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Table 3
Body Weight Changes Summary

Proprietary Info

Proprietary Info

Key Page

General Footnotes

Provantis version 10.1.0.1

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
Absolute Weight Gain	Absolute Weight Gain (g)

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
Absolute Weight Gain	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Automatic Transformations

<u>Measurement</u>	<u>Transformation Order</u>
Absolute Weight Gain	Identity (No Transformation), Log, Rank

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Proprie	Dose	Group 4	30 mg/kg	SC

Pairwise Comparisons

<u>Group</u>	<u>Vs</u>	<u>Group</u>
1		2
1		3
1		4

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Table 4
Food Consumption Summary

Proprietary Info

Proprietary Info

Key Page

General Footnotes

Provantis version 10.1.0.1

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
Food Mean Daily Consumption	Food Mean Consumption

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
Food Mean Daily Consumption	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Automatic Transformations

<u>Measurement</u>	<u>Transformation Order</u>
Food Mean Daily Consumption	Identity (No Transformation), Log, Rank

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet [Pr] (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet [Pr] (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet [Pr] (30)	Dose	Group 4	30 mg/kg	SC

Pairwise Comparisons

<u>Group</u>	<u>Vs</u>	<u>Group</u>
1		2
1		3
1		4

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Table 5

**Toxicokinetic Parameters of [Proprietary Info] [Proprietary] and [Proprietary] after Weekly SC
Administration of [Proprietary Info] [Pro] for 5 weeks in Male and Female Sprague Dawley Rats**

Compound	Group	Sex	Dose (mg/kg)	C _{max} ± SE (ng/ml)	AUC _{last} ± SE (day*ng/ml)
[Proprietary Info]					

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Table 6
Hematology Summary

Proprietary Info

Proprietary Info

Key Page

General Footnotes

Provantis version 10.1.0.1

"." indicates Not Applicable

Statistical significance indicated on a group with an N < 3 is not valid

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
White Blood Cells	White Blood Cells
Red Blood Cells	Red Blood Cells
Hemoglobin	Hemoglobin
Hematocrit	Hematocrit
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
RDW	Red Blood Cell Distribution Width
Platelet Count	Platelet Count
MeanPlatelet Volume	Mean Platelet Volume
Percent Neutrophils	Percent Neutrophils
Percent Lymphocytes	Percent Lymphocytes
Percent Monocytes	Percent Monocytes
Percent Eosinophils	Percent Eosinophils
Percent Basophils	Percent Basophils
Neutrophils (Absolute)	Absolute Neutrophils
Lymphocytes (Absolute)	Absolute Lymphocytes
Monocytes (Absolute)	Absolute Monocytes
Eosinophils (Absolute)	Absolute Eosinophils
Basophils (Absolute)	Absolute Basophils
Percent Reticulocyte	Percent Reticulocytes
Reticulocyte (Absolute)	Absolute Reticulocytes

Unit Descriptions

<u>Headings Used</u>	<u>Description</u>
%	%
10^9/L	10^9/L
fL	fL
g/dL	g/dL
pg	pg
x10^3/uL	x10^3/uL
x10^6/uL	x10^6/uL

Table 6
Hematology Summary

Proprietary Info

Proprietary Info

Key Page

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
White Blood Cells	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Red Blood Cells	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Hemoglobin	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Hematocrit	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Mean Corpuscular Volume	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Mean Corpuscular Hemoglobin	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Mean Corpuscular HGB Conc.	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
RBC Distribution Width	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Platelet Count	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Mean Platelet Volume	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Percent Neutrophils	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Percent Lymphocytes	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Percent Monocytes	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Percent Eosinophils	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Table 6
Hematology Summary

Proprietary Info

Proprietary Info

Key Page

Measurement/Statistics (Continued)

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
Percent Basophils	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Neutrophils (Absolute)	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Lymphocytes (Absolute)	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Monocytes (Absolute)	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Eosinophils (Absolute)	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Basophils (Absolute)	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Percent Reticulocytes	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Reticulocyte (Absolute)	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Automatic Transformations

<u>Measurement</u>	<u>Transformation Order</u>
White Blood Cells	Identity (No Transformation), Log, Rank
Red Blood Cells	Identity (No Transformation), Log, Rank
Hemoglobin	Identity (No Transformation), Log, Rank
Hematocrit	Identity (No Transformation), Log, Rank
Mean Corpuscular Volume	Identity (No Transformation), Log, Rank
Mean Corpuscular Hemoglobin	Identity (No Transformation), Log, Rank
Mean Corpuscular HGB Conc.	Identity (No Transformation), Log, Rank
RBC Distribution Width	Identity (No Transformation), Log, Rank
Platelet Count	Identity (No Transformation), Log, Rank
Mean Platelet Volume	Identity (No Transformation), Log, Rank
Percent Neutrophils	Identity (No Transformation), Log, Rank
Percent Lymphocytes	Identity (No Transformation), Log, Rank
Percent Monocytes	Identity (No Transformation), Log, Rank
Percent Eosinophils	Identity (No Transformation), Log, Rank
Percent Basophils	Identity (No Transformation), Log, Rank

Table 6
Hematology Summary

Proprietary Info

Proprietary Info

Key Page

Automatic Transformations (Continued)

<u>Measurement</u>	<u>Transformation Order</u>
Neutrophils (Absolute)	Identity (No Transformation), Log, Rank
Lymphocytes (Absolute)	Identity (No Transformation), Log, Rank
Monocytes (Absolute)	Identity (No Transformation), Log, Rank
Eosinophils (Absolute)	Identity (No Transformation), Log, Rank
Basophils (Absolute)	Identity (No Transformation), Log, Rank
Percent Reticulocytes	Identity (No Transformation), Log, Rank
Reticulocyte (Absolute)	Identity (No Transformation), Log, Rank

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Pairwise Comparisons

<u>Group</u>	<u>Vs</u>	<u>Group</u>
1		2
1		3
1		4

Table 6
Hematology Summary

Proprietary Info

Proprietary Info

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Table 7
Clinical Chemistry Summary

Proprietary Info

Proprietary Info

Key Page

General Footnotes

Provantis version 10.1.0.1

"." indicates Not Applicable

Statistical significance indicated on a group with an N < 3 is not valid

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
Blood Urea Nitrogen	Blood Urea Nitrogen
Creatinine	Creatinine
Glucose	Glucose
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
Alkaline Phosphatase	Alkaline Phosphatase
Total Bilirubin	Total Bilirubin
Sodium	Sodium
Potassium	Potassium
Chloride	Chloride
Calcium	Calcium
Phosphorus	Phosphorus
Total Protein	Total Protein
Albumin	Albumin
Globulin	Globulin
Alb/Glo Ratio	Albumin/Globulin Ratio
Cholesterol	Cholesterol
Triglyceride	Triglyceride

Unit Descriptions

<u>Headings Used</u>	<u>Description</u>
g/dL	g/dL
mg/dL	mg/dL
mmol/L	mmol/L
U/L	U/L

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic</u> <u>/Adjusted</u>	<u>Transformation</u>
Blood Urea Nitrogen	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Table 7
Clinical Chemistry Summary

Proprietary Info

Proprietary Info

Key Page

Measurement/Statistics (Continued)

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
Creatinine	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Glucose	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Aspartate Aminotransferase	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Alanine Aminotransferase	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Alkaline Phosphatase	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Total Bilirubin	Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Sodium	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Potassium	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Chloride	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Calcium	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Phosphorus	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Total Protein	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Albumin	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Globulin	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Albumin/Globulin Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Table 7
Clinical Chemistry Summary

Proprietary Info

Proprietary Info

Key Page

Measurement/Statistics (Continued)

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic</u> <u>/Adjusted</u>	<u>Transformation</u>
Cholesterol	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Triglyceride	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Automatic Transformations

<u>Measurement</u>	<u>Transformation Order</u>
Blood Urea Nitrogen	Identity (No Transformation), Log, Rank
Creatinine	Identity (No Transformation), Log, Rank
Glucose	Identity (No Transformation), Log, Rank
Aspartate Aminotransferase	Identity (No Transformation), Log, Rank
Alanine Aminotransferase	Identity (No Transformation), Log, Rank
Alkaline Phosphatase	Identity (No Transformation), Log, Rank
Total Bilirubin	Identity (No Transformation), Log, Rank
Sodium	Identity (No Transformation), Log, Rank
Potassium	Identity (No Transformation), Log, Rank
Chloride	Identity (No Transformation), Log, Rank
Calcium	Identity (No Transformation), Log, Rank
Phosphorus	Identity (No Transformation), Log, Rank
Total Protein	Identity (No Transformation), Log, Rank
Albumin	Identity (No Transformation), Log, Rank
Globulin	Identity (No Transformation), Log, Rank
Albumin/Globulin Ratio	Identity (No Transformation), Log, Rank
Cholesterol	Identity (No Transformation), Log, Rank
Triglyceride	Identity (No Transformation), Log, Rank

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Pairwise Comparisons

<u>Group</u>	<u>Vs</u>	<u>Group</u>
1		2

Table 7
Clinical Chemistry Summary

Proprietary Info

Proprietary Info

Key Page

Pairwise Comparisons (Continued)

<u>Group</u>	<u>Vs</u>	<u>Group</u>
1		3
1		4

Table 7
Clinical Chemistry Summary

Proprietary Info

Proprietary Info

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Table 8
Urinalysis Summary

Proprietary Info

Proprietary Info

Key Page

General Footnotes

Provantis version 10.1.0.1

"." indicates Not Applicable

Statistical significance indicated on a group with an N < 3 is not valid

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
Specific Gravity	Specific Gravity
UA pH	UA pH
UA Urobilinogen	UA Urobilinogen

Unit Descriptions

<u>Headings Used</u>	<u>Description</u>
EU/dL	EU/dL

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
Specific Gravity	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Identity (No Transformation)
UA pH	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
UA Urobilinogen	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Automatic Transformations

<u>Measurement</u>	<u>Transformation Order</u>
UA pH	Identity (No Transformation), Log, Rank
UA Urobilinogen	Identity (No Transformation), Log, Rank

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Table 8
Urinalysis Summary

Proprietary Info

Proprietary Info

Key Page

Pairwise Comparisons

<u>Group</u>	<u>Vs</u>	<u>Group</u>
1		2
1		3
1		4

Table 8
Urinalysis Summary

Proprietary Info

Proprietary Info

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Table 9
Organ Weights Summary

Proprietary Info

Proprietary Info

Key Page

General Footnotes

Provantis version 10.1.0.1

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
Adrenal Glands Wt	Adrenal Glands Weight
Brain Weight	Brain Weight
Heart Weight	Heart Weight
Kidneys Weight	Kidneys Weight
Liver Weight	Liver Weight
Ovaries Weight	Ovaries Weight
Spleen Weight	Spleen Weight
Testes Weight	Testes Weight
Thymus Weight	Thymus Weight
Adrenal/Body weight	Adrenals/Terminal Bodyweight Ratio
Brain/Body weight	Brain / Terminal Bodyweight Ratio
Heart/Body weight	Heart/ Terminal Bodyweight Ratio
Kidney/Body weight	Kidney/Terminal Bodyweight Ratio
Liver/Body weight	Liver/Terminal Bodyweight Ratio
Ovaries/Body weight	Ovaries/Terminal Bodyweight Ratio
Spleen/Body weight	Spleen/Terminal Bodyweight Ratio
Testes/Body weight	Testes/Terminal Bodyweight Ratio
Thymus/Body weight	Thymus/Terminal Bodyweight Ratio
Adrenal/ Brain	Adrenals/Brain Ratio
Heart/ Brain	Heart/Brain Ratio
Kidneys/ Brain	Kidneys/Brain Ratio
Liver/ Brain	Liver/Brain Ratio
Ovaries/ Brain	Ovaries/Brain Ratio
Spleen/ Brain	Spleen/Brain Ratio
Testes/ Brain	Testes/Brain Ratio
Thymus/ Brain	Thymus/Brain Ratio

Unit Descriptions

<u>Headings Used</u>	<u>Description</u>
%	%
g	g

Table 9
Organ Weights Summary

Proprietary Info

Proprietary Info

Key Page

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
Adrenal Glands Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Brain Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Heart Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Kidneys Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Liver Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Ovaries Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Spleen Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Testes Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Thymus Weight	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Adrenals/Terminal Bodyweight R	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Brain / Terminal BW Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Heart/ Terminal BWt Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Kidney/Terminal Bwt Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Liver/TrmBW	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Table 9
Organ Weights Summary

Proprietary Info

Proprietary Info

Key Page

Measurement/Statistics (Continued)

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
Ovaries/Terminal Bodyweight Ra	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Spleen/Terminal BW Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Testes/Terminal BW Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Thymus/Terminal BW Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Adrenals/Brain Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Heart/Brain Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Kidneys/Brain Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Liver/Brain Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Ovaries/Brain Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Spleen/Brain Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Testes/Brain Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic
Thymus/Brain Ratio	Mean Standard Deviation Count (N)	Anova & Dunnett's 2 Sided	Arithmetic	Automatic

Automatic Transformations

<u>Measurement</u>	<u>Transformation Order</u>
Adrenal Glands Weight	Identity (No Transformation), Log, Rank
Brain Weight	Identity (No Transformation), Log, Rank

Table 9
Organ Weights Summary

Proprietary Info

Proprietary Info

Key Page

Automatic Transformations (Continued)

<u>Measurement</u>	<u>Transformation Order</u>
Heart Weight	Identity (No Transformation), Log, Rank
Kidneys Weight	Identity (No Transformation), Log, Rank
Liver Weight	Identity (No Transformation), Log, Rank
Ovaries Weight	Identity (No Transformation), Log, Rank
Spleen Weight	Identity (No Transformation), Log, Rank
Testes Weight	Identity (No Transformation), Log, Rank
Thymus Weight	Identity (No Transformation), Log, Rank
Adrenals/Terminal Bodyweight R	Identity (No Transformation), Log, Rank
Brain / Terminal BW Ratio	Identity (No Transformation), Log, Rank
Heart/ Terminal BWt Ratio	Identity (No Transformation), Log, Rank
Kidney/Terminal Bwt Ratio	Identity (No Transformation), Log, Rank
Liver/TmBW	Identity (No Transformation), Log, Rank
Ovaries/Terminal Bodyweight Ra	Identity (No Transformation), Log, Rank
Spleen/Terminal BW Ratio	Identity (No Transformation), Log, Rank
Testes/Terminal BW Ratio	Identity (No Transformation), Log, Rank
Thymus/Terminal BW Ratio	Identity (No Transformation), Log, Rank
Adrenals/Brain Ratio	Identity (No Transformation), Log, Rank
Heart/Brain Ratio	Identity (No Transformation), Log, Rank
Kidneys/Brain Ratio	Identity (No Transformation), Log, Rank
Liver/Brain Ratio	Identity (No Transformation), Log, Rank
Ovaries/Brain Ratio	Identity (No Transformation), Log, Rank
Spleen/Brain Ratio	Identity (No Transformation), Log, Rank
Testes/Brain Ratio	Identity (No Transformation), Log, Rank
Thymus/Brain Ratio	Identity (No Transformation), Log, Rank

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Pairwise Comparisons

<u>Group</u>	<u>Vs</u>	<u>Group</u>
1		2
1		3

Table 9
Organ Weights Summary

Proprietary Info

Proprietary Info

Key Page

Pairwise Comparisons (Continued)

<u>Group</u>	<u>Vs</u>	<u>Group</u>
1		4

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix A

PROTOCOL AND AMENDMENTS

I. GLP-MULTIPLE (5-WEEKLY) REPEAT SUBCUTANEOUS DOSE TOXICITY STUDY WITH [Proprietary] [Pro] IN SPRAGUE DAWLEY RATS**II. SRI STUDY NUMBER: M398-18****III. SPONSOR**

National Institute of Allergy and Infectious Diseases
Division of AIDS
5601 Fishers Lane, [Redacted by]
Bethesda, MD 20892-9830

Contract and TO Number: HHSN272201400006I/TO- HHSN27200007
Sponsor's Representative: [Redacted by agreement]

IV. TESTING FACILITY

SRI International
Biosciences Division
333 Ravenswood Avenue
Menlo Park, CA 94025
Study Director: [Redacted by agreement]

V. PROPOSED IN-LIFE SCHEDULE

Start of In-life (first dose): December 12, 2018
Termination (final necropsy): February 22, 2019

VI. APPROVALS

[Redacted by agreement]

[Redacted by agreement]

Date

12/6/18

Date

12/6/18

Date

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

VII. PURPOSE OF STUDY

The purpose of this study is to provide data of suitable quality and integrity to support applications to the U.S. Food and Drug Administration (FDA) and other regulatory agencies. Therefore, this study will be performed in accordance with the U.S. FDA "Good Laboratory Practice for Nonclinical Laboratory Studies" (GLP) as described in 21 CFR Part 58.

VIII. STUDY OBJECTIVE

The objective of this study is to determine potential toxicity of [Proprietary] [Prop] a new formulation of [Proprietary] [Propriet] 12 mg/ml), [Proprietary] [Propriet] 6.9 mg/ml) and [Proprietary] [Propriet] 3.3 mg/ml), in adult male and female Sprague Dawley rats following a 5-weekly repeat subcutaneous (s.c.) administration.

IX. SPONSOR RESPONSIBILITIES

The Sponsor is responsible for the following:

1. Documentation on the strength, purity, composition, physical properties, stability, and other pertinent information on the bulk test article in the form of a Certificate or Record of Analysis and a Certificate of Stability or other documentation for the bulk test article for inclusion in the final report.
2. Stability, homogeneity and concentration of the formulated test article under conditions of use.
3. Providing sufficient quantity of test article.

X. EXPERIMENTAL DESIGN

The design of the study is summarized in the table on the next page.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Group	Treatment	Dose Level (mg/kg) ^a	Dose Conc. (mg/ml)	Volume (ml/kg) ^b	Total No. of Animals	No. of Animals at Necropsy		TK Satellite Group ^c
						Day 30 (Main)	Day 72 (Recovery)	
1	Excipient	Equivalent to 30 mg/kg [Prop]	0	5	15M/15F	10M/10F	5M/5F	-
2	[Proprietary] [Pro]	1.5	0.3	5	24M/24F	10M/10F	5M/5F	9M/9F
3	[Proprietary] [Pro]	15	3	5	24M/24F	10M/10F	5M/5F	9M/9F
4	[Proprietary] [Pro]	30	6	5	24M/24F	10M/10F	5M/5F	9M/9F
Total No. of Rats					87M/87F	40M/40F	20M/20F	27M/27F

^a Based on [Prop] for [Proprietary] [Pro] fixed dose [Proprietary Info] combination (same as M332-17 non GLP multiple dose study batch and ratio). The doses in mg/kg for each component are as follows: Group 2: 1.5 mg/kg [Propri] 0.8625 mg/kg [Propri] 0.4125 mg/kg [Propri] Group 3: 15 mg/kg [Propri] 8.625 mg/kg [Propri] 4.125 mg/kg [Propri] Group 4: 30 mg/kg [Propri] 17.25 mg/kg [Propri] 8.25 mg/kg [Propri]

^b The dose volumes may be adjusted to achieve the target dose levels based on actual measured concentration of dose solution. Any change will be approved by the Study Director and documented in the study records. Variances in volumes administered should not be more than $\pm 30\%$ and must be within the IACUC-approved dose volume administration guideline limit.

^c Satellite group will be used to collect toxicokinetic samples only. Body weights will be recorded for dose administration calculations and will not be included in body weight analyses. No other in-life evaluations will be conducted on this subset of animals. Animals will be euthanized by an overdose intraperitoneal injection of sodium pentobarbital after their last blood collection. A necropsy will not be performed on any animal in the TK satellite groups found dead or sacrificed in moribund condition and no other terminal samples will be collected from these animals.

Species and Strain

Sprague Dawley rat

Route of Administration

Subcutaneous (s.c.)

Frequency

Once a week for 5 weeks

Dosing Volume

Dose volumes will be calculated based on the animal's most recent body weight to achieve the target dose levels based on 12 mg/ml [Propri] anchored [Proprietary Info] concentration of dose solution. Maximum injection volume will be in accordance with IACUC guidelines.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Duration of In-Life Phase

72 days

XI. MATERIALS AND METHODS

A. Test and Control Articles

1. Test Article

[Proprietary] [Prop] a new formulation of [Proprietary] [Propriet] 12 mg/ml), [Proprietary] [Propriet] 6.9 mg/ml) and [Proprietary] [Propriet] 3.3 mg/ml)

Supplier

To be included in the final report

Manufacturer

To be included in the final report

Lot Number

To be included in the final report

Physical Description

To be included in the final report

Storage Conditions

2-8°C

Characterization of Test Article

The Sponsor is responsible for characterization and stability of the test article and will provide a Certificate of Analysis (CofA), or equivalent documentation, to SRI for inclusion in the final report. The raw data generated by the Sponsor in support of this CofA or its equivalent will not be verified or maintained by SRI.

2. Vehicle Control

Excipient control

Supplier

To be included in the final report

Manufacturer

To be included in the final report

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18

Lot Number

To be included in the final report

Physical Description

To be included in the final report

Storage Conditions

2-8°C

Characterization of Vehicle Control

The Sponsor is responsible for characterization and stability of the excipient control under the specified storage conditions and will provide the CofA to SRI for inclusion in the final report. Information on the identity, purity, and stability of the excipient control article may be obtained by recording all of the pertinent information provided on the container labels or in a CofA provided by the supplier.

3. Preparation of Dose Formulations

Dose formulations will be provided by the Sponsor as ready-to-dose formulations at the concentrations specified in the table above.

Storage of Dose Formulations

Dose formulations will be stored refrigerated at 2-8°C until the day of use. Formulation(s) will be brought to 37°C temperature prior to administration to the animals.

4. Characterization of Dose Formulations

The Sponsor is responsible for stability, homogeneity, and concentration analyses of the test articles in the vehicle. The raw analytical data generated in support of this study will not be verified or maintained by SRI. SRI will rely on the formal CofA provided with the formulation for confirmation of concentration, quality and stability.

5. Test Article Handling

At a minimum, personnel handling the test, and control article formulations will wear eye protection, gloves, and a protective smock or laboratory coat.

6. Disposition

At the end of the study, any remaining partially used and unused containers of excipient control or test article (kept refrigerated) will be shipped to the Sponsor unless the Sponsor issues other directions.

Residual dose formulations will be discarded when the final report is submitted, or when samples no longer afford evaluation.

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with [Proprietary Info] [Pro] in Sprague Dawley Rats
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Empty control, test article containers will be destroyed by SRI on submission of the final report to the Sponsor.

See Section XII.D, "Regulatory Compliance," for information about retention of records and study samples.

7. Method for Assuring Correct Dosing

The administration of each dose formulation will be properly documented, and the amount administered to each animal will be recorded.

B. Test System

1. Species

Rat

Strain

Sprague Dawley

Supplier

[Proprietary Info] or other reputable supplier

Number of Animals

174 assigned to test

Sex

87 males and 87 females

Age at First Dose

6-8 weeks (males) and 8-10 weeks (females)

Weight Range at First Dose

190–260 g (males); ~190–260 g (females)

2. Animal Care

General procedures for animal care and housing will be in accordance with the current Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) recommendations, current requirements stated in the Guide for the Care and Use of Laboratory Animals (National Research Council), and current requirements as stated by the U.S. Department of Agriculture through the Animal Welfare Act and Animal Welfare Regulations (November 2013).

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Quarantine

At least 3 days

Housing

1-3 per cage

Cages

Microisolator cages with hardwood chip bedding

Light Cycle

12 hr light/12 hr dark

Temperature

68–79°F

Humidity

30–70% Brief excursions outside this range may occur; excursions of less than 4 hr/day will not be considered deviations from the protocol.

Ventilation

At least 10 room volumes per hour, with no recirculation of air

Food

Envigo Teklad Certified Global 18% rodent diet, #2018C or Purina Certified Rodent Chow #5002, ad libitum. Feed is analyzed periodically to ensure that contaminants known to be capable of interfering with the study and reasonably expected to be present in such feed are not present at levels that would affect the study. Documentation of feed analyses is maintained at SRI for reference. A copy of the lot specific reports provided by the supplier will be maintained in the study records.

Water

Water (purified, reverse osmosis) will be provided ad libitum. Based on previous reports, no contaminants that could interfere with and affect the results of the study are expected to be present in the water. Copies of annual analysis reports are maintained at SRI for reference.

3. Assignment of Animals to Study

Day

No more than 6 days before initiation of treatment

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
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Randomization

Animals will be randomly assigned to treatment groups via a computerized or manual body weight stratification procedure. Animals may be excluded based on health, behavior, or inappropriate weight.

Identification

Animals will be individually identified by a unique ear punch or by another approved method.

4. Welfare of the Animals

Every effort will be made to minimize, if not eliminate, pain and suffering in all animals in this study. Moribund animals and animals experiencing undue pain and suffering will be euthanized at the discretion of the Study Director, attending veterinarian, or other qualified person. The Study Director will make every effort to protect the scientific validity of the study.

C. Experimental Procedure (In-Life Evaluations)

1. Preparation of Animals

Animals will not be fasted before dose administration.

2. Dose Administration

Weekly subcutaneous (s.c.) injection for 5 weeks to a single site on the dorsal, scapular region. The amount of dose volume administration will be calculated based on latest body weight. The injection site will be cleaned, fur removed and cleaned with alcohol wipe and dried prior to administration of the test article. Injection sites will begin on the dorsal, scapular region at either side of spine (right or left) and on subsequent weeks, it will alternate to the opposite side (left or right) of spine, progressing 0.5 cm posterior to the prior site. The injection sites will weekly progress in a zig-zag pattern to avoid injecting on the same area. Additionally, each injection site will be marked (adjacent to the injection location) and this marking will be refreshed as needed to maintain a visual identification of the injection site. This route of administration is proposed for clinical use of the test article in humans.

3. Mortality/Morbidity

Animals will be checked at least once daily.

4. Clinical Observations

Recorded once daily and approximately 2–4 hr postdose on Days 1, 8, 15, 22 and 29, then weekly in recovery phase or more often as clinical signs warrant, and on necropsy days. Animals will be examined for any altered clinical signs, including gross motor and behavioral activity, and observable changes in appearance.

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5. Body Weights

Body weights will be recorded on Days 1, 8, 15, 22 and 29 (predose on each dosing day) for the purpose of dose calculation, weekly thereafter and at each necropsy.

Body weights will be recorded for animals found dead and for any euthanized early, but these weights will not be included in the statistical evaluations.

6. Food Consumption

Quantitatively measured for approximately a 24 hr period once weekly for each cage throughout the study. The total cage consumption per interval will be divided by the number of animals in the cage to determine the average daily food consumption per animal.

7. Ophthalmologic Examination

All animals (including extras) will have a pretest ophthalmic examination performed by a board-certified veterinary ophthalmologist, and all surviving animals will be re-examined by the ophthalmologist within the week before their scheduled necropsy (Main necropsy Day 30 and Recovery necropsy Day 72). If there are no adverse ophthalmologic effects seen in the Main subset animals at termination time point, then ophthalmologic examinations will not be performed on the Recovery subset animals.

8. Plasma Drug Levels

Method of Collection

Blood will be collected from the retro-orbital sinus of TK Satellite rats under 60:40% CO₂:O₂ anesthesia, or by the use of other approved routes of blood collection (tail or jugular vein), into tubes containing K₂EDTA, processed to plasma, and then stored frozen at ≤-60°C.

Volume

~ 300 µl whole blood (~150 µl of plasma) per sample

Frequency

TK Satellite **Groups 2-4** rats will be sampled 3 rats/sex/time point as follows:

1 hr predose and 1 hr postdose on dosing days (Days 1, 8, 15, 22 and 29). Additional samples will be collected on Days 36, 43, 50, 57, 64 and 71.

Method of Analysis

Drug levels of [Proprietary] [Proprietary] and [Proprietary] will be measured in plasma samples using a bioanalytical method provided by the Sponsor and validated by SRI. Details of the bioanalytical method and validation results will be included in a separate validation report (SRI Study No. B181-18).

