Test Report (Bioanalytics)

(ABF TR 01/14: PMI Mouse Study 15015)

Titel:	**Determination of HPMA, total NNAL, SPMA, CEMA, 8-OHdG, MDA, 4-HNE and 9 eicosanoids in mice urine samples and of Nic/Cot in mice plasma samples of PMI Study 15015**
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PO / SOW (Date):	PO No (145 urine samples): 7100515118 (22.10.2013) PO No (40 plasma samples): 7100571295 (08.05.2014)

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Abbreviations

4-HNE	4-Hydroxynonenal
8-OHdG	8-Hydroxydeoxyguanosine
8-i-PGF$_{2\alpha}$	8-iso-Prostaglandine F$_{2\alpha}$
11-dh-TXB$_2$	11-dehydro Thromboxane B$_2$
12-HETE	12-Hydroxy-5***Z***,8***Z***,10***E***,14***Z***-eicosatetraenoic acid
2,3-d-8-i-PGF$_{2\alpha}$	2,3-dinor-8-iso-Prostaglandine F$_{2\alpha}$
2,3-d-TXB$_2$	2,3-dinor Thromboxane B$_2$
APCI	Atmospheric pressure chemical ionization
CEMA	Cyanoethylmercapturic acid
Cot	Cotinine
CV	Coefficient of variation
ESI	Electrospray ionization
GC-MS	Gas chromatography-mass spectrometry
HPLC	High pressure liquid chromatography
HPMA	3-Hydroxypropylmercapturic acid
IS	Internal standard
LC-MS/MS	Liquid chromatography with tandem mass spectrometry
LOD	Limit of detection
LTE$_4$	Leukotriene E$_4$
LLOQ	Lower limit of quantification
MDA	Malondialdehyde
MRM	Multi-reaction monitoring
Nic	Nicotine
NNAL	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol
PGF$_{2\alpha}$	Prostaglandine F$_{2\alpha}$
PI	Principal Investigator
QC	Quality control
SD	Standard deviation of the mean
SOP	Standard operating procedure
SPE	Solid phase extraction
SPMA	S-Phenylmercapturic acid
SR	Short report
Suppl.	Supplementary
t-PGDM	tetranor-Prostaglandine D Metabolite
t-PGEM	tetranor-Prostaglandine E Metabolite
TR	Test report
ULOQ	Upper limit of quantification

1 Introduction

A total of 145 mice urine samples and 40 mice plasma samples were analyzed. Biological samples were received in 4 shipments of urine samples and an additional shipment of plasma samples between December 19th 2013 and May 26th 2014. The analyzed biomarkers are listed in Table 1.
Urine volumes per sample were between 80 and 1500 µl. Plasma volumes per sample were about 90 µl (60 – 110 µl).
In case of total sample volumes below 400 and 100 µl for urine and plasma, respectively, the samples were diluted with water to yield the minimum sample volumes as indicated in the related quotation. The respective dilution factors were taken into account for calculation of analyte concentrations. They are included in the corresponding Short Report (SR).
Biomarkers, biological matrix, principle of method, ABF SOP No and ABF staff responsible for the analysis are listed in Table 1.

Table 1: Biomarkers analyzed by ABF in the PMI Mouse Study 15015 samples

No	Biomarker	Matrix (Unit)	Method priniciple	ABF SOP No, Version, Date	ABF staff
1	HPMA	Urine (ng/ml)	LC-MS/MS	SOP 38, Version 1.0, 14.11.2013	Gerhard Gilch Claudia Bernstein Dinamis Janket
2	Total NNAL	Urine (pg/ml)	LC-MS/MS	SOP 07, Version 2.4, 07.01.2013; SOP 07, Version 2.5, 15.01.2014	Gerhard Gilch Dinamis Janket
3	SPMA	Urine (ng/ml)	LC-MS/MS	SOP 37, Version 1.0, 30.10.2013	Gerhard Gilch Claudia Bernstein Dinamis Janket
4	CEMA				
5	8-OHdG	Urine (ng/ml)	LC-MS/MS	SOP 09, Version 1.0, 31.10.2013	Markus Piller
6	MDA	Urine (pmol/ml)	GC-MS	SOP 39, Version 1.0, 19.12.2013	Heinz-Werner Hagedorn Kirsten Riedel
7	4-HNE	Urine (pmol/ml)			
8	t-PGDM	Urine (ng/ml)	LC-MS/MS	SOP 34, Version 2.0, 17.06.2013; SOP 34, Version 2.1, 04.02.2014	Claudia Bernstein Max Scherer Nikola Pluym Dinamis Janket
9	t-PGEM				
10	2,3-d-8-i-$PGF_{2\alpha}$				
11	2,3-d-TXB_2				
12	11-dh-TXB_2				
13	$PGF_{2\alpha}$				
14	8-i-$PGF_{2\alpha}$				
15	LTE_4				
16	12-HETE				
17	Nicotine	Plasma (ng/ml)	LC-MS/MS	SOP 19, Version 2.4, 26.07.2012	Markus Piller
18	Cotinine				

2 Authorization and Signature Page

Table 2: Signatures approving that summaries, results and conclusions are found to be consistent and scientifically rational

Function in the present study	Name	Title/Function in ABF	Test Report approved: Date and Signature
Laboratory management	Prof. Gerhard Scherer	General manager ABF	7.7.14
PI of the study (bio-analytical part) Substitute PI	Dr. Max Scherer Dr. Nikola Pluym	Laboratory Manager/Chemist Laboratory Manager/Chemist	7.7.14 7.7.14
Quality Assurance (QA)	Karl-Heinz Zeidler	QA authorized person	7.7.14
Sponsor	Philip Morris International (PMI) Maciej Cabanski, PhD	-	Information only
Test Facility	PMI, Singapore Blaine Phillips, PhD (Study Director)	-	Information only

3 Compliance Statement

Bioanalysis were conducted using SOPs adherent to ISO 17025 and to the principles of 21 CFR Part 58 (Good Laboratory Practice (GLP) Regulation). The persons listed in Table 3 confirm the validity of this statement by their signature.

Table 3: Signatures for the validity of the GLP compliance statement

Function in the present study	Name	Title/Function in ABF	Compliance statement valid: Date and Signature
PI (Bioanalysis)	Dr. Max Scherer	Laboratory Manager/Chemist	7.7.14 .....
Substitute PI	Dr. Nikola Pluym	Laboratory Manager/Chemist	7.7.14 .....
Quality Assurance (QA)	Karl-Heinz Zeidler	QA authorized person	7.7.14 .....
Laboratory management	Prof. Gerhard Scherer	General manager ABF	7.7.14 .....

