Method Validation Report

Method Validation Report

DCN: 11-350-V2

Determination of Omeprazole in Heparinized Human Plasma by LC-MS-MS

Validation of the Analytical Method

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April 2002

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QUALITY ASSURANCE AUDITS AND INSPECTIONS

Phase	Date of Audit or Inspection	Date Reported to CEDRA Project Director	Date Reported to CEDRA Management
Folders	January 16, 2002	January 16, 2002	January 17, 2002
Tables	January 23, 2002	January 23, 2002	January 24, 2002
Tables and Solutions	January 24, 2002	January 24, 2002	January 24, 2002
Folders	March 1, 2002	March 1, 2002	March 1, 2002
Tables	March 19, 2002	March 19, 2002	March 20, 2002
Folder	March 22, 2002	March 22, 2002	March 25, 2002
Report	April 10, 2002	April 10, 2002	April 18, 2002

This study was audited and inspected by CEDRA's Quality Assurance Unit and the findings reported on the dates listed above.

Emily Wienen 4/18/02

Emily Wienen
Quality Assurance Unit

Determination of Omeprazole in Heparinized Human Plasma by LC-MS-MS

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GLP COMPLIANCE STATEMENT

These analyses were conducted and reported in compliance with applicable US FDA Good Laboratory Practice (GLP) Regulations, 21 CFR 58, Dec. 22, 1978, and all subsequent amendments, per CEDRA SOPs.

4/18/02

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Michael P. Sullivan, M.S.
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Determination of Omeprazole in Heparinized Human Plasma by LC-MS-MS
Validation of the Analytical Method

1.0 Method Summary

Heparinized human plasma was analyzed for omeprazole according to CEDRA procedure ATM-601, effective December 4, 2001. The method was validated for a range of 1.00 to 500 ng/mL based on the analysis of 0.100 mL of human plasma. Plasma containing omeprazole and the internal standard, lansoprazole, was extracted with an organic solvent mixture. Following centrifugation, the upper organic layer was removed and evaporated before being reconstituted in mobile phase. An aliquot of the extract was injected onto a SCIEX API 3000 LC-MS-MS equipped with an HPLC column. Peak areas of the m/z 344→194 product ion were measured against the m/z 368→164 product ion of the internal standard. Quantitation was performed using a weighted ($1/x^2$) linear least squares regression analysis generated from fortified plasma calibration standards prepared immediately prior to each run.

2.0 Preparation of Solutions

Stock solutions of omeprazole were dissolved in methanol, filled to volume with sodium carbonate solution (0.1 M), and stored at approximately 4 °C. Calibration standard intermediate solutions and calibration spiking solutions of omeprazole were prepared in methanol and sodium carbonate solution (1:4), and stored at approximately 4 °C. Calibration standards were prepared

to yield 1.00, 2.00, 5.00, 10.0, 50.0, 200, 450, and 500 ng/mL by fortifying 0.100 mL of heparinized human plasma with 10.0 µL of the appropriate spiking solution immediately prior to each analysis.

Heparinized human plasma was fortified with the QC intermediate solution at the appropriate concentrations. The QC samples were stored at approximately -20 °C in 0.100 mL aliquots. High, medium, and low QC samples were prepared at 375, 175, and 3.00 ng/mL, respectively, of omeprazole.

The lansoprazole internal standard working solution that expired on February 11, 2002, was inadvertently used on February 13, 2002. Data were accepted since the same amount of internal standard working solution was added to standards and QC samples, all of which were within acceptance criteria. The internal standard working solution was prepared to yield a concentration of approximately 1.00 µg/mL of lansoprazole. Each sample was fortified with 10.0 µL of this solution.

The following reference compounds and blank matrix were used during analysis. Omeprazole was purchased from USP (lot H, 100% purity, CEDRA logbook 770-70). Lansoprazole was purchased from Sigma Chemical Company (lot 041K1743, CEDRA logbook 770-78). The heparinized human plasma used during analysis was purchased from Golden West Biologicals, Inc.

3.0 Assay Validation

The assay procedure was validated according to CEDRA SOP PS-002, Revision 9, effective December 21, 2001. Calibration standards prepared at eight different omeprazole concentrations were assayed on three separate days, and the lower limit of quantitation (LLOQ) was established at 1.00 ng/mL. The results of these analyses are presented in Tables 1 through 4.

3.1 Linearity

The assay procedure was found to be linear over the range of 1.00 to 500 ng/mL. The weighting of $1/x^2$ was selected based on power for weights calculations. Weighted linear least squares regression analyses gave a mean correlation coefficient of 0.9992 over the three validation days (Table 1). The mean value for the y-intercept was 0.0016 and the mean value for the slope was 0.0096.

3.2 Standard Curves

Precision and accuracy were evaluated by treating the peak areas of the calibration standards as unknowns and entering them into the derived equation for the least squares regression line to obtain "amount found" values. Results from the standard curve data may be found in Table 2. The coefficient of variation (CV) ranged from 0.64% to 5.5%. The absolute deviation of the mean from the theoretical concentration ranged from 0.00% to 3.1%.

3.3 Lower Limit of Quantitation Evaluation

Precision and accuracy at the LLOQ were verified by analyzing at least two samples at the lowest standard concentration (1.00 ng/mL) on each day of validation. The interday CV was 11.9% and the interday absolute deviation of the mean from the theoretical concentration was 4.7%. The intraday precision and accuracy at the LLOQ were verified by analyzing six samples at the lowest standard concentration during one day of validation. The intraday CV was 7.9% and the intraday absolute deviation was 13.3%. The results are shown in Tables 3 and 4.

3.4 Quality Control Samples

At least three samples from each QC pool (high, medium, and low) were processed on each day of validation. The interday CV for the three QC pools ranged from 3.2% to 4.4%. The interday absolute deviation of the mean from theoretical concentration ranged from 7.1% to 8.8%. On one day of validation, six samples from each QC pool were processed. The intraday CV ranged from 2.6% to 5.7%. The intraday absolute deviation ranged from 7.9% to 9.3%. Results of these analyses are shown in Tables 5 and 6.

On one day of validation, very high QC samples were prepared at 2500 ng/mL and diluted 1:10 prior to analysis. The CV was 2.9% and the absolute deviation of the mean from theoretical concentration was 5.7%. Results of this analysis are shown in Table 7.

3.5 Short-Term Stability Studies

Benchtop, freeze/thaw, and extract stability in heparinized human plasma were performed. Three replicates from each QC pool (375, 175, and 3.00 ng/mL) were thawed and placed on the benchtop at room temperature for approximately twenty-five hours prior to extraction. A different set of triplicate samples from each QC pool was taken through four freeze/thaw cycles and then analyzed. A third set of triplicate samples was extracted and injected; the extracts were then reinjected after approximately one hundred twenty-five hours at room temperature.

At least two-thirds of the stability samples in each pool were within ±15% of their theoretical concentrations. Based on these findings, it is concluded that omeprazole is stable under these test conditions. Results of these studies may be found in Tables 8 through 10.

Reinjection stability was performed on February 13, 2002, by reinjecting the BDMBM run in its entirety. The run was within acceptance criteria.

3.6 Recovery

Extraction recovery was determined by comparing peak areas of extracted standards against those of nonextracted standards at three concentrations spanning the calibration curve.

The average recovery of omeprazole ranged from 102% to 115%. The recovery of the internal standard (lansoprazole) was 99.7%. The results are given in Tables 11 and 12.

3.7 Matrix Effect on Analytical Recovery

Six different lots of heparinized human plasma were fortified to the level of standard D (10.0 ng/mL), and extracted to examine the effect of variations in matrix on analytical recovery. The amount recovered ranged from 101% to 110% for omeprazole. These results may be found in Table 13. Based on these results, analytical recovery was unaffected by variations in matrix.

3.8 Specificity

Six lots of blank heparinized human plasma were analyzed on January 2, 2002, to identify any interferences at the retention times of omeprazole or the internal standard. No significant interferences were observed at either retention time.

3.9 Over-the-Counter Drugs

On February 27, 2002, a solution of common over-the-counter drugs (acetaminophen, acetylsalicylic acid, brompheniramine, caffeine, chlorpheniramine, cimetidine, dextromethorphan, diphenhydramine, ibuprofen, ketoprofen, naproxen, phenylpropanolamine, pseudoephedrine, ranitidine, salicylic acid, and triprolidine) was injected in triplicate directly

onto the LC-MS-MS to determine whether interferences exist. No interferences were observed at the retention times of omeprazole or the internal standard.

3.10 Extended Stability at -20 °C

A measure of the extended stability of omeprazole in heparinized human plasma at -20 °C was evaluated at concentrations of 375, 175, and 3.00 ng/mL. Heparinized human plasma pools were fortified with the analyte on December 13, 2001, aliquotted, and stored at approximately -20 °C. Subsequent analysis of these samples on February 13, 2002, against a freshly prepared calibration curve, provided insight into the extended stability of the analyte. The eight-week extended stability for omeprazole in heparinized human plasma is presented in Table 14. All the stability samples in each pool were within ±15% of their theoretical concentrations.

3.11 Discussion of Rejected Data

The BDQLL run was rejected due to unacceptable contamination in blanks. The BDUBM2 run was rejected due to carry-over in the OTC-1 sample.

4.0 Archiving

The data, report, and electronic media will be archived off-site for a minimum of fifteen years according to CEDRA Standard Operating Procedures PS-016 and PS-077.

5.0 Appendices

Appendix A contains the raw data worksheets. Appendix B contains example chromatograms from the analysis of validation samples. Appendix C contains an example standard curve plot. Appendix D contains the list of contributors.