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
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9. Toxicokinetics Analysis

Plasma concentrations of the test articles will be plotted versus time for each animal. The plasma drug level data will be analyzed using Phoenix® WinNonlin® (version 6.3 or higher) software to perform noncompartmental assessments. The dose administered will be input to the program as mg/kg, and as a result no additional corrections for individual body weights of the animals will be necessary.

The following parameters and constants will be determined if the data allow: maximal plasma concentration (C_{\max}), time to maximum plasma concentration (T_{\max}), and area under the plasma concentration-time curve to the last time point (AUC_{last}). Values will be calculated for each individual animal.

Other methods of analysis may be used or other parameters calculated, as appropriate, based on the plasma drug level data.

Disposition

Residual bioanalytical samples will be discarded on submission of the final report.

10. Clinical Pathology Evaluations

Preparation of Animals

Animals will **not be fasted** before blood collection.

Method of Collection

Blood will be collected from the retro-orbital sinus of rats under 60% CO₂/40% O₂ anesthesia. Hematology samples will be collected using K₃EDTA as the anticoagulant. No anticoagulant will be used for clinical chemistry samples.

Frequency

Day 30 (Main Group) and Day 72 (Recovery Group).

Parameters that will be evaluated are listed below. In some cases, automated analyzers report additional parameters not specified in the protocol. Results for the additional parameter(s) will be included in the data package, but will not be summarized, analyzed, or reported, and their collection will not be considered deviations from the protocol.

If manual WBC differential counts have to be conducted, some parameters that are not specified in the protocol may be evaluated and reported. This will not be considered a deviation from the protocol.

Hematology Parameters

- Hematocrit (HCT)
- Hemoglobin (HGB)

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- Red blood cell count (RBC)
- Red blood cell distribution width (RDW)
- White blood cell count (WBC)
- WBC differential and absolute counts
 - Absolute neutrophil [ANE]
 - Percent neutrophil [PNE]
 - Absolute lymphocyte [ALY]
 - Percent lymphocyte [PLY]
 - Absolute monocyte [AMO]
 - Percent monocyte [PMO]
 - Absolute eosinophil [AEO]
 - Percent eosinophil [PEO]
 - Absolute basophil [ABA]
 - Percent basophil [PBA]
- Mean corpuscular hemoglobin (MCH)
- Mean corpuscular volume (MCV)
- Mean corpuscular hemoglobin concentration (MCHC)
- Platelet count (PLT)
- Mean platelet volume (MPV)
- Absolute Reticulocyte (ARET)
- Percent Reticulocyte (PRET)

Clinical Chemistry Parameters

- Total Bilirubin (TBI)
- Creatinine (CRE)
- Sodium (SOD)
- Potassium (POT)
- Chloride (CHL)
- Cholesterol (CHO)
- Triglyceride (TRI)
- Glucose (GLU)
- Blood urea nitrogen (BUN)
- Aspartate aminotransferase (AST)
- Alanine aminotransferase (ALT)
- Alkaline phosphatase (ALP)
- Calcium (CAL)
- Phosphorus (PHO)
- Total protein (TPR)
- Albumin (ALB)
- Albumin/globulin ratio (AGR)
- Globulin (GLO)

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with [Proprietary Info] [Pro] in Sprague Dawley Rats
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11. Urinalysis

Method of Collection

Urine will be collected by placing animals in metabolism cages overnight. No preservative will be used for the collection. Total urine volume will be recorded.

Frequency

The week prior to each necropsy (Days 30 and 72)

Urinalysis Parameters

- Color (noted at time of collection)
- Total Volume (total urine output measured at time of collection)
- Clarity (noted at time of collection)
- Specific gravity
- Microscopic examination of urine sediment
- Bilirubin
- Glucose
- Ketones
- Leukocytes
- Nitrite
- Occult blood
- pH
- Protein
- Urobilinogen

D. Necropsy

Interval

Day 30 (Main Group) and Day 72 (Recovery Group). Necropsies will also be performed for any animals found dead or euthanized in moribund condition.

Euthanasia

An overdose of sodium pentobarbital will be administered via intraperitoneal (ip) or intravenous (iv) injection. Alternatively, CO2 compressed gas inhalation in conjunction with an approved secondary method (cervical dislocation or bilateral thoracotomy) may be used.

Observations

External examination of all body orifices and an examination of all cranial, thoracic, and abdominal organs will be performed, and all gross findings will be recorded.

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Tissues Retained

The following tissues will be collected from all animals in the Main Group and the Recovery Group, including those found dead and moribund animals. Tissues will be retained in 10% neutral buffered formalin, except where noted:

- All gross lesions (including tissue masses and abnormal regional lymph nodes)
- Adrenal glands
- Aorta
- Bone (femur with femoro-tibial joint)
- Bone, sternum (marrow histology)
- Bone marrow smear, sternum (for cytology, except for found dead animals)
- Brain (fore-, mid-, and hindbrain)
- Cecum
- Cervix
- Colon
- Duodenum
- Epididymides
- Esophagus
- Eyes, with optic nerve (fixed with modified Davidson's solution)
- Heart
- Identification; (retained in formalin; not processed for histology)
- Ileum
- Injection site(s) tissue. Only representative sections of the injection site(s) will be collected
- Jejunum
- Kidneys
- Liver
- Lungs with bronchi
- Lymph nodes, mandibular and mesenteric
- Mammary gland (females, males when present)
- Ovaries
- Pancreas
- Pituitary gland
- Prostate
- Rectum
- Salivary gland, mandibular
- Sciatic nerve
- Seminal vesicles
- Skeletal muscle
- Skin, ventral abdomen, taken with mammary gland
- Spinal cord retained within spinal column (thoracolumbar only)

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- Spleen
- Stomach (including nonglandular stomach)
- Testes (fixed with modified Davidson's solution)
- Thymus
- Thyroid/parathyroid glands
- Trachea
- Urinary bladder
- Uterus
- Vagina

Final Body/Organ Weights

Body weight will be recorded on the day of necropsy for body-to-organ weight ratios. The following organs will be weighed. Paired organs will be weighed together.

- Adrenal glands
- Brain
- Heart
- Kidneys
- Liver
- Spleen
- Ovaries
- Testes, without epididymides
- Thymus

Organ weights will be recorded for animals found dead or sacrificed in moribund condition, but these data will not be included in statistical evaluations.

E. Histopathologic Examination

Tissues

Tissues listed under "Retained Tissues" will be processed and evaluated for the following:

- All Main animals in the control and high dose groups (Groups 1 and 4)
- Animals with an unscheduled death or euthanized in moribund condition
- Any tissue identified as a target organ of toxicity by the pathologist (examined in all other dose groups)
- Any other tissue deemed necessary by the pathologist
- All gross lesions will be processed for all animals
- Analysis of only one parathyroid gland per animal is sufficient

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
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- Bone marrow smear for cytology will be processed but only analyzed at the discretion of the Study Director and/or pathologist based on hematology and/or bone marrow histopathology findings.
- If neurological clinical signs are not present, only a representative sample of the thoracolumbar (or thoracic) section of the spinal cord will be collected, processed and evaluated. If neurological clinical signs are observed, representative sections of all available spinal cord tissues (cervical, thoracic and lumbar sections) will be collected, processed and evaluated.

Tissue Sections

Sections of the tissues will be embedded in paraffin, cut approximately 5 µm thick, and stained with hematoxylin and eosin by a histology laboratory qualified by SRI.

Evaluated By

A board-certified veterinary pathologist.

Method

Each lesion will be listed and coded by the most specific topographic and morphologic diagnoses, severity, and distribution, using International Harmonization of Nomenclature and Diagnostic Criteria for Lesions (INHAND) as a guide. A four-step grading system (minimal, mild, moderate, and marked) will be used to define gradable lesions for comparison between treated and control groups. Data will be recorded and summarized using Provantis® version 10.1.0.1 or later. Other appropriate programs may be used. Records of gross findings for a specimen from postmortem observations will be available to the pathologist when examining that specimen microscopically.

F. Evaluation of Data Parameters

Mean and standard deviation will be calculated for body weight, clinical pathology, food consumption, urinalysis pH, urobilinogen and specific gravity and organ weight data at each evaluation interval. Calculations will be performed using Provantis® version 10.1.0.1 and MS Excel 2010 or later. Other appropriate programs may be used.

Proposed Statistical Tests

Body weight, food consumption, clinical pathology, urinalysis pH, urobilinogen and specific gravity and organ weight data will be evaluated by one-way analysis of variance (ANOVA), followed by Dunnett's test (if the ANOVA is significant). All other numeric parameters will be evaluated by Student's t-test, unless specified otherwise. If appropriate, other post hoc analyses may also be performed. For clinical pathology data, values for parameters that are not within the detection threshold will not be included in the statistical evaluation.

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Criteria for Null Hypothesis Rejection

$p \leq 0.05$

G. Control of Bias

While evaluating the responses of the animals and conducting the analyses, the technical staff will be aware of the treatment history of each animal and sample. Based on the relatively objective endpoints to be examined, bias is not expected to influence the results of the study.

XII. REGULATORY COMPLIANCE

A. Good Laboratory Practice Compliance

This study is intended to be submitted to and reviewed by the U.S. FDA or an equivalent regulatory agency, and this study therefore will be performed in accordance with the U.S. FDA “Good Laboratory Practice for Nonclinical Laboratory Studies,” as described in 21 CFR Part 58, with the following exceptions:

- Various pre-initiation study activities (e.g., receipt and quarantine of animals, pre-initiation body weights and randomization) may be performed prior to the approval of the protocol. These activities will be conducted according to testing facility SOPs, but because they may be conducted before the protocol is signed, they may not be considered by the FDA to have been conducted in compliance with GLP requirements.
- Animal water, bedding, and food analysis will not be performed under GLP compliance by the vendors.

B. Standard Operating Procedures (SOPs)

All operations pertaining to this study, unless specifically defined in this protocol, will be performed according to the SOPs of the laboratory. All deviations from any SOP and the reasons for the deviations will be documented and acknowledged by the Study Director.

C. Protocol Amendments and Deviations

All changes or revisions made to the approved protocol by any involved party and the reasons for the changes and revisions will be documented, signed, and dated by the Study Director and the Sponsor’s Representative. Amendments will be maintained with the protocol. Verbal or email approval for changes in the protocol may be granted by the Sponsor’s Representative, but a written amendment as described above will follow.

All deviations from the protocol and the reasons for the deviations will be documented and acknowledged by the Study Director. The Sponsor’s Representative

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will be informed of the occurrence of any deviations that might affect the results of the study, and any corrective actions taken.

D. Retention of Records and Study Samples

A copy of the final report, including all appendices, raw data and histopathology slides will be retained and stored by SRI International for a period of one year. An archival sample of the test and control articles will be maintained by SRI for at least 5 years or as long as samples afford evaluation (21 CFR 58.105[d]). At the end of the retention period, the Sponsor will be contacted for instructions regarding disposition of the raw data and histopathology slides. All other pathology materials (blocks and wet tissue specimens) will be disposed of upon submission of the final report.

XIII. REPORTING

The final report will accurately and completely describe the study design, procedures, and findings. An analysis and summary of the data followed by the conclusions derived from the analyses will also be included. A draft report will be issued prior to submission of the final report.

PROTOCOL AMENDMENT NO. 1

PROTOCOL TITLE GLP-Multiple (5 Weekly) Repeat Subcutaneous Dose Toxicity and Toxicokinetics Study with [Proprietary] [Pro] in Sprague Dawley Rats

SRI Study Number: M398-18

Sponsor: National Institute of Allergy and Infectious Diseases
Division of AIDS
5601 Fishers Lane [Redacted by amendment]
Bethesda, MD 20892-9830

Sponsor's Representative: [Redacted by agreement]

SRI Study Director [Redacted]

This amendment modifies the following lines/sections of the study protocol. Additions are in bold and italics: *addition*. Deleted text has been struck through: ~~deleted~~.

Section XI. MATERIALS AND METHODS, page 5, 8:

A. Test and Control Articles

Storage of Dose Formulations

Dose formulations will be stored refrigerated at 2°-8°C, until the day of use. Formulation(s) will be brought to 37° ± 1° C temperature prior to administration to the animals.

C. Experimental Procedure (In-Life Evaluations)

2. Dose Administration

Weekly subcutaneous (s.c.) injection for 5 weeks to a single site on the dorsal, ~~scapular~~ region. The amount of dose volume administration will be calculated based on latest body weight. The injection site will be cleaned, fur removed and cleaned with alcohol wipe and dried prior to administration of the test article. Injection sites will begin on the dorsal, scapular region at either side of spine (right or left) and on subsequent weeks, it will alternate to the opposite side (left or right) of spine, progressing 0.5 cm posterior to the prior site. The injection sites will weekly progress in a zig-zag pattern to avoid injecting on the same area. Additionally, each injection site will be marked (adjacent to the injection location) and this marking will be refreshed as needed to maintain a visual identification of the injection site. This route of administration is proposed for clinical use of the test article in humans.

Reason for Change: Text clarification in Storage of Dose Formulation and Dose Administration sections.

Effect on the Study: No impact to study because study has not started yet.

Effective Date: 12/11/2018

PROTOCOL AMENDMENT NO. 1

APPROVALS

Redacted by agreement

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2/11/18

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PROTOCOL AMENDMENT NO. 2

PROTOCOL TITLE GLP-Multiple (5 Weekly) Repeat Subcutaneous Dose Toxicity and Toxicokinetics Study with Proprietary Pro in Sprague Dawley Rats

SRI Study Number: M398-18

Sponsor: National Institute of Allergy and Infectious Diseases
Division of AIDS
5601 Fishers Lane, Redacted by
Bethesda, MD 20892-9830

Sponsor's Representative: Redacted by agreement

SRI Study Director

This amendment modifies the following lines/sections of the study protocol. Additions are in bold and italics: *addition*. Deleted text has been struck through: ~~deleted~~.

Section IV. TESTING FACILITY, page 1:

Study Director:

Redacted by agreement

Reason for Change: Redacted by agreement will be on personal time off (PTO) starting on December 20, 2018.

Effect on the Study: This change has no impact on the validity of the study because the replacement Study Director is qualified to take on the study.

Effective Date: 12/20/2018

APPROVALS

Redacted by agreement

9-18

PROTOCOL AMENDMENT NO. 3

PROTOCOL TITLE GLP-Multiple (5 Weekly) Repeat Subcutaneous Dose Toxicity and Toxicokinetics Study with Proprietary Pro in Sprague Dawley Rats

SRI Study Number: M398-18

Sponsor: National Institute of Allergy and Infectious Diseases
Division of AIDS
5601 Fishers Lane Redacted by agreement
Bethesda, MD 20892-9830

Sponsor's Representative: Redacted by agreement

SRI Study Director

This amendment modifies the following lines/sections of the study protocol. Additions are in bold and italics: ***addition***. Deleted text has been struck through: ~~deleted~~.

Section IV. TESTING FACILITY, page 1:

Study Director:

Redacted by agreement

Reason for Change: Redacted by agreement has returned from personal time off (PTO) and is being reinstated as Study Director for this study.

Effect on the Study: This change has no impact on the validity of the study because Redacted by agreement was previously approved as Study Director.

Effective Date: Upon signature of Study Director

APPROVALS

Redacted by agreement

Date

1/11/19

Date

PROTOCOL AMENDMENT NO. 4

PROTOCOL TITLE GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with Proprietary Pro in Sprague Dawley Rats

SRI Study Number: M398-18

Sponsor: National Institute of Allergy and Infectious Diseases
Division of AIDS
5601 Fishers Lane Redacted by agreement
Bethesda, MD 20892-9830

Sponsor's Representative: Redacted by agreement

SRI Study Director

This amendment modifies the following lines/sections of the study protocol. Additions are in bold and italics: *addition*. Deleted text has been struck through: ~~deleted~~.

Section I. PROTOCOL TITLE, page 1:

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity and ~~Toxicokinetics~~ Study with Proprietary

Reason for Change: Text clarification in protocol title which was inadvertently written with mistakes in Protocol Amendments 1-3.

Effect on the Study: No impact to study as this is a simple text clarification in study title.

Effective Date: Upon the Study Director's signature

APPROVALS

Redacted by agreement

1/19

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix B

CERTIFICATES OF ANALYSIS

COPY

LN 5/17/19

Proprietary Info

CERTIFICATE OF ANALYSIS

Proprietary Pro Drug Combination Suspension

Lot Number

Date of Manufacturing

Page 1 of 1

Proprietary Info

11/26/2018

Product Name:

Proprietary Pro Drug Combination Suspension for subcutaneous injection (Group 1 — 0.0 mg/kg)

Manufacturer:

Proprietary Info

Lot Number:

Proprietary Info

Storage and Expiration

Store at 2-8°C

Expiration / Retest Date 4/26/19

Test	Specification	Result
Appearance	White, turbid suspension	White turbid suspension
Identity	Matches nominal mass of APIs, DSPC, and mPEG2000-DSPE	conforms
Proprietary Info	0 mg/mL ± 0 mg/mL	0 mg/ml
	0 mg/mL ± 0 mg/mL	0 mg/m
	0 mg/mL ± 0 mg/mL	0 mg/ml
	28.5 mg/mL ± 2.85 mg/mL	27.46 mg/ml
	72.1 mg/mL ± 7.21 mg/mL	76.64 mg/ml
Osmolality	250 – 450 mmol/Kg	332 mmol/Kg
pH	6.5 – 8.5	8.5
Endotoxin USP <85>	< 50 EU/mL	< 5 EU/ml
Sterility USP <71>	No growth on FTM or TSB	Pass

Approval Signatures

	Name, Title	Signature and Date
Author	Redacted by agreement	[Signature] 5/2/19
Approver		

COPY

UN5/17/19

Proprietary Info

CERTIFICATE OF ANALYSIS

Proprietary Pro Drug Combination Suspension

Lot Number

Proprietary Info

Date of Manufacturing

11/27/2018

Page 1 of 1

Product Name:

Proprietary Pro Drug Combination Suspension for subcutaneous
injection (Group 2 — 1.5 mg/kg)

Manufacturer:

Proprietary Info

Lot Number:

Proprietary Info

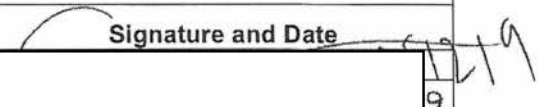
Storage and Expiration

Store at 2-8°C

Expiration / Retest Date 4/27/19

Test	Specification	Result
Appearance	White, turbid suspension	White turbid suspension
Identity	Matches nominal mass of APIs, DSPC, and mPEG2000-DSPE	conforms
Proprietary Info	0.30 mg/mL \pm 0.03 mg/mL	0.30 mg/ml
	0.09 mg/mL \pm 0.01 mg/mL	0.08 mg/ml
	0.17 mg/mL \pm 0.02 mg/mL	0.17 mg/ml
Osmolality	250 – 350 mmol/Kg	250 mmol/Kg
pH	6.5 – 8.5	8.43
Endotoxin USP <85>	< 50 EU/mL	< 5 EU/ml
Sterility USP <71>	No growth on FTM or TSB	Pass

Approval Signatures

	Name, Title	Signature and Date
Author	Redacted by agreement	
Approver		9

COPY 6/5/17/19

Proprietary Info

CERTIFICATE OF ANALYSIS

Proprietary Pro Drug Combination Suspension

Lot Number

Date of Manufacturing

Page 1 of 1

Proprietary Info

11/27/2018

Product Name:

Proprietary Pro Drug Combination Suspension for subcutaneous injection (Group 3 — 15 mg/kg)

Manufacturer:

Lot Number:

Proprietary Info

Proprietary Info

Storage and Expiration

Store at 2-8°C

Expiration / Retest Date 4/27/19

Test	Specification	Result
Appearance	White, turbid suspension	White turbid suspension
Identity	Matches nominal mass of APIs, DSPC, and mPEG2000-DSPE	conforms
Proprietary Info	3.00 mg/mL \pm 0.30 mg/mL	3.00 mg/ml
	0.86 mg/mL \pm 0.09 mg/mL	0.80 mg/ml
	1.71 mg/mL \pm 0.17 mg/mL	1.72 mg/ml
Osmolality	250 – 350 mmol/Kg	262 mmol/Kg
pH	6.5 – 8.5	8.10
Endotoxin USP <85>	< 50 EU/mL	< 5 EU/ml
Sterility USP <71>	No growth on FTM or TSB	Pass

Approval Signatures

	Name, Title	Signature and Date
Author	Redacted by agreement	05/12/19
Approver		5.12.19

COPY LN 5/17/19

Proprietary Info

CERTIFICATE OF ANALYSIS

Proprietary Pro Drug Combination Suspension

Lot Number

Proprietary Info

Date of Manufacturing
11/27/2018

Page 1 of 1

Product Name:

Proprietary Pro Drug Combination Suspension for subcutaneous
injection (Group 4 — 30 mg/kg)

Manufacturer:

Lot Number:

Proprietary Info

Proprietary Info

Storage and Expiration

Store at 2-8°C

Expiration / Retest Date 4/27/19

Test	Specification	Result
Appearance	White, turbid suspension	White turbid suspension
Identity	Matches nominal mass of APIs, DSPC, and mPEG2000-DSPE	conforms
Proprietary Info	6.00 mg/mL \pm 0.60 mg/mL	6.00 mg/ml
	1.72 mg/mL \pm 0.17 mg/mL	1.61 mg/ml
	3.43 mg/mL \pm 0.34 mg/mL	3.44 mg/ml
Osmolality	250 – 350 mmol/Kg	278 mmol/kg
pH	6.5 – 8.5	7.56
Endotoxin USP <85>	< 50 EU/mL	< 5 EU/ml
Sterility USP <71>	No growth on FTM or TSB	Pass

Approval Signatures

	Name, Title	Signature and Date
Author	Redacted by agreement	05/12/19
Approver		12.19

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix C

INDIVIDUAL CLINICAL OBSERVATIONS

Page 2028 of 3822 to Page 2540 of 3822

Withheld pursuant to exemption

Proprietary Info

of the Freedom of Information and Privacy Act

Individual Clinical Observations

Proprietary Info

Proprietary Info

Key Page

General Footnotes

Provantis version 10.1.0.1
"." indicates Not Applicable

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Proprietary Pro (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Proprietary Pro (15)	Dose	Group 3	15 mg/kg	SC
4	Proprietary Pro (30)	Dose	Group 4	30 mg/kg	SC

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix D

INDIVIDUAL BODY WEIGHTS

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix D-1

INDIVIDUAL BODY WEIGHTS

Page 2544 of 3822 to Page 2561 of 3822

Withheld pursuant to exemption

Proprietary Info

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M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Propriet] [Pr] in Sprague Dawley Rats

Key Page

General Footnotes

Provantis version 10.1.0.1

"-" indicates Not Applicable

Measurement Descriptions

Headings Used

Body Weight

Description

Body Weight

Measurement/Statistics

Measurement

Body Weight

Descriptive

Mean

Standard Deviation

Count (N)

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	[Propriet] [Pr] (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	[Propriet] [Pr] (15)	Dose	Group 3	15 mg/kg	SC
4	[Propriet] [Proprie]	Dose	Group 4	30 mg/kg	SC

Comment Abbreviations

RC = Result Comment

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix D-2

INDIVIDUAL BODY WEIGHT CHANGES

Page 2564 of 3822 to Page 2579 of 3822

Withheld pursuant to exemption

Proprietary Info

of the Freedom of Information and Privacy Act

Individual Body Weight Changes

Proprietary Info

Proprietary Info

Key Page

General Footnotes

Provantis version 10.1.0.1

"-" indicates Not Applicable

Measurement Descriptions

Headings Used

Absolute Weight Gain

Description

Absolute Weight Gain (g)

Measurement/Statistics

Measurement

Absolute Weight Gain

Descriptive

Mean

Standard Deviation

Count (N)

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Proprie	Dose	Group 4	30 mg/kg	SC

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix E

INDIVIDUAL FOOD CONSUMPTION

Page 2582 of 3822 to Page 2597 of 3822

Withheld pursuant to exemption

Proprietary Info

of the Freedom of Information and Privacy Act

Key Page**General Footnotes**

Provantis version 10.1.0.1

"-" indicates Not Applicable

Measurement DescriptionsHeadings Used

Food Mean Daily Consumption

Description

Food Mean Consumption

Measurement/StatisticsMeasurement

Food Mean Daily Consumption

Descriptive

Mean

Standard Deviation

Count (N)

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Proprie	Dose	Group 4	30 mg/kg	SC

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix F

OPHTHALMOLOGY REPORTS

Redacted by agreement

Redacted by agreement

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Dear Redacted by agreement

I examined 120 study rats (60 males and 60 females) and 14 extra rats (6 male, 8 females) associated with **Study M398-18** on **December 10, 2018**. This was a prestudy examination. Eyes were examined with a Kowa SL-17 hand held slit lamp biomicroscope and indirect ophthalmoscopy using a Volk 2.2 diopter double aspheric lens. The pupils were pharmacologically dilated with 1% tropicamide prior to examination. The eyelids, conjunctiva, cornea and the anterior compartment including the aqueous humor iris, lens and anterior vitreous humor were examined with a biomicroscope. The retinal vessels, optic nerve and posterior vitreous were examined with indirect ophthalmoscopy.

Proprietary Info

Sincerely,

Redacted by agreement

12/10/18

Redacted by agreement

Redacted by agreement

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Dear Redacted by agreement

I examined 119 study rats (59 males and 60 females) associated with **Study M398-18** on **January 7, 2019**. Eyes were examined with a Kowa SL-17 hand held slit lamp biomicroscope and indirect ophthalmoscopy using a Volk 2.2 diopter double aspheric lens. The pupils were pharmacologically dilated with 1% tropicamide prior to examination. The eyelids, conjunctiva, cornea and the anterior compartment including the aqueous humor iris, lens and anterior vitreous humor were examined with a biomicroscope. The retinal vessels, optic nerve and posterior vitreous were examined with indirect ophthalmoscopy.

Proprietary Info

Sincerely,

Redacted by agreement

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Appendix G

BIOANALYTICAL CHEMISTRY

Bioanalytical Scientist:

Redacted by agreement

11/12/19
Date

Approved by:

11/07/19
Date

SRI International
Biosciences Division

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Appendix G-1

BIOANALYTICAL METHOD

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

I. INTRODUCTION

Rat plasma samples from SRI Study No. M398-18 were analyzed for [Proprietary] [Proprietary] and [Proprietary] according to the Bioanalytical Sample Analysis Plan (Appendix G-3) and the analytical method detailed in SRI Test Method 106.202 (Appendix G-4); K₂ EDTA was used as the anticoagulant. This method was validated using a methanol protein precipitation extraction followed by tandem mass spectrometric (LC-MS/MS) detection. Refer to the report for SRI Study No. B181-18 for details and results from this validation. The analytical range was 5.00–1000 ng/ml for [Proprietary] and [Proprietary] and 25.0-5000 ng/ml for [Proprietary] with 0.0200 ml sample volumes. The internal standards used for this assay were [Proprietary Info] [Proprietary Info] and [Proprietary Info]

Incurred sample reanalysis (ISR) was performed during this study to ensure assay performance and to verify the results.

II. REFERENCE STANDARDS

The certificates of analysis for the analytes and internal standards are provided in Appendix G-5.

Reference Standard Description

Reference Standard	Supplier	Lot Number	Correction Factor	Storage Conditions	Expiration
[Proprietary Info]			0.997	Refrigerated, Protected from light	Current lot
			0.993	Refrigerated, Protected from light	Current lot
			0.940	Refrigerated	Current lot
			0.980 ^b	-20°C	Retest 06-30-24
			0.970 ^b	-20°C	Retest 04-30-20
			0.970 ^b	-20°C	Retest 10-31-20

^a [Proprietary] was supplied as [Proprietary] monohydrate. The final correction factor used during stock solution preparation is based on the amount of [Proprietary] present when weighing.

^b The purity was assumed as 100% during weighing.

Pooled control K₂ EDTA rat plasma ([Proprietary Info]) which was used in the preparation of calibration curves, QC samples, assay blanks, and sample dilution, was obtained from [Proprietary Info] 05-21-19 and stored in a -20°C freezer until use.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

III. SAMPLE RECEIPT AND STORAGE

The Bioanalytical Chemistry group at SRI received rat plasma samples from the Toxicology group on 02-21-19. A total of 285 frozen, intact samples were received and transferred to an ultra-low temperature freezer ($\leq -60^{\circ}\text{C}$) prior to analysis. A total of 285 samples were analyzed during this study.