4 Laboratory personnel and responsibilities

Responsibilities of the involved ABF personnel are listed in Table 1 and in the Signature Page (Table 2).

5 Study samples

Biological samples were collected, stored and shipped to ABF by

Philip Morris International Research Laboratories Pte Ltd
Attn Dr Blaine Phillips
#02-07, 50 Science Park Road
The Kendall
Singapore Science Park II
Singapore 117406

All operations with the study samples at ABF were performed according to ABF SOP 101 (Sample Custody Chain), Version 1.3 (24.01.2013) and 1.4 (24.01.2014), respectively.

Mice urine samples were shipped in 4 separate shipments frozen on dry ice by PMI Singapore on the following dates:

Shipment 1:	24 mice urine samples received at ABF November 19th 2013 (Volume: 300-1500 µl)
Shipment 2:	40 mice urine samples received at ABF December 13th 2013 (Volume: 350-850 µl)
Shipment 3:	41 mice urine samples received at ABF March 07th 2014 (Volume: 80-850 µl)
Shipment 4:	40 mice urine samples received at ABF May 08th 2014 (Volume: 190-900 µl)

Mice plasma samples were shipped frozen on dry ice by PMI Singapore and received at ABF May 21st 2014 (Volume 60-110 µl).

All samples were frozen and properly labeled upon receipt at ABF. Receipt of samples was confirmed by e-mails to PMI at Neuchatel and Singapore on November 19th, December 13th 2013, March 07th, May 09th, and May 21st 2014, respectively.

6 Analytical methods

The analytical methods applied, including analytes measured, ABF SOP No, version and release date, are listed in Table 1. Characteristics of the applied methods (specifications, method principles, etc.) for urine samples are summarized in the Study Plan 1.0/16-Dec-2013 Chapter 4. Nicotine/Cotinine determination in mice plasma samples was included in the study after completion of the Study Plan and therefore it is not specified in the Study Plan.

7 Method calibrations

Descriptions of reference compounds, internal standards (IS), working solutions, calibrators and criteria for acceptance of calibrations are given in Suppl. Files 1-18.

8 Quality control (QC) samples

A summary description of all control materials used in this project is given in Suppl. Files 1-18.
For 4-HNE, 2,3-d-8-i-$PGF_{2\alpha}$ and $PGF_{2\alpha}$, QC samples could not be evaluated due to insufficient stability of the analytes over the entire study. In case of 2,3-d-8-i-$PGF_{2\alpha}$ and $PGF_{2\alpha}$, QC samples at three different concentration levels were prepared freshly for each batch (shipment) in duplicate right before sample clean-up and incorporated in the assay. The concentrations were evaluated against the theoretical concentrations of the spiked calibrators as target values and found to be consistent for all analytes and shipments, respectively (cf. Suppl. Files 10 and 13).

9 Results

The results chapter of this Test Report contains the following sections:

- Analytical run lists
- Method calibrations
- Results for Quality Control (QC) samples
- Test results
- Chromatograms

9.1 Analytical run lists

The analytical run list (RL) for each compound can be found in the respective Suppl. Files 1-18.

9.2 Method calibrations

The obtained calibration lines and functions for all analytes are shown in the corresponding Suppl. Files 1-18.

9.3 Results for Quality Control (QC) samples

Results for the QC samples are shown in Suppl. Files 1-18.

9.4 Chromatograms

Chromatograms of all analytical runs performed for this project (blanks, calibrators, QC samples, study samples) are compiled in Suppl. Files 19-25.
Where several analytes are determined simultaneously in multiplexed assays, chromatograms of all analytes in one method are compiled in one supplement.

9.5 Test results

Single analysis was performed for all samples and analytes. Please note that some of the samples had to be diluted prior to analysis due to the low urine volumes available. The resulting dilution factor was taken into account for the calculation of the analyte concentrations summarized in the TR and also listed in the corresponding SR.

Cumulated SRs for results of single shipments were sent to Dr. Maciej Cabanski (PMI Neuchatel) with CC to Dr. Blaine Phillips (PMI, Singapore) on the following dates:

Shipment 1: ABF_SR_PMI_15015_Mice_Ship1_Rev1.xls, 11.12.2013
Shipment 2: ABF_SR_PMI_15015_Mice_Ship1+2.xls, 10.01.2014
Shipment 3: ABF_SR_PMI_15015_Mice_Ship1+2+3.xls, 31.03.2014

The complete results (for all shipments) of the bioanalysis of the study samples were compiled in two separate Excel-files – one file per matrix – and provided as SR.
The SRs (Excel-files: ABF_SR_PMI_15015_Mice_Ship1+2+3+4.xlsx; ABF_SR_PMI_15015_Mice_Nic_Cot.xlsx) were sent to

Dr. Maciej Cabanski (PMI Neuchatel)
with CC to Dr. Blaine Phillips (PMI, Singapore)

on May 28th 2014.

Pdf-files of the final SRs are attached as Suppl. Files 26, 27 to this Test Report.

Table 4 shows information and references summarized for:

- Calibrations (Data and diagrams)
- QC samples (Data and diagrams)
- Analytical run lists

Table 5, Table 6 and Table 7 show the results for the individual samples.

Table 4: General information and reference to the corresponding Suppl. Files for the results obtained with Methods 1-7