Table 1

Standard Curve Parameters
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Intercept	Slope	Correlation Coefficient
12/28/2001	BD8LL	0.0008	0.0092	0.9988
01/02/2002	BDBAM	0.0020	0.0094	0.9994
01/03/2002	BDCAM	0.0021	0.0101	0.9994
	n	3	3	3
	Mean	0.0016	0.0096	0.9992

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 2

Standard Curve Data:
Precision and Accuracy
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Found (ng/mL)							
12/28/2001	BD8LL	0.981	2.08	4.95	10.1	50.2	184	480	493
01/02/2002	BDBAM	1.03	1.87	5.11	10.1	50.8	202	448	492
01/03/2002	BDCAM	1.00	2.03	4.87	9.38	50.3	200	464	515
	n	3	3	3	3	3	3	3	3
	Amount Added (ng/mL)	1.00	2.00	5.00	10.0	50.0	200	450	500
	Mean (ng/mL)	1.00	1.99	4.98	9.86	50.4	195	464	500
	SD (n-1)	0.02	0.11	0.12	0.42	0.3	9.9	16	13
	CV (%)	2.5	5.5	2.5	4.2	0.64	5.1	3.4	2.6
	Absolute Deviation (%)	0.37	0.33	0.47	1.4	0.87	2.3	3.1	0.00

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 3

Lower Limit of Quantitation Data:
Interday Precision and Accuracy
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Found (ng/mL)
12/28/2001	BD8LL	1.05
		1.03
		1.28
		1.13
		1.17
		1.14
01/02/2002	BDBAM	0.900
		0.894
01/03/2002	BDCAM	0.895
		1.02
		1.01
	n	11
	Amount Added (ng/mL)	1.00
	Mean (ng/mL)	1.05
	SD (n-1)	0.12
	CV (%)	11.9
	Absolute Deviation (%)	4.7

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 4

Lower Limit of Quantitation Data:
Intraday Precision and Accuracy
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Found (ng/mL)
12/28/2001	BD8LL	1.05
		1.03
		1.28
		1.13
		1.17
		1.14
	n	6
	Amount Added (ng/mL)	1.00
	Mean (ng/mL)	1.13
	SD (n-1)	0.09
	CV (%)	7.9
	Absolute Deviation (%)	13.3

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 5

Quality Control Data:
Interday Precision and Accuracy
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Found (ng/mL)		
12/28/2001	BD8LL	346	164	2.85
		332	157	2.65
		330	155	2.97
		349	165	2.57
		352	164	2.63
		331	162	2.66
01/02/2002	BDBAM	348	169	2.76
		361	160	2.71
		352	174	2.72
01/03/2002	BDCAM	327	158	2.85
		339	165	2.82
		335	157	2.90
	n	12	12	12
	Amount Added (ng/mL)	375	175	3.00
	Mean (ng/mL)	342	163	2.76
	SD (n-1)	11	6	0.12
	CV (%)	3.2	3.4	4.4
	Absolute Deviation (%)	8.8	7.1	8.1

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 6

Quality Control Data:
Intraday Precision and Accuracy
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Found (ng/mL)		
12/28/2001	BD8LL	346	164	2.85
		332	157	2.65
		330	155	2.97
		349	165	2.57
		352	164	2.63
		331	162	2.66
	n	6	6	6
	Amount Added (ng/mL)	375	175	3.00
	Mean (ng/mL)	340	161	2.72
	SD (n-1)	10	4	0.15
	CV (%)	3.0	2.6	5.7
	Absolute Deviation (%)	9.3	7.9	9.3

Note: Calculations performed with [illegible] Microsoft Excel 97.

Table 7

Dilution Quality Control Data:
Precision and Accuracy
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Found (ng/mL)
12/28/2001	BD8LL	2420
		2290
		2260
		2360
		2420
		2390
	n	6
	Amount Added (ng/mL)	2500 (10X)
	Mean (ng/mL)	2360
	SD (n-1)	70
	CV (%)	2.9
	Absolute Deviation (%)	5.7

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 8

25-Hour Benchtop Stability
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Added (ng/mL)	Stability Samples (ng/mL)	% Deviation from Amount Added
01/03/2002	BDCAM	375	340	-9.3
			341	-9.1
			343	-8.5
		175	163	-6.9
			158	-9.7
			165	-5.7
		3.00	2.58	-14.0
			2.62	-12.7
			2.73	-9.0

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 9

4-Cycle Freeze/Thaw Stability
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Added (ng/mL)	Stability Samples (ng/mL)	% Deviation from Amount Added
01/02/2002	BDBAM	375	363	-3.2
			361	-3.7
			346	-7.7
		175	168	-4.0
			167	-4.6
			173	-1.1
		3.00	2.81	-6.3
			2.62	-12.7
			2.76	-8.0

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 10

125-Hour Extract Stability
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Folder ID	Amount Added (ng/mL)	Stability Samples (ng/mL)	% Deviation from Amount Added
BDBAM	375	329	-12.3
		342	-8.8
		333	-11.2
	175	166	-5.1
		164	-6.3
		162	-7.4
	3.00	2.89	-3.7
		2.50	-16.7
		2.95	-1.7

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 11

Recovery of Omeprazole
from Heparinized Human Plasma
Masterfile No.: 11-350-V2

		Peak Area					
		1.00 ng/mL		10.0 ng/mL		500 ng/mL	
Date	Folder ID	Extracted	Non-Extracted	Extracted	Non-Extracted	Extracted	Non-Extracted
01/03/2002	BDCAM	1513	1208	12411	12238	676043	668659
		1601	1389	13084	12492	705646	615620
		1408	1342	12746	12898	683707	745878
	n	3	3	3	3	3	3
	Mean	1507	1313	12747	12543	688465	676719
	% Recovery	115		102		102	

Note: Calculations performed with machine precision of Microsoft Excel 97

Table 12

Recovery of Internal Standard (Lansoprazole)
from Heparinized Human Plasma
Masterfile No.: 11-350-V2

		Peak Area	
		Internal Standard	
Date	Folder ID	Extracted	Non-Extracted
01/03/2002	BDCAM	124256	115982
		120472	124280
		130119	137450
		128286	122737
		130118	129412
		123098	130838
		130085	138851
		135769	142983
		133483	117184
	n	9	9
	Mean	128410	128857
	% Recovery	99.7	

Note: Calculations performed with machine precision of Microsoft Excel 97.

Table 13

Matrix Effect on Analytical Recovery[+]
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Added (ng/mL)	Plasma Log Number	Amount Found (ng/mL)	Analytical Recovery (%)
01/02/2002	BDBAM	10.0	783-01J	10.7	107
			783-51A	11.0	110
			783-51M	10.2	102
			783-67E	10.3	103
			783-67G	10.1	101
			783-67D	10.5	105

[+] Matrix effect samples prepared by fortifying different blank plasma lots with Standard D spiking solution and working internal standard. The samples were then extracted per ATM-601.
Note: Calculations performed with machine precision of Microsoft Excel 97

Table 14

8-Week Extended Stability
for Omeprazole in Heparinized Human Plasma
Masterfile No.: 11-350-V2

Date	Folder ID	Amount Added (ng/mL)	Stability Samples+ (ng/mL)	% Deviation from Amount Added
02/13/2002	BDMBM	375	366	-2.4
			378	0.80
			360	-4.0
		175	166	-5.1
			172	-1.7
			175	0.00
		3.00	2.89	-3.7
			2.91	-3.0
			3.07	2.3

+ Stability samples were prepared on 12/13/2001 and stored at -20 °C. The QCs were quantitated against a standard curve prepared on 02/13/2002.
Note: Calculations performed with machine precision of Microsoft Excel 97.

DCN: 11-350-V2

Appendix A

Raw Data Worksheets

Printed 01/03/2002 by IR

Filename: BD8LL
Date: 12/28/2001

Page 1

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept: 0.0008
Slope: 0.0092
Correlation coeff.: 0.9988
Weighted (1/x*x)

Standard ID	Status	Theor Conc (ng/mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Percent Deviation	Back Cal Analyte (ng/mL)	Ratio/ Conc
Std A		1.00	597	60873	0.00981	-1.9	0.981	0.0098
Std B		2.00	1201	60243	0.01994	4.1	2.08	0.0100
Std C		5.00	2559	55316	0.04626	-1.1	4.95	0.0093
Std D		10.0	5243	55959	0.09369	1.1	10.1	0.0094
Std E		50.0	27442	59340	0.46245	0.45	50.2	0.0092
Std F		200	100970	59533	1.69603	-7.8	184	0.0085
Std G		450	232507	52707	4.41131	6.6	480	0.0098
Std H		500	254333	56143	4.53009	-1.4	493	0.0091

TECHNICAL REVIEW
SIGNATURE [signature]
DATE 1/2/02

QC REVIEW #1
SIGNATURE [signature]
DATE 1-3-02

QC REVIEW #2
SIGNATURE [signature]
DATE 1/3/02

PROJECT DIRECTOR REVIEW
SIGNATURE [signature]
DATE 1/13/02

QA REVIEW
SIGNATURE [signature]
DATE 1-16-02

Printed 01/03/2002 by
QA review by

Filename: BD8LL
Date: 12/28/2001

Page 2

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No.: 11-350-V2
Client Study Number

Intercept: 0.0008
Slope: 0.0092
Correlation coeff.: 0.9988
Weighted (1/x*x)