The freezer storage temperatures stated in this report are nominal. The temperature of the sample storage freezers did not go above -60°C from the dates of sample receipt until the final analysis of the samples. Any recorded departure from the manufacturer's specifications for a particular freezer unit would result in a facility deviation. No deviations were generated as a result of this over the course of this study.

IV. RESULTS

A. Summary of Runs Performed

A description of all analytical runs performed, including the date of extraction, date of analysis, and run outcome, is presented in Table G-1. Representative chromatographs from Run MF1, including blank plasma extracts, calibration standards, quality control (QC) samples, and study samples, are included in Appendix G-6.

B. Calibration Standard Acceptance Criteria and Results

The calibration curve ranged from 5.00 ng/ml (lower limit of quantitation, LLOQ) to 1000 ng/ml (upper limit of quantitation, ULOQ) for [Proprietary] and [Proprietary] and from 25.0 ng/ml to 5000 ng/ml for [Proprietary]. As freeze thaw stability and sufficient long-term storage stability in matrix were generated during the validation study, SRI Study No. B181-18, calibration standards were prepared in bulk on 07-08-19 and stored in a $\leq -60^{\circ}\text{C}$ freezer until use. A total of eight calibration standards, extracted in duplicate, were used in the construction of each calibration curve. The correlation coefficient (r) in each run was at least 0.9989 for [Proprietary] using a least-squares linear regression with a $1/x^2$ weighting (Table G-2). The correlation coefficient (r) in each run was at least 0.9995 for [Proprietary] and 0.9991 for [Proprietary] using a least-squares linear regression with a $1/x$ weighting (Tables G-3 and G-4). A representative calibration curve for each analyte from Run MF1 are shown in Figures G-1 to G-3.

For a calibration curve to be considered acceptable for each analytical run, at least 75% of the calibration standards must be accurate to within 15% of the nominal concentration ($\pm 20\%$ at the LLOQ). In Run MF6 the second ULOQ calibration standard was excluded from the calibration curve and statistics for all three analytes as the import file for this run erroneously contained the incorrect vial number, so the second highest calibration standard was injected instead of the ULOQ standard. As the first ULOQ standard successfully injected, and as all other calibration standards, QC samples and study samples showed the correct vial numbers in the import file, the run was accepted.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-5 shows the inter-batch back-calculated concentrations of [Proprietary] in the calibration standards from all of the accepted analytical runs. The inter-batch precision (defined as %CV) ranged from 1.8% to 3.0%, and the inter-batch accuracy ranged from 95.4% to 102.6%.

Table G-6 shows the inter-batch back-calculated concentrations of [Proprietary] in the calibration standards from all of the accepted analytical runs. The inter-batch precision ranged from 1.2% to 3.4%, and the inter-batch accuracy ranged from 93.7% to 104.0%.

Table G-7 shows the inter-batch back-calculated concentrations of [Proprietary] in the calibration standards from all of the accepted analytical runs. The inter-batch precision ranged from 1.6% to 6.1%, and the inter-batch accuracy ranged from 90.8% to 105.5%.

C. Quality Control Sample Acceptance Criteria and Results

QC samples in K₂ EDTA rat plasma were spiked with [Proprietary] and [Proprietary] at low (15.0 ng/ml), mid (400 ng/ml) and high (800 ng/ml) concentrations. These QC samples were also spiked with [Proprietary] at 75.0 ng/ml (low), 2000 ng/ml (mid) and 4000 ng/ml (high) concentrations. These QC samples were prepared in bulk on 07-08-19 before being aliquoted into smaller volumes and stored in an ultra-low temperature freezer ($\leq -60^{\circ}\text{C}$) prior to analysis. These QC samples were extracted in replicates of two at each concentration in each analytical batch. For an analytical batch to be acceptable, at least 67% of the low, mid and high QC samples must be within 15% of the nominal concentration, with at least one QC sample at each concentration satisfying this criterion.

Table G-8 shows the inter-batch back-calculated concentrations of [Proprietary] in QC samples from all reported analytical runs. The inter-batch precision ranged from 1.9% to 4.8%, and the inter-batch accuracy ranged from 95.6% to 99.0%.

Table G-9 shows the inter-batch back-calculated concentrations of [Proprietary] in QC samples from all reported analytical runs. The inter-batch precision ranged from 2.3% to 2.9%, and the inter-batch accuracy ranged from 98.4% to 99.0%.

Table G-10 shows the inter-batch back-calculated concentrations of [Proprietary] in QC samples from all reported analytical runs. The inter-batch precision ranged from 1.7% to 2.5%, and the inter-batch accuracy ranged from 95.1% to 98.4%.

In addition to calibration standards and QC samples, pooled plasma samples containing no analyte or internal standard (BI/BI) and pooled plasma samples containing internal standard only (BI/IS) were analyzed in each run. These samples were positioned throughout the run in order to identify either analyte contamination or auto-injector carryover. For [Proprietary] and [Proprietary] there was no evidence of significant chromatographic interferences in these samples at the analyte or internal standard retention time, defined as a peak at the analyte retention time with a peak area $>20\%$ of the mean analyte peak area at the LLOQ, or a peak at the internal standard retention time with a peak area $>5\%$ of the mean peak area of the extracted internal standard across samples. For

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

[Proprietary] significant carryover was observed in both carryover blanks across all runs. The sample preceding the second carryover blank in run MF6 was not an injection from the ULOQ calibration standard (Standard 8), but from the preceding Standard 7 due to a vial number error in the batch import file. Therefore, it does not represent the true carryover value. This pertains to all three analytes.

In all analytical runs, the second BI/BI sample also showed evidence of significant carryover for [Proprietary] as the injection preceding this was a high QC sample. The first BI/BI sample and both BI/IS samples did not show a significant response at the analyte retention time. As both carryover blanks were affected in these runs, a carryover impact assessment was performed in these batches. Results from the carryover impact assessment, which are stored with the raw data and are not reported here, indicated that no study sample was significantly affected by carryover by more than 5%, which would warrant sample reanalysis per SRI SOP 006.061, except for sample 136F-Group 2-Day 29-Predose. For this sample, originally analyzed in Run MF2, the % carryover impact was determined to be 5.43%. This sample was reanalyzed (n=1) in Run MF7. A carryover blank was injected before this study sample to prevent carryover from the preceding high QC sample affecting it. Carryover impact assessment performed for Run MF7 indicates that this study sample is not affected by carryover, and therefore the reassay value will be reported. The values obtained on original analysis and reanalysis, and the reported value for this study sample are shown in Table G-17.

Carryover for [Proprietary] was observed during the validation study, SRI Study No. B181-18. The carryover originates from the column and not the autosampler, and as chromatographic limitations already existed because of the differences in analyte polarity, it was not practical to fully eliminate the carryover. Tables G-11 to G-13 compare the analyte peak areas from the BI/BI, BI/IS, and carryover samples with the mean LLOQ calibration standard analyte peak areas from all reported runs.

D. Incurred Sample Reanalysis

Incurred sample reanalysis (ISR) was performed on 29 study samples (10.2%) in order to confirm the integrity of the bioanalytical method. Samples that had been previously analyzed and had the results accepted were reanalyzed in replicates of n=1 and the resulting concentration compared with the original reported concentration. The results generated from ISR are not intended to replace the original result and are generated for comparative purposes only. According to SRI SOP 006.062, in order for an ISR result to be considered comparable to the original result, the difference between the two results must be $\leq 20\%$. At least 67% of the ISR samples must meet the acceptance criteria in order for the overall ISR evaluation to be considered successful.

ISR of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA rat plasma samples satisfied the acceptance criterion, with 100% of all reassayed samples meeting the acceptance criterion as defined above. The complete results and outcome of ISR analysis are reported in Tables G-14 to G-16.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

E. Sample Analysis Results

Tables G-20 to G-37 shows the final concentrations of each analyte from individual K₂ EDTA rat plasma samples. Also included for toxicokinetic (TK) purposes are the mean and standard deviation (SD) per time point per sex. Samples with values < LLOQ were excluded from the calculation of the mean \pm SD. Note that the complete TK analysis is separate from the bioanalytical report and appears as an appendix to the report for SRI Study No. M398-18 (Appendix H).

Samples with values less than the LLOQ are reported as lower than the level of quantitation (<LLOQ).

Some study samples were reassayed with sample dilution as the original value was higher than the upper limit of quantitation (>ULOQ). The values obtained on original analysis and reanalysis, and the reported values are shown in Tables G-17 to G-19.

V. DEVIATIONS

There were no deviations to SRI SOPs that had any impact on the integrity of the study.

VI. DATA MANAGEMENT

LC-MS/MS data were acquired, peak areas were integrated, the calibration line regressions were calculated, and the final concentrations were generated using AB Sciex Analyst software, version 1.6.2. All concentration values calculated by the Analyst software have been rounded to three significant figures. The inter-batch calibration curve and QC statistics described in this report were generated, using unrounded values, with this software. The mean and standard deviation values for each sample analysis timepoint were calculated using Microsoft Excel 2016, and are reported to three significant figures.

VII. CONCLUSION

Rat plasma samples from SRI Study No. M398-18 were analyzed for [Proprietary] [Proprietary] and [Proprietary] using the validated analytical method detailed in SRI Test Method 106.202 (Appendix G-4). All sample results generated from this study were acceptable.

Interim long-term matrix storage stability for 25 days at $\leq -60^{\circ}\text{C}$ was established during validation study, SRI Study No. B181-18. Additional stability is still ongoing, and an amended validation report will be created on completion.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

VIII. DEFINITIONS AND ABBREVIATIONS

Accuracy:	$\frac{\text{Calculated concentration}}{\text{Nominal concentration}} * 100$
Bl/Bl:	Double blank, containing no analyte or internal standard
Bl/IS:	Blank, containing only internal standard
CV:	Coefficient of variation; $\text{SD}/\text{mean} * 100$
DMSO:	Dimethyl sulfoxide
K ₂ EDTA:	Di-potassium ethylenediaminetetraacetic acid
IS:	Internal standard [Proprietary Info] [Proprietary Info] [Proprietary Info]
ISR:	Incurred sample reanalysis
LC-MS/MS:	Liquid chromatography-mass spectrometer; tandem or triple-quadrupole mass spectrometer
LLOQ:	Lower limit of quantitation
QC:	Quality Control
SD:	Standard Deviation
TK:	Toxicokinetic
ULOQ:	Upper limit of quantitation

IX. REFERENCES

1. SRI Test Method 106.202 *Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma*
2. SRI Report B181-18 "Method Validation Report for the Quantitative Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma"
3. SRI SOP 006.061 *Bioanalytical Sample Analysis*
4. SRI SOP 006.062 *Bioanalytical Sample Reanalysis*

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix G-2

BIOANALYTICAL FIGURES AND TABLES

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

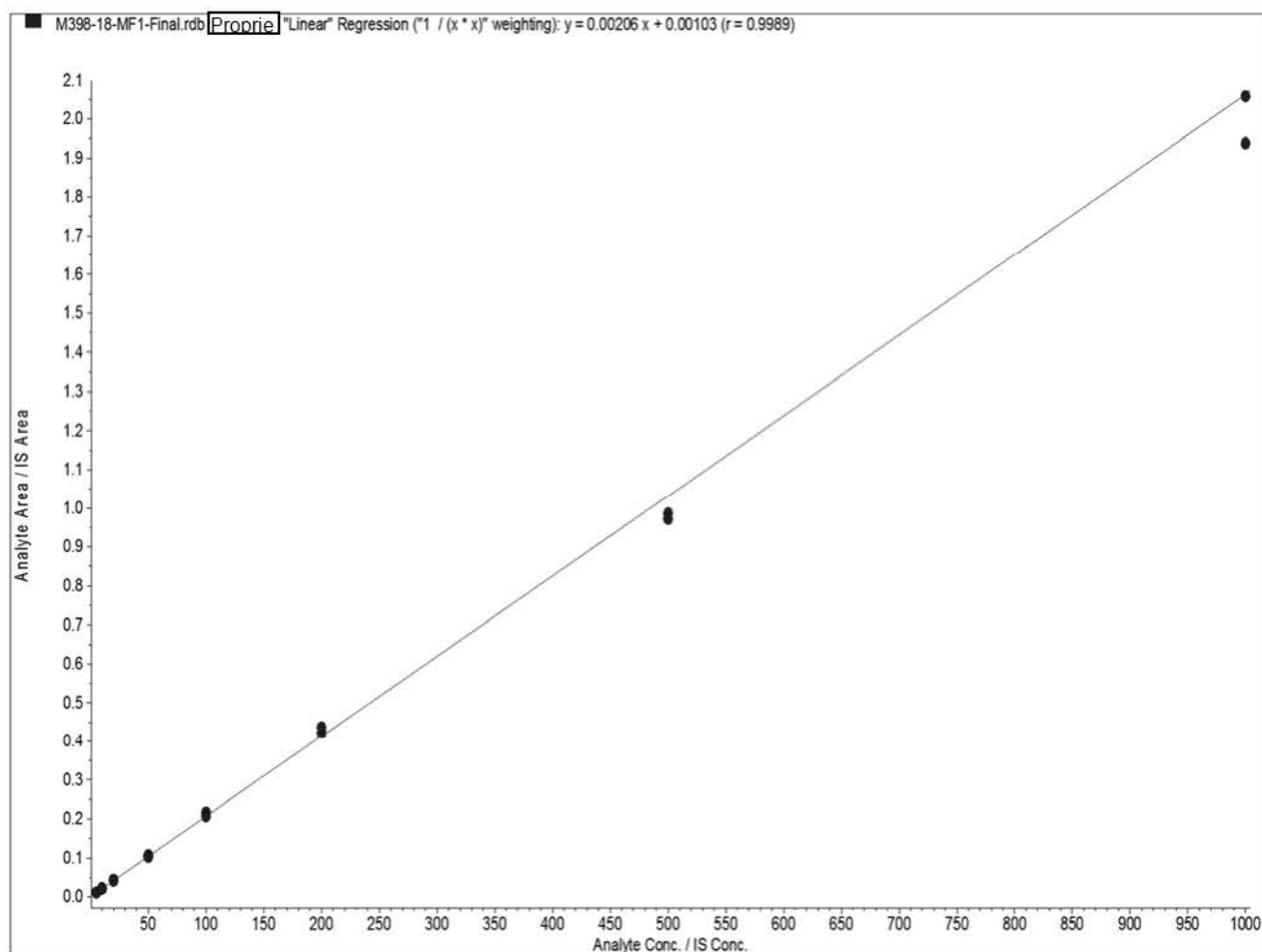


Figure G-1. Representative [Proprietary] Calibration Curve from Run MF1.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

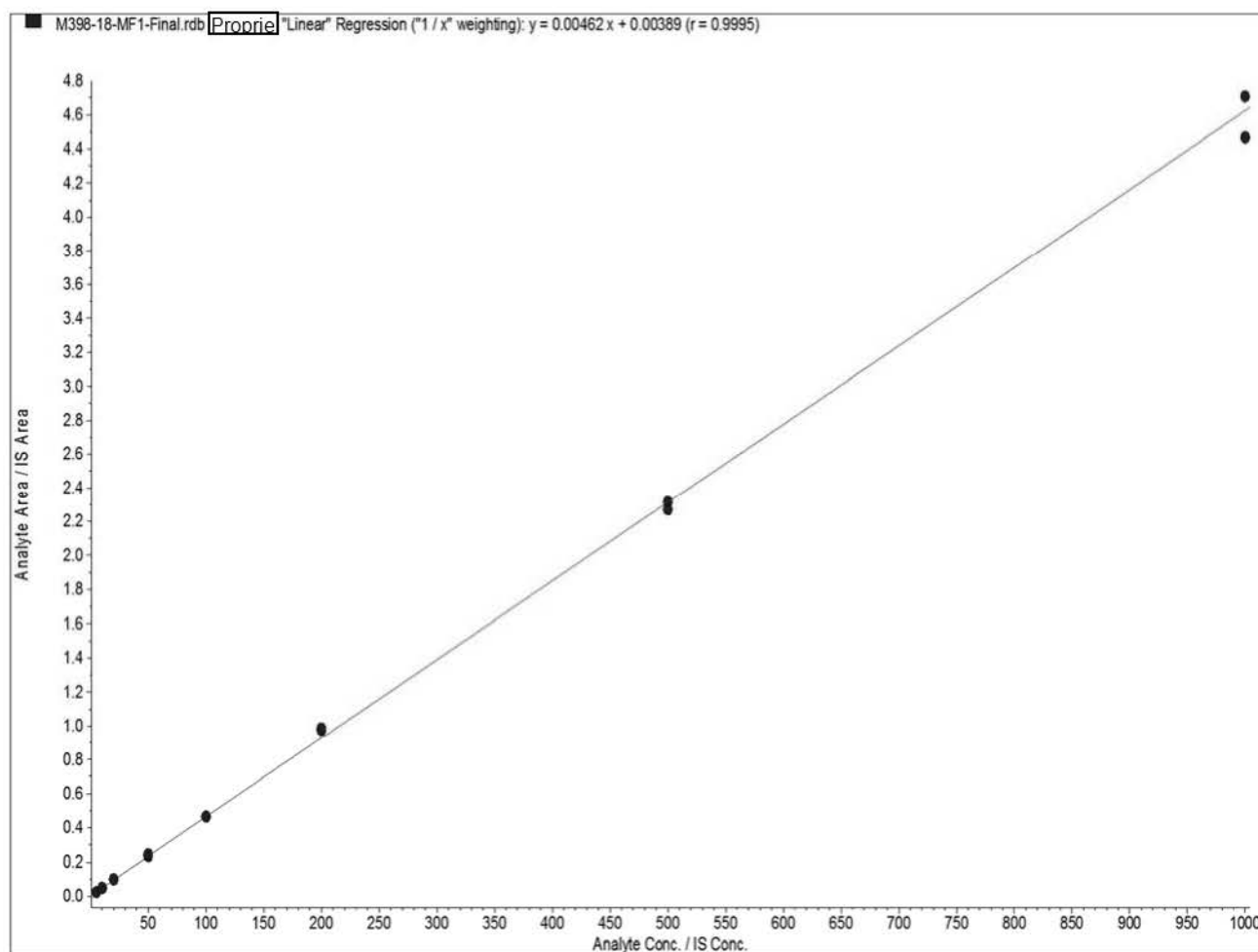


Figure G-2. Representative [Proprietary] Calibration Curve from Run MF1.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

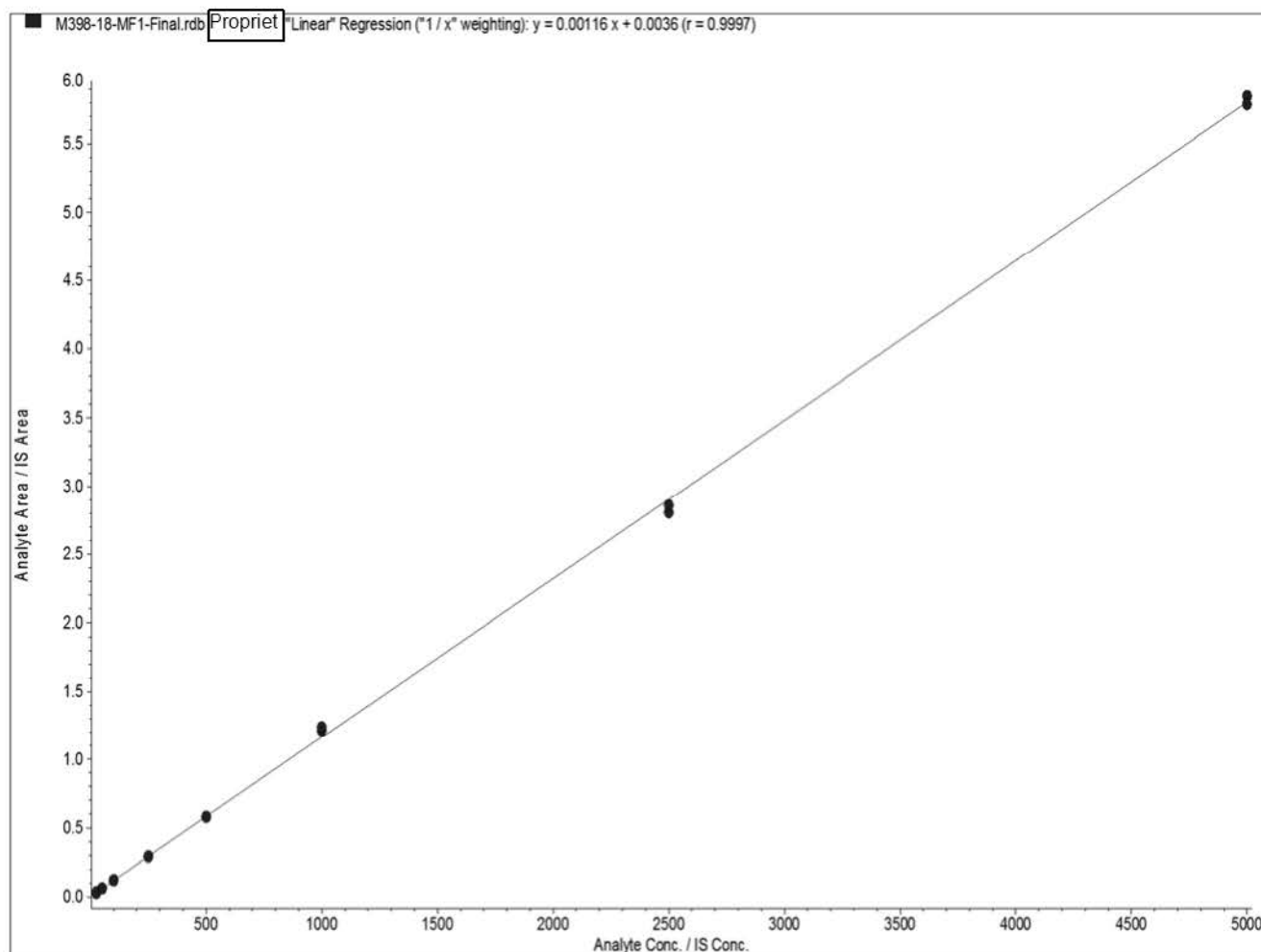


Figure G-3. Representative [Proprietary] Calibration Curve from Run MF1.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-1

Summary of Analytical Runs

Run Number	Date Extracted	Date Analyzed	Outcome (Pass/Fail)	Run Description
MF1	16-Jul-19	16-Jul-19	Pass	Group 2 (Males and Females)
MF2	17-Jul-19	17-Jul-19	Pass	Group 2 (Females); Group 3 (Males)
MF3	19-Jul-19	19-Jul-19	Pass	Group 3 (Females); Group 4 (Males)
MF4	22-Jul-19	22-Jul-19	Pass	Group 4 (Males and Females); Dilution Repeats
MF5	23-Jul-19	23-Jul-19	Pass	Dilution Repeats [Proprietary] only)
MF6	24-Jul-19	24-Jul-19	Pass	Incurred Sample Reanalysis (ISR)
MF7	26-Jul-19	26-Jul-19	Pass	Reassay ^a [Proprietary] only)

^a One sample was reassayed in this batch for [Proprietary] as Carryover Impact Assessment indicated that it was affected by carryover in the original analysis in the batch MF2. Refer to the Section C of this report for further details.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-2

Summary of Calibration Curve Parameters for [Proprietary Info]

Run Number	Slope	Intercept	Correlation Coefficient (r)
MF1	0.00206	0.00103	0.9989
MF2	0.00202	0.00108	0.9993
MF3	0.00201	0.00115	0.9992
MF4	0.00179	0.00111	0.9991
MF6	0.00177	0.00110	0.9991
MF7	0.00177	0.00101	0.9996

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-3

Summary of Calibration Curve Parameters for [Proprietary]

Run Number	Slope	Intercept	Correlation Coefficient (r)
MF1	0.00462	0.00389	0.9995
MF2	0.00446	0.00345	0.9995
MF3	0.00441	0.00436	0.9997
MF4	0.00392	0.00304	0.9998
MF6	0.00392	0.00276	0.9997

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-4

Summary of Calibration Curve Parameters for [Proprietary]

Run Number	Slope	Intercept	Correlation Coefficient (r)
MF1	0.00116	0.00360	0.9997
MF2	0.00114	0.00408	0.9996
MF3	0.00113	0.00534	0.9994
MF4	0.00129	0.00642	0.9991
MF5	0.00132	0.00553	0.9995
MF6	0.00133	0.00474	0.9996

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-5

Back-Calculated Concentrations of [Proprietary] Calibration Standards (ng/ml)

Run Number	Standard Description															
	5.00	%Acc	10.0	%Acc	20.0	%Acc	50.0	%Acc	100	%Acc	200	%Acc	500	%Acc	1000	%Acc
MF1	4.97	99.5	9.71	97.1	20.9	104.5	51.3	102.7	105	104.7	204	102.0	478	95.6	998	99.8
	4.90	98.1	10.6	105.7	19.6	98.2	49.3	98.7	100	100.0	211	105.6	471	94.2	939	93.9
MF2	4.87	97.4	9.56	95.6	19.8	99.1	50.0	100.1	98.6	98.6	207	103.5	469	93.8	1030	102.8
	5.23	104.6	9.83	98.3	20.7	103.5	52.0	103.9	101	101.5	200	100.0	483	96.5	1010	100.7
MF3	4.94	98.8	10.2	102.3	20.7	103.6	48.6	97.2	100	100.4	204	101.8	453	90.6	986	98.6
	4.90	97.9	10.2	101.5	20.4	102.2	50.0	99.9	104	103.8	207	103.3	483	96.7	1010	101.5
MF4	4.78	95.7	9.97	99.7	20.4	102.1	49.0	98.1	102	101.9	199	99.4	460	92.1	997	99.7
	5.15	103.0	10.0	100.2	20.5	102.5	50.6	101.2	103	103.4	212	105.9	476	95.3	999	99.9
MF6	4.80	96.0	9.63	96.3	21.4	106.9	48.7	97.5	99.9	99.9	201	100.4	491	98.3	973	97.3
	5.16	103.1	10.1	101.1	20.5	102.6	50.1	100.3	100	100.5	211	105.4	472	94.4	484 ^a	NA
MF7	4.86	97.2	10.4	103.9	20.2	101.0	50.2	100.5	100	100.2	202	101.1	508	101.5	973	97.3
	5.00	99.9	9.90	99.0	21.0	105.0	48.9	97.9	100	100.3	202	101.2	481	96.3	977	97.7
Mean	4.96		10.0		20.5		49.9		101		205		477		990	
SD	0.145		0.305		0.485		1.05		1.84		4.53		14.2		24.2	
%CV	2.9		3.0		2.4		2.1		1.8		2.2		3.0		2.4	
%Accuracy	99.3		100.1		102.6		99.8		101.3		102.5		95.4		99.0	
n	12		12		12		12		12		12		12		11	

^a Result is outside acceptance criterion ($\pm 15\%$) and was excluded from the calibration curve and statistics due to a wrong vial number in the batch import file.