No	Matrix	Analytes	Calibrations per analyte (N)[1]	Calibration (Data & Diagrams)	Samples (N)	QC low samples (N)[1]	QC med samples (N)[1]	QC high samples (N)[1]	QC (Data & Diagrams)	Analytical run list
1	Urine	HPMA	1	**Suppl. File 1**, Sheets: Cal_HPMA	145	2	2	2	**Suppl. File 1**, Sheets: QC_HPMA	**Suppl. File 1**, Sheets: RL_HPMA
2	Urine	total NNAL	1	**Suppl. File 2**, Sheets: Cal_NNAL	145	2	2	2	**Suppl. File 2**, Sheets: QC_NNAL	**Suppl. File 2**, Sheets: RL_NNAL
3	Urine	SPMA	1	**Suppl. File 3**, Sheets: Cal_SPMA	145	2	2	2	**Suppl. File 3**, Sheets: QC_SPMA	**Suppl. File 3**, Sheets: RL_SPMA
		CEMA	1	**Suppl. File 4**, Sheets: Cal_CEMA	145	2	2	2	**Suppl. File 4**, Sheets: QC_CEMA	**Suppl. File 4**, Sheets: RL_CEMA
4	Urine	8-OHdG	1	**Suppl. File 5**, Sheets: Cal_8-OHdG	145	2	2	2	**Suppl. File 5**, Sheets: QC_8-OHdG	**Suppl. File 5**, Sheets: RL_8-OHdG
5	Urine	MDA	1	**Suppl. File 6**, Sheets: Cal_MDA	145	2	2	2	**Suppl. File 6**, Sheets: QC_MDA	**Suppl. File 6**, Sheets: RL_MDA
		4-HNE	1	**Suppl. File 7**, Sheets: Cal_4-HNE	145	n.a.	n.a.	n.a.	n.a. see Chapter 8	**Suppl. File 7**, Sheets: RL_4-HNE

6	Urine	t-PGDM	1	**Suppl. File 8,** Sheets: Cal_t-PGDM	145	2	2	2	**Suppl. File 8,** Sheets: QC_t-PGDM	**Suppl. File 8,** Sheets: RL_t-PGDM
		t-PGEM	1	**Suppl. File 9,** Sheets: Cal_t-PGEM	145	2	2	2	**Suppl. File 9,** Sheets: QC_t-PGEM	**Suppl. File 9,** Sheets: RL_t-PGEM
		2,3-d-8-i-$PGF_{2\alpha}$	1	**Suppl. File 10,** Sheets: Cal_2,3-d-8-i-$PGF_{2\alpha}$	145	n.a.	n.a.	n.a.	**Suppl. File 10,** Sheets: QC_2,3-d-8-i-$PGF_{2\alpha}$	**Suppl. File 10,** Sheets: RL_2,3-d-8-i-$PGF_{2\alpha}$
		2,3-d-TXB_2	1	**Suppl. File 11,** Sheets: Cal_2,3-d-TXB_2	145	2	2	2	**Suppl. File 11,** Sheets: QC_2,3-d-TXB_2	**Suppl. File 11,** Sheets: RL_2,3-d-TXB_2
		11-dh-TXB_2	1	**Suppl. File 12,** Sheets: Cal_11-dh-TXB_2	145	2	2	2	**Suppl. File 12,** Sheets: RL_2,3-d-TXB_2	**Suppl. File 12,** Sheets: RL_2,3-d-TXB_2
		$PGF_{2\alpha}$	1	**Suppl. File 13,** Sheets: Cal_$PGF_{2\alpha}$	145	n.a.	n.a.	n.a.	**Suppl. File 13,** Sheets: QC_$PGF_{2\alpha}$	**Suppl. File 13,** Sheets: RL_$PGF_{2\alpha}$
		8-i-$PGF_{2\alpha}$	1	**Suppl. File 14,** Sheets: Cal_8-i-$PGF_{2\alpha}$	145	2	2	2	**Suppl. File 14,** Sheets: QC_8-i-$PGF_{2\alpha}$	**Suppl. File 14,** Sheets: RL_8-i-$PGF_{2\alpha}$
		LTE_4	1	**Suppl. File 15,** Sheets: Cal_LTE_4	145	2	2	2	**Suppl. File 15,** Sheets: QC_LTE_4	**Suppl. File 15,** Sheets: RL_LTE_4
		12-HETE	1	**Suppl. File 16,** Sheets: Cal_12-HETE	145	2	2	2	**Suppl. File 16,** Sheets: QC_12-HETE	**Suppl. File 16,** Sheets: RL_12-HETE
7	Plasma	Nic	1	**Suppl. File 17,** Sheets: Cal_Nic	40	2	2	2	**Suppl. File 17,** Sheets: QC_Nic	**Suppl. File 17,** Sheets: RL_Nic
		Cot	1	**Suppl. File 18,** Sheets: Cal_Cot	40	2	2	2	**Suppl. File 18,** Sheets: QC_Cot	**Suppl. File 18,** Sheets: RL_Cot

[1]: Figures indicate the numbers per batch and shipment

Table 5: Results for HPMA, NNAL, SPMA, CEMA, 8-OHdG, MDA, and 4-HNE in mice urine samples

Animal ID	HPMA (ng/ml)	NNAL (pg/ml)	SPMA (ng/ml)	CEMA (ng/ml)	8-OHdG (ng/ml)	MDA (pmol/ml)	4-HNE (pmol/ml)
6519	3943	0.0*	2.5	1.2	51.9	4961	59.8
6523	5074	0.0*	3.1	1.6	96.0	8898	120.7
6526	6323	207.9	82.4	319.5	59.5	6376	73.6
6314	4285	91.0	5.7	9.1	56.1	4828	92.0
6334	2929	0.0*	2.3	3.4	49.5	4571	71.4
6528	6247	155.2	75.1	336.2	56.1	5396	69.2
6294	5899	221.6	92.4	359.5	46.8	4775	60.1
6338	2496	0.0*	1.3	2.3	33.1	5887	23.0
6521	3949	0.0*	2.9	1.0	52.0	5313	71.1
6306	4570	182.0	53.2	203.6	44.6	5826	94.5
6322	2872	0.0*	2.2	5.1	47.9	4605	118.6
6302	6433	370.4	49.3	188.1	56.1	7743	214.6
6518	3491	0.0*	2.3	1.0	55.3	8344	58.3
6530	5708	301.5	56.6	212.8	60.9	7520	74.1
6520	4642	0.0*	3.3	2.1	71.6	6329	87.6
6298	8043	738.3	133.4	445.0	32.4	5445	49.6
6522	2680	0.0*	2.0	0.3	43.6	6364	52.7
6310	4516	0.0*	3.2	4.4	56.4	5984	97.3
6524	3212	0.0*	2.0	0.0*	45.0	3854	52.3
6525	5007	0.0*	3.5	0.9	65.0	6457	186.3
6326	2722	0.0*	1.2	1.5	42.8	4455	59.1
6527	6973	345.7	151.7	589.0	51.2	4755	134.9
6318	3788	70.8	2.9	5.0	59.6	5269	93.9
6529	6631	366.5	95.4	319.0	46.9	6618	84.7
6979	527	0.0*	0.1	0.0*	6.9	677	6.1
6968	4701	135.6	41.3	171.9	60.6	8221	80.4
6980	2875	0.0*	0.8	1.0	43.9	4563	70.4
6697	2836	0.0*	1.7	8.7	43.2	4499	50.9
6688	3635	162.2	64.4	239.1	34.4	5265	45.2
8318	5819	261.1	92.7	318.0	49.4	4953	58.2
6965	2649	0.0*	0.9	1.3	44.7	5651	55.1
6975	1762	0.0*	0.4	4.0	39.3	3219	28.9
8317	2554	0.0*	1.4	1.4	33.6	4463	30.8
6684	2077	0.0*	1.0	1.4	37.9	4733	30.3