Quality Control Samples	Status	Theor Conc (ng/mL)	Sample Volume (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Percent Deviation	Normalized Conc (ng/mL)
QC VERY HIGH 1		2500	0.0100	120578	54288	2.22108	242	-3.4	2420
QC VERY HIGH 2		2500	0.0100	122865	58229	2.11003	229	-8.2	2290
QC VERY HIGH 3		2500	0.0100	123546	59416	2.07934	226	-9.5	2260
QC VERY HIGH 4		2500	0.0100	115953	53510	2.16694	236	-5.7	2360
QC VERY HIGH 5		2500	0.0100	130205	58573	2.22295	242	-3.3	2420
QC VERY HIGH 6		2500	0.0100	126767	57609	2.20047	239	-4.3	2390
QC HIGH 1		375		168585	53006	3.18049	346	-7.8	
QC HIGH 2		375		174997	57390	3.04926	332	-11.6	
QC HIGH 3		375		168944	55709	3.03262	330	-12.0	
QC HIGH 4		375		178695	55727	3.20661	349	-7.0	
QC HIGH 5		375		184966	57107	3.23894	352	-6.1	
QC HIGH 6		375		177461	58377	3.03991	331	-11.8	
QC MED 1		175		85971	56970	1.50906	164	-6.2	
QC MED 2		175		74237	51393	1.44450	157	-10.2	
QC MED 3		175		80070	56151	1.42598	155	-11.4	
QC MED 4		175		88367	58341	1.51466	165	-5.9	
QC MED 5		175		81649	54083	1.50970	164	-6.2	
QC MED 6		175		84915	57084	1.48754	162	-7.6	
QC LOW 1		3.00		1530	56680	0.02699	2.85	-5.0	
QC LOW 2		3.00		1487	59069	0.02517	2.65	-11.6	
QC LOW 3		3.00		1519	54141	0.02806	2.97	-1.1	
QC LOW 4		3.00		1412	57828	0.02442	2.57	-14.3	
QC LOW 5		3.00		1400	55966	0.02502	2.63	-12.2	
QC LOW 6		3.00		1541	60978	0.02527	2.66	-11.3	

Printed 01/03/2002 by TR
QA review by

Filename. BD8LL
Date. 12/28/2001

Page 3

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions. 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept: 0.0008
Slope: 0.0092
Correlation coeff.: 0.9988
Weighted (1/x*x)

Sample ID	Status	Vol (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Normalized Conc (ng/mL)
Blank-Blank 1			0	0	NA	NA	
Blank Blank 2			0	0	NA	NA	
Blank IS			0	58141	NM	< 1.00	
LLOQ 1			453	43488	0.01042	1.05	
LLOQ 2			611	59567	0.01026	1.03	
LLOQ 3			726	57967	0.01252	1.28	
LLOQ 4			676	60238	0.01122	1.13	
LLOQ 5			997	86242	0.01156	1.17	
LLOQ 6			849	75112	0.01130	1.14	
OTC_1			0	0	NA	NA	
OTC_2			0	0	NA	NA	
OTC_3			0	0	NA	NA	

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Filename: BDBAM
Date: 01/02/2002

Page 1

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept: 0.0020
Slope: 0.0094
Correlation coeff.: 0.9994
Weighted (1/x*x)

Standard ID	Status	Theor Conc (ng/mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Percent Deviation	Back Cal Analyte (ng/mL)	Ratio/ Conc
Std A		1.00	689	59145	0.01165	2.7	1.03	0.0116
Std B		2.00	1119	57295	0.01953	-6.6	1.87	0.0098
Std C		5.00	3021	60516	0.04992	2.2	5.11	0.0100
Std D		10.0	5805	60002	0.09675	1.0	10.1	0.0097
Std E		50.0	29060	60775	0.47816	1.5	50.8	0.0096
Std F		200	121122	63839	1.89730	1.0	202	0.0095
Std G		450	249872	59395	4.20695	-0.36	448	0.0093
Std H		500	259983	56278	4.61962	-1.5	492	0.0092

Quality Control Samples	Status	Theor Conc (ng/mL)	Sample Volume (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Percent Deviation	Normalized Conc (ng/mL)
QC HIGH 1		375		204537	62650	3.26476	348	-7.2	
QC HIGH 2		375		208265	61535	3.38450	361	-3.8	
QC HIGH 3		375		223103	67531	3.30371	352	-6.1	
QC MED 1		175		95064	60000	1.58440	169	-3.6	
QC MED 2		175		98500	65470	1.50451	160	-8.4	
QC MED 3		175		102478	62780	1.63234	174	-0.66	
QC LOW 1		3.00		1657	59400	0.02790	2.76	-8.0	
QC LOW 2		3.00		1786	65065	0.02745	2.71	-9.6	
QC LOW 3		3.00		1732	62843	0.02756	2.72	-9.2	

TECHNICAL REVIEW
SIGNATURE [signature]
DATE 1/3/02

QC REVIEW #1
SIGNATURE [signature]
DATE 1/9/02

QC REVIEW #2
SIGNATURE Kathryn Rogers
DATE 1/9/02

PROJECT DIRECTOR REVIEW
SIGNATURE [signature]
DATE 1/13/02

QA REVIEW
SIGNATURE Michele Malone
DATE 1-16-02

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QA review by

Filename BDBAM
Date 01/02/2002

Page 2

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept: 0.0020
Slope: 0.0094
Correlation coeff.: 0.9994
Weighted (1/x*x)

Sample ID	Status	Vol (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Normalized Conc (ng/mL)
Spec_1_(783-1J)			0	0	NA	NA	
Spec_2_(783-51A)			0	0	NA	NA	
Spec_3_(783-51M)			0	0	NA	NA	
Spec_4_(783-67E)			0	0	NA	NA	
Spec_5_(783-67G)			120	54	NA	NA	
Spec_6_(783-67D)			0	0	NA	NA	
Blank Blank			0	0	NA	NA	
Blank IS			0	57469	NM	< 1.00	
LLOQ_1			614	58702	0.01046	0.900	
LLOQ_2			575	55299	0.01040	0.894	
Spec_D1_(783-1J)			5911	57840	0.10220	10.7	
Spec_D2_(783-51A)			6316	60225	0.10487	11.0	
Spec_D3_(783-51M)			5851	59664	0.09807	10.2	
Spec_D4_(783-67E)			6085	61933	0.09825	10.3	
Spec_D5_(783-67G)			5593	57992	0.09644	10.1	
Spec_D6_(783-67D)			6086	60637	0.10037	10.5	
QC LOW_1_XTS			2933	100784	0.02910	2.89	
QC LOW_2_XTS			3225	126416	0.02551	2.50	
QC LOW_3_XTS			4218	142256	0.02965	2.95	
QC MED_1_XTS			177469	113654	1.56131	166	
QC MED_2_XTS			183605	119204	1.54026	164	
QC MED_3_XTS			200519	131596	1.52375	162	
QC HIGH_1_XTS			390353	126364	3.08912	329	
QC HIGH_2_XTS			361624	112732	3.20782	342	
QC HIGH_3_XTS			461072	147607	3.12365	333	
QC LOW_1_FTS			1773	62515	0.02836	2.81	
QC LOW_2_FTS			1782	66916	0.02663	2.62	
QC LOW_3_FTS			1874	67066	0.02794	2.76	
QC MED_1_FTS			104098	65825	1.58144	168	
QC MED_2_FTS			97416	62301	1.56363	167	
QC MED_3_FTS			107794	66219	1.62784	173	
QC HIGH_1_FTS			220196	64650	3.40597	363	
QC HIGH_2_FTS			225304	66568	3.38457	361	
QC HIGH_3_FTS			226452	69646	3.25147	346	

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Filename: BDCAM
Date: 01/03/2002

Page 1

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No.: 11-350-V2
Client Study Number

Intercept: 0.0021
Slope: 0.0101
Correlation coeff.: 0.9994
Weighted (1/x*x)

Standard ID	Status	Theor Conc (ng/mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Percent Deviation	Back Cal Analyte (ng/mL)	Ratio/ Conc
Std A 1		1 00	1513	124256	0.01218	0.25	1.00	0 0122
Std A 2	D9	1 00	1601	120472	0.01329	11.3	1.11	0.0133
Std A 3	D9	1 00	1408	130119	0.01082	-13.2	0.868	0.0108
Std B		2 00	2671	118256	0.02259	1.7	2.03	0.0113
Std C		5 00	6695	130876	0.05116	-2.7	4.87	0.0102
Std D 1		10.0	12411	128286	0.09674	-6.2	9.38	0.0097
Std D 2	D9	10.0	13084	130118	0.10055	-2.4	9.76	0.0101
Std D 3	D9	10.0	12746	123098	0.10354	0.59	10.1	0.0104
Std E		50.0	68800	134951	0.50981	0.65	50.3	0.0102
Std F		200	267011	132079	2.02160	0.08	200	0.0101
Std G		450	660509	141012	4.68406	3.1	464	0.0104
Std H 1		500	676043	130085	5.19693	3.0	515	0.0104
Std H 2	D9	500	705646	135769	5.19740	3.0	515	0.0104
Std H 3	D9	500	683707	133483	5.12205	1 5	507	0.0102

D9 Not included in calculations; used for recovery only.