NA: Not Applicable.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-6

Back-Calculated Concentrations of [Proprietary] Calibration Standards (ng/ml)

Run Number	Standard Description															
	5.00	%Acc	10.0	%Acc	20.0	%Acc	50.0	%Acc	100	%Acc	200	%Acc	500	%Acc	1000	%Acc
MF1	4.62	92.3	9.63	96.3	20.9	104.7	50.3	100.7	100	100.0	210	105.0	500	100.0	1020	101.8
	4.58	91.6	9.97	99.7	20.6	102.9	51.8	103.7	100	100.2	213	106.3	491	98.1	966	96.6
MF2	4.66	93.1	10.2	101.8	20.5	102.3	50.6	101.3	99.2	99.2	212	106.0	489	97.9	973	97.3
	4.61	92.3	9.86	98.6	20.7	103.4	51.4	102.9	101	101.1	205	102.3	488	97.5	1030	103.1
MF3	4.62	92.4	9.30	93.0	20.5	102.6	48.6	97.2	101	100.6	211	105.5	494	98.8	995	99.5
	4.91	98.1	10.3	102.6	21.1	105.3	50.0	99.9	105	104.8	205	102.3	484	96.7	1010	100.8
MF4	4.83	96.7	9.67	96.7	21.1	105.7	51.7	103.4	100	100.3	200	100.0	484	96.8	992	99.2
	4.64	92.9	9.29	92.9	20.9	104.3	52.0	104.0	101	101.4	207	103.3	514	102.9	996	99.6
MF6	4.58	91.6	9.91	99.1	20.7	103.3	48.3	96.6	100	100.3	208	104.2	502	100.4	978	97.8
	4.82	96.3	10.0	100.2	20.5	102.5	49.9	99.9	103	102.8	210	105.0	500	100.0	507 ^a	NA
Mean	4.69		9.81		20.7		50.5		101		208		495		995	
SD	0.119		0.334		0.244		1.31		1.62		4.00		9.58		21.2	
%CV	2.5		3.4		1.2		2.6		1.6		1.9		1.9		2.1	
%Accuracy	93.7		98.1		103.7		100.9		101.1		104.0		98.9		99.5	
n	10		10		10		10		10		10		10		9	

^a Result is outside acceptance criterion (±15%) and was excluded from the calibration curve and statistics due to a wrong vial number in the batch import file.

NA: Not Applicable.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-7

Back-Calculated Concentrations of [Proprietary] Calibration Standards (ng/ml)

Run Number	Standard Description															
	25.0	%Acc	50.0	%Acc	100	%Acc	250	%Acc	500	%Acc	1000	%Acc	2500	%Acc	5000	%Acc
MF1	22.7	90.8	50.6	101.2	101	101.0	247	98.7	497	99.4	1040	104.3	2420	96.7	5040	100.8
	25.5	102.2	49.9	99.9	102	101.8	249	99.5	497	99.3	1060	106.4	2460	98.5	4990	99.7
MF2	23.7	94.7	50.2	100.5	107	107.1	248	99.2	516	103.3	1060	105.8	2470	98.7	4910	98.3
	22.2	88.7	49.9	99.8	104	104.3	245	98.0	500	100.1	1030	103.3	2410	96.3	5100	102.1
MF3	20.7	82.9	47.8	95.5	104	103.6	247	98.9	507	101.5	1090	109.1	2450	98.2	4990	99.8
	23.5	94.1	52.3	104.5	103	102.7	249	99.4	531	106.2	1070	106.7	2480	99.1	4890	97.7
MF4	21.4	85.8	50.0	100.0	101	101.0	272	108.8	527	105.4	1060	106.2	2440	97.6	5130	102.5
	20.8	83.3	48.6	97.3	103	103.0	257	102.7	531	106.2	1060	105.6	2500	99.9	4740	94.7
MF5	23.3	93.3	46.9	93.9	102	102.4	251	100.4	491	98.2	1060	106.5	2490	99.5	5050	101.0
	22.1	88.5	51.6	103.1	107	107.1	250	99.9	520	104.1	1070	106.8	2450	98.0	4860	97.2
MF6	22.5	90.1	48.0	96.1	104	103.9	255	101.9	513	102.5	1020	101.9	2560	102.2	4860	97.2
	23.8	95.2	48.6	97.2	103	102.9	254	101.8	519	103.8	1040	103.9	2480	99.4	2440 ^a	NA
Mean	22.7		49.5		103		252		512		1060		2470		4960	
SD	1.38		1.59		2.01		7.26		13.9		19.2		39.1		119	
%CV	6.1		3.2		1.9		2.9		2.7		1.8		1.6		2.4	
%Accuracy	90.8		99.1		103.4		100.8		102.5		105.5		98.7		99.2	
n	12		12		12		12		12		12		12		11	

^a Result is outside acceptance criterion ($\pm 15\%$) and was excluded from the calibration curve and statistics due to a wrong vial number in the batch import file.

NA: Not Applicable.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-8

Back-Calculated Concentrations of [Proprietary] Quality Control Samples (ng/ml)

Run Number	QC Description					
	15.0	%Acc	400	%Acc	800	%Acc
MF1	14.7	98.3	356	89.1	801	100.1
	15.5	103.0	382	95.5	754	94.3
MF2	14.6	97.2	393	98.3	776	97.0
	16.4	109.3	377	94.2	772	96.5
MF3	14.4	96.3	377	94.2	751	93.9
	15.5	103.6	399	99.8	771	96.4
MF4	14.3	95.4	369	92.1	775	96.9
	15.5	103.3	390	97.4	782	97.7
MF6	14.1	93.7	395	98.7	751	93.9
	14.1	94.1	379	94.8	764	95.5
MF7	14.6	97.2	385	96.4	767	95.9
	14.4	96.0	385	96.3	785	98.1
Mean	14.8		382		771	
SD	0.714		11.9		14.7	
%CV	4.8		3.1		1.9	
%Accuracy	99.0		95.6		96.3	
n	12		12		12	

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-9

Back-Calculated Concentrations of [Proprietary] Quality Control Samples (ng/ml)

Run Number	QC Description					
	15.0	%Acc	400	%Acc	800	%Acc
MF1	14.4	96.3	382	95.4	782	97.7
	15.3	102.3	395	98.7	795	99.4
MF2	14.3	95.0	392	98.1	767	95.8
	15.5	103.5	395	98.8	783	97.9
MF3	14.6	97.6	395	98.9	762	95.3
	15.2	101.1	403	100.8	809	101.2
MF4	14.8	98.3	403	100.7	821	102.6
	14.9	99.3	414	103.4	802	100.2
MF6	15.1	100.9	389	97.3	795	99.4
	14.4	95.8	389	97.2	754	94.3
Mean	14.9		396		787	
SD	0.432		8.97		21.4	
%CV	2.9		2.3		2.7	
%Accuracy	99.0		98.9		98.4	
n	10		10		10	

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-10

Back-Calculated Concentrations of [Proprietary] Quality Control Samples (ng/ml)

Run Number	QC Description					
	75.0	%Acc	2000	%Acc	4000	%Acc
MF1	72.0	96.1	1910	95.6	3800	95.0
	69.3	92.4	1940	97.0	3920	97.9
MF2	72.1	96.2	1990	99.5	3930	98.2
	71.8	95.7	1930	96.4	3930	98.2
MF3	71.0	94.7	2020	100.8	3860	96.4
	69.0	92.0	1960	98.2	3910	97.8
MF4	71.0	94.6	2070	103.7	4060	101.6
	70.5	94.0	1970	98.4	3960	99.1
MF5	72.7	97.0	2010	100.5	3950	98.7
	72.2	96.3	1960	98.0	3830	95.8
MF6	71.6	95.4	1900	95.1	3820	95.5
	72.9	97.2	1950	97.3	3780	94.4
Mean	71.3		1970		3900	
SD	1.25		48.7		81.6	
%CV	1.7		2.5		2.1	
%Accuracy	95.1		98.4		97.4	
n	12		12		12	

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-11

Selectivity Determination and Carryover in [Proprietary] Assay BI/BI and BI/IS samples

Run Number	Peak Area							
	LLOQ	Mean LLOQ	BI/BI	% Difference	BI/IS	% Difference	Carryover	% Difference
MF1	19382	19589	705	3.6	457	2.3	5641	28.8
	19795		4360	22.3	1585	8.1	5185	26.5
MF2	21183	20395	452	2.2	836	4.1	5016	24.6
	19607		4573	22.4	1442	7.1	4906	24.1
MF3	20704	20149	165	0.8	1207	6.0	5271	26.2
	19593		4988	24.8	1820	9.0	5297	26.3
MF4	18530	18979	446	2.3	645	3.4	5081	26.8
	19427		4020	21.2	1106	5.8	4605	24.3
MF6	18364	18815	531	2.8	459	2.4	5642	30.0
	19265		4090	21.7	1476	7.8	3679 ^a	NA
MF7	18079	18543	833	4.5	0	0.0	5174	27.9
	19006		4303	23.2	1492	8.0	6562	35.4

% Difference is calculated using the mean of the LLOQ peak areas.

^a Due to a wrong vial number in the batch import file, the sample preceding this carryover sample was not an injection from the ULOQ calibration standard (Std8), but from the preceding Std7. Therefore, it does not represent the true carryover value. Refer to the Section C of this report for additional information.

NA: Not Applicable.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18

Table G-12

Selectivity Determination and Carryover in Proprietary Assay BI/BI and BI/IS samples

Run Number	Peak Area							
	LLOQ	Mean LLOQ	BI/BI	% Difference	BI/IS	% Difference	Carryover	% Difference
MF1	19336	19906	0	0.0	0	0.0	3451	17.3
	20475		2827	14.2	1030	5.2	3442	17.3
MF2	20635	19628	0	0.0	408	2.1	2979	15.2
	18621		2484	12.7	1099	5.6	2828	14.4
MF3	20254	20525	240	1.2	591	2.9	3574	17.4
	20795		3166	15.4	965	4.7	3252	15.8
MF4	18683	18849	271	1.4	413	2.2	2961	15.7
	19014		2511	13.3	1181	6.3	2914	15.5
MF6	17935	18681	173	0.9	264	1.4	3730	20.0
	19426		2720	14.6	993	5.3	1943 ^a	NA

% Difference is calculated using the mean of the LLOQ peak areas.

^a Due to a wrong vial number in the batch import file, the sample preceding this carryover sample was not an injection from the ULOQ calibration standard (Std8), but from the preceding Std7. Therefore, it does not represent the true carryover value. Refer to the Section C of this report for additional information.

NA: Not Applicable.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-13

Selectivity Determination and Carryover in [Proprietary] Assay BI/BI and BI/IS samples

Run Number	Peak Area							
	LLOQ	Mean LLOQ	BI/BI	% Difference	BI/IS	% Difference	Carryover	% Difference
MF1	36303	37662	350	0.9	0	0.0	640	1.7
	39021		2233	5.9	947	2.5	869	2.3
MF2	40002	37466	0	0.0	1404	3.7	2929	7.8
	34930		1950	5.2	1268	3.4	2499	6.7
MF3	34814	36554	521	1.4	2016	5.5	3000	8.2
	38293		2852	7.8	1981	5.4	2110	5.8
MF4	32421	32302	229	0.7	877	2.7	1210	3.7
	32182		1067	3.3	1090	3.4	786	2.4
MF5	32249	31470	0	0.0	200	0.6	1158	3.7
	30690		2161	6.9	1536	4.9	1331	4.2
MF6	31254	32300	0	0.0	1159	3.6	767	2.4
	33345		2173	6.7	1348	4.2	1737 ^a	NA

% Difference is calculated using the mean of the LLOQ peak areas.

^a Due to a wrong vial number in the batch import file, the sample preceding this carryover sample was not an injection from the ULOQ calibration standard (Std8), but from the preceding Std7. Therefore, it does not represent the true carryover value. Refer to the Section C of this report for additional information.

NA: Not Applicable.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-14

Incurred Sample Re-analysis (ISR) of [Proprietary] in K₂ EDTA Rat Plasma Samples (ng/ml)

Animal Number	Sex	Group	Day	Timepoint (H)	Original Concentration	ISR Concentration	% Difference	Analytical Run (Original, ISR)
[Proprietary Info]								

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-15

Incurred Sample Re-analysis (ISR) of [Proprietary] in K₂ EDTA Rat Plasma Samples (ng/ml)

Animal Number	Sex	Group	Day	Timepoint (H)	Original Concentration	ISR Concentration	% Difference	Analytical Run (Original, ISR)
Proprietary Info								

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-16

Incurred Sample Re-analysis (ISR) of [Proprietary] in K₂ EDTA Rat Plasma Samples (ng/ml)

Animal Number	Sex	Group	Day	Timepoint (H)	Original Concentration	ISR Concentration	% Difference	Analytical Run (Original; ISR)
Proprietary Info								

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Table G-17

Sample Reassay of Lopinavir in K₂ EDTA Rat Plasma Samples (ng/ml)

Animal Number-Sex-Group-Day-Timepoint	Original Concentration	Reassay Concentration	% Difference (Between Reassay and Original)	Reported Value	Reason for Reported Value	Analytical Run (Original; Reassay)
[Proprietary Info]	10.2	9.91	-2.9	9.91	a	MF2; MF7
	>ULOQ	1520	NA	1520	b	MF3; MF4

^a This sample was reassayed in run MF7 as it was affected by carryover in the original analysis (run MF2) based on the carryover impact assessment. Carryover impact assessment of run MF7 indicates that reassayed result was not affected by carryover, therefore this value is accepted as the final reported value.

^b The original value was above the quantitation limit (1000 ng/ml). The sample was reassayed with sample dilution to give the reported result, above.

ULOQ: Upper Limit of Quantitation.

NA: Not Applicable.

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Table G-18

Sample Reassay of [Proprietary] in K₂ EDTA Rat Plasma Samples (ng/ml)

Animal Number-Sex-Group-Day-Timepoint	Original Concentration	Reassay Concentration	% Difference (Between Reassay and Original)	Reported Value	Reason for Reported Value	Analytical Run (Original; Reassay)
[Proprietary Info]	>ULOQ	1480	NA	1480	a	MF3; MF4

^a The original value was above the quantitation limit (1000 ng/ml). The sample was reassayed with sample dilution to give the reported result, above.

ULOQ: Upper Limit of Quantitation.

NA: Not Applicable.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-19

Sample Reassay of [Proprietary] in K₂ EDTA Rat Plasma Samples (ng/ml)

Animal Number-Sex-Group-Day-Timepoint	Original Concentration	Reassay Concentration	% Difference (Between Reassay and Original)	Reported Value	Reason for Reported Value	Analytical Run (Original; Reassay)
[Proprietary Info]	>ULOQ	5570	NA	5570	a	MF3; MF4
	>ULOQ	7150	NA	7150	a	MF3; MF4
	>ULOQ	6660	NA	6660	a	MF3; MF4
	>ULOQ	5540	NA	5540	a	MF3; MF4
	>ULOQ	6720	NA	6720	a	MF3; MF4
	>ULOQ	5670	NA	5670	a	MF4; MF5
	>ULOQ	5850	NA	5850	a	MF4; MF5
	>ULOQ	6160	NA	6160	a	MF4; MF5

^a The original value was above the quantitation limit (5000 ng/ml). The sample was reassayed with sample dilution to give the reported result, above.

ULOQ: Upper Limit of Quantitation.

NA: Not Applicable.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-20

Back-Calculated Concentrations of [Proprietary] in Group 2 (1.5 mg/kg [Proprietary Info])
Male K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-21

Back-Calculated Concentrations of [Proprietary] in Group 2 (1.5 mg/kg [Proprietary Info])
Female K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-22

Back-Calculated Concentrations of [Proprietary] in Group 3 (15 mg/kg [Proprietary Info])
Male K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-23

Back-Calculated Concentrations of [Proprietary] in Group 3 (15 mg/kg [Proprietary Info])
Female K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-24

Back-Calculated Concentrations of [Proprietary] in Group 4 (30 mg/kg Lopinavir)
Male K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
Proprietary Info							

with **Proprietary Info** **Pro** **in Sprague Dawley Rats**

**Back-Calculated Concentrations of [Proprietary] in Group 4 (30 mg/kg Lopinavir)
Female K₂ EDTA Rat Plasma Samples**

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
Proprietary Info							

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Table G-26

**Back-Calculated Concentrations of [Proprietary] in Group 2 (0.4125 mg/kg Ritonavir)
Male K₂ EDTA Rat Plasma Samples**

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
Proprietary Info							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-27

Back-Calculated Concentrations of [Proprietary] in Group 2 (0.4125 mg/kg Ritonavir)
Female K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-28

Back-Calculated Concentrations of [Proprietary] in Group 3 (4.125 mg/kg Ritonavir)
Male K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
Proprietary Info							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-29

Back-Calculated Concentrations of [Proprietary] in Group 3 (4.125 mg/kg Ritonavir)
Female K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-30

Back-Calculated Concentrations of [Proprietary] in Group 4 (8.25 mg/kg [Proprietary])
Male K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
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Proprietary Info

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-31

Back-Calculated Concentrations of [Proprietary] in Group 4 (8.25 mg/kg [Proprietary Info])
Female K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-32

Back-Calculated Concentrations of [Proprietary] in Group 2 (0.8625 g/kg [Proprietary Info])
Male K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-33

Back-Calculated Concentrations of [Proprietary] in Group 2 (0.8625 mg/kg [Proprietary Info])
Female K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-34

Back-Calculated Concentrations of [Proprietary] in Group 3 (8.625 mg/kg [Proprietary Info])
Male K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-35

Back-Calculated Concentrations of [Proprietary] in Group 3 (8.625 mg/kg [Proprietary Info])
Female K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-36

Back-Calculated Concentrations of [Proprietary] in Group 4 (17.25 mg/kg [Proprietary Info])
Male K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
[Proprietary Info]							

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table G-37

Back-Calculated Concentrations of [Proprietary] in Group 4 (17.25 mg/kg [Proprietary Info])
Female K₂ EDTA Rat Plasma Samples

Animal Number	Day	Timepoint (Hours)	Dilution Factor	Concentration (ng/ml)	Mean Concentration (ng/ml)	SD	Analytical Run
Proprietary Info							

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix G-3

BIOANALYTICAL SAMPLE ANALYSIS PLAN

**Bioanalytical Sample Analysis Plan for the Analysis of Study
Samples from SRI International Study Number M398-18
“GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity
Study with [Proprietary Info] [Proprietary Info] in Sprague Dawley Rats”**

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Date

07/11/19

Date

SCOPE

This sample analysis plan will be limited to the analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA rat plasma samples from SRI International Study M398-18 “GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with [Proprietary] [Pro] in Sprague Dawley Rats”. [Proprietary] [Proprietary] and [Proprietary] will be extracted from rat plasma using 0.0200 ml sample volumes, using a protein precipitation extraction procedure followed by LC-MS/MS detection. The internal standards used in this assay are [Proprietary Info] [Proprietary Info] and [Proprietary Info]. This method was fully validated, with long term storage stability in matrix still ongoing at this time. Refer to SRI Report B181-18 for full details of this validation.

This sample analysis plan is based on SRI SOP 006.061, *Bioanalytical Sample Analysis*. Further details on the conduct of a typical study are described in this SOP.

OBJECTIVE

The objective of this sample analysis plan is to describe the laboratory procedure used, the analytical curve range, the anticoagulant, matrix, and species used, the study samples, and the assay acceptance criteria. Following completion of analysis, a report will be written that will detail the assay performance and the results obtained from sample analysis.

SUMMARY OF METHOD

Full details of the methodology used during the conduct of sample analysis will be detailed in SRI Test Method 106.202: *Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma*.

[Proprietary] [Proprietary] [Proprietary] and the internal standards are extracted from K₂ EDTA rat plasma, using 0.0200 ml sample volumes, using a protein precipitation procedure. Following centrifugation, the supernatant is then further diluted with water:methanol (90:10, v:v) with 0.1% acetic acid before analysis by high performance liquid chromatography with tandem mass spectrometric detection (LC-MS/MS).

CALIBRATION STANDARD AND QUALITY CONTROL SAMPLES

The calibration standards (n=2 per analytical batch) contain the following concentrations of [Proprietary] and [Proprietary] in K₂ EDTA rat plasma: 5.00, 10.0, 20.0, 50.0, 100, 200, 500, and 1000 ng/ml. These calibration standards also contain [Proprietary] at 25.0, 50.0, 100, 250, 500, 1000, 2500, and 5000 ng/ml. Calibration standards may be either freshly prepared on the day of analysis, or prepared in advance and stored at ≤-60°C for no longer than 25 days, the period of matrix storage stability established to date in the validation study. Also included with each batch will be at least n=2 blank samples containing no analyte or internal standard (BI/BI) and at least n=2 blank samples containing no analyte but containing internal standard (BI/IS).

Quality Control (QC) samples contain the following concentrations of [Proprietary] and [Proprietary] in K₂ EDTA rat plasma: 15.0 ng/ml (low), 400 ng/ml (mid), and 800 ng/ml (high). These calibration standards also contain [Proprietary] at 75.0 ng/ml (low), 2000 ng/ml (mid), and

4000 ng/ml (high) concentrations. These QC samples will be prepared in advance and stored in a $\leq -60^{\circ}\text{C}$ freezer. A dilution QC, prepared at 5000 ng/ml [Proprietary] and [Proprietary] and 25000 ng/ml [Proprietary Info] has been successfully validated using a 10-fold and a 50-fold dilution. QC samples will be analyzed in at least $n \geq 2$ replicates in each analytical batch. The dilution QC, if used, should be extracted in multiples of least $n=3$, although it is not necessary to extract a dilution QC in a batch where samples have been diluted providing that the dilution factor selected was previously validated. If a new dilution scheme is required, then this will be validated in replicates of 6.

ACCEPTANCE CRITERIA

The linearity of the assay will be assessed by the correlation coefficient (r) obtained from the linear regression analysis of the peak area ratios, with perfect fit of the data to the linear equation yielding an r value of 1.000. The minimum value for r for an assay to be acceptable is 0.990. A linear weighting of $1/x$ will be applied to the [Proprietary] and [Proprietary] calibration curves, while a linear weighting of $1/x^2$ will be applied to the [Proprietary] calibration curves.

In order for the calibration curve to be considered acceptable there will not be more than a 15% difference between the nominal and observed concentrations, except at the lower limit of quantitation (LLOQ) where a 20% deviation is permitted. At least 75% of the calibration standards will fulfill this criterion. Individual calibration standards which do not fulfill the criterion will be excluded from the regression.

For the QC samples to be considered acceptable, at least 50% of the individual replicates at each concentration must be within $\pm 15\%$ of the nominal concentration, and at least 67% of the QCs in a batch must meet this acceptance criterion. For dilution QCs, at least 67% of the QCs at each validated dilution factor used must be within 15% of their nominal concentrations.

In all analytical batches, at least $n=2$ samples containing no analyte or internal standard (BI/BI) will be extracted. Any peak detected at the retention time of the analyte should be less than 20% of the analyte mean peak area observed for the extracted samples at the LLOQ. Any peak detected at the retention time of the internal standard should be less than 5% of the mean peak area observed for the extracted samples containing the internal standard.

In all analytical batches, at least $n=2$ samples containing no analyte but with internal standard included (BI/IS) will be extracted to confirm the suitability of the internal standard for use in the assay at that concentration. Any peak detected at the retention time of the analyte as a result of the internal standard addition should be less than 20% of the analyte mean peak area observed for the extracted samples at the LLOQ.

STABILITY INFORMATION

The following stability parameters were successfully established during the validation studies B181-18 and B185-18.

Room temperature stability in matrix	25 hours established
Freeze thaw stability in matrix	5 cycles established
Reinjection (autosampler) stability	94 hours (refrigerated) established
Post-preparative extract stability	99 hours (refrigerated) established
Whole blood processing stability	4 hours
Effect of hemolysis	0.5% and 2% hemolysis; no impact
Refrigerated stock stability	40 days
Long term matrix storage stability	25 days at $\leq -60^{\circ}\text{C}$; ongoing

SAMPLE INFORMATION

The Bioanalytical Chemistry group at SRI received K₂ EDTA rat plasma samples from the Toxicology group on February 21, 2019. A total of 285 frozen samples were received and transferred to an ultra-low temperature freezer ($\leq -60^{\circ}\text{C}$) upon arrival. A total of 285 samples will be analyzed per the study protocol.

INCURRED SAMPLE REANALYSIS

Incurred sample reanalysis (ISR) will be performed during this study on at least 10% of study samples, or 21 samples, whichever number is greater. Per SRI SOP 006.062 *Bioanalytical Sample Reanalysis*, there must be a $\leq 20\%$ difference between the two results in order for an ISR result to be considered comparable to the original result. At least 67% of the ISR samples must meet the acceptance criteria in order for the overall ISR evaluation to be considered successful.

REFERENCES

SRI Test Method 106.202: Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma

SRI SOP 006.061: Bioanalytical Sample Analysis

SRI SOP 006.062: Bioanalytical Sample Reanalysis

SRI Report B181-18: Method Validation Report for the Quantitative Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma

SRI Report B185-18: Method Validation Report for the Quantitative Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Dog Plasma

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix G-4

**SRI TEST METHOD 106.202: “ANALYSIS OF [Proprietary Info] [Proprietary Info] AND
[Proprietary Info] IN K₂ EDTA RAT PLASMA”**

**TEST METHOD****Classification:** Project
Supersedes: NA (Original)**TM No.:** 106.202**Page:** 1 of 26**Effective:** JUL 15 2019**Subject:** Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma**A. PURPOSE/SCOPE**

This Test Method describes procedures to be employed for the analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA rat plasma using a protein precipitation extraction procedure and analysis by LC-MS/MS.

During sample analysis, SRI SOPs 006.061 *Bioanalytical Sample Analysis* and 006.062 *Bioanalytical Sample Reanalysis* will also be followed.

B. BACKGROUND/GENERAL

This Test Method will fully detail the experimental procedures used in the analysis, detection and quantitation of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA rat plasma. To summarize, [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA rat plasma (0.0200 ml sample size) will be extracted, using [Proprietary Info] [Proprietary Info] and [Proprietary Info] as the internal standard, by a protein precipitation extraction procedure. The supernatant is then diluted prior to injection on the LC-MS/MS system. The range of the assay is 5.00 – 1000 ng/ml [Proprietary] and [Proprietary] and 25.0 – 5000 ng/ml [Proprietary Info]

SIGNATURES**Prepared by:****Reviewed by:****Management Approval:****QAU Review:**

Redacted by agreement

07/12/19
Date07/15/19
Date7-15-19
Date07/15/2019
Date**SRI PROPRIETARY / CONFIDENTIAL**

**TEST METHOD****Classification:** Project**Supersedes:** NA (Original)**Subject:** Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma**TM No.:** 106.202**Page:** 2 of 26**Effective:** July 15, 2019**C. HEALTH AND SAFETY**

All personnel must observe standard laboratory safety practices. All personnel must wear protective equipment appropriate to the area in which they will work, which may include, but not be limited to: safety glasses, protective clothing and gloves.

D. TRAINING

All personnel involved in handling chemicals, equipment, and instruments must have attended the pertinent laboratory safety classes from SRI's Environmental Health & Safety Department and must have attended GLP training courses. Training must be documented.

E. EQUIPMENT AND MATERIALS

Chemicals, consumables or equipment may be substituted provided that equivalent assay performance is obtained.

E.1 Chemicals

- [Proprietary] [Proprietary] and [Proprietary] USP, Current Lot
- [Proprietary Info] [Proprietary Info] and [Proprietary Info] Medical Isotopes, Inc.
- Ammonium hydroxide, reagent grade
- Acetic acid, LC-MS grade
- Milli-Q water, Millipore
- Formic acid, reagent grade
- Dimethyl Sulfoxide (DMSO), reagent grade
- Methanol, HPLC grade
- Acetonitrile, HPLC grade
- Isopropanol, reagent grade
- K₂ EDTA rat plasma, BioIVT

E.2 Consumables

- HPLC column: Phenomenex Synergi Polar RP 100 x 2mm, 4µm
- 0.5 µm stainless-steel pre-column frit (Upchurch Scientific)
- Assorted disposable pipette tips
- Disposable 1.5 ml and 2.0 ml polypropylene microcentrifuge tubes

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**TEST METHOD****Classification:** Project**Supersedes:** NA (Original)**Subject:** Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma**TM No.:** 106.202**Page:** 3 of 26**Effective:** July 15, 2019

- Disposable 15 ml conical polypropylene test tubes and caps
- Disposable glass vials and caps, assorted sizes
- Glass autosampler vials with inserts and caps

E.3 Equipment

- Air displacement pipettor, Rainin
- Positive displacement pipettor, Gilson
- Repeater pipettor, Eppendorf
- Mettler Toledo AG 285 balance
- VWR Mini Vortexer
- Beckman Coulter Microfuge® 18 Centrifuge, 20 Centrifuge
- Shimadzu Corp. LC-20AD Prominence Pumps (incorporates Shimadzu Corp. CBM-20A Prominence Communications Bus Module and Shimadzu DGU-20A_{3R} Prominence degasser
- Shimadzu Corp. CTO-20AC Prominence Column Oven
- CTC Analytics HTS-xt Autosampler
- AB Sciex 5500 Mass Spectrometer

F. PROCEDURES

Note: SRI Forms 106.202A through 106.202E will be used to assist in raw data recording for the experimental phases of this study. The completed attachments or other documentation must be stored in the study file.