8323	2291	0.0*	2.1	5.1	33.4	4657	24.9
8325	3741	0.0*	2.0	4.3	60.3	9630	89.4
6696	4716	0.0*	2.7	12.9	90.1	11496	60.9
6687	6239	323.4	81.2	349.8	46.3	7935	53.3
8330	2690	83.5	3.9	9.5	32.2	3619	9.7
6987	2236	0.0*	1.2	5.3	33.3	2461	22.5
6686	2270	0.0*	1.1	1.3	40.0	6091	61.1
6969	3785	111.2	44.0	180.8	34.6	4388	32.1
8324	2382	0.0*	1.2	2.9	50.6	5212	59.8
6982	4322	270.8	86.2	291.8	22.1	3125	0.0*
6690	2031	0.0*	1.9	2.2	40.0	2556	12.5
6983	2525	30.2	2.0	5.2	35.0	3310	28.7
6689	2898	109.0	11.5	44.6	31.9	3947	17.5
6966	2600	0.0*	0.3	1.2	44.7	4566	39.7
6986	2066	0.0*	0.5	2.4	36.8	4176	23.5
8326	1618	0.0*	0.8	3.6	34.2	2341	19.5
6972	2740	0.0*	1.3	3.2	49.5	4685	34.5
6984	2290	42.5	1.4	2.6	47.7	3918	19.2
6978	2287	0.0*	1.8	7.2	47.9	3274	22.0
6964	2663	0.0*	0.7	0.7	49.0	3719	15.4
8328	6931	46.2	4.9	16.2	97.4	8593	69.3
6970	3088	0.0*	1.7	4.6	46.7	6048	33.6
8329	2455	78.0	2.3	8.6	44.1	2530	5.6
8322	3913	0.0*	2.9	6.1	56.5	6107	50.7
6694	4888	0.0*	2.3	11.2	75.7	9564	36.8
6967	2364	35.5	1.1	11.8	26.8	3846	40.4
8319	3679	0.0*	3.1	6.9	59.1	5950	41.4
6974	2798	0.0*	0.6	4.1	55.9	4884	47.5
6691	3666	0.0*	3.4	5.6	40.4	3917	35.1
6976	3232	0.0*	1.6	6.9	56.8	6436	40.6
8460	5011	152.7	6.2	14.3	57.2	5515	40.9
8651	6271	100.2	4.1	12.5	56.6	4929	27.5
8475	3704	40.8	1.4	2.8	45.2	4419	18.5
8459	2706	31.6	3.5	13.5	46.2	5207	32.2
8648	6754	0.0*	3.0	8.1	63.8	11464	0.0*
8479	2525	70.4	3.1	6.3	48.2	4336	20.9
8484	3403	0.0*	1.2	4.8	57.3	6711	49.0
8486	3867	0.0*	1.7	5.2	69.2	4475	0.0*

8463	3692	0.0*	4.4	13.4	71.3	6400	35.2
8470	2569	0.0*	1.7	3.0	61.1	3879	11.6
8652	3239	0.0*	1.0	10.7	84.8	4567	29.7
8645	3994	0.0*	4.7	12.1	79.4	5749	48.8
8477	2153	63.6	3.6	6.9	26.9	2718	45.0
8483	2236	0.0*	1.3	3.6	49.7	2882	0.0*
8655	3156	27.9	3.6	9.0	33.2	5315	0.0*
8471	3849	0.0*	2.4	5.9	77.1	5056	0.0*
8641	8058	951.5	143.7	525.3	52.9	7557	52.0
8474	4677	0.0*	2.7	3.7	78.6	5935	51.9
8481	2765	0.0*	2.2	2.5	65.8	4441	70.2
8653	5009	56.1	2.1	5.8	77.7	8312	105.2
8469	2246	38.8	2.9	8.0	25.8	2592	0.0*
8462	4972	118.3	3.5	8.5	60.7	5592	35.1
8646	5281	63.8	2.1	4.7	86.0	9667	47.2
8455	7529	958.7	123.7	546.0	68.3	9412	71.8
8478	4331	0.0*	3.9	15.3	33.6	2580	11.2
8467	3712	70.9	2.8	7.7	37.3	5682	34.6
8643	7282	777.2	81.6	346.1	52.8	7656	63.8
8457	5919	369.5	63.6	252.5	42.1	6398	73.3
8647	3773	0.0*	1.7	5.6	72.2	6010	29.1
8451	4707	821.7	89.4	395.6	39.4	4593	21.2
8480	2360	59.3	2.3	7.5	35.6	2133	17.6
8452	9295	480.5	117.4	417.6	52.4	9200	104.2
8472	3679	0.0*	1.8	4.1	56.6	5424	57.9
8482	2735	0.0*	1.2	2.9	48.3	3517	8.1
8454	5129	251.2	41.5	153.9	48.5	6797	73.2
8473	3556	0.0*	1.8	3.7	55.4	3845	48.3
8466	3261	65.1	2.4	5.5	32.3	2790	0.0*
8476	1825	29.7	1.5	2.8	30.2	2872	20.0
8458	14683	1789.0	294.8	1146.6	45.9	7833	0.0*
8490	2816	0.0*	1.3	5.1	49.9	3144	15.0
8468	2475	45.7	2.4	7.2	31.9	4624	20.4
8927	6561	417.7	77.1	193.5	75.1	9910	83.1
8805	1472	0.0*	0.9	0.0*	38.3	3501	32.5
10032	2498	36.7	5.2	10.0	50.4	2886	19.8
10093	4297	0.0*	5.0	9.6	58.7	5515	63.7
8804	2187	0.0*	1.7	0.0*	46.7	4249	33.7