Quality Control Samples	Status	Theor Conc (ng/mL)	Sample Volume (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Percent Deviation	Normalized Conc (ng/mL)
QC HIGH 1		375		470299	142615	3.29768	327	-12.9	
QC HIGH 2		375		457972	133952	3.41893	339	-9.7	
QC HIGH 3		375		487594	144354	3.37777	335	-10.8	
QC MED 1		175		210382	132097	1.59263	158	-9.9	
QC MED 2		175		237109	142674	1.66189	165	-6.0	
QC MED 3		175		228879	144428	1 58473	157	-10.4	
QC LOW 1		3.00		4270	138752	0.03077	2.85	-5.1	
QC LOW 2		3.00		4064	133074	0.03054	2.82	-5.9	
QC LOW 3		3 00		4447	142130	0 03129	2.90	-3.4	

TECHNICAL REVIEW
SIGNATURE [signature]
DATE 1/4/02

QC REVIEW #1
SIGNATURE Kathryn Rogers
DATE 1/7/02

QC REVIEW #2
SIGNATURE Maria Sumbillo
DATE 1-8-02

PROJECT DIRECTOR REVIEW
SIGNATURE [signature]
DATE 1/13/02

QA REVIEW
SIGNATURE Michele Malone
DATE 1-16-02

Printed 01/07/2002 by
QA review by

Filename: BDCAM
Date: 01/03/2002

Page 2

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No : 11-350-V2
Client Study Number:

Intercept: 0.0021
Slope: 0.0101
Correlation coeff.: 0.9994
Weighted (1/x*x)

Sample ID	Status	Vol (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Normalized Conc (ng/mL)
Blank Blank 1			0	0	NA	NA	
Blank Blank 2			0	0	NA	NA	
Blank IS			110	108297	0.00102	< 1.00	
LLOQ_1			1313	118461	0.01108	0.895	
LLOQ_2			1568	127432	0.01230	1.02	
LLOQ_3			1469	120292	0.01221	1.01	
Std A 1 REC			1208	115982	0.01042	0.828	
Std A 2 REC			1389	124280	0.01118	0.903	
Std A 3 REC			1342	137450	0.00976	0.764	
Std D 1 REC			12238	122737	0.09971	9.68	
Std D 2 REC			12492	129412	0.09653	9.36	
Std D 3 REC			12898	130838	0.09858	9.57	
Std H 1 REC			668659	138851	4.81566	477	
Std H 2 REC			615620	142983	4.30555	427	
Std H 3 REC			745878	117184	6.36502	631	
QC LOW 1 BTS			3598	128216	0.02806	2.58	
QC LOW 2 BTS			3685	129136	0.02854	2.62	
QC LOW 3 BTS			4065	137466	0.02957	2.73	
QC MED 1 BTS			186870	113142	1.65164	163	
QC MED 2 BTS			223759	139954	1.59880	158	
QC MED 3 BTS			219403	131994	1.66222	165	
QC HIGH 1 BTS			424170	123647	3.43049	340	
QC HIGH 2 BTS			483401	140552	3.43930	341	
QC HIGH 3 BTS			455229	131548	3.46055	343	

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Filename: BDMBM
Date. 02/13/2002

Page 1

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept: -0.0003
Slope. 0.0121
Correlation coeff.: 0.9991
Weighted (1/x*x)

Standard ID	Status	Theor Conc (ng/mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Percent Deviation	Back Cal Analyte (ng/mL)	Ratio/ Conc
Std A		1.00	2979	246582	0.01208	2.5	1.02	0.0121
Std B		2.00	5008	222347	0.02252	-5.5	1.89	0.0113
Std C		5.00	12524	205684	0.06089	1 4	5.07	0 0122
Std D		10.0	23809	198371	0 12002	-0.31	9 97	0.0120
Std E		50 0	120326	198117	0 60735	0 70	50.3	0 0121
Std F		200	450196	197888	2.27500	-5 7	189	0.0114
Std G		450	954722	170443	5 60142	3 1	464	0 0124
Std H		500	1046943	167150	6 26349	3 8	519	0.0125

Quality Control Samples	Status	Theor Conc (ng/mL)	Sample Volume (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Percent Deviation	Normalized Conc (ng/mL)
QC HIGH 1		375		676130	153089	4.41658	366	-2.4	
QC HIGH 2		375		703818	154224	4.56361	378	0.84	
QC HIGH 3		375		715108	164777	4.33985	360	-4 1	
QC MED 1		175		324164	161570	2.00634	166	-5 0	
QC MED 2		175		352222	169565	2.07721	172	-1.6	
QC MED 3		175		342010	162119	2.10962	175	-0.10	
QC LOW 1		3.00		5785	167418	0 03455	2 89	-3 8	
QC LOW 2		3.00		5577	160173	0 03482	2 91	-3.0	
QC LOW 3		3.00		5664	154132	0.03675	3.07	2 3	

TECHNICAL REVIEW
SIGNATURE [signature]
DATE 2/14/02

QC REVIEW #1
SIGNATURE [signature]
DATE 2/15/02

QC REVIEW #2
SIGNATURE [signature]
DATE 2-17-02

PROJECT DIRECTOR REVIEW
SIGNATURE [signature]
DATE 2/18/02

QA REVIEW
SIGNATURE [signature]
DATE 3/1/02

Printed 02/15/2002 by
QA review by

Filename. BDMBM
Date 02/13/2002

Page 2

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions· 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept -0.0003
Slope· 0.0121
Correlation coeff.. 0.9991
Weighted (1/x*x)

Sample ID	Status	Vol (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Normalized Conc (ng/mL)
Blank-Blank 1			0	0	NA	NA	
Blank Blank 2			0	0	NA	NA	
Blank IS			0	268759	NM	< 1.00	

Printed 02/18/2002 by _____

Filename BDMBMRS
Date 02/13/2002

Page 1

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept 0.0001
Slope 0.0125
Correlation coeff.: 0.9990
Weighted (1/x*x)

Standard ID	Status	Theor Conc (ng/mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Percent Deviation	Back Cal Analyte (ng/mL)	Ratio/ Conc
Std A		1.00	2574	198391	0.01297	2 8	1 03	0.0130
Std B		2.00	4598	191026	0 02407	-4 2	1 92	0.0120
Std C		5.00	11943	193808	0.06162	-1 6	4 92	0.0123
Std D		10 0	25103	210401	0 11931	-4 7	9 53	0.0119
Std E		50 0	122051	188852	0 64628	3 3	51 7	0 0129
Std F		200	526401	218630	2 40773	-3 7	193	0 0120
Std G		450	1120500	193890	5 77905	2 7	462	0.0128
Std H		500	1424345	216108	6 59089	5 4	527	0.0132

Quality Control Samples	Status	Theor Conc (ng/mL)	Sample Volume (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Percent Deviation	Normalized Conc (ng/mL)
QC HIGH 1		375		896041	190649	4 69995	376	0 22	
QC HIGH 2		375		906447	195788	4 62974	370	-1.3	
QC HIGH 3		375		821940	185173	4 43877	355	-5 4	
QC MED 1		175		402834	193378	2.08314	167	-4.8	
QC MED 2		175		445378	214591	2 07547	166	-5.2	
QC MED 3		175		409597	190876	2.14588	172	-2.0	
QC LOW 1		3.00		7677	205829	0 03730	2 97	-0.88	
QC LOW 2		3 00		7116	193096	0 03685	2 94	-2.1	
QC LOW 3		3 00		7293	189949	0 03839	3 06	2.0	

TECHNICAL REVIEW
SIGNATURE [signature]
DATE 2/15/02

QC REVIEW #1
SIGNATURE [signature]
DATE 2/15/02

QC REVIEW #2
SIGNATURE [signature]
DATE 2-20-02

PROJECT DIRECTOR REVIEW
SIGNATURE [signature]
DATE 2/22/02

QA REVIEW
SIGNATURE [signature]
DATE 3/1/02

Printed 02/18/2002 by
QA review by

Filename: BDMBMRS
Date: 02/13/2002

Page 2

Omeprazole in Human Plasma
Internal Standard Lansoprazole
Parent -> Product Ions. 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept 0.0001
Slope 0.0125
Correlation coeff.: 0.9990
Weighted (1/x*x)

Sample ID	Status	Vol (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Normalized Conc (ng/mL)
Blank-Blank 1			0	0	NA	NA	
Blank Blank 2			292	0	NA	NA	
Blank IS			0	190646	NM	< 1.00	

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Filename BD7BM
Date 02/27/2002

Page 1

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No ' 11-350-V2
Client Study Number:

Intercept. 0.0015
Slope. 0.0110
Correlation coeff.: 0.9993
Weighted (1/x*x)

Standard ID	Status	Theor Conc (ng/mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Percent Deviation	Back Cal Analyte (ng/mL)	Ratio/ Conc
Std A		1.00	633	50124	0 01263	1.1	1.01	0.0126
Std B		2 00	1132	49537	0 02285	-3 0	1.94	0.0114
Std C	D1	5.00	2508	54475	0 04604	-19 0	4.05	0.0092
Std D		10.0	5870	51267	0 11450	2.8	10.3	0.0114
Std E		50.0	26707	46979	0 56849	3.2	51.6	0.0114
Std F	D1	200	115933	40253	2 88011	31 0	262	0.0144
Std G		450	273649	55050	4 97092	8 51	452	0.0110
Std H		500	415222	79328	5 23424	-4 7	476	0 0105

D1 Standard not included in calculations, outlier

Quality Control Samples	Status	Theor Conc (ng/mL)	Sample Volume (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Percent Deviation	Normalized Conc (ng/mL)
QC HIGH 1	OR	375		284614	83771	3 39752	309	-17 6	
QC HIGH 2		375		235392	60476	3 89232	354	-5 6	
QC HIGH 3		375		237414	59393	3 99734	364	-3.0	
QC MED 1		175		127465	66457	1 91801	174	-0.32	
QC MED 2	OR	175		119994	49919	2 40377	219	24 9	
QC MED 3		175		132539	67775	1 95557	178	1.6	
QC LOW 1		3.00		1905	63983	0 02977	2.57	-14.3	
QC LOW 2		3.00		2013	62966	0 03197	2 77	-7 6	
QC LOW 3		3.00		2064	64087	0 03221	2 79	-6.9	

OR QC Out of Range

TECHNICAL REVIEW
SIGNATURE [signature]
DATE 3/1/02

QC REVIEW #1
SIGNATURE [signature]
DATE 3/4/02

QC REVIEW #2
SIGNATURE Maria Jumbillo
DATE 3/7/02

PROJECT DIRECTOR REVIEW
SIGNATURE [signature]
DATE 3/8/02

QA REVIEW
SIGNATURE Alma Martinez
DATE 3/22/02

Printed 03/05/2002 by MCS
QA review by DM

Filename. BD7BM
Date: 02/27/2002

Page 2

Omeprazole in Human Plasma
Internal Standard: Lansoprazole
Parent -> Product Ions: 344->194
Masterfile No.: 11-350-V2
Client Study Number:

Intercept: 0.0015
Slope: 0.0110
Correlation coeff.: 0.9993
Weighted (1/x*x)

Sample ID	Status	Vol (mL)	Area Analyte	Area Int Std	Ratio Analyte/ Int Std	Conc Found (ng/mL)	Normalized Conc (ng/mL)
Blank-Blank 1			0	0	NA	NA	
Blank Blank 2			0	0	NA	NA	
Blank IS			0	48447	NM	< 1.00	
OTC 1			0	0	NA	NA	
OTC 2			0	0	NA	NA	
OTC 3			0	0	NA	NA	

DCN: 11-350-V2

Appendix B

Example Chromatograms from the Analysis of Validation Samples

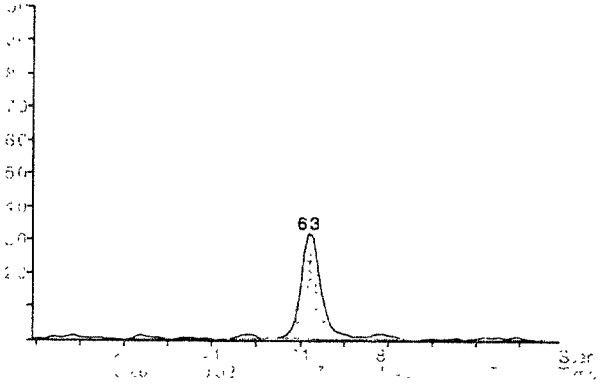
MacQuan, version 1.6
Printed: Wed, Jan 2, 2002 08:31
Calibration File: BD8LL Calibration Path: Snoopy:Desktop Folder:AA PROJECTS:bd8ll:
Comments: No Comments

BD8LL1011 **Std A** Fri, Dec 28, 2001 17:53
Std A

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	3.0
Quant Thres.	0.8
Min. Width	9
Mult. Width	2
Base. Width	20
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	597
Height	92
Start Time	1:12
End Time	1:31
Integration Width	0:18 9
Retention Time	1:19
Integration Type	A - BB

intensity: 300 cps



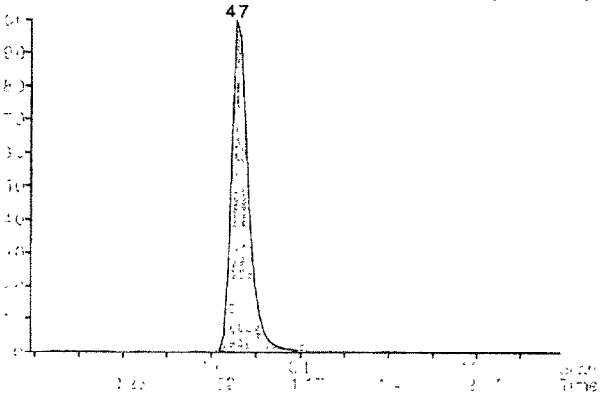
BD8LL1011 **Std A** Fri, Dec 28, 2001 17:53
Std A

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	10.0
Quant Thres.	1.5
Min. Width	6
Mult. Width	2
Base. Width	17
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	60873
Height	10886
Start Time	0:54.2
End Time	1:16
Integration Width	0:21.4
Retention Time	0:59.2
Integration Type	A - BB

intensity: 10909 cps



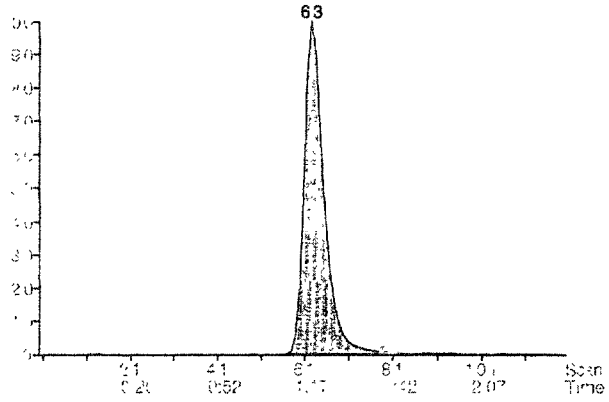
MacQuan, version 1.6
Printed: Wed, Jan 2, 2002 08:31
Calibration File: BD8LL Calibration Path: Snoopy:Desktop Folder:AA PROJECTS:bd8ll:
Comments: No Comments

BD8LL1015 **Std E** Fri, Dec 28, 2001 18:04
Std E

2:29 in 1 period
Omeprazole
Internal Standard: I.S
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	3.0
Quant Thres.	0.8
Min. Width	9
Mult. Width	2
Base. Width	20
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	27442
Height	4200
Start Time	1:12
End Time	1:37
Integration Width	0:25.2
Retention Time	1:19
Integration Type	A - BB

intensity: 4207 cps



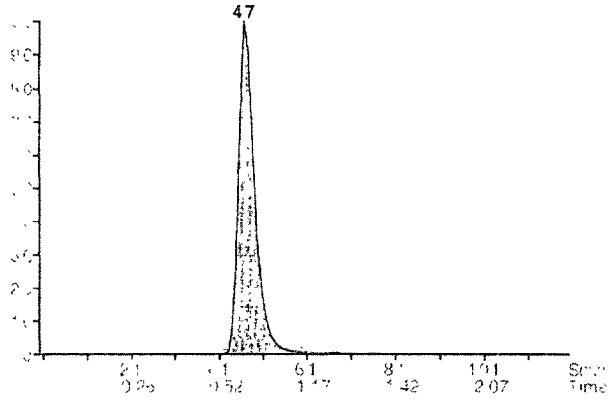
BD8LL1015 **Std E** Fri, Dec 28, 2001 18:04
Std E

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	10.0
Quant Thres.	1.5
Min. Width	6
Mult. Width	2
Base. Width	17
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	59340
Height	10816
Start Time	0:52.9
End Time	1:14
Integration Width	0:21.4
Retention Time	0:59.2
Integration Type	A - BB

intensity: 10828 cps

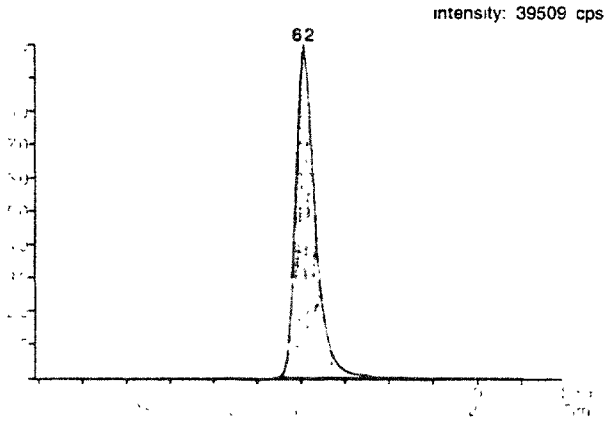


MacQuan, version 1.6
Printed: Wed, Jan 2, 2002 08:31
Calibration File: BD8LL Calibration Path: Snoopy:Desktop Folder:AA PROJECTS:bd8ll
Comments: No Comments

BD8LL1018 **Std H** Fri, Dec 28, 2001 18:12
Std H

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	3.0
Quant Thres.	0.8
Min. Width	9
Mult. Width	2
Base. Width	20
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	254333
Height	39421
Start Time	1:11
End Time	1:36
Integration Width	0:25.2
Retention Time	1:18
Integration Type	A - BB

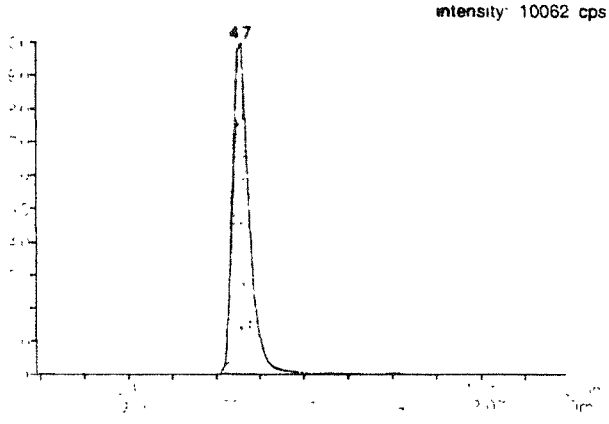


BD8LL1018 **Std H** Fri, Dec 28, 2001 18:12
Std H

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	10.0
Quant Thres.	1.5
Min. Width	6
Mult. Width	2
Base. Width	17
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	56143
Height	10041
Start Time	0:52.9
End Time	1:14
Integration Width	0:21.4
Retention Time	0:59.2
Integration Type	A - BB



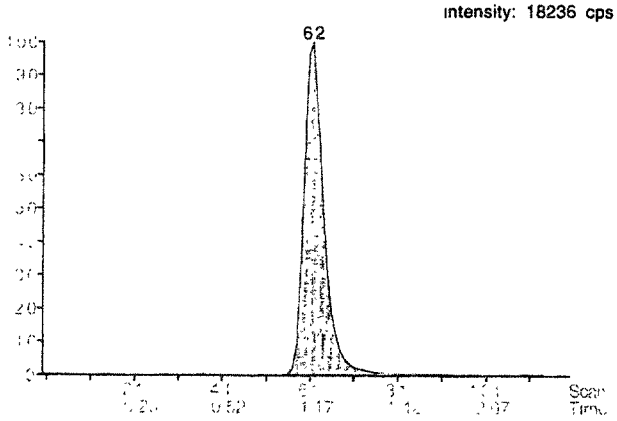
MacQuan, version 1.6
Printed: Wed, Jan 2, 2002 08:31
Calibration File: BD8LL Calibration Path: Snoopy:Desktop Folder:AA PROJECTS:bd8ll:
Comments: No Comments