F.1 Preparation of Reagents

Volumes of these reagents can be adjusted as long as proportionality is maintained and their preparation is documented in the raw data.

F.1.1 2% Acetic Acid in Water (Mobile Phase A)

Add 20.0 ml of acetic acid to 1000 ml of Milli-Q water in a glass bottle and store the solution at room temperature. The expiration date for this solution is one month after preparation.

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**TEST METHOD****Classification:** Project**Supersedes:** NA (Original)**Subject:** Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma**TM No.:** 106.202**Page:** 4 of 26**Effective:** July 15, 2019**F.1.2 0.1% Acetic Acid in Acetonitrile (Mobile Phase B)**

Add 1.00 ml of acetic acid to 1000 ml of acetonitrile in a glass bottle and store the solution at room temperature. The expiration date for this solution is one month after preparation.

F.1.3 Acetonitrile : Isopropanol (80:20, v:v) with 1% Ammonium Hydroxide (Needle Rinse 1)

Add 400 ml acetonitrile to 100 ml isopropanol and 5.00 ml ammonium hydroxide in a glass bottle and store the solution at room temperature. The expiration date for this solution is one month after preparation.

F.1.4 Water : Methanol (90:10, v:v) with 1% Formic Acid (Needle Rinse 2)

Add 450 ml Milli-Q water to 50.0 ml methanol and 5.00 ml formic acid in a glass bottle and store the solution at room temperature. The expiration date for this solution is one month after preparation.

F.1.5 0.2% Acetic Acid in Methanol (Diluent Solution)

Add 0.400 ml acetic acid to 200 ml methanol in a glass bottle and store the solution at room temperature. The expiration date for this solution is one month after preparation.

F.1.6 Water : Methanol (90:10, v:v) with 0.1% Acetic Acid (Reconstitution Solution)

Add 180 ml Milli-Q water to 20.0 ml methanol and 0.200 ml acetic acid in a glass bottle and store the solution at room temperature. The expiration date for this solution is one month after preparation.

F.2 Preparation of Stock and Spiking Solutions

The following standard preparation scheme is a suggested approach. Appropriate modifications to reach the targeted nominal calibrant and quality control (QC) standard concentrations are acceptable. For example, if the targeted nominal concentration is not achieved when the analyte calibration standard primary stock solution is obtained, the volume of this stock solution used in subsequent dilutions can be modified in order to achieve the targeted nominal calibration standard matrix concentrations. The actual volumes of standards used will be documented in the raw data. Volumes of these stock solutions can be adjusted as long as proportionality is maintained and their preparation is documented in the study binder.

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**TEST METHOD****Classification:** Project**Supersedes:** NA (Original)**Subject:** Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma**TM No.:** 106.202**Page:** 5 of 26**Effective:** July 15, 2019

Analytical reference standards are corrected for purity, water and salt content, if applicable. Internal standard stocks may not be corrected for purity, water or salt.

Example purity calculation:

$$\text{Purity} = \frac{[\text{HPLC \% purity} \times (100 - \% \text{ water} - \% \text{ residual solvent})]}{100} \times \frac{\text{Free base molecular weight}}{\text{Salt form molecular weight}}$$

F.2.1 Preparation of [Proprietary] [Proprietary] and [Proprietary] Stock Solutions (1.00 mg/ml)

Accurately weigh out approximately 5.00 mg of [Proprietary] into a glass vial and dilute to a concentration of 1.00 mg/ml using dimethyl sulfoxide (DMSO). The purity of the compound must be taken into account when preparing this stock (Stock A). Repeat this step to produce a second stock solution at the same concentration (Stock B). Repeat to get duplicate weighings for [Proprietary] at the same concentration.

To prepare [Proprietary] stock solutions, weigh approximately 5.00 mg of [Proprietary] into a glass vial and dilute to a concentration of 1.00 mg/ml using Milli-Q water. Repeat this step to produce a second stock solution at the same concentration.

Store all stock solutions refrigerated (set point 5 °C ± 3 °C) until use.

F.2.2 Preparation of [Proprietary Info] [Proprietary Info] and [Proprietary Info] Stock Solutions (Internal Standard), 1.00 mg/ml

These Internal Standards are supplied by Medical Isotopes, Inc. as 1.00 mg amounts in a glass vial. Add 1.00 ml of DMSO to the [Proprietary Info] and [Proprietary Info] to produce a 1.00 mg/ml stock. Repeat for [Proprietary Info] using Milli-Q water instead of DMSO.

Store all internal standard stock solutions refrigerated (set point 5 °C ± 3 °C) until use.

F.2.3 Preparation of [Proprietary Info] [Proprietary Info] and [Proprietary Info] Internal Standard Secondary Stock Solutions

Accurately add 0.0100 ml of the 1.00 mg/ml [Proprietary Info] and [Proprietary Info] internal standard stock solutions, and 0.0500 ml of the 1.00 mg/ml [Proprietary Info] internal standard stock solution into a glass vial containing 9.930 ml of 0.2%

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acetic acid in methanol. The final concentration of the internal standard secondary stock solution will be 1.00 µg/ml [Proprietary Info] and [Proprietary Info] and 5.00 µg/ml [Proprietary Info]. This solution can be stored refrigerated (set point 5 °C ± 3 °C) until use.

F.2.4 Preparation of [Proprietary Info] [Proprietary Info] and [Proprietary Info] Internal Standard Spiking Solution

Accurately add 2.50 ml of the internal standard secondary stock solution into a glass bottle containing 97.5 ml of 0.2% acetic acid in methanol. The final concentration of the internal standard spiking solution will be 25.0 ng/ml [Proprietary Info] and [Proprietary Info] and 125 ng/ml [Proprietary Info]. This solution can be stored refrigerated (set point 5 °C ± 3 °C) until use.

Per SRI SOP 006.063, *Reference Material Receipt and Stock, Spiking Solution and Calibration and Quality Control Sample Preparation / Expiration* internal standard stock and spiking solutions will be given a default expiration date of 6 months after preparation.

F.2.5 Stock Verification

In order to determine the accuracy of preparation, the duplicate stock solutions will be verified prior to use. A suggested approach for the preparation of stock verification solutions is given here, although alternative final concentrations may be used providing that a suitable analyte and internal standard response is achieved. The duplicate stock solutions prepared in step F.2.1 should be diluted by spiking 0.0100 ml of the 1.00 mg/ml [Proprietary] and [Proprietary] stock solutions and 0.0500 ml of the 1.00 mg/ml [Proprietary] stock solution into 9.930 ml of Diluent Solution. These duplicate vials are briefly vortexed and 0.100 ml is removed and added to a vial containing 0.900 ml Diluent Solution. Vortex, then remove 0.0325 ml of this solution and place into a separate vial containing 0.0203 ml of internal standard spiking solution and 0.947 ml of Reconstitution Solution. The final concentration of [Proprietary] and [Proprietary] is 3.25 ng/ml and the final concentration of [Proprietary] is 16.3 ng/ml. The final concentration of [Proprietary Info] and [Proprietary Info] is 0.508 ng/ml and the final concentration of [Proprietary Info] is 2.54 ng/ml. The duplicate samples are injected in replicates of $n \geq 3$ onto the LC-MS/MS system.

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To be considered acceptable for use, the stocks must agree to within 5% of each other, calculated as follows:

% difference =

$$\frac{(\text{Mean of peak area ratio of stock A} - \text{Mean of peak area ratio of stock B})}{(\text{Mean of peak area ratio of stock A} + \text{Mean of peak area ratio of stock B})/2} \times 100$$

If these stocks agree within 5% of each other, one single stock may be used for the preparation of both calibrants and Quality Control (QC) samples.

Alternatively, one stock may be used for the preparation of calibrants while the other stock can be used for the preparation of QC samples.

If these stocks do not agree, a third weighing may be performed and the three stocks compared against each other. If two stocks agree with each other these may be used to prepare calibrants and QCs, and the other stock can be discarded.

F.2.6 Test Mix Preparation

A solution prepared at the LLOQ level (or below Low QC concentration) shall be prepared and injected at the start and the end of each bioanalytical run (system suitability). This solution will contain both analyte and internal standard. To prepare at the LLOQ level, spike 0.0100 ml of the 1.00 mg/ml [Proprietary] and [Proprietary] stock solutions and 0.0500 ml of the 1.00 mg/ml [Proprietary] stock solution into 9.930 ml of Diluent Solution. Vortex, remove 0.100 ml, and add to a vial containing 0.900 ml of Diluent Solution. Vortex, remove 0.0100 ml, and add to a vial containing 0.990 ml of Diluent Solution. This solution may be stored refrigerated for up to 3 months from the date of preparation. On the day of use, remove 0.0203 ml of this solution and place into a separate vial containing 0.0203 ml of internal standard spiking solution and 0.959 ml of Reconstitution Solution. The final concentration of [Proprietary] and [Proprietary] is 0.0203 ng/ml and the final concentration of [Proprietary] is 0.102 ng/ml. The final concentration of [Proprietary Info] and [Proprietary Info] is 0.508 ng/ml and the final concentration of [Proprietary Info] is 2.54 ng/ml. The final concentrations mimic the final theoretical concentrations of [Proprietary] [Proprietary] and [Proprietary] and internal standards seen in LLOQ samples post-extraction.

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F.2.7 Remove approximately 40.0 ml of control K₂ EDTA rat plasma from storage and allow it to equilibrate to room temperature. The matrix may be centrifuged at approximately 3000 RPM for 10 minutes prior to use to remove excess particulates. Prepare QC samples in polypropylene vials as shown in the table below. Note that the Solution Spiking Volumes are combined with the Matrix Volumes. Volumes of these QC samples can be adjusted as long as proportionality is maintained and their preparation is properly documented in the study raw data.

Quality Control Sample Preparation						
QC ID	Spiking Solution ID	Spiking Solution Concentration (µg/ml)	Spiking Volume (ml)	Matrix Volume (ml)	Final Volume (ml)	Nominal Matrix Concentration (ng/ml)
QC- Low	QC-Mid	0.400 / 0.400 / 2.00	0.0375	0.9625	1.00	15.0 / 15.0 / 75.0
QC- Mid	QC-Dil	5.00 / 5.00 / 25.0	0.0800	0.920	1.00	400 / 400 / 2000
QC- High	QC-Dil	5.00 / 5.00 / 25.0	0.160	0.840	1.00	800 / 800 / 4000
QC- Dil	[Proprietary] Stock A/B;	1000	0.0100	1.930	2.00	5000
	[Proprietary] Stock A/B;	1000	0.0100			5000
	[Proprietary] Stock A/B.	1000	0.0500			25000

Either Stock A or Stock B may be used, assuming equivalency is achieved.

The values in the “Spiking Solution Concentration” and the “Nominal Matrix Concentration” columns represent the concentrations of [Proprietary] [Proprietary] and [Proprietary] respectively.

These QC samples may be aliquoted into appropriate volumes into polypropylene tubes (suggested 150 µl volumes) and stored in a ≤-60 °C freezer until use, providing that sufficient stability in matrix has been successfully validated under these conditions. QC samples may also be freshly prepared on the day of extraction.

F.3 Extraction Procedure

Each bioanalytical run will be comprised of bracketing calibration curves (8 points) each with a matrix blank sample (matrix with neither analyte nor internal standard spiked) and a control blank (matrix with only internal standard included). It is recommended that a carryover blank (matrix blank) be injected after each upper limit of quantitation (ULOQ) calibration standard to assess any carryover present. Duplicate System Suitability samples will be injected, one before the first calibration curve and one at the end of the batch. Interspersed between the calibration curves will be $n \geq 2$ QC samples at low, mid and high concentration.

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The dilution QC, when used, should be extracted in multiples of $n=3$. It is not required to run the dilution QC with a batch where samples are diluted, provided that the level of sample dilution did not exceed what was previously validated. However, for troubleshooting practices, the dilution QC may be analyzed with each batch, at the discretion of the bioanalytical scientist. If study samples are diluted with multiple dilution factors, then the dilution QC may be similarly diluted (with replicates of $n=3$ for each dilution factor used), or alternatively, the highest dilution factor used for study samples will be used for the extraction of the dilution QC. It is also acceptable if low dilution factors are applied to study samples to use a high QC in place of the dilution QC, in order that the diluted sample falls within the calibration range. If the level of dilution required for study samples exceeds the dilution factor previously validated, then the dilution QC will need to be revalidated at the dilution factor required, in replicates of 6.

In order to facilitate the equilibration of the instrument, multiple injections of extracts (Conditioning Samples) may be injected before each batch. It is recommended to prepare conditioning samples near the LLOQ level, but providing that internal standard is present in the sample, the actual concentration used may change. Conditioning samples will be pooled, where more than one calibration standard or QC sample, at different concentrations, are combined. Individual study samples, calibration standards, and QC samples will not be used as conditioning samples without pooling. It is not acceptable to condition a batch using an old standard curve from a previous batch. It is acceptable to prepare either multiple pooled conditioning samples, or to re-inject the pooled sample from the same vial, depending on the final extract volume. The conditioning injections will be included as part of the analytical batch and will be printed with the rest of the batch. Approximately 10 conditioning injections will be analyzed prior to the start of each batch. If one batch is analyzed immediately following another, later batches may not require conditioning injections, although duplicate system suitability injections will be included.

Remove the calibration standard spiking solutions, internal standard spiking solution, QC samples and control matrix (approximately 10.0 ml) from storage and allow them to equilibrate to room temperature.

Follow the scheme listed below to prepare the calibration standards. The calibration standards are prepared in polypropylene tubes. Calibration standards may be discarded after use. Note that the Spiking Solution Volumes are combined with the Matrix Volumes.

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Preparation of Calibration Standards in Matrix						
Calibration Standard ID	Spiking Solution ID	Spiking Solution Concentration (µg/ml)	Spiking Volume (ml)	Matrix Volume (ml)	Final Volume (ml)	Nominal Matrix Concentration (ng/ml)
Std-1	Std-5	0.100 / 0.100 / 0.500	0.0250	0.475	0.500	5.00 / 5.00 / 25.0
Std-2	Std-5	0.100 / 0.100 / 0.500	0.0500	0.450	0.500	10.0 / 10.0 / 50.0
Std-3	Std-5	0.100 / 0.100 / 0.500	0.100	0.400	0.500	20.0 / 20.0 / 100
Std-4	Std-8	1.00 / 1.00 / 5.00	0.0250	0.475	0.500	50.0 / 50.0 / 250
Std-5	Std-8	1.00 / 1.00 / 5.00	0.0500	0.450	0.500	100 / 100 / 500
Std-6	Std-8	1.00 / 1.00 / 5.00	0.100	0.400	0.500	200 / 200 / 1000
Std-7	Std-9	10.0 / 10.0 / 50.0	0.0250	0.475	0.500	500 / 500 / 2500
Std-8	Std-9	10.0 / 10.0 / 50.0	0.0500	0.450	0.500	1000 / 1000 / 5000
Std-9	[Proprietary] Stock A/B;	1000	0.0100	0.930	1.00	10000
	[Proprietary] Stock A/B;	1000	0.0100			10000
	[Proprietary] Stock A/B	1000	0.0500			50000

Either Stock A or Stock B may be used, assuming equivalency is achieved.

The values in the "Spiking Solution Concentration" and the "Nominal Matrix Concentration" columns represent the concentrations of [Proprietary] [Proprietary] and [Proprietary] respectively.

These calibration standards may be aliquoted into appropriate volumes into polypropylene tubes (suggested 150 µl volumes) and stored in a ≤-60 °C freezer until use, providing that sufficient stability in matrix has been successfully validated under these conditions. Calibration standards may also be freshly prepared on the day of extraction.

- F.3.1** Transfer 0.0200 ml of each calibration standard, QC sample, study sample and blank into separate 1.50 ml microcentrifuge tubes. If needed, extra samples may be extracted in order to be used as Conditioning Samples. These should be pooled before use.
- F.3.2** Add 0.100 ml of 0.2% acetic acid in methanol to the matrix blanks. Cap tubes and vortex for approximately 5 seconds.
- F.3.3** Add 0.100 ml of the Internal Standard Spiking Solution to each calibration standard, QC standard, study sample and control blank. Cap tubes and vortex for approximately 5 seconds.
- F.3.4** Centrifuge tubes at approximately 18000g for approximately 10 minutes.
- F.3.5** Transfer 0.0250 ml of the supernatant into a 2.00 ml HPLC vial containing 1.00 ml Reconstitution Solution. Cap and vortex briefly to mix.

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F.3.6 Store on the autosampler (set point 5 °C ± 3 °C) or refrigerated (set point 5 °C ± 3 °C).

F.4 Analytical Conditions

Equipment can be substituted provided that equivalent assay performance is obtained.

Refer to Figures 1-3 in this Test Method for an example of representative chromatograms of each analyte at the LLOQ level.

F.4.1 HPLC Conditions

Autosampler:	CTC Analytics HTS-xt
Pumps:	Shimadzu LC-20AD Prominence. Incorporates Shimadzu CBM-20A Prominence communications bus module and Shimadzu DGU-20A _{3R} Prominence degasser Shimadzu CTO-20AC Prominence
Column Oven:	Set point 5 °C
Autosampler Temp:	
Column Oven Temp:	Set point 25 °C
Column:	Phenomenex Synergi Polar RP 100 x 2 mm, 4µm
Pre-column Frit:	0.5 µm stainless-steel Precolumn Frit (Upchurch Scientific)
Flow Rate:	0.350 ml/min
Run Time:	8.0 minutes
Injection Volume:	10 µl*
Mobile Phase A:	2% acetic acid in water
Mobile Phase B:	0.1% acetic acid in acetonitrile
Needle Rinse 1:	Acetonitrile:isopropanol (80:20, v:v) with 1% ammonium hydroxide
Needle Rinse 2:	Water:methanol (90:10, v:v) with 1% formic acid
Pre clean with Needle	1*, 1*
Rinses 1 and 2:	
Post clean with Needle	2*, 2*
Rinse 1 and 2:	
Valve clean with Needle	2*, 2*
Rinse 1 and 2:	
Retention Time:	4.3 minutes [Proprietary] and IS) 4.2 minutes [Proprietary] and IS) 1.4 minutes [Proprietary] and IS)

* may be modified to improve performance

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Time (min)	% A	% B
0.01	98	2
2.00	98	2
2.10	50	50
4.00	2	98
5.50	2	98
5.51	98	2
8.00	98	2

Switching Valve program

Total Time (minutes)	Position
0.0 to 0.2*	Divert to Waste
0.2 to 5.0*	Divert to MS
5.0 to 8.0*	Divert to Waste

* may be modified to improve performance

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Mass Spectrometer: AB Sciex 5500 Mass Spectrometer

Interface: Turbo IonSpray positive-ion mode

Scan Mode: Multiple Reaction Monitoring (MRM)

IS: 5500V*

EP: 10V*

DP:	71V*	Proprietary Info	81V*	Proprietary Info
	121V		76V*	
	76V*		56V*	
CE:	21V*		19V*	
	25V*		25V*	
	33V*		35V*	
CXP:	38V*		20V*	
	26V*		24V*	
	14V*		14V*	

Resolution Q1, Q3: Unit, Unit

CUR Gas: 20*

CAD Gas: 8*

GS1: 60*

GS2: 60*

Source Temp: 650 °C*

Dwell: 80* ms

Nominal	[Proprietary]	m/z 629.3* → 447.2*
Transitions:	[Proprietary]	m/z 721.3* → 296.1*
	[Proprietary]	m/z 288.1* → 176.1*
	[Proprietary Info]	m/z 637.4* → 447.2*
	[Proprietary Info]	m/z 727.4* → 302.2*
	[Proprietary Info]	m/z 294.1* → 182.1*

* May be modified to improve performance. The eventual m/z ratios used must be within ± 0.3 amu from the masses quoted above.)

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F.5.1 Chromatograms will be automatically integrated using AB Sciex Analyst software (Version 1.6.2) or equivalent and visually inspected for an acceptable integration.

F.5.2 Compute the 1/x weighted least-squares linear regression [Proprietary] and [Proprietary] and the 1/x² weighted least-squares linear regression [Proprietary Info] using Analyst software, relating the peak area ratios (relative to internal standard) of the calibration standards to their respective nominal concentrations (ng/ml in plasma) for [Proprietary] [Proprietary] and [Proprietary]

F.5.3 Using the peak area ratios (relative to the internal standard) of the standards and the regression equation constants, concentrations for analyte in the QC samples and study samples can be interpolated.

F.5.4 Compute the correlation coefficient for the standard data.

F.6. Acceptance Criteria**F.6.1 System Suitability Standard**

There are no formal acceptance criteria for the System Suitability samples. The system suitability sample will be injected at the beginning and at the end of a run and inspected to ensure signal-to-noise ratio and peak shape are adequate for quantitation. Any chromatographic change between these injections which may have an impact on the ability to accurately quantitate the samples will be noted, however there is no formal acceptance criteria for this. The system suitability injections will be printed with the other chromatograms in the analytical batch.


F.6.2 Calibration Standard Acceptance Criteria

F.6.2.1 The lower limit of quantitation (LLOQ) standard back-calculated concentration must be within $\pm 20\%$ of theoretical nominal concentration.

F.6.2.2 To meet acceptance criteria, the back-calculated concentration of a calibration standards (excluding at the LLOQ level) must be within 15% of their nominal theoretical concentrations.

F.6.2.3 A minimum of three-quarters of calibration standards must meet these criteria.

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F.6.2.4 Any standards failing to meet the acceptance criteria will be excluded from the regression, starting with the calibration standard which is furthest away from the nominal concentration.

F.6.3 Quality Control (QC) Sample Acceptance Criteria.

F.6.3.1 To meet acceptance criteria, the back-calculated concentration of a QC sample must be within 15% of their nominal theoretical concentrations.

F.6.3.2 At least two-thirds of all assay QCs (low, mid and high) must meet the acceptance criteria.

F.6.3.3 At least 50% of the QCs at each level must meet the acceptance criteria.

F.6.3.4 For dilution QCs, which are generally assayed using multiples of n=3 replicates, at least 67% (rounded) of the QCs must be within 15% of their nominal theoretical concentrations. Failure of a dilution QC does not mean that the batch itself has failed if the low, mid and high QCs meet acceptance criteria as defined above. However, any samples diluted in a batch with a failed dilution QC should be repeated and the value from this batch discarded. If more than one dilution scheme was followed in a batch of samples, with corresponding dilution QCs prepared using different dilution factors, only the dilution QC which failed acceptance criteria will be rejected and the associated samples repeated.


F.6.4 Blank Acceptance Criteria

At least 50% of matrix blanks (including carryover blanks, BI/BI) and 50% of control blanks (BI/IS) must have a response (peak area) less than or equal to 20% of the mean accepted LLOQ calibration standards. Carryover blanks should be positioned in the run in a manner capable of determining assay carryover, for example, after each ULOQ calibration standard injection.

F.7 Data Reporting

Concentrations found below the lowest calibration standard concentration, will be reported as below the quantitation limit. Where no peak is detected (ND), the result will be flagged as (<LLOQ). Over-diluted samples falling below the calibration range (assuming insufficient to reassay) will be reported as <LLOQ (LLOQ value x dilution factor).

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G. STABILITY/METHOD PARAMETERS

G.1 Solutions

<u>Parameter Evaluated</u>	<u>Validated Result</u>	<u>Study Reference</u>
Analyte Stability in Stock Solutions at 5±3 °C:	40 days	B185-18

G.2 Matrix, K₂ EDTA Rat Plasma

<u>Parameter Evaluated</u>	<u>Validated Result</u>	<u>Study Reference</u>
Room Temperature Stability in Matrix:	25 hours	B181-18
Freeze/Thaw Stability in Matrix:	5 cycles	B181-18
Re-injection Stability:	94 hours, refrigerated	B181-18
Post Preparative Extract Stability:	99 hours, refrigerated	B181-18
Validated Dilution Factor:	10-fold, 50-fold	B181-18
Long-Term Stability in Matrix at ≤-60°C:	25 days	B181-18
Effect of 2% Hemolysis:	No impact	B181-18
Whole Blood Stability:	4 hours, refrigerated	B181-18
Maximum Batch Size:	101 samples	B181-18
Incurred Sample Reanalysis:	TBD	M398-18

TBD: To be determined.