10043	3496	0.0*	5.8	16.1	75.3	4027	35.6
8792	3047	0.0*	3.3	7.7	54.0	4996	48.3
10086	2111	0.0*	2.1	0.0*	38.7	3736	30.8
8791	4214	0.0*	3.8	9.5	49.2	4002	65.7
10098	3955	130.2	5.3	11.5	65.8	6832	67.0
8789	3150	0.0*	3.9	10.2	62.6	4252	22.0
10037	2543	0.0*	3.1	0.0*	53.0	4215	42.4
8926	6388	240.4	61.6	156.6	71.5	10624	115.7
10096	3989	0.0*	6.2	18.6	63.0	4312	20.6
8799	2977	0.0*	3.3	6.8	73.6	4845	44.3
10087	1715	0.0*	1.8	0.0*	34.8	3495	32.7
8779	9122	283.5	161.6	592.5	72.5	10405	68.9
10089	8462	148.4	115.2	334.1	112.2	12293	135.1
8815	2892	0.0*	2.7	4.9	51.5	6639	77.4
10036	4229	0.0*	4.7	0.0*	99.0	9839	80.7
8807	3499	0.0*	3.1	0.0*	57.3	5466	42.7
10095	3498	0.0*	3.0	0.0*	69.1	5731	63.2
8810	1790	0.0*	1.9	0.0*	44.0	3042	24.7
10097	3365	0.0*	4.9	0.0*	68.0	4159	22.9
10030	4522	0.0*	6.0	6.1	75.0	5368	53.7
8796	3987	0.0*	3.5	6.9	52.9	6359	48.8
10041	2851	0.0*	5.2	10.9	68.7	2555	16.8
8925	4880	239.0	68.9	233.5	56.1	5340	52.9
10090	9155	298.8	246.3	587.7	90.2	9558	146.8
8777	8733	299.2	181.4	607.6	85.4	9209	95.0
10094	2243	0.0*	2.5	0.0*	60.1	3402	27.6
8813	7513	0.0*	3.6	6.4	125.6	13256	159.7
10085	3498	0.0*	3.6	0.0*	66.5	4820	28.1
8786	5041	0.0*	4.6	11.6	94.4	6746	39.0
10039	2551	0.0*	2.8	0.0*	61.3	4375	33.4
8924	13205	533.0	174.1	583.3	100.9	10570	124.4
10092	3444	0.0*	5.0	10.8	60.5	3677	41.5
8806	2273	0.0*	1.2	0.0*	44.0	3324	42.1
10099	3778	62.7	5.3	8.8	43.7	5004	40.3
8795	3862	0.0*	3.0	0.0*	91.4	5422	58.8

*<LOD

Table 6: Results for eicosanoids (t-PGDM, t-PGEM, 2,3-d-8-i-$PGF_{2\alpha}$, 2,3-d-TXB_2, 11-dh-TXB_2, $PGF_{2\alpha}$, 8-i-$PGF_{2\alpha}$, LTE_4, 12-HETE) in mice urine samples

Animal ID	t-PGDM (ng/ml)	t-PGEM (ng/ml)	2,3-d-8-i-$PGF_{2\alpha}$ (ng/ml)	2,3-d-TXB_2 (ng/ml)	11-dh-TXB_2 (ng/ml)	$PGF_{2\alpha}$ (ng/ml)	8-i-$PGF_{2\alpha}$ (ng/ml)	LTE_4 (ng/ml)	12-HETE (ng/ml)
6519	0.00*	29.94	5.02	123.72	1.26	11.71	0.00*	0.15	0.26
6523	0.00*	19.48	5.49	108.53	0.98	8.40	1.13	0.17	0.12
6526	0.00*	23.88	4.67	67.73	1.55	5.36	0.94	0.16	0.08
6314	0.00*	27.46	3.10	101.19	1.07	4.24	0.54	0.12	0.06
6334	0.00*	25.68	2.58	62.48	0.94	5.68	1.06	0.11	0.14
6528	0.00*	78.54	8.35	224.53	1.91	16.62	0.00*	0.27	0.19
6294	0.00*	29.43	3.59	55.01	0.51	5.43	0.01	0.12	0.07
6338	0.00*	0.00*	1.05	17.04	0.89	3.35	0.36	0.00*	0.02
6521	0.00*	0.00*	3.21	115.11	1.14	4.85	0.73	0.69	0.18
6306	0.00*	31.53	3.85	51.26	0.79	6.34	1.13	0.27	0.11
6322	0.00*	124.35	10.78	342.15	2.92	25.26	0.12	0.99	0.40
6302	0.00*	21.81	5.68	78.86	0.92	7.92	0.13	0.17	0.09
6518	0.00*	0.00*	1.21	36.92	0.82	4.20	0.00*	0.14	0.09
6530	0.00*	108.38	18.06	364.32	3.06	23.35	4.17	0.86	0.28
6520	0.00*	37.76	5.65	132.69	0.88	5.82	0.89	0.19	0.10
6298	0.00*	48.74	0.94	15.49	1.61	3.84	0.36	0.15	0.08
6522	0.00*	40.66	2.15	63.59	0.69	5.84	0.36	0.09	0.08
6310	0.00*	0.00*	2.88	74.84	0.95	9.70	0.81	0.27	0.18
6524	0.00*	45.61	3.19	105.69	0.92	7.05	0.02	0.23	0.18
6525	0.00*	0.00*	5.02	111.65	0.95	10.26	0.00*	0.14	0.28
6326	0.00*	0.00*	2.13	42.18	0.77	6.44	0.73	0.13	0.09
6527	0.00*	0.00*	4.40	79.05	0.78	4.94	0.00*	0.08	0.12
6318	0.00*	0.00*	3.87	121.65	0.74	7.13	0.84	0.12	0.08
6529	0.00*	36.64	4.11	90.54	0.71	6.18	0.00*	0.00*	0.08
6979	0.00*	0.00*	0.73	11.54	3.01	9.79	0.00*	0.00*	0.25
6968	0.00*	18.23	1.88	22.89	1.28	4.38	1.36	0.00*	0.07
6980	0.00*	26.76	1.72	52.94	0.89	4.34	0.87	0.00*	0.07
6697	0.00*	0.00*	1.23	29.15	0.96	4.36	0.00*	0.07	0.30
6688	9.82	27.48	1.68	27.00	1.29	2.53	0.32	0.00*	0.09
8318	9.96	15.06	0.36	27.02	0.60	1.70	0.73	0.00*	0.00*
6965	0.00*	17.76	2.21	54.07	0.74	1.36	0.89	0.00*	0.09
6975	0.00*	0.00*	1.27	33.92	1.19	1.13	0.61	0.00*	0.06