BD8LL1038 **QC VERY HIGH 1** Fri, Dec 28, 2001 19:06
QC VERY HIGH 1

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	3.0
Quant Thres.	0.8
Min. Width	9
Mult. Width	2
Base. Width	20
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	120578
Height	18207
Start Time	1:11
End Time	1:36
Integration Width	0:25 2
Retention Time	1:18
Integration Type	A - BB

Intensity: 18236 cps



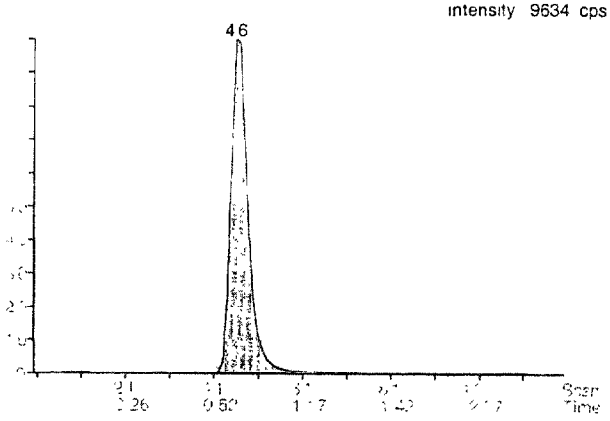
BD8LL1038 **QC VERY HIGH 1** Fri, Dec 28, 2001 19:06
QC VERY HIGH 1

2:29 in 1 period
I.S.
use as Internal Standard

1 2:29 MRM, 119 scans
368 1->164 0

Noise Thres	10 0
Quant Thres	1 5
Min Width	6
Mult Width	2
Base. Width	17
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	54288
Height	9608
Start Time	0:52.9
End Time	1:14
Integration Width	0:21.4
Retention Time	0:58.0
Integration Type	A - BB

Intensity 9634 cps



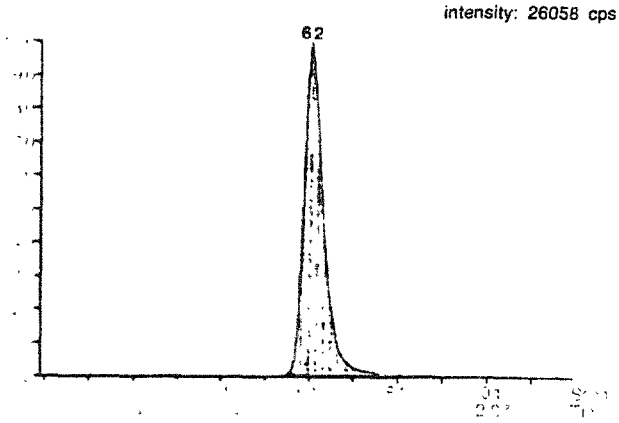
MacQuan, version 1.6
Printed: Wed, Jan 2, 2002 08:31
Calibration File: BD8LL Calibration Path: Snoopy:Desktop Folder:AA PROJECTS:bd8ll
Comments: No Comments

BD8LL1032 **QC HIGH 1** Fri, Dec 28, 2001 18 50
QC HIGH 1

2.29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	3.0
Quant Thres.	0.8
Min. Width	9
Mult. Width	2
Base. Width	20
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	168585
Height	26011
Start Time	1:11
End Time	1:36
Integration Width	0:25.2
Retention Time	1:18
Integration Type	A - BB

intensity: 26058 cps



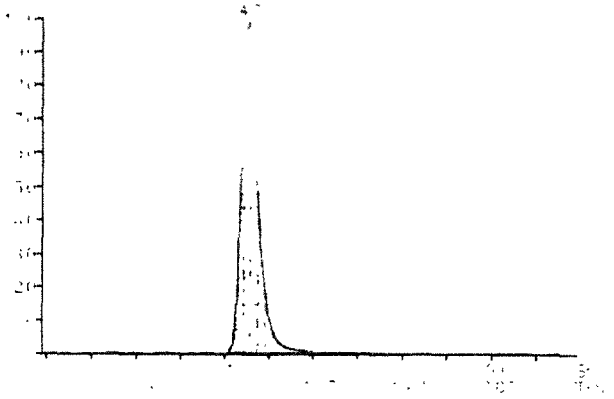
BD8LL1032 **QC HIGH 1** Fri, Dec 28, 2001 18 50
QC HIGH 1

2:29 in 1 period
I.S.
use as Internal Standard

intensity 9579 cps

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	10.0
Quant Thres.	1.5
Min. Width	6
Mult. Width	2
Base. Width	17
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	53006
Height	9563
Start Time	0:52.9
End Time	1:14
Integration Width	0:21.4
Retention Time	0:59.2
Integration Type	A - BB



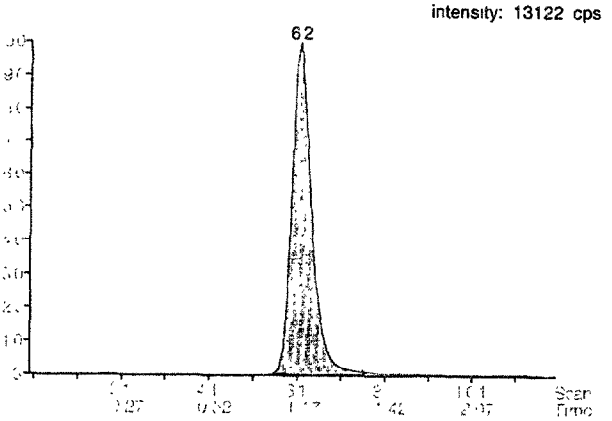
MacQuan, version 1.6
Printed: Wed, Jan 2, 2002 08:31
Calibration File: BD8LL Calibration Path: Snoopy:Desktop Folder:AA PROJECTS:bd8ll:
Comments: No Comments

BD8LL1026 **QC MED 1** Fri, Dec 28, 2001 18:34
QC MED 1

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	3.0
Quant Thres.	0.8
Min. Width	9
Mult. Width	2
Base. Width	20
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	85971
Height	13093
Start Time	1:11
End Time	1:36
Integration Width	0:25.2
Retention Time	1:18
Integration Type	A - BB

intensity: 13122 cps



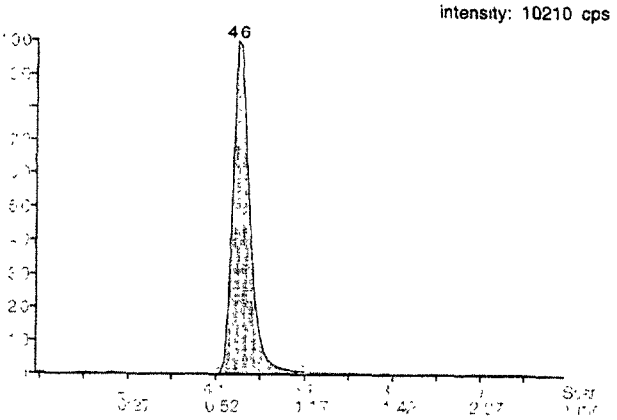
BD8LL1026 **QC MED 1** Fri, Dec 28, 2001 18:34
QC MED 1

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	10.0
Quant Thres.	1 5
Min. Width	6
Mult. Width	2
Base. Width	17
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	56970
Height	10186
Start Time	0:53.0
End Time	1:14
Integration Width	0:21.4
Retention Time	0:58.0
Integration Type	A - BB

intensity: 10210 cps



MacQuan, version 1.6

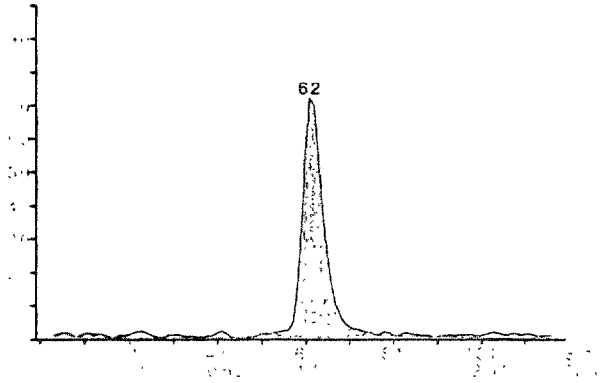
Printed: Wed, Jan 2, 2002 08:31
Calibration File: BD8LL Calibration Path: Snoopy:Desktop Folder.AA PROJECTS:bd8ll:
Comments: No Comments

BD8LL1020 **QC LOW 1** Fri, Dec 28, 2001 18:17
QC LOW 1

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	3.0
Quant Thres.	0.8
Min. Width	9
Mult. Width	2
Base. Width	20
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	1530
Height	214
Start Time	1.08
End Time	1:33
Integration Width	0:25.2
Retention Time	1:18
Integration Type	A - BB

intensity: 300 cps



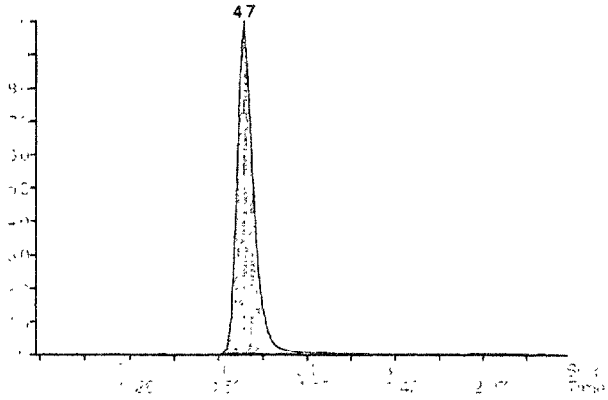
BD8LL1020 **QC LOW 1** Fri, Dec 28, 2001 18:17
QC LOW 1