H. REFERENCES

- H.1 B181-18: "Method Validation Report for the Quantitative Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Rat Plasma"
- H.2 B185-18: "Method Validation Report for the Quantitative Analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA Dog Plasma".
- H.3 M398-18: "GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with
- H.4 [Proprietary] [Pro] in Sprague Dawley Rats".
- H.5 SRI SOP 006.061, *Bioanalytical Sample Analysis*
- H.6 SRI SOP 006.062, *Bioanalytical Sample Reanalysis*
- H.7 SRI SOP 006.063, *Reference Material Receipt and Stock, Spiking Solution and Calibration and Quality Control Sample Preparation / Expiration*

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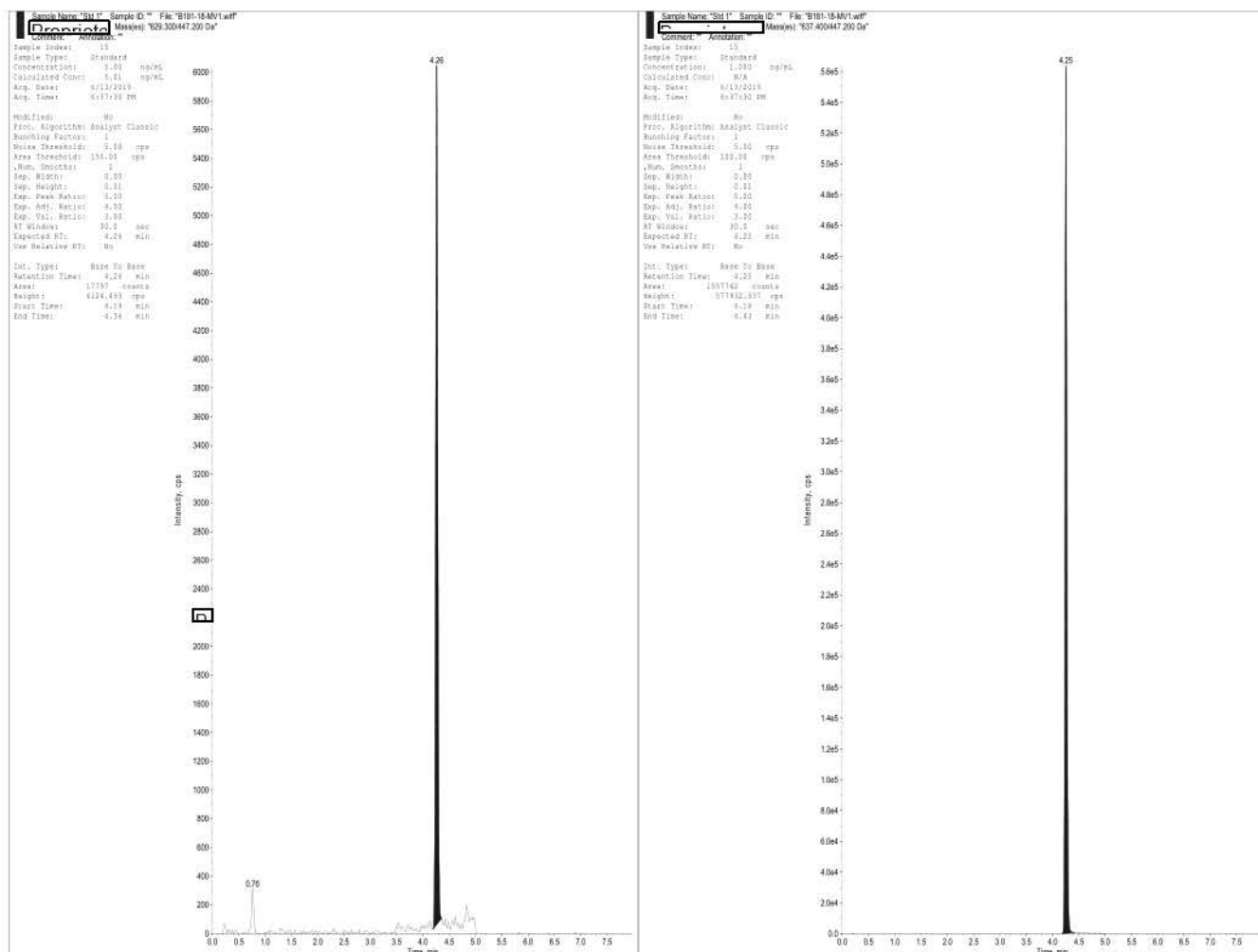
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I. FIGURES

I.1 Figure 1. Representative Proprietary Chromatogram of a K₂ EDTA Rat Plasma Sample Spiked at the Lower Limit of Quantitation (LLOQ)



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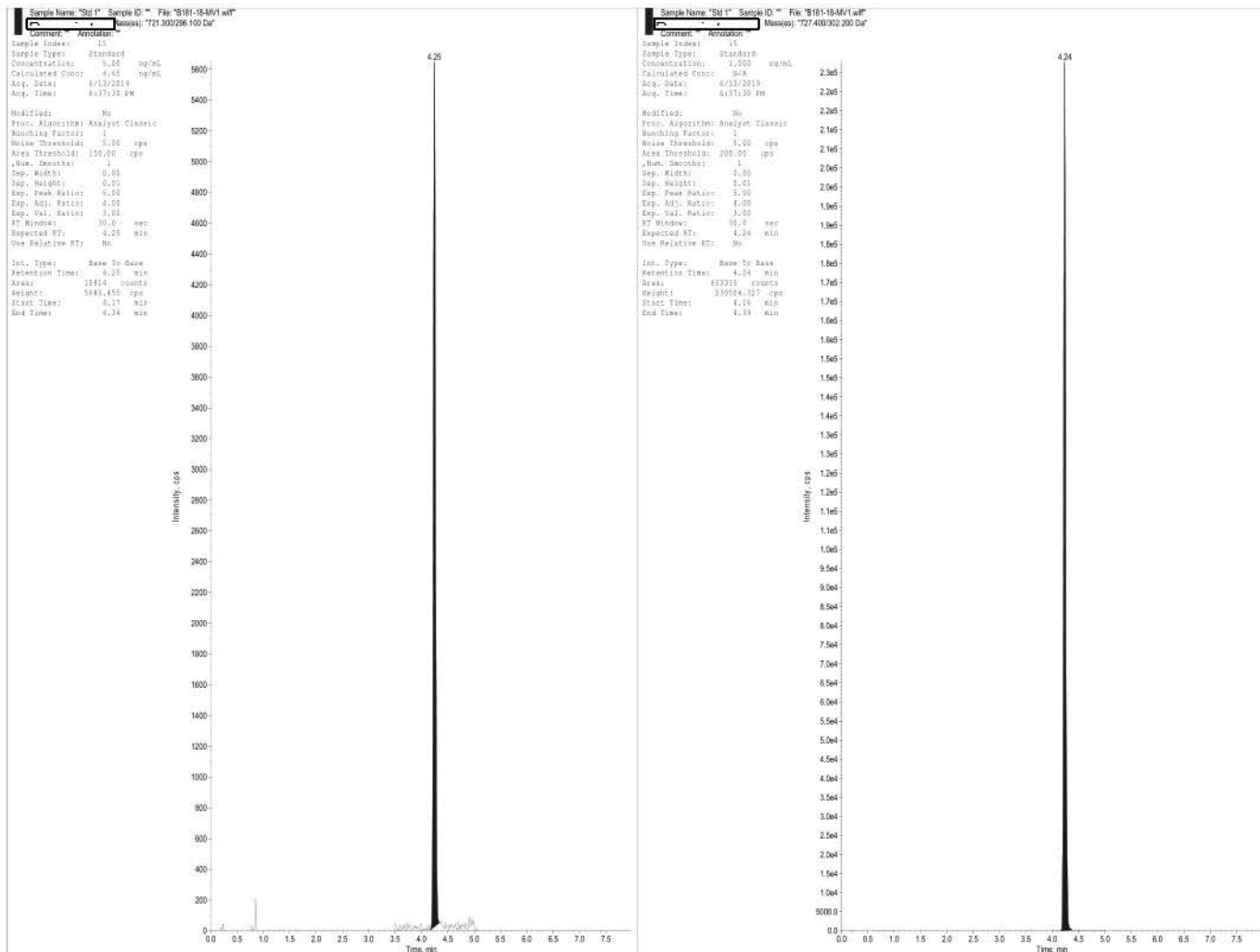
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I.2 Figure 2. Representative [Proprietary] Chromatogram of a K₂ EDTA Rat Plasma Sample Spiked at the Lower Limit of Quantitation (LLOQ)



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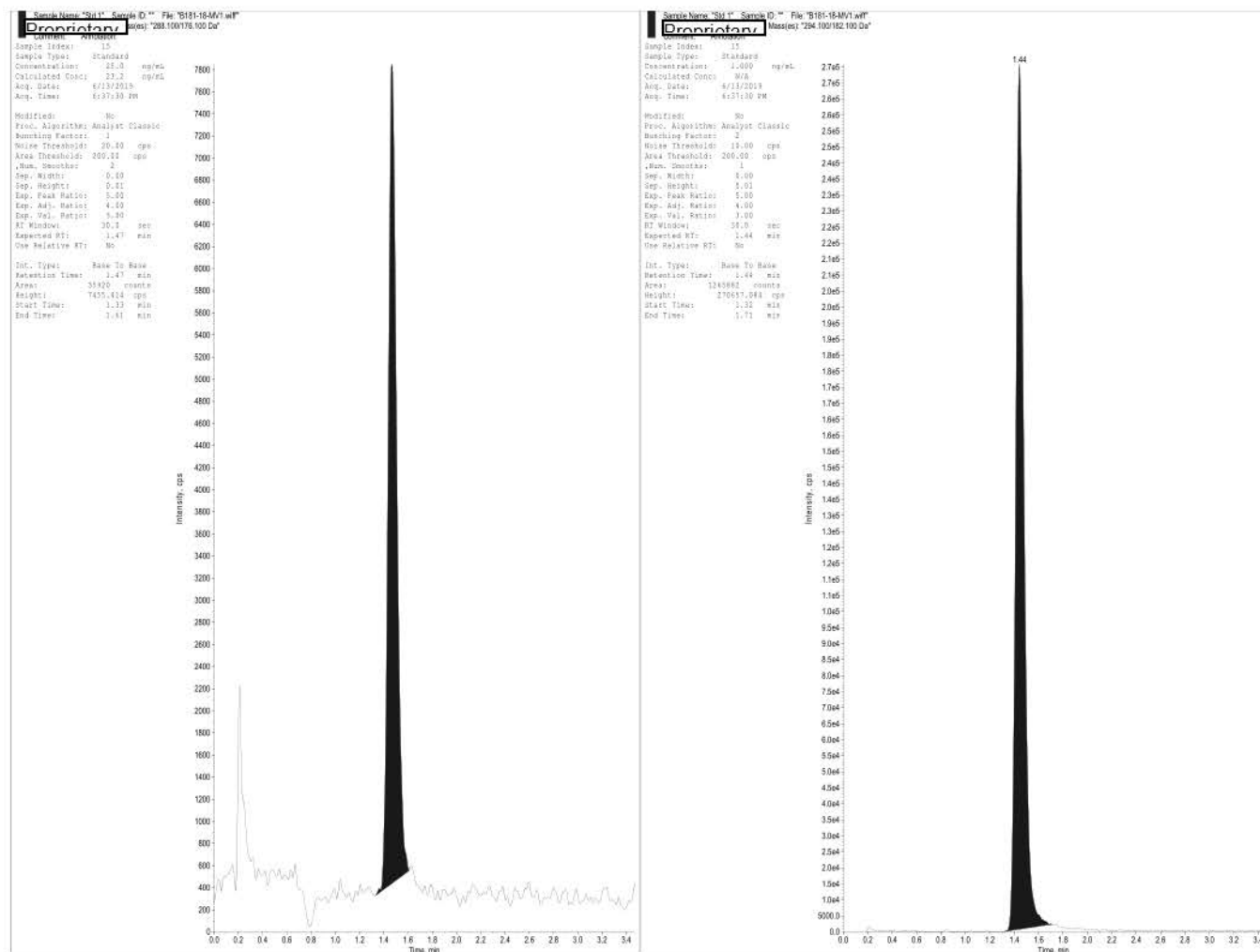
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I.3 Figure 3. Representative [Proprietary] Chromatogram of a K₂ EDTA Rat Plasma Sample Spiked at the Lower Limit of Quantitation (LLOQ)



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J. ATTACHMENTS

- J.1** Extraction Form (SRI Form 106.202A)
- J.2** Methodology and Reagent List (SRI Form 106.202B)
- J.3** Instrument Analytical Conditions and Reagents (SRI Form 106.202C)
- J.4** Instrument Reagent Preparation (SRI Form 106.202D)
- J.5** Extraction Reagent Preparation (SRI Form 106.202E)

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Study ID:

Batch ID:

EXTRACTION FORM

Preparation of Calibration Standards in Matrix						
Calibration Standard ID	Spiking Solution ID	Spiking Solution Concentration (µg/ml)	Spiking Volume (ml)	Matrix Volume (ml)	Final Volume (ml)	Nominal Matrix Concentration (ng/ml)
Std-1	Std-5	0.100 / 0.100 / 0.500	0.0250	0.475	0.500	5.00 / 5.00 / 25.0
Std-2	Std-5	0.100 / 0.100 / 0.500	0.0500	0.450	0.500	10.0 / 10.0 / 50.0
Std-3	Std-5	0.100 / 0.100 / 0.500	0.100	0.400	0.500	20.0 / 20.0 / 100
Std-4	Std-8	1.00 / 1.00 / 5.00	0.0250	0.475	0.500	50.0 / 50.0 / 250
Std-5	Std-8	1.00 / 1.00 / 5.00	0.0500	0.450	0.500	100 / 100 / 500
Std-6	Std-8	1.00 / 1.00 / 5.00	0.100	0.400	0.500	200 / 200 / 1000
Std-7	Std-9	10.0 / 10.0 / 50.0	0.0250	0.475	0.500	500 / 500 / 2500
Std-8	Std-9	10.0 / 10.0 / 50.0	0.0500	0.450	0.500	1000 / 1000 / 5000
Std-9	Proprietary Stock A/B;	1000	0.0100	0.930	1.00	10000
	Proprietary Stock A/B;	1000	0.0100			10000
	Proprietary Stock A/B	1000	0.0500			50000

Preparation of Quality Control Samples in Matrix						
QC ID	Spiking Solution ID	Spiking Solution Concentration (µg/ml)	Spiking Volume (ml)	Matrix Volume (ml)	Final Volume (ml)	Nominal Matrix Concentration (ng/ml)
QC-Low	QC-Mid	0.400 / 0.400 / 2.00	0.0375	0.9625	1.00	15.0 / 15.0 / 75.0
QC-Mid	QC-Dil	5.00 / 5.00 / 25.0	0.0800	0.920	1.00	400 / 400 / 2000
QC-High	QC-Dil	5.00 / 5.00 / 25.0	0.160	0.840	1.00	800 / 800 / 4000
QC-Dil	Proprietary Stock A/B;	1000	0.0100	1.930	2.00	5000
	Proprietary Stock A/B;	1000	0.0100			5000
	Proprietary Stock A/B	1000	0.0500			25000

Species: _____ Anticoagulant/Matrix: _____ Matrix Supplier: _____

Lot: _____ Matrix Expiration Date: _____

Pipette IDs: _____

Calibration Spiking Solution: _____ Expiration Date: _____

QC Sample Spiking Solution: _____ Expiration Date: _____

Prepared by: _____ Date: _____

SRI Form 106.202A
07/15/19**SRI PROPRIETARY / CONFIDENTIAL**

Obtained via FOIA by White Coat Waste Project

Study ID:

Batch ID:

METHODOLOGY AND REAGENT LIST

Step	Description	Equipment or Pipettes used	Step completed (check)
1	Transfer 0.0200 ml of each calibration standard, QC sample, study sample and blank into separate 1.50 ml microcentrifuge tubes.		
2	Add 0.100 ml of 0.2% acetic acid in methanol to the matrix blanks. Cap and vortex for approximately 5 seconds.		
3	Add 0.100 ml of the Internal Standard Spiking Solution to each calibration standard, QC sample, study sample and control blank. Cap and vortex for approximately 5 seconds.		
4	Centrifuge tubes at approximately 18000 g for approximately 10 minutes.		
5	Transfer 0.0250 ml of the supernatant into a 2.00 ml HPLC vial containing 1.00 ml Reconstitution Solution. Cap and vortex briefly to mix.		
6	Store on the autosampler (set point 5°C ± 3°C) or refrigerated (5°C ± 3°C).	End of extraction (time):	

Ⓐ Eppendorf Repeater Plus / M4 (circle one) Equipment ID: _____ Exp: _____

Dilution Scheme (1:_____)	Add _____ ul sample to _____ ul control matrix and vortex.	Pipettes:
Dilution Scheme (1:_____)	Add _____ ul sample to _____ ul control matrix and vortex.	
Dilution Scheme (1:_____)	Add _____ ul sample to _____ ul control matrix and vortex.	

Procedure Performed by: _____ Date: _____

Study ID:

Batch ID:

METHODOLOGY AND REAGENT LIST (cont.)**Additional information, if required:**

Test Mix Dilution: Remove the Test Mix in 2% acetic acid in methanol from storage (ID: _____ Exp: _____) and remove 0.0203 ml of this solution and place into a separate HPLC vial containing 0.0203 ml of internal standard spiking solution and 0.959 ml of Reconstitution Solution. Store with batch.

Pipettes: _____

REAGENT LIST

Reagent Description	Assigned ID	Supplier	Lot #	Grade	Exp.
K ₂ EDTA Rat Plasma	NA			NA	
Internal Standard		NA	NA	NA	
0.2% Acetic Acid in Methanol (Diluent)		NA	NA	NA	
Water:Methanol (90:10, v:v) with 0.1% Acetic Acid (Reconstitution Solution)		NA	NA	NA	
Initial/Date:					

Study ID:	Batch ID:
-----------	-----------

INSTRUMENT ANALYTICAL CONDITIONS AND REAGENTS

HPLC Column ID.	Vendor:	Calibration due date
Phenomenex Synergi Polar RP 100 x 2 mm, 4µm	Description:	NA
	Dimension:	
	S/N:	
Column Heater	Equipment Tracking #- _____	
Column Temp (Set Point 25°C)	Set Point _____ °C	NA
Pump ID	Equipment Tracking #- _____	
Pump Pressures at Start	_____ psi	NA
Autosampler ID	Equipment Tracking #- _____	
Autosampler Temp (Set Point 5°C ± 3°C)	Set Point _____ °C	NA
Mass Spectrometer	Equipment Tracking #- _____	
		Exp. Date
Mobile Phase A		
Mobile Phase B		
Needle Rinse 1		
Needle Rinse 2		
Number of Conditioning Injections		NA

NA: Not Applicable

Initial: _____ Date: _____

Additional Comments / Incidents during analysis:

SRI Form 106.202C
07/15/19

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Obtained via FOIA by White Coat Waste Project

INSTRUMENT REAGENT PREPARATION

Study Number: _____

Mobile Phase A:

Assigned ID: _____

2% Acetic Acid in Water

Add _____ ml (nominal 20.0 ml) of acetic acid to _____ ml (nominal 1000 ml) of Milli-Q Water. This solution should be stored at room temperature for up to one month after preparation.

Expiration Date: _____

Mobile Phase B:

Assigned ID: _____

0.1% Acetic Acid in Acetonitrile

Add _____ ml (nominal 1.00 ml) of acetic acid to _____ ml (nominal 1000 ml) of acetonitrile. This solution should be stored at room temperature for up to one month after preparation.

Expiration Date: _____

Needle Rinse 1:

Assigned ID: _____

Acetonitrile:Isopropanol (80:20, v:v) with 1% Ammonium Hydroxide

Add _____ ml (nominal 400 ml) of acetonitrile to _____ ml (nominal 100 ml) isopropanol and add _____ ml (nominal 5.00 ml) ammonium hydroxide in a glass bottle. This solution should be stored at room temperature for up to one month after preparation.

Expiration Date: _____

Needle Rinse 2:

Assigned ID: _____

Water:Methanol (90:10, v:v) with 1% Formic Acid

Add _____ ml (nominal 450 ml) of Milli-Q water to _____ ml (nominal 50.0 ml) methanol and add _____ ml (nominal 5.00 ml) formic acid in a glass bottle. This solution should be stored at room temperature for up to one month after preparation.

Expiration Date: _____

Milli-Q water: Decanted from Milli-Q unit on the day of use. Unit ID: _____ Exp: _____

Is resistivity $\geq 18.0 \text{ M}\Omega\text{-cm}$? Y / N (circle) Is TOC $< 50.0 \text{ ppb}$? Y / N (circle)

Ammonium Hydroxide:

Supplier: _____ Lot: _____ Grade: _____ Expire: _____

Acetic Acid:

Supplier: _____ Lot: _____ Grade: _____ Expire: _____

Formic Acid:

Supplier: _____ Lot: _____ Grade: _____ Expire: _____

Methanol:

Supplier: _____ Lot: _____ Grade: _____ Expire: _____

Acetonitrile:

Supplier: _____ Lot: _____ Grade: _____ Expire: _____

Isopropanol:

Supplier: _____ Lot: _____ Grade: _____ Expire: _____

Prepared by: _____ Date: _____

SRI Form 106.202D

07/15/19

SRI PROPRIETARY / CONFIDENTIAL

EXTRACTION / STOCK REAGENT PREPARATION

Study Number: _____

0.2% Acetic Acid in Methanol (Diluent):

Assigned ID: _____

Add _____ ml (nominal 0.400 ml) of acetic acid to _____ ml (nominal 200 ml) of methanol. This solution should be stored at room temperature for up to one month after preparation.

Expiration Date: _____

Water:Methanol (90:10, v:v) with 0.1% acetic acid (Reconstitution Solution):

Assigned ID: _____

Add _____ ml (nominal 0.200 ml) of acetic acid to _____ ml (nominal 180 ml) Milli-Q water and _____ ml (nominal 20.0 ml) of methanol. This solution should be stored at room temperature for up to one month after preparation.

Expiration Date: _____

Test Mix (System Suitability):

Assigned ID: _____

To prepare at the LLOQ level, spike 0.0100 ml of the 1.00 mg/ml [Proprietary] and [Proprietary] stock solutions and 0.0500 ml of the 1.00 mg/ml [Proprietary] stock solution into 9.930 ml of Diluent Solution. Vortex, remove 0.100 ml, and add to a vial containing 0.900 ml of Diluent Solution. Vortex, remove 0.0100 ml, and add to a vial containing 0.990 ml of Diluent Solution. This solution may be stored refrigerated for up to 3 months from the date of preparation.

On the day of use, remove 0.0203 ml of this solution and place into a separate vial containing 0.0203 ml of internal standard spiking solution and 0.959 ml of Reconstitution Solution.

Expiration Date: _____ Storage Unit / Temperature: _____

Milli-Q water: Decanted from Milli-Q unit on the day of use. Unit ID: _____ Exp: _____

Is resistivity $\geq 18.0 \text{ M}\Omega\text{-cm}$? Y / N (circle) Is TOC $< 50.0 \text{ ppb}$? Y / N (circle)

Acetic Acid:

Supplier: _____ Lot: _____ Grade: _____ Expire: _____

Methanol:

Supplier: _____ Lot: _____ Grade: _____ Expire: _____

[Proprietary] Stock Solution (1.00 mg/ml) ID: _____ Expire: _____

[Proprietary] Stock Solution (1.00 mg/ml) ID: _____ Expire: _____

[Proprietary] Stock Solution (1.00 mg/ml) ID: _____ Expire: _____

Internal Standard Spiking Solution ID: _____ Expire: _____

Diluent ID: _____ Expire: _____

Reconstitution Solution ID: _____ Expire: _____

Pipettes: _____

Prepared by: _____ Date: _____

SRI Form 106.202E
07/15/19

SRI PROPRIETARY / CONFIDENTIAL

Obtained via FOIA by White Coat Waste Project

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix G-5

BIOANALYTICAL CERTIFICATES OF ANALYSIS

Proprietary Info

CERTIFICATE OF ANALYSIS

Proprietary Pro Drug Combination Suspension

Lot Number

Proprietary Info

Date of Manufacturing

11/26/2018

Page 1 of 1

Product Name:

Proprietary Pro Drug Combination Suspension for subcutaneous injection (Group 1 — 0.0 mg/kg)

Manufacturer:

Lot Number:

Proprietary Info

Proprietary Info

Storage and Expiration

Store at 2-8°C

Expiration / Retest Date 4/26/19

Test	Specification	Result
Appearance	White, turbid suspension	White turbid suspension
Identity	Matches nominal mass of APIs, DSPC, and mPEG2000-DSPE	conforms
Proprietary Info	0 mg/mL \pm 0 mg/mL	0 mg/ml
	0 mg/mL \pm 0 mg/mL	0 mg/m
	0 mg/mL \pm 0 mg/mL	0 mg/ml
	28.5 mg/mL \pm 2.85 mg/mL	27.46 mg/ml
	72.1 mg/mL \pm 7.21 mg/mL	76.64 mg/ml
Osmolality	250 – 450 mmol/Kg	332 mmol/Kg
pH	6.5 – 8.5	8.5
Endotoxin USP <85>	< 50 EU/mL	< 5 EU/ml
Sterility USP <71>	No growth on FTM or TSB	Pass

Approval Signatures

	Name, Title	Signature and Date
Author	Redacted by agreement	05/21/19
Approver		

Proprietary Info

CERTIFICATE OF ANALYSIS

Proprietary Pro Drug Combination Suspension

Lot Number

Proprietary Info

Date of Manufacturing
11/27/2018

Page 1 of 1

Product Name: Proprietary Pro Drug Combination Suspension for subcutaneous injection (Group 2 — 1.5 mg/kg)

Manufacturer:

Lot Number:

Proprietary Info

Proprietary Info

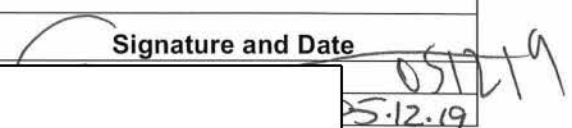
Storage and Expiration

Store at 2-8°C

Expiration / Retest Date 4/27/19

Test	Specification	Result
Appearance	White, turbid suspension	White turbid suspension
Identity	Matches nominal mass of APIs, DSPC, and mPEG2000-DSPE	conforms
Proprietary Info	0.30 mg/mL \pm 0.03 mg/mL	0.30 mg/ml
	0.09 mg/mL \pm 0.01 mg/mL	0.08 mg/ml
	0.17 mg/mL \pm 0.02 mg/mL	0.17 mg/ml
Osmolality	250 – 350 mmol/Kg	250 mmol/Kg
pH	6.5 – 8.5	8.43
Endotoxin USP <85>	< 50 EU/mL	< 5 EU/ml
Sterility USP <71>	No growth on FTM or TSB	Pass

Approval Signatures

	Name, Title	Signature and Date
Author	Redacted by agreement	 05/12/19
Approver		

Proprietary Info

CERTIFICATE OF ANALYSIS

Proprietary Pro Drug Combination Suspension

Lot Number

Proprietary Info

Date of Manufacturing
11/27/2018

Page 1 of 1

Product Name:

Proprietary Pro Drug Combination Suspension for subcutaneous
injection (Group 3 — 15 mg/kg)

Manufacturer:

Lot Number:

Proprietary Info

Proprietary Info

Storage and Expiration

Store at 2-8°C

Expiration / Retest Date 4/27/19

Test	Specification	Result
Appearance	White, turbid suspension	White turbid suspension
Identity	Matches nominal mass of APIs, DSPC, and mPEG2000-DSPE	conforms
Proprietary Info	3.00 mg/mL \pm 0.30 mg/mL	3.00 mg/ml
	0.86 mg/mL \pm 0.09 mg/mL	0.80 mg/ml
	1.71 mg/mL \pm 0.17 mg/mL	1.72 mg/ml
Osmolality	250 – 350 mmol/Kg	262 mmol/Kg
pH	6.5 – 8.5	8.10
Endotoxin USP <85>	< 50 EU/mL	< 5 EU/ml
Sterility USP <71>	No growth on FTM or TSB	Pass

Approval Signatures

	Name, Title	Signature and Date
Author	Redacted by agreement	05/12/19 5.12.19
Approver		

Proprietary Info

CERTIFICATE OF ANALYSIS

Proprietary Pro Drug Combination Suspension

Lot Number

Proprietary Info

Date of Manufacturing
11/27/2018

Page 1 of 1

Product Name: Proprietary Pro Drug Combination Suspension for subcutaneous injection (Group 4 — 30 mg/kg)

Manufacturer:

Lot Number:

Proprietary Info

Proprietary Info

Storage and Expiration

Store at 2-8°C

Expiration / Retest Date 4/27/19

Test	Specification	Result
Appearance	White, turbid suspension	White turbid suspension
Identity	Matches nominal mass of APIs, DSPC, and mPEG2000-DSPE	conforms
Proprietary Info	6.00 mg/mL \pm 0.60 mg/mL	6.00 mg/ml
	1.72 mg/mL \pm 0.17 mg/mL	1.61 mg/ml
	3.43 mg/mL \pm 0.34 mg/mL	3.44 mg/ml
Osmolality	250 – 350 mmol/Kg	278 mmol/kg
pH	6.5 – 8.5	7.56
Endotoxin USP <85>	< 50 EU/mL	< 5 EU/ml
Sterility USP <71>	No growth on FTM or TSB	Pass