8317	0.00*	0.00*	0.39	42.11	0.87	1.59	0.84	0.00*	0.05
6684	0.00*	0.00*	1.43	38.03	0.74	4.57	0.99	0.00*	0.08
8323	0.00*	36.29	2.02	46.61	1.35	4.42	0.80	0.14	0.00*
8325	0.00*	18.05	2.43	33.68	1.21	3.82	1.63	0.17	0.08
6696	0.00*	0.00*	3.02	53.20	0.69	4.94	1.36	0.00*	0.00*
6687	0.00*	0.00*	2.53	37.53	0.87	2.42	0.76	0.11	0.00*
8330	0.00*	0.00*	0.67	51.56	1.82	6.37	0.00*	1.57	0.46
6987	0.00*	0.00*	1.61	44.74	0.77	3.08	0.00*	0.34	0.11
6686	0.00*	34.43	1.84	32.53	0.82	3.62	0.90	0.10	0.07
6969	0.00*	23.36	1.45	29.75	1.11	2.84	0.73	0.20	0.07
8324	0.00*	38.48	2.15	26.95	0.79	3.22	1.13	0.07	0.10
6982	0.00*	0.00*	1.36	22.33	1.08	1.79	0.49	0.00*	0.07
6690	0.00*	0.00*	1.62	19.55	1.01	2.73	0.00*	0.07	0.07
6983	0.00*	0.00*	1.83	38.11	0.76	2.72	0.36	0.00*	0.00*
6689	0.00*	0.00*	1.41	17.48	0.80	4.55	0.00*	0.00*	0.05
6966	0.00*	0.00*	1.49	67.48	0.90	3.74	0.45	0.00*	0.04
6986	0.00*	0.00*	1.28	46.70	0.61	3.16	0.45	0.00*	0.06
8326	0.00*	0.00*	1.89	33.81	0.79	3.30	0.00*	0.00*	0.07
6972	15.81	30.35	1.81	42.57	0.66	2.89	0.44	0.19	0.05
6984	0.00*	29.47	1.16	40.10	1.05	4.34	0.00*	0.00*	0.09
6978	0.00*	0.00*	1.46	27.73	1.04	4.74	0.41	0.09	0.09
6964	0.00*	29.29	1.52	55.94	0.94	4.64	0.85	0.00*	0.06
8328	0.00*	0.00*	4.66	117.56	0.93	4.65	0.88	0.14	0.08
6970	0.00*	27.34	2.24	32.05	0.72	8.46	0.00*	0.00*	0.10
8329	0.00*	0.00*	0.91	26.63	1.68	3.96	0.00*	0.00*	0.08
8322	0.00*	0.00*	2.46	49.37	0.90	4.09	0.67	0.13	0.04
6694	0.00*	21.10	2.03	55.51	1.27	5.50	0.98	0.00*	0.06
6967	0.00*	0.00*	0.97	15.77	0.96	3.06	0.68	0.00*	0.06
8319	0.00*	0.00*	2.16	46.65	0.44	3.07	0.76	0.15	0.05
6974	0.00*	18.46	1.87	31.03	0.92	1.87	0.33	0.11	0.11
6691	0.00*	24.59	2.44	77.20	1.06	2.91	0.44	0.05	0.13
6976	18.32	27.41	3.03	76.13	0.69	3.81	0.81	0.00*	0.06
8460	0.00*	0.00*	4.57	106.85	0.95	2.95	0.00*	0.17	0.09
8651	0.00*	0.00*	5.90	110.52	0.74	2.41	0.07	0.19	0.09
8475	0.00*	0.00*	5.18	168.06	0.68	4.54	0.24	0.07	0.09
8459	4.40	0.00*	4.87	63.50	0.88	2.94	0.00*	0.05	0.07
8648	7.36	0.00*	4.17	136.44	1.31	5.37	0.00*	0.11	0.06
8479	0.00*	0.00*	5.18	160.47	0.83	4.53	0.00*	0.04	0.06

8484	0.00*	0.00*	6.85	202.64	0.68	4.31	0.00*	0.03	0.06
8486	0.00*	0.00*	4.05	136.44	1.45	2.94	0.00*	0.06	0.06
8463	0.00*	0.00*	3.23	74.87	1.20	3.94	0.00*	0.04	0.06
8470	4.43	0.00*	3.19	106.94	0.67	3.04	0.00*	0.00*	0.07
8652	0.00*	0.00*	3.88	228.34	2.71	9.97	0.00*	0.00*	0.34
8645	5.53	0.00*	6.92	157.99	1.25	3.04	0.00*	0.02	0.05
8477	0.00*	0.00*	3.80	63.14	1.27	2.69	0.00*	0.05	0.10
8483	4.31	0.00*	2.45	182.61	0.54	3.44	0.07	0.00*	0.06
8655	2.85	0.00*	5.43	70.69	0.96	3.30	0.30	0.02	0.04
8471	4.85	0.00*	4.11	155.81	1.15	2.18	0.10	0.01	0.05
8641	0.00*	0.00*	7.39	53.26	1.03	3.60	0.64	0.03	0.06
8474	0.00*	0.00*	4.09	156.69	1.80	6.12	0.31	0.18	0.28
8481	4.11	0.00*	6.22	223.78	1.04	2.40	0.32	0.05	0.05
8653	6.42	0.00*	7.21	190.76	0.98	5.33	0.93	0.04	0.10
8469	2.40	0.00*	5.36	141.34	1.16	2.08	0.12	0.00*	0.06
8462	0.00*	0.00*	1.95	71.38	0.80	2.07	0.17	0.22	0.17
8646	4.41	0.00*	6.05	170.88	0.63	3.59	0.52	0.10	0.12
8455	2.52	0.00*	9.31	68.58	1.16	2.77	1.02	0.00*	0.12
8478	0.00*	0.00*	6.15	137.98	1.42	5.53	0.13	0.08	0.00*
8467	3.06	0.00*	12.06	60.64	0.64	1.90	0.00*	0.05	0.00*
8643	2.66	0.00*	7.73	71.34	0.53	3.60	0.00*	0.03	0.00*
8457	8.40	0.00*	3.25	47.12	0.84	2.13	0.37	0.04	0.00*
8647	8.95	0.00*	10.21	219.01	0.74	2.49	0.00*	0.07	0.00*
8451	5.43	0.00*	5.28	66.41	1.29	2.86	0.00*	0.02	0.17
8480	0.00*	0.00*	2.85	55.23	0.94	2.20	0.08	0.06	0.10
8452	7.31	0.00*	8.99	79.38	0.93	3.20	0.00*	0.06	0.00*
8472	0.00*	0.00*	8.00	145.46	0.33	2.54	0.00*	0.05	0.00*
8482	0.00*	0.00*	3.39	97.13	0.67	2.51	0.51	0.04	0.00*
8454	4.05	0.00*	4.18	27.58	0.89	2.93	0.00*	0.00*	0.00*
8473	4.03	0.00*	4.19	71.57	0.78	1.96	0.39	0.08	0.00*
8466	2.01	0.00*	4.35	20.66	0.74	2.18	0.00*	0.15	0.00*
8476	0.00*	0.00*	1.66	30.69	0.82	1.72	0.21	0.10	0.00*
8458	7.28	0.00*	4.01	57.08	1.90	4.02	0.00*	0.09	0.00*
8490	0.00*	0.00*	4.15	104.68	0.47	2.83	0.00*	0.04	0.08
8468	4.57	0.00*	4.69	33.88	0.44	2.60	0.00*	0.02	0.05
8927	0.00*	0.00*	8.87	48.40	1.25	2.81	0.00*	0.00*	0.00*
8805	6.94	0.00*	5.76	98.88	0.72	1.79	0.00*	0.00*	0.00*
10032	6.13	0.00*	7.37	154.53	0.94	3.31	0.00*	0.00*	0.00*