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	10.0
Quant Thres.	1.5
Min. Width	6
Mult. Width	2
Base. Width	17
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	56680
Height	10526
Start Time	0:52.9
End Time	1:14
Integration Width	0:21.4
Retention Time	0:59 2
Integration Type	A - BB

intensity: 10554 cps



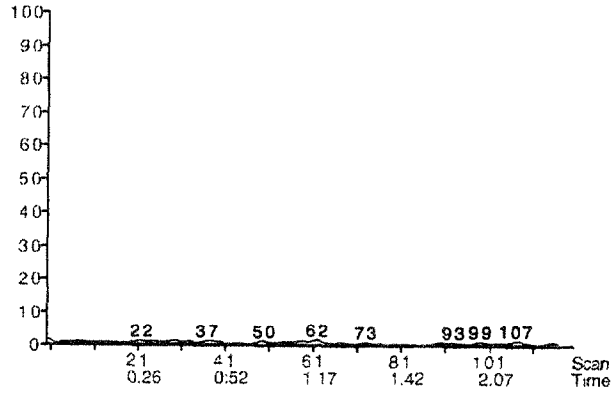
MacQuan, version 1.6
Printed: Thu, Jan 3, 2002 06:45
Calibration File: BDBAM Calibration Path: Apollo HD:Desktop Folder:AA Projects:bdbam:
Comments: No Comments

bdbam1003 **Spec_1_(783-1J)** Wed, Jan 2, 2002 22:01
Spec_1_(783-1J)

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	2.5
Quant Thres.	1.1
Min. Width	6
Mult. Width	2
Base. Width	21
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	0
Height	0
Start Time	0:00.0
End Time	0:00.0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 400 cps



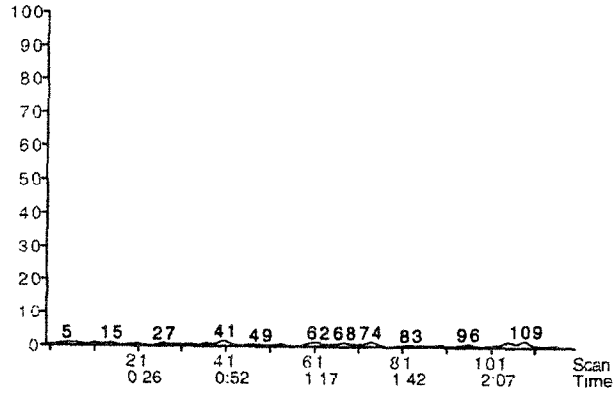
bdbam1003 **Spec_1_(783-1J)** Wed, Jan 2, 2002 22:01
Spec_1_(783-1J)

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	2.1
Quant Thres.	1.5
Min. Width	4
Mult. Width	2
Base. Width	18
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	0
Height	0
Start Time	0:00.0
End Time	0:00.0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 400 cps



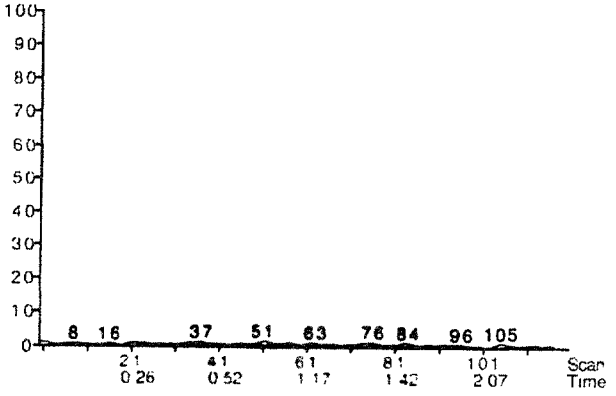
MacQuan, version 1.6
Printed: Thu, Jan 3, 2002 06:45
Calibration File: BDBAM Calibration Path: Apollo HD:Desktop Folder:AA Projects:bdbam:
Comments: No Comments

bdbam1005 **Spec_3_(783-51M)** Wed, Jan 2, 2002 22:06
Spec_3_(783-51M)

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	2.5
Quant Thres.	1.1
Min. Width	6
Mult. Width	2
Base. Width	21
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	0
Height	0
Start Time	0:00.0
End Time	0:00.0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 400 cps



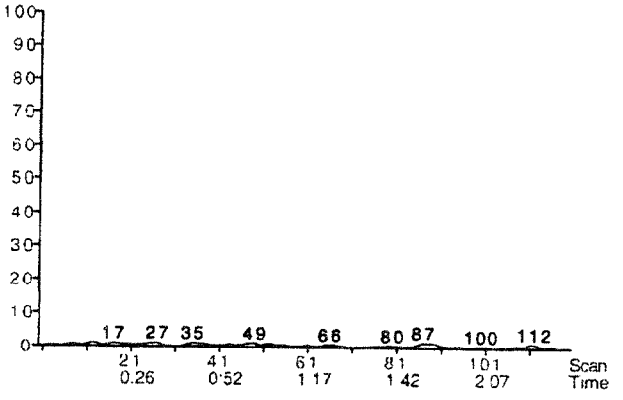
bdbam1005 **Spec_3_(783-51M)** Wed, Jan 2, 2002 22:06
Spec_3_(783-51M)

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	2.1
Quant Thres.	1.5
Min. Width	4
Mult. Width	2
Base. Width	18
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	0
Height	0
Start Time	0:00.0
End Time	0:00.0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 400 cps



MacQuan, version 1.6
Printed: Thu, Jan 3, 2002 06:45
Calibration File: BDBAM Calibration Path: Apollo HD:Desktop Folder:AA Projects:bdbam:
Comments: No Comments

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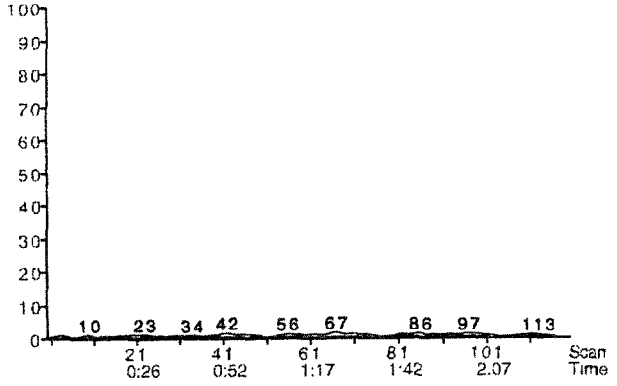
bdbam1006 **Spec_4_(783-67E)** Wed, Jan 2, 2002 22:09
Spec_4_(783-67E)

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	2.5
Quant Thres.	1.1
Min. Width	6
Mult. Width	2
Base. Width	21
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	0
Height	0
Start Time	0:00.0
End Time	0:00.0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 400 cps



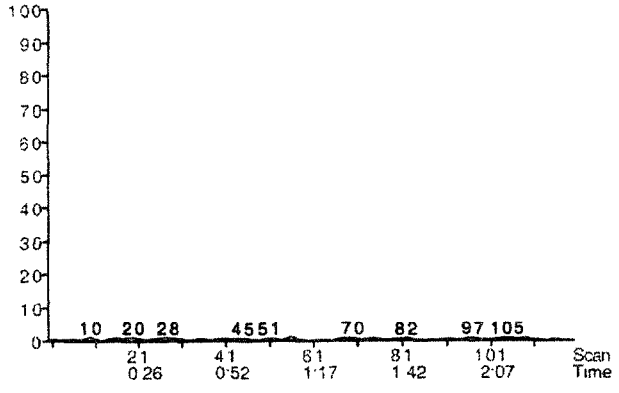
bdbam1006 **Spec_4_(783-67E)** Wed, Jan 2, 2002 22:09
Spec_4_(783-67E)

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	2.1
Quant Thres.	1.5
Min. Width	4
Mult. Width	2
Base. Width	18
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	0
Height	0
Start Time	0:00.0
End Time	0:00.0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 400 cps



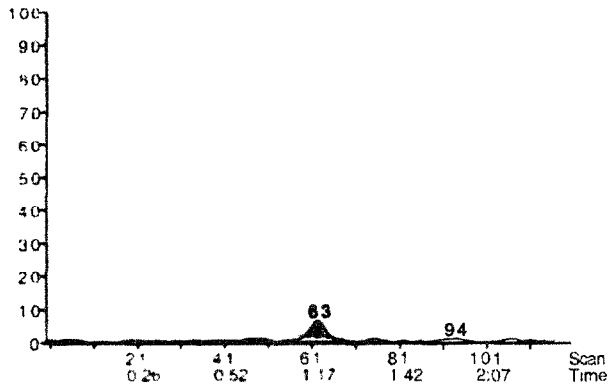
MacQuan, version 1.6
Printed: Thu, Jan 3, 2002 06:45
Calibration File: BDBAM Calibration Path: Apollo HD:Desktop Folder:AA Projects:bdbam
Comments: No Comments

bdbam1007 **Spec_5_(783-67G)** **Wed, Jan 2, 2002 22:12**
Spec_5_(783-67G)

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	2.5
Quant Thres.	1.1
Min. Width	6
Mult. Width	2
Base. Width	21
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	120
Height	23
Start Time	1:13
End Time	1:23
Integration Width	0:10.1
Retention Time	1:19
Integration Type	A - BB

intensity: 400 cps



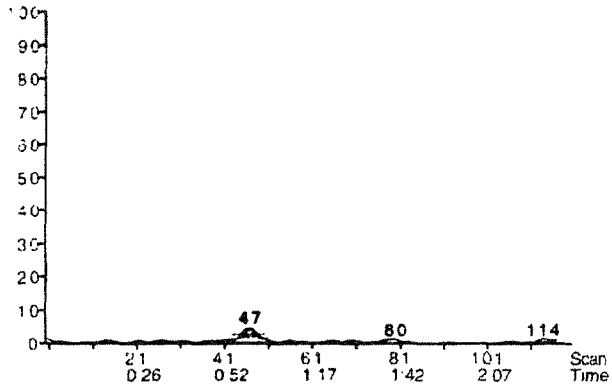
bdbam1007 **Spec_5_(783-67G)** **Wed, Jan 2, 2002 22:12**
Spec_5_(783-67G)