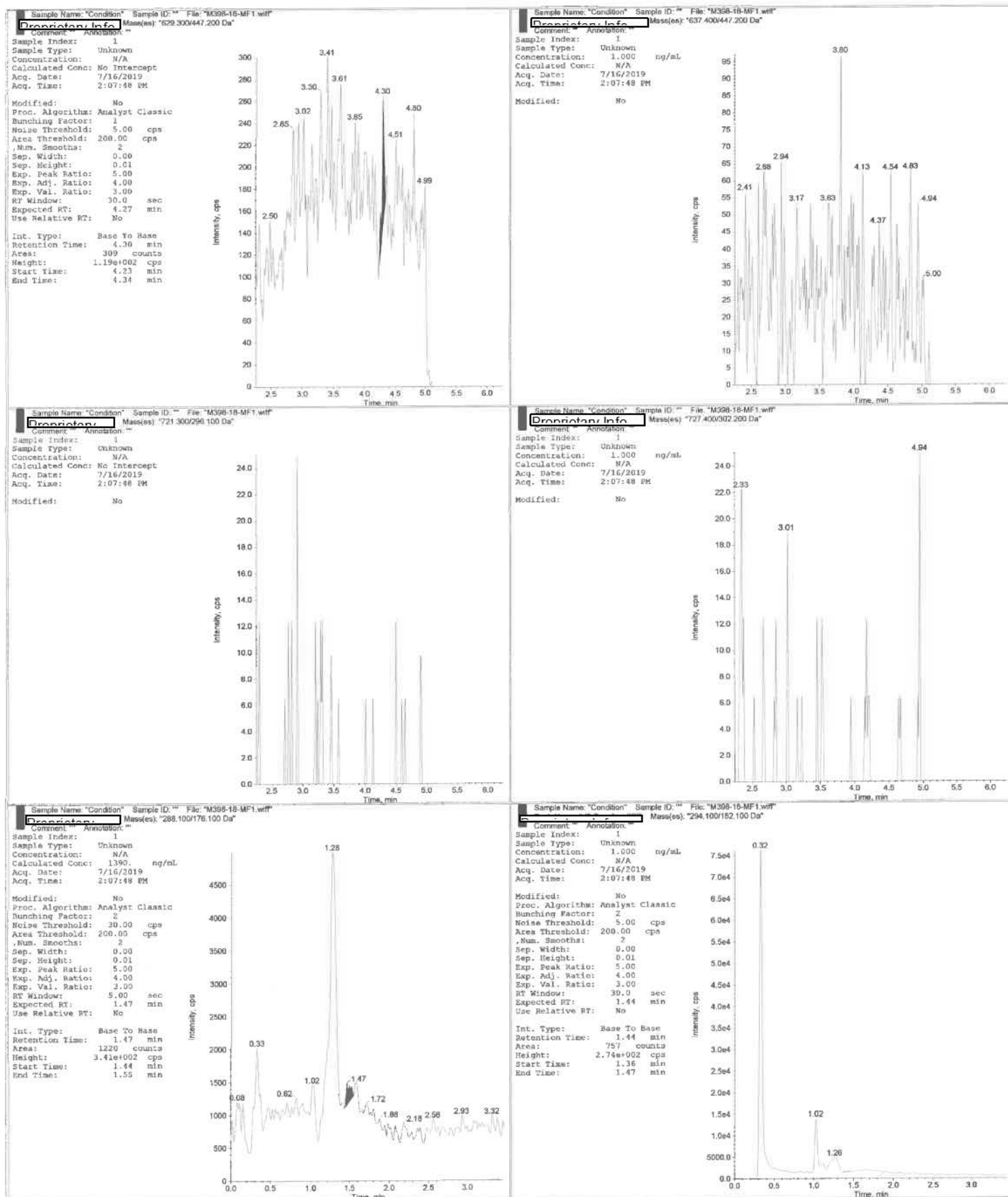
Approval Signatures

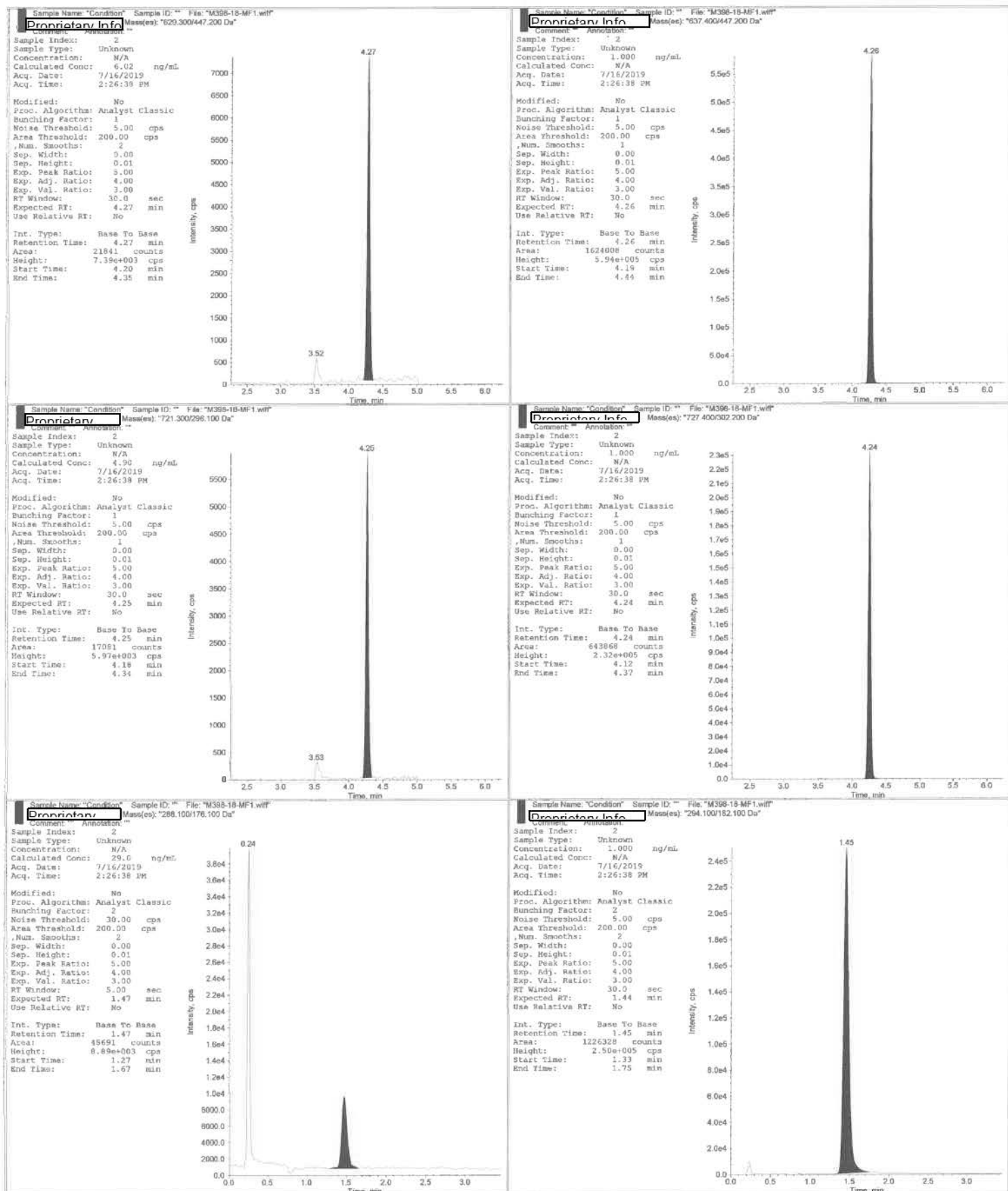
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Approver		5.12.19

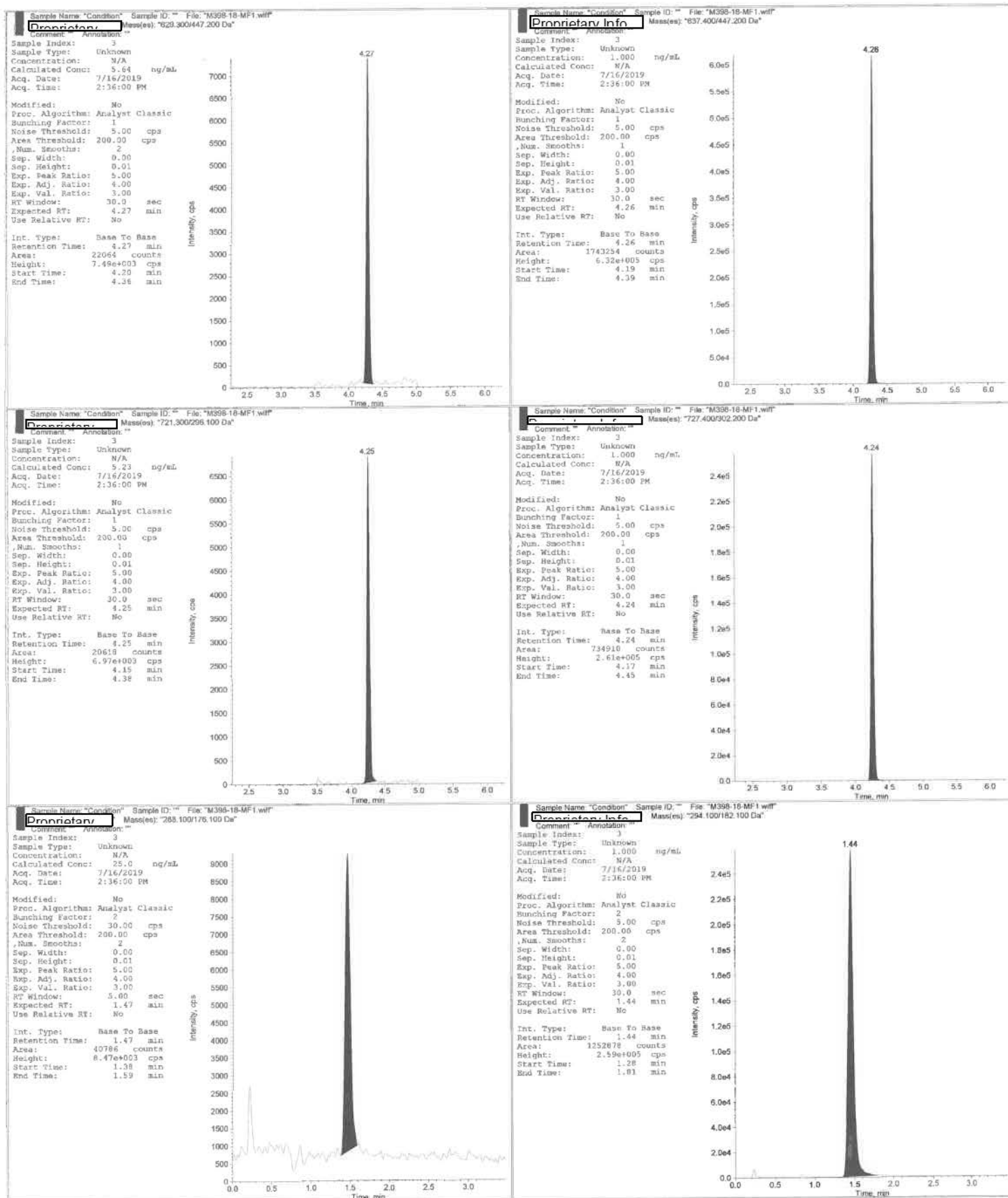
**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