10093	8.75	0.00*	10.39	187.31	0.55	2.02	0.00*	0.00*	0.00*
8804	9.81	0.00*	4.43	61.50	1.71	1.31	0.00*	0.00*	0.00*
10043	0.00*	0.00*	4.02	196.04	1.10	2.93	0.00*	0.00*	0.00*
8792	8.90	0.00*	10.83	170.18	0.99	2.23	0.00*	0.00*	0.00*
10086	4.79	0.00*	4.97	83.29	0.77	1.09	0.00*	0.00*	0.00*
8791	7.46	0.00*	10.94	46.72	0.59	1.64	0.00*	0.00*	0.00*
10098	9.51	0.00*	6.96	123.17	1.19	2.09	0.00*	0.00*	0.16
8789	14.01	0.00*	7.17	173.07	0.77	1.71	0.00*	0.00*	0.00*
10037	11.68	0.00*	5.58	179.30	1.56	2.65	0.00*	0.00*	0.00*
8926	15.99	0.00*	8.86	39.76	1.89	2.75	0.00*	0.00*	0.00*
10096	8.63	0.00*	3.39	117.25	0.87	1.25	0.00*	0.00*	0.00*
8799	5.52	0.00*	7.62	105.01	0.00*	2.07	0.00*	0.00*	0.00*
10087	6.82	0.00*	3.08	51.28	0.24	2.00	0.00*	0.00*	0.00*
8779	12.18	0.00*	9.15	56.09	1.86	2.17	0.00*	0.00*	0.00*
10089	7.70	0.00*	11.22	117.99	0.82	2.90	0.00*	0.00*	0.00*
8815	10.31	0.00*	8.19	137.28	1.19	2.10	0.00*	0.00*	0.00*
10036	14.62	0.00*	11.46	99.36	2.47	4.00	0.00*	0.00*	0.00*
8807	29.22	0.00*	5.04	130.03	2.01	2.38	0.00*	0.00*	0.00*
10095	15.53	0.00*	3.53	155.34	1.60	1.36	0.29	0.00*	0.00*
8810	5.00	0.00*	4.87	97.74	1.33	4.51	0.00*	0.00*	0.00*
10097	17.13	0.00*	5.75	78.90	1.27	3.12	0.00*	0.00*	0.00*
10030	13.78	0.00*	4.63	103.73	1.24	1.99	0.00*	0.00*	0.00*
8796	14.62	0.00*	6.19	100.66	2.07	1.66	0.00*	0.00*	0.00*
10041	8.31	0.00*	5.09	106.17	1.49	1.75	0.00*	0.00*	0.00*
8925	17.70	0.00*	6.54	98.58	1.95	2.27	0.00*	0.00*	0.00*
10090	17.00	0.00*	6.38	91.39	1.79	2.13	0.00*	0.00*	0.00*
8777	11.49	5.81	13.45	101.88	1.45	1.71	0.00*	0.00*	0.00*
10094	7.75	0.00*	2.30	120.86	0.96	1.64	0.00*	0.00*	0.00*
8813	15.03	0.00*	10.06	299.75	3.51	3.52	0.00*	0.00*	0.00*
10085	8.79	0.00*	6.01	183.13	1.34	2.53	0.00*	0.00*	0.00*
8786	13.84	0.00*	6.91	106.99	3.03	4.48	0.00*	0.00*	0.00*
10039	8.99	0.00*	5.51	84.53	1.22	3.91	0.00*	0.00*	0.00*
8924	14.64	0.00*	8.17	55.28	3.39	1.78	0.00*	0.00*	0.00*
10092	11.35	0.00*	5.53	137.51	1.09	2.27	0.00*	0.00*	0.00*
8806	7.09	0.00*	1.98	78.31	0.36	2.04	0.00*	0.00*	0.00*
10099	9.41	0.00*	6.98	84.58	2.61	2.38	0.00*	0.00*	0.00*
8795	13.14	0.00*	5.35	194.33	1.86	3.34	0.00*	0.00*	0.00*

* <LOD

Table 7: Results for nicotine and cotinine in mice plasma samples

Animal ID	Nicotine (ng/ml)	Cotinine (ng/ml)
10068	181.7	196.9
10075	0.0*	0.4
10078	0.0*	0.0*
10052	0.0*	0.0*
10071	160.2	368.5
10063	58.3	144.9
10048	7.5	1.9
10072	96.3	295.5
10065	53.8	227.7
10055	134.9	580.1
10061	68.5	382.7
10054	182.8	548.6
10064	101.6	265.7
10057	88.0	307.8
10049	0.0*	2.5
10053	127.6	252.6
10067	193.6	203.8
10045	0.0*	0.9
10046	0.0*	0.0*
10069	147.6	246.5
10066	66.5	246.9
10076	0.0*	0.0*
10047	0.0*	0.0*
10058	79.2	271.3
10050	0.0*	0.0*
10062	111.7	454.2
10073	85.5	293.6
10082	16.7	0.0*
10074	0.0*	0.0*
10059	140.3	259.4
10084	0.0*	1.0
10070	95.4	446.1
10079	59.9	131.6
10056	85.0	238.1
10083	5.2	1.2
10080	134.9	320.4
10060	97.4	319.8
10051	9.2	0.0*
10077	6.1	2.2
10081	96.0	189.6