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	2.1
Quant Thres.	1.5
Min. Width	4
Mult. Width	2
Base. Width	18
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	54
Height	14
Start Time	0:55.4
End Time	1:02
Integration Width	0:06.3
Retention Time	0:59.2
Integration Type	A - BB

intensity: 400 cps



MacQuan, version 1.6 Page 8 of 53
Printed: Thu, Jan 3, 2002 06:45
Calibration File: BDBAM Calibration Path: Apollo HD:Desktop Folder:AA Projects:bdbam:
Comments: No Comments

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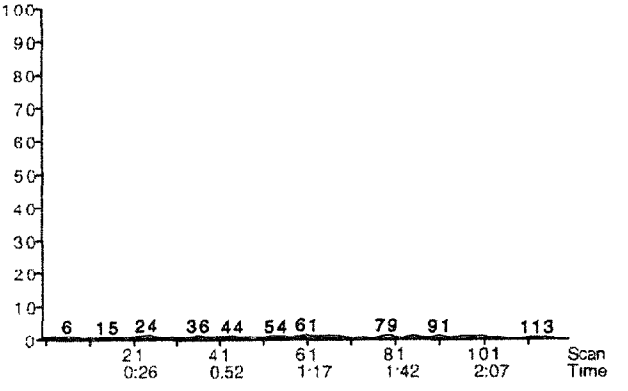
bdbam1008 **Spec_6_(783-67D)** Wed, Jan 2, 2002 22:15
Spec_6_(783-67D)

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194.0

Noise Thres.	2.5
Quant Thres.	1.1
Min. Width	6
Mult. Width	2
Base. Width	21
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	0
Height	0
Start Time	0:00.0
End Time	0:00.0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 400 cps



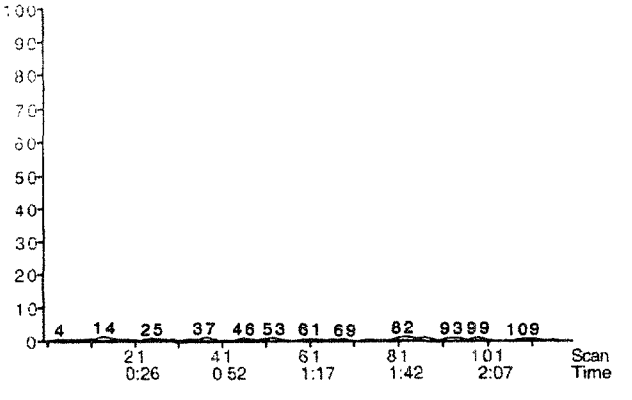
bdbam1008 **Spec_6_(783-67D)** Wed, Jan 2, 2002 22:15
Spec_6_(783-67D)

2:29 in 1 period
I.S.
use as Internal Standard

1: 2.29 MRM, 119 scans
368.1->164.0

Noise Thres.	2.1
Quant Thres.	1 5
Min. Width	4
Mult. Width	2
Base. Width	18
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	0
Height	0
Start Time	0:00.0
End Time	0:00.0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 400 cps



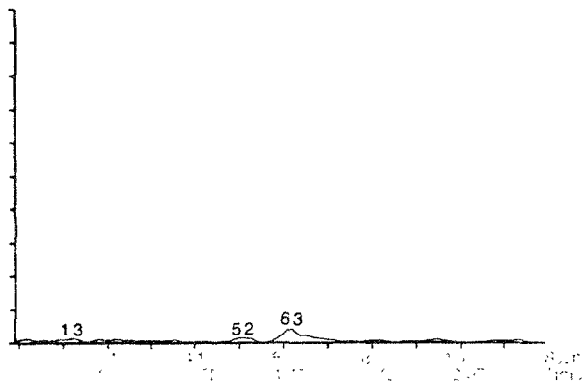
MacQuan, version 1.6
Printed: Wed, Jan 2, 2002 08:31
Calibration File: BD8LL Calibration Path Snoopy:Desktop Folder:AA PROJECTS:bd8ll:
Comments: No Comments

BD8LL1004 **Blank IS** Fri, Dec 28, 2001 17:33
Blank IS

2:29 in 1 period
Omeprazole
Internal Standard: I.S.
Use Area
Absolute Retention Time
1: 2:29 MRM, 119 scans
344.2->194 0

Noise Thres.	3.0
Quant Thres.	0.8
Min. Width	9
Mult Width	2
Base. Width	20
RT Win. (secs)	5
Smooth	2
Expected RT	1:18
Area	0
Height	0
Start Time	0:00 0
End Time	0:00 0
Integration Width	0:00.0
Retention Time	0:00.0
Integration Type	

intensity: 300 cps



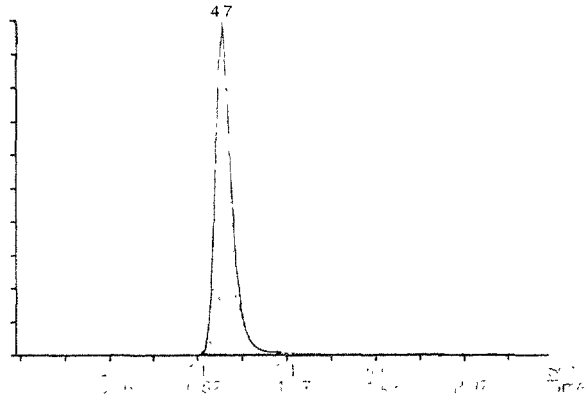
BD8LL1004 **Blank IS** Fri, Dec 28, 2001 17:33
Blank IS

2:29 in 1 period
I.S.
use as Internal Standard

1: 2:29 MRM, 119 scans
368.1->164.0

Noise Thres.	10.0
Quant Thres	1.5
Min. Width	6
Mult. Width	2
Base. Width	17
RT Win. (secs)	20
Smooth	2
Expected RT	0:59.2
Area	58141
Height	10871
Start Time	0:52.9
End Time	1:14
Integration Width	0:21.4
Retention Time	0:59.2
Integration Type	A - BB

intensity 10889 cps



DCN: 11-350-V2

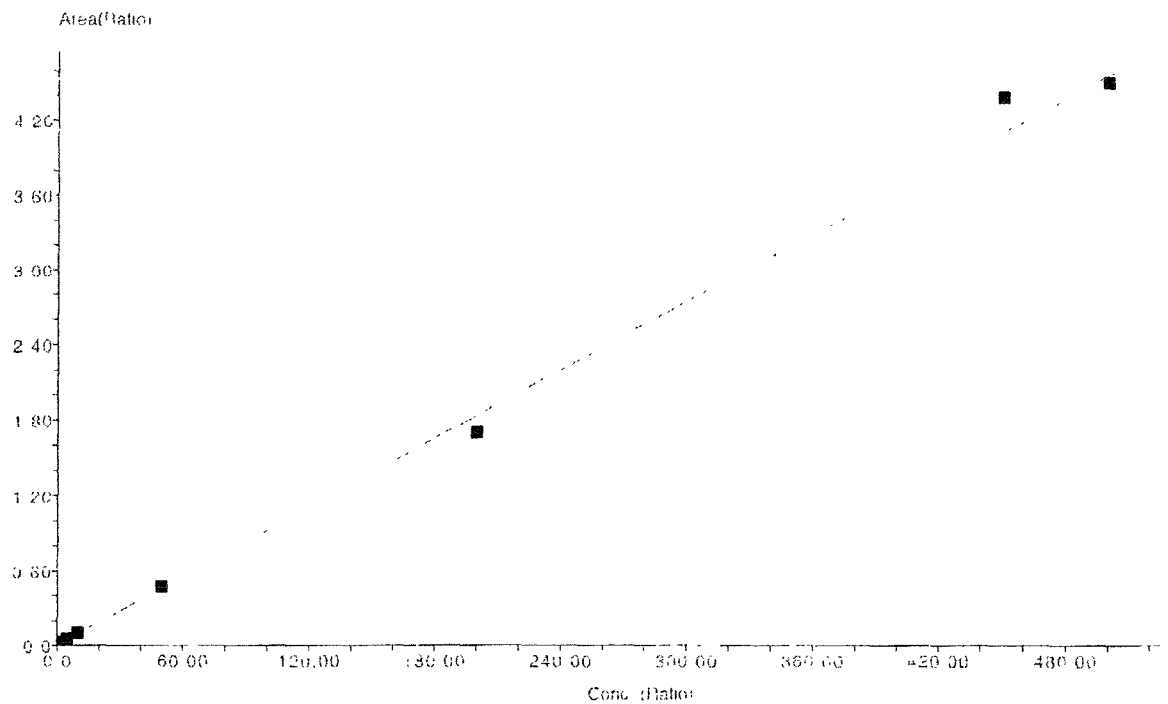
Appendix C

Example Standard Curve Plot

MacQuan, version 1 6
Printed· Wed, Jan 2, 2002 08:31
Calibration File. BD8LL Calibration Path: Snoopy:Desktop Folder:AA PROJECTS.bd8ll:
Comments: No Comments

Omeprazole 344.2->194.0 Internal Standard: I.S.
Weighted (1/x*x)

Intercept = 0.000796
Slope = 0.009192
Correlation Coeff. = 0 998809



DCN: 11-350-V2

Appendix D

List of Contributors

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