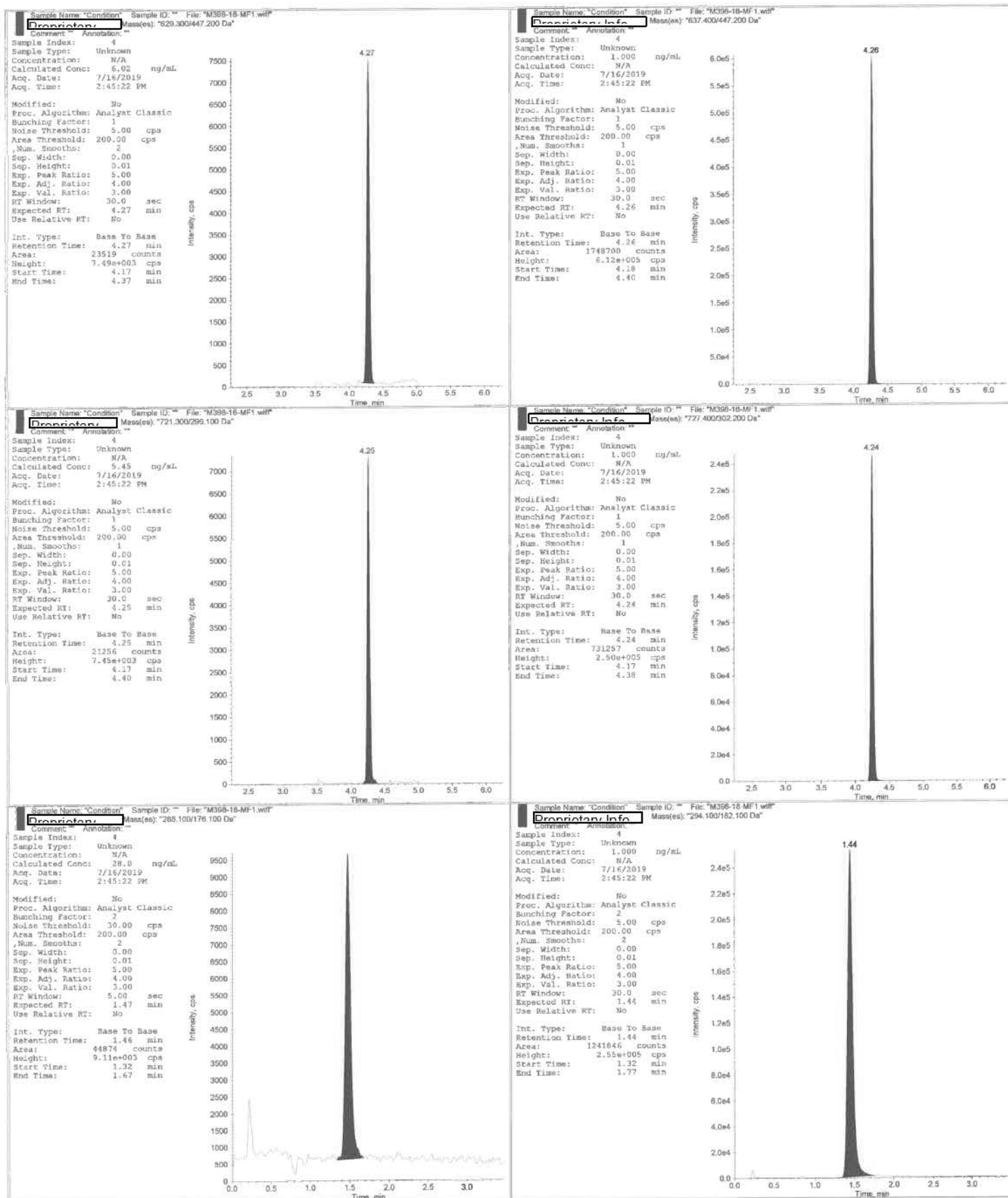
Appendix G-6

REPRESENTATIVE CHROMATOGRAPHS



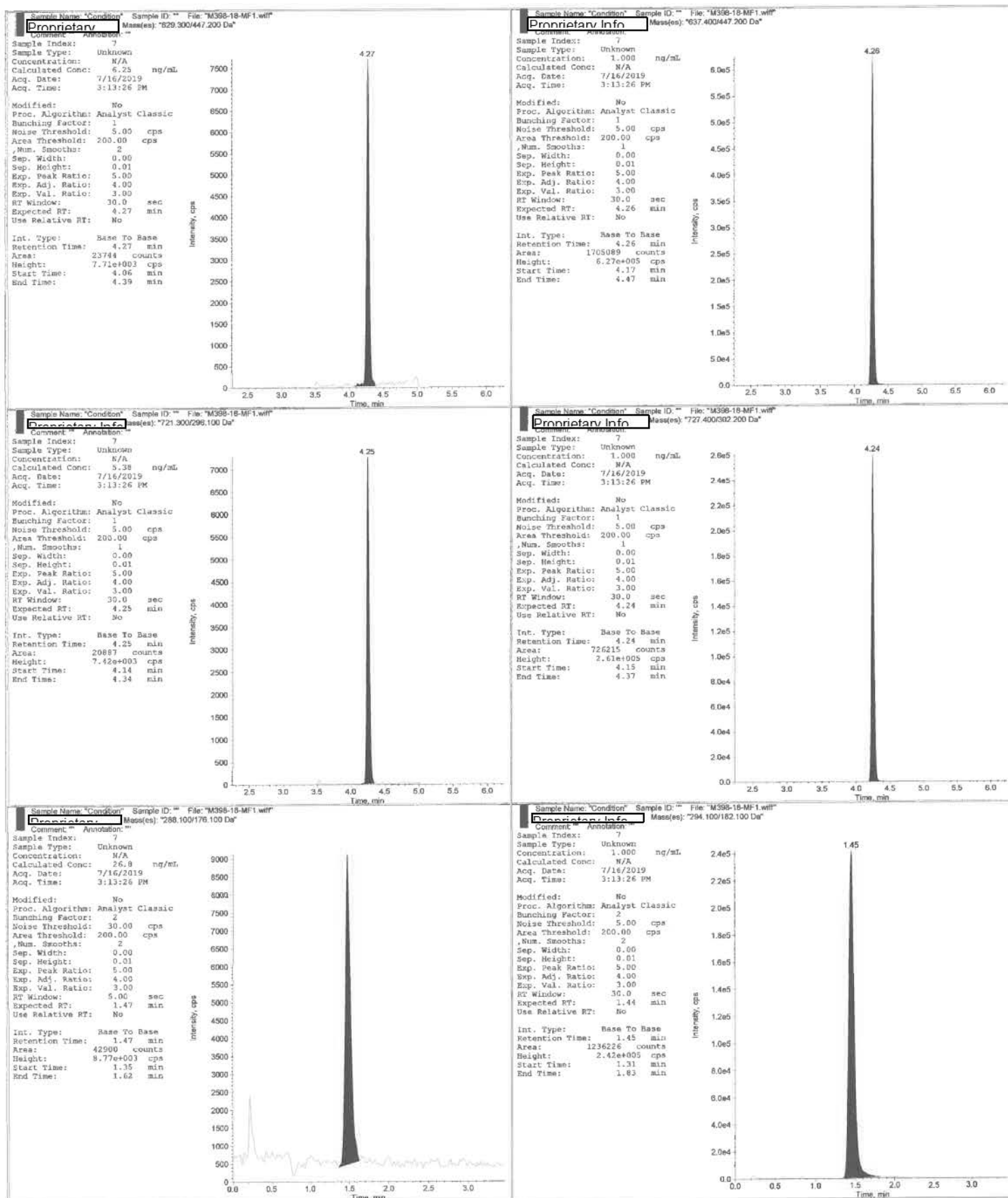


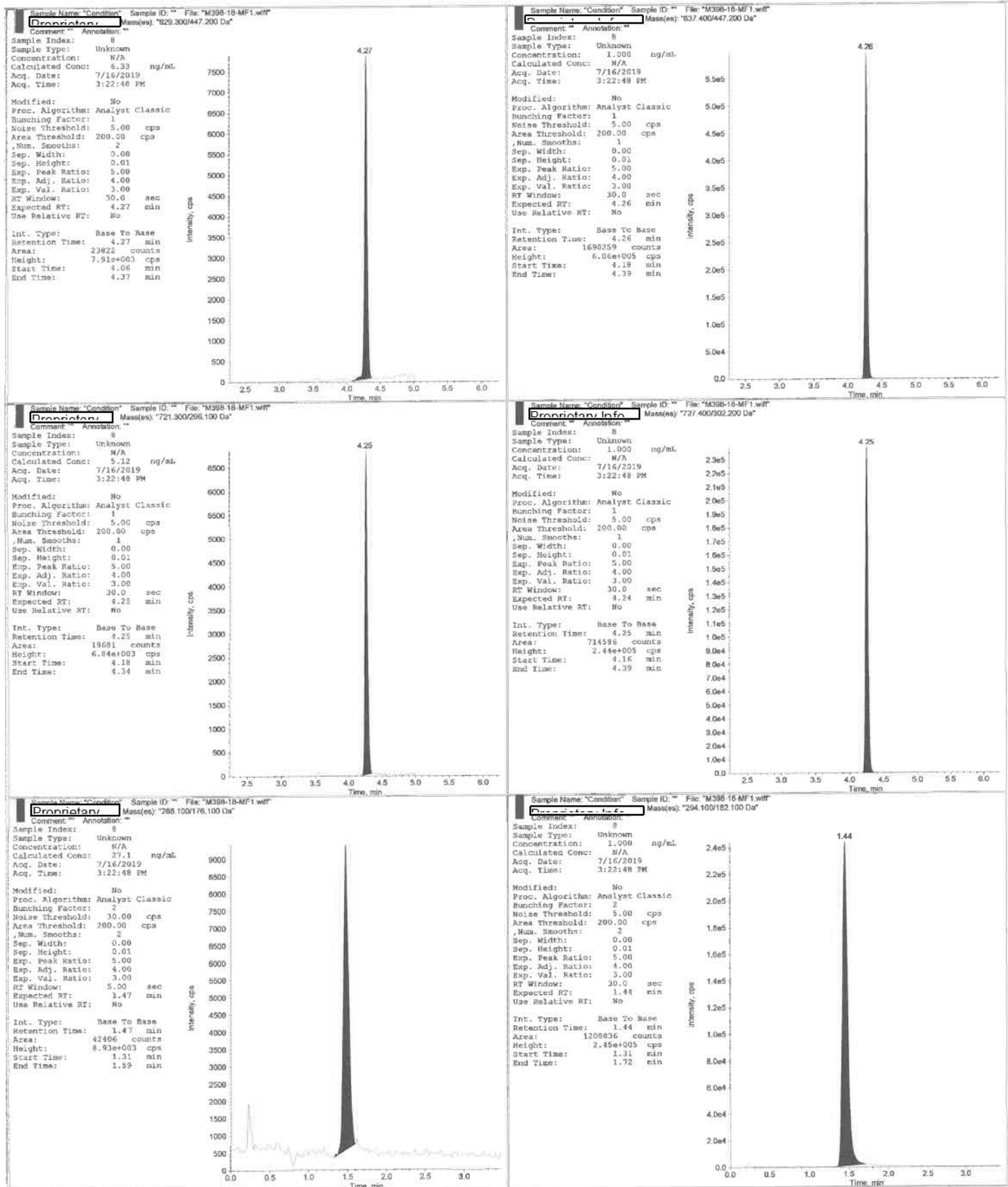


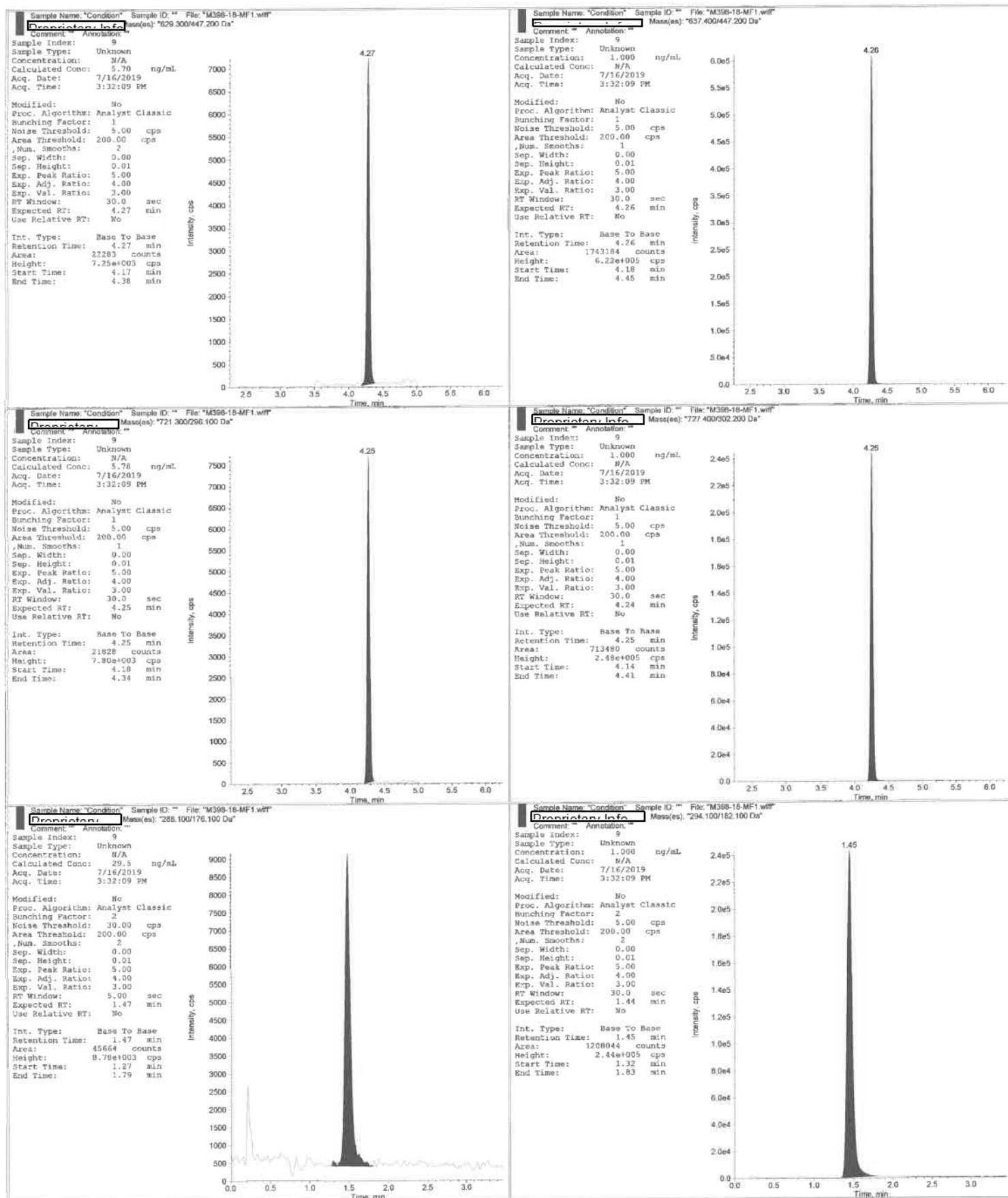


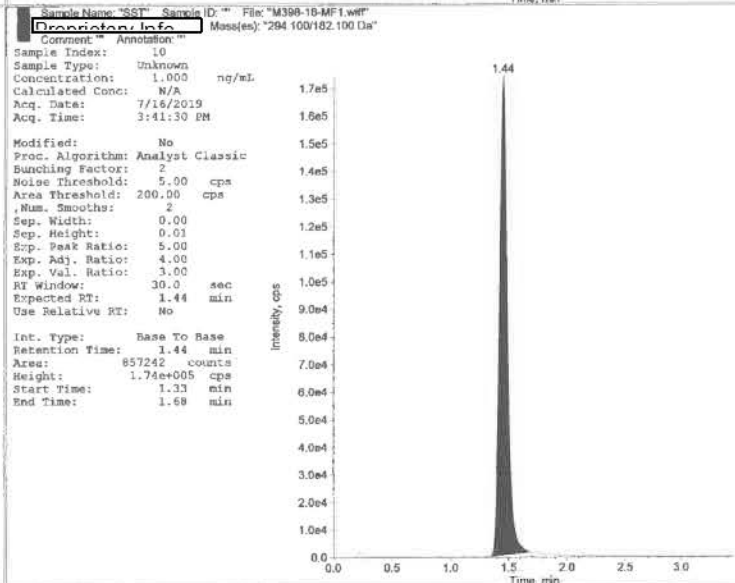
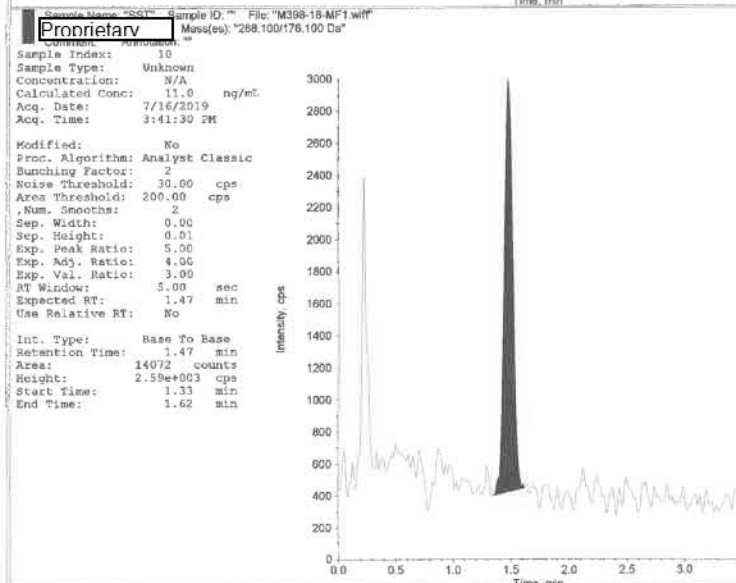
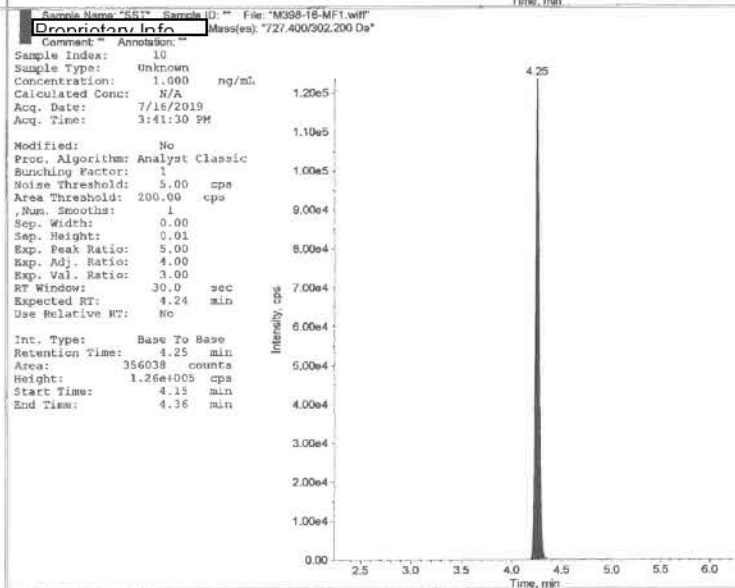
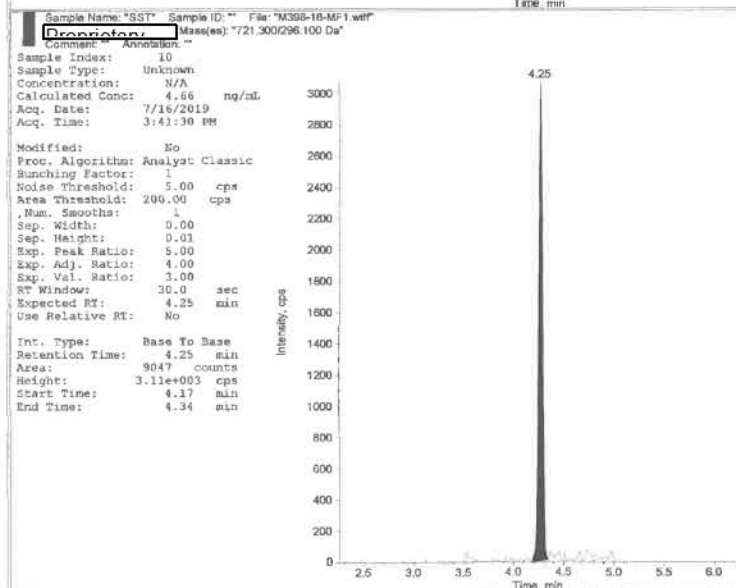
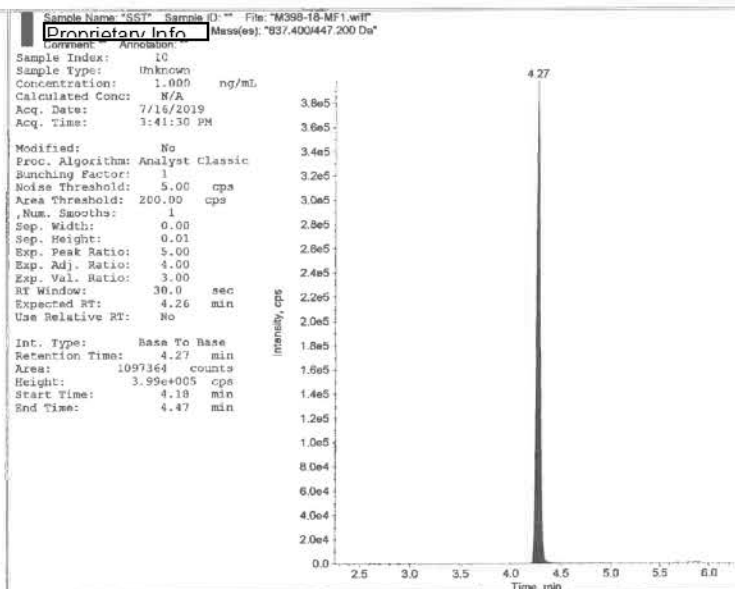
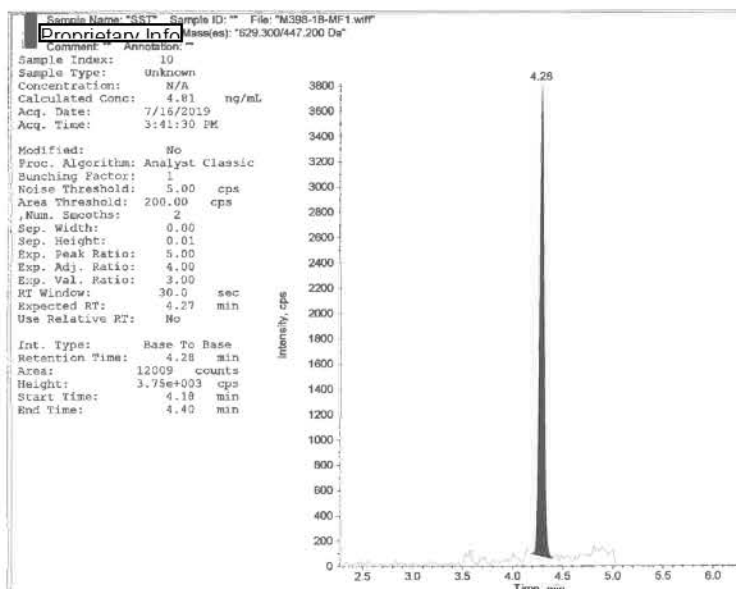


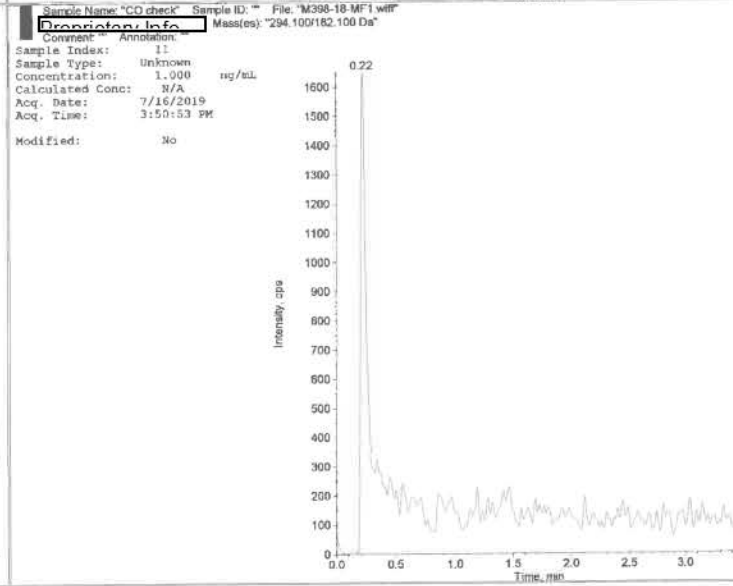
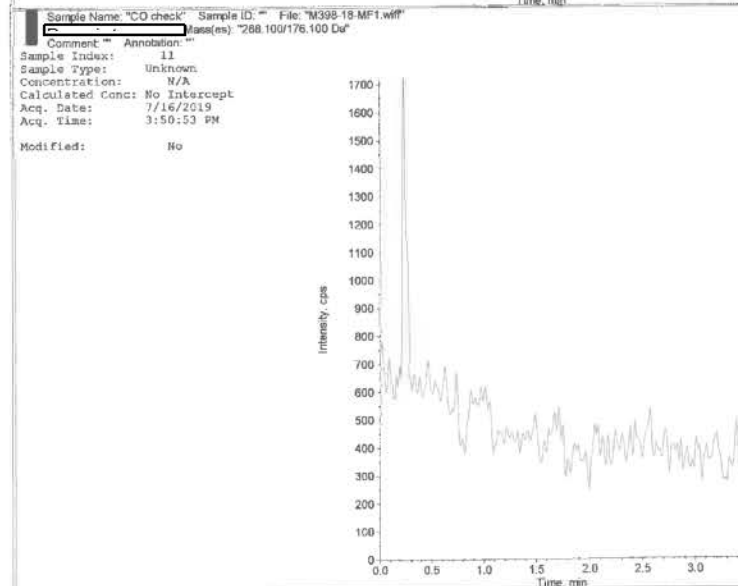
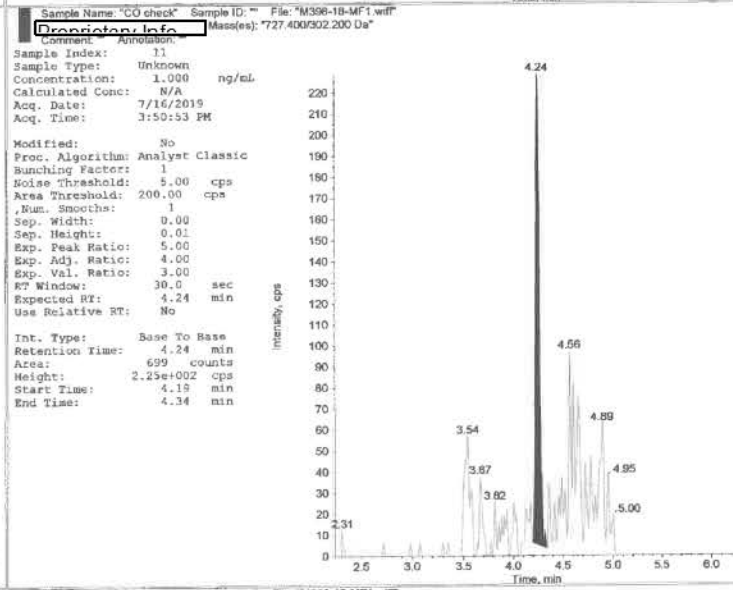
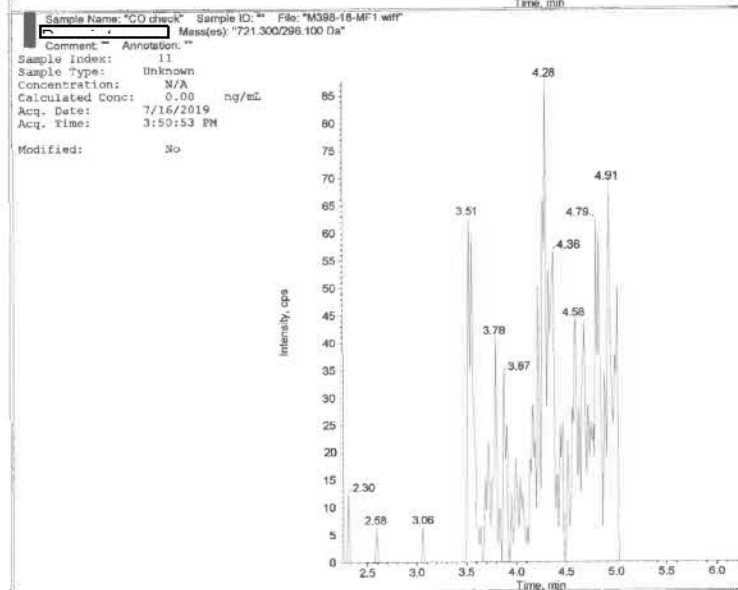
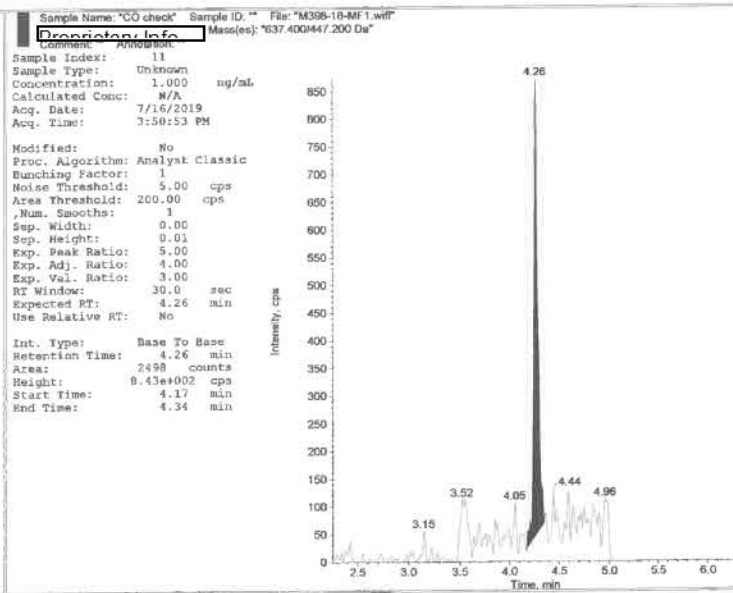
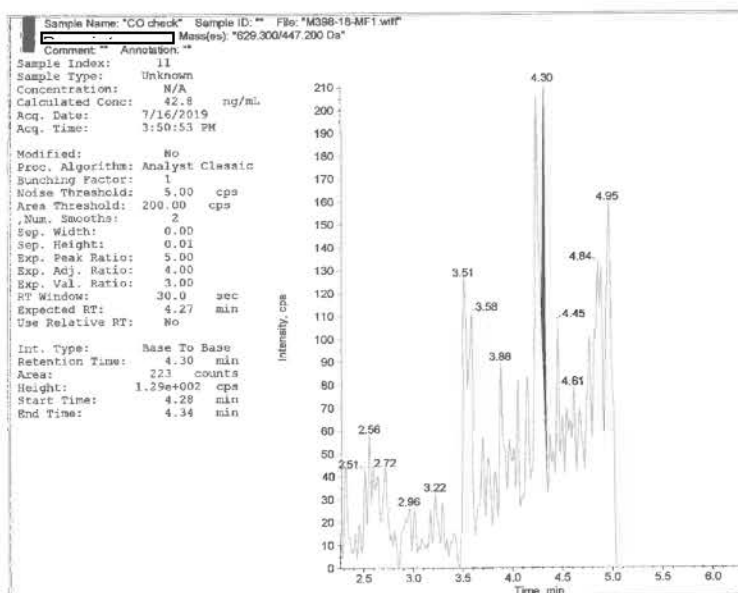


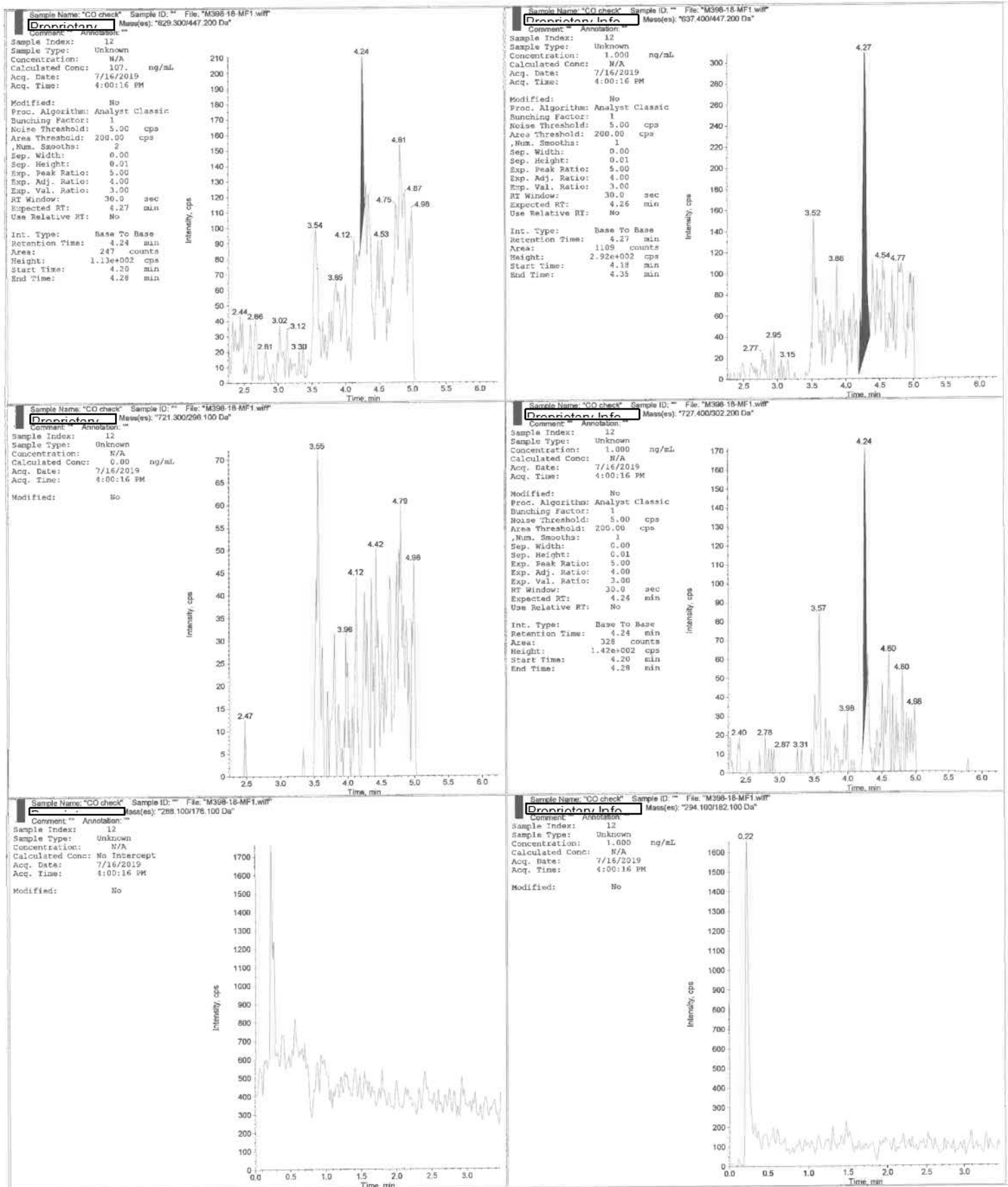


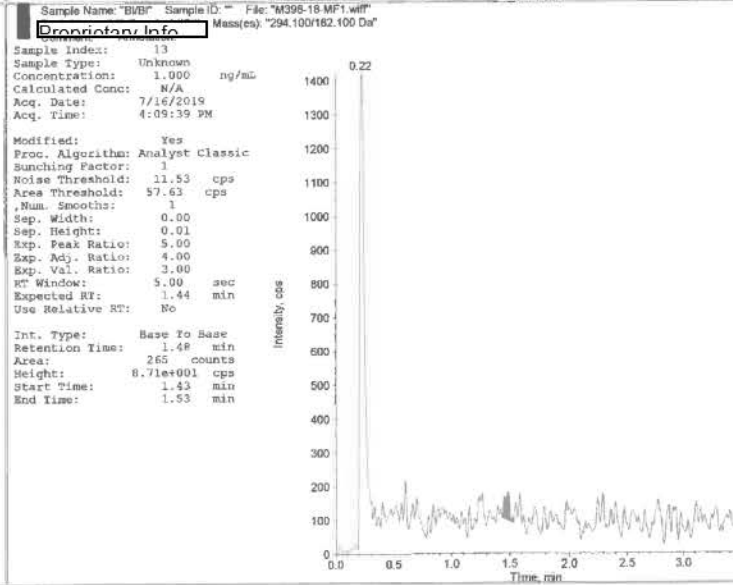
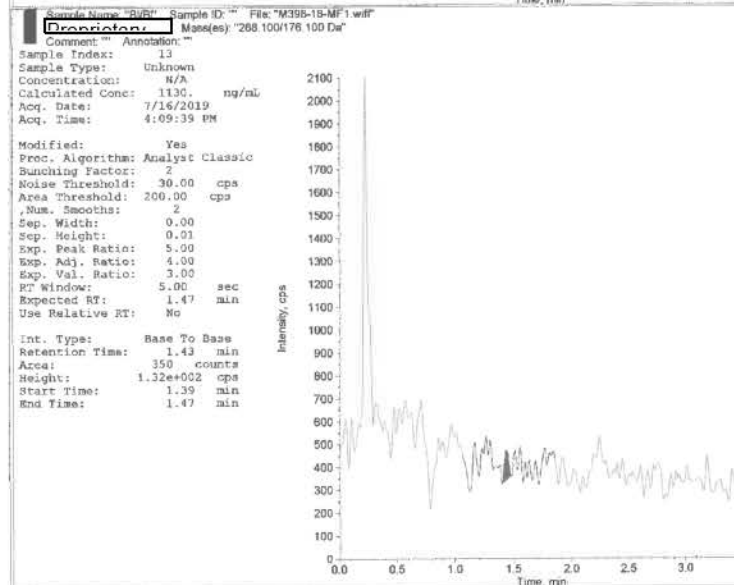
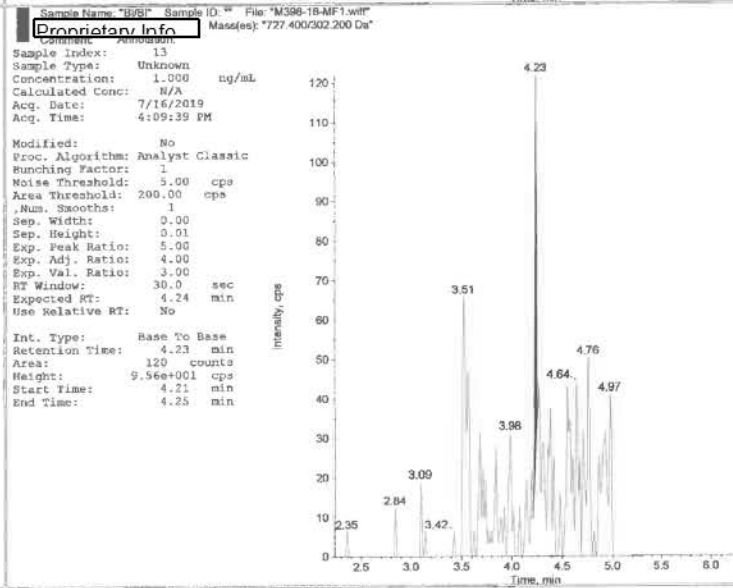
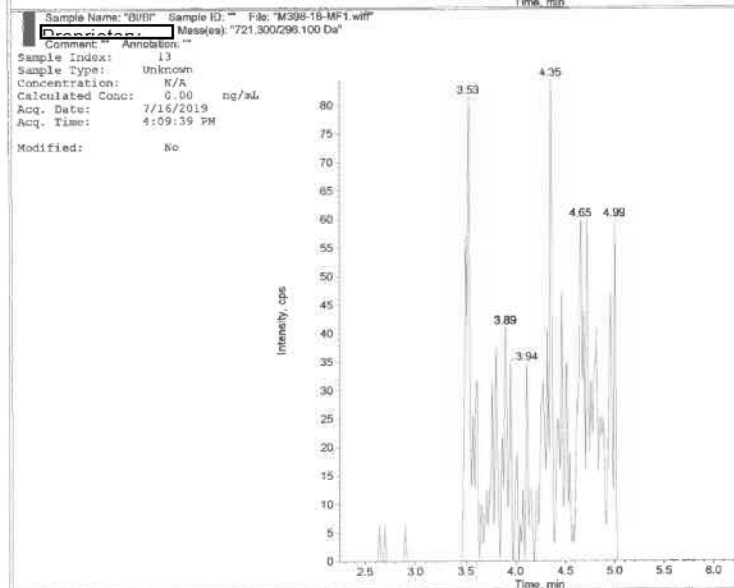
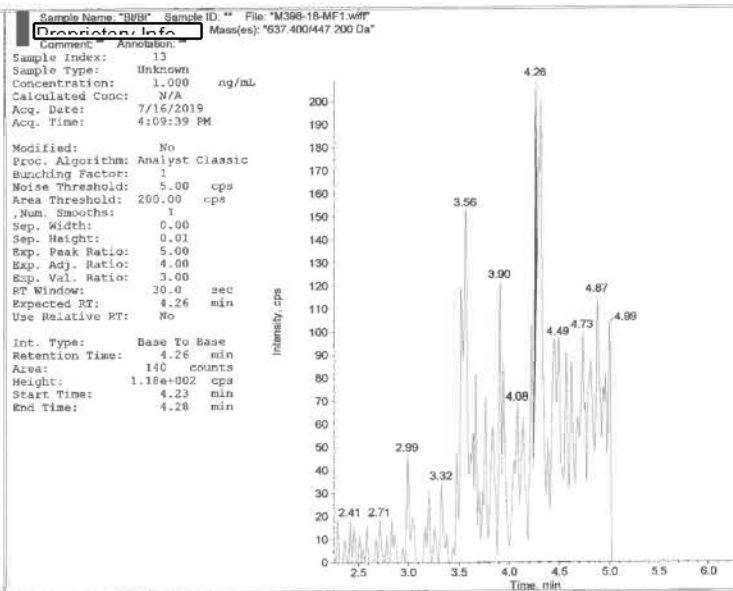
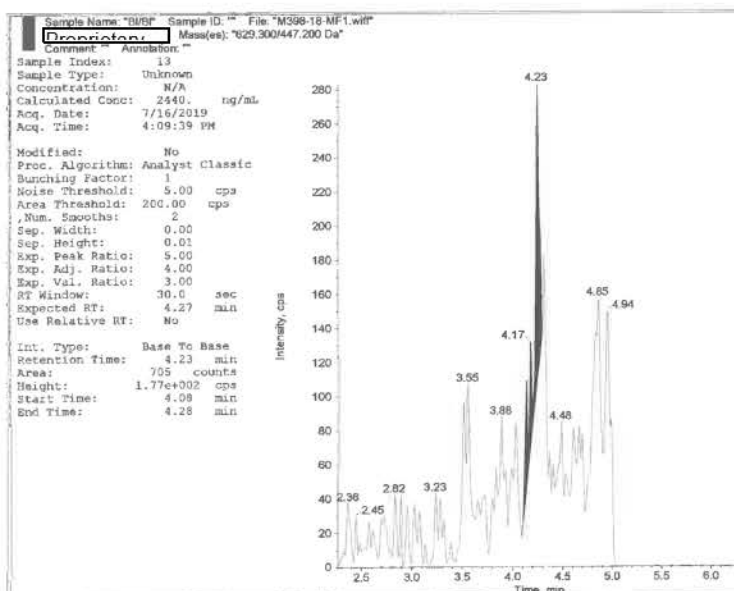


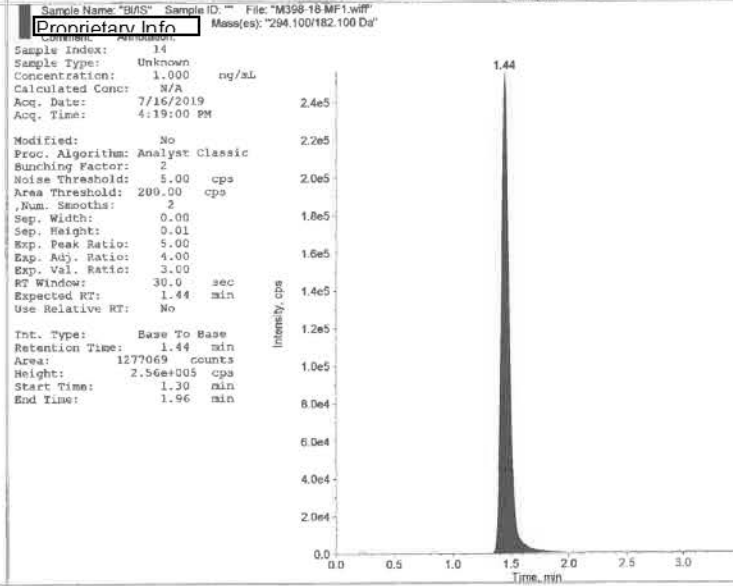
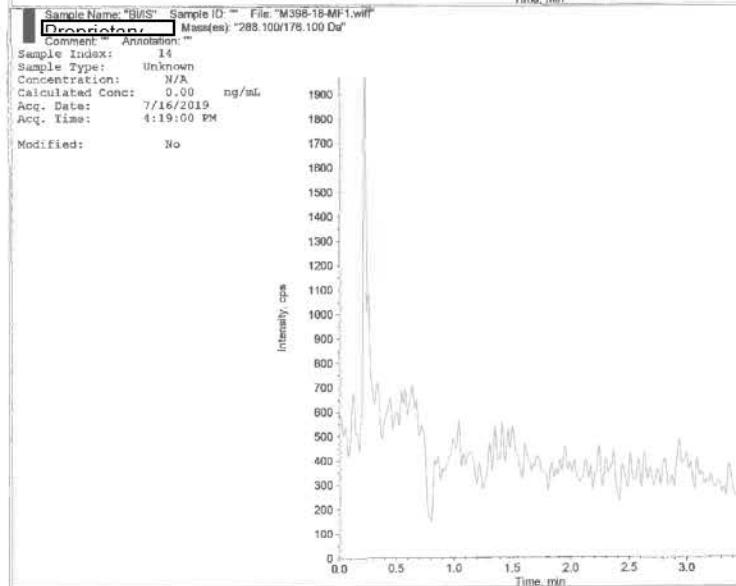