*<LOD

10 Deviations

Generally, all methods were validated for human urine and plasma, respectively, and modified for diluted mouse samples. The obtained analyte concentrations were found to be consistent and within the validated concentration range, whenever quantifiable peaks were detected. Moreover, all QC samples and calibrators met the acceptance criteria throughout the entire study (cf. Suppl. Files 1-18) and therefore the deviation can be regarded as uncritical.
When evaluating and interpreting the results for the urinary biomarkers, it has to be taken into account that samples had to be diluted prior to analysis, due to low urine volumes. According to our experience, sample dilution has no impact on the results. However, there is of course an influence on the levels of LOD, LLOQ and ULOQ, which differ from the validated values (obtained with undiluted human urine samples).

11 Conclusions

The bioanalytical results of this study were obtained at ABF by using validated SOPs. As indicated in Section 10 of this TR, only minor deviations from the valid SOPs concerning sample dilution were necessary. Method suitability was proven for all analytes throughout the entire study.
In conclusion, all methods are applicable for the quantification of the respective biomarkers in diluted mice urine and plasma samples.

12 List of Supplementary files

Table 8: List of supplementary files

Suppl. File No	File Type	File name	Contents
1	xls (read only)	PMI15015_Supplement1_HPMA	***HPMA in urine (Method 1)***: Identity of reference substances, IS and reference material; calibration data and diagrams; QC data and diagrams; analytical run lists.
2	xls (read only)	PMI15015_Supplement2_NNAL	***NNAL in urine (Method 2)***: Identity of reference substances, IS and reference material; calibration data and diagrams; QC data and diagrams; analytical run lists.
3	xls (read only)	PMI15015_Supplement3_SPMA	***SPMA in urine (Method 3)***: Identity of reference substances, IS and reference material; calibration data and diagrams; QC data and diagrams; analytical run lists.
4	xls (read only)	PMI15015_Supplement4_CEMA	***CEMA in urine (Method 3)***: Identity of reference substances, IS and reference material; calibration data and diagrams; QC data and diagrams; analytical run lists.
5	xls (read only)	PMI15015_Supplement5_8-OHdG	***8-OHdG in urine (Method 4)***: Identity of reference substances, IS and reference material; calibration data and diagrams; QC data and diagrams; analytical run lists.
6	xls (read only)	PMI15015_Supplement6_MDA	***MDA in urine (Method 5)***: Identity of reference substances, IS and reference material; calibration data and diagrams; QC data and diagrams; analytical run lists.
7	xls (read only)	PMI15015_Supplement7_4-HNE	***4-HNE in urine (Method 5)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
8	xls (read only)	PMI15015_Supplement8_t-PGDM	***t-PGDM in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
9	xls (read only)	PMI15015_Supplement9_t-PGEM	***t-PGEM in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
10	xls (read only)	PMI15015_Supplement10_2,3-d-8-i-$PGF_{2\alpha}$	***2,3-d-8-i-$PGF_{2\alpha}$ in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
11	xls (read only)	PMI15015_Supplement11_2,3-d-TXB_2	***2,3-d-TXB_2 in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
12	xls (read only)	PMI15015_Supplement12_11-dh-TXB_2	***11-dh-TXB_2 in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.

13	xls (read only)	PMI15015_Supplement13_$PGF_{2\alpha}$	***$PGF_{2\alpha}$ in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
14	xls (read only)	PMI15015_Supplement14_8-i-$PGF_{2\alpha}$	***8-i-$PGF_{2\alpha}$ in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
15	xls (read only)	PMI15015_Supplement15_LTE_4	***LTE_4 in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
16	xls (read only)	PMI15015_Supplement16_12-HETE	***12-HETE in urine (Method 6)***: Identity of reference substances, IS and reference material; calibration data and diagrams; analytical run lists.
17	xls (read only)	PMI15015_Supplement17_Nic	***Nic in plasma (Method 7)***: Identity of reference substances, IS and reference material; calibration data and diagrams; QC data and diagrams; analytical run lists.
18	xls (read only)	PMI15015_Supplement18_Cot	***Cot in plasma (Method 7)***: Identity of reference substances, IS and reference material; calibration data and diagrams; QC data and diagrams; analytical run lists.
19	pdf	PMI15015_Supplement19_HPMA_Chromatograms	Chromatograms for HPMA analysis in mouse urine
20	pdf	PMI15015_Supplement20_NNAL_Chromatograms	Chromatograms for NNAL analysis in mouse urine
21	pdf	PMI15015_Supplement21_SPMA_CEMA_ Chromatograms	Chromatograms for SPMA and CEMA analysis in mouse urine
22	pdf	PMI15015_Supplement22_8-OHdG_Chromatograms	Chromatograms for 8-OHdG analysis in mouse urine
23	pdf	PMI15015_Supplement23_MDA_4-HNE_ Chromatograms	Chromatograms for MDA and 4-HNE analysis in mouse urine
24	pdf	PMI15015_Supplement24_Eicosanoids_Chromatograms	Chromatograms for eicosanoid analysis in mouse urine (t-PGDM, t-PGEM, 2,3-d-8-i-$PGF_{2\alpha}$, 2,3-d-TXB_2, 11-dh-TXB_2, $PGF_{2\alpha}$, 8-i-$PGF_{2\alpha}$, LTE_4, 12-HETE)
25	pdf	PMI15015_Supplement25_Nic_Cot_Chromatograms	Chromatograms for Nic and Cot analysis in mouse urine
26	pdf	PMI15015_Supplement26_ABF_SR_Ship1+2+3+4	Summary of the bioanalytical results (SR provided to PMI in Excel format by May 28th 2014)
27	pdf	PMI15015_Supplement27_ABF_SR_Nic_Cot_Rev2	Summary of the bioanalytical results (SR provided to PMI in Excel format by May 28th 2014)

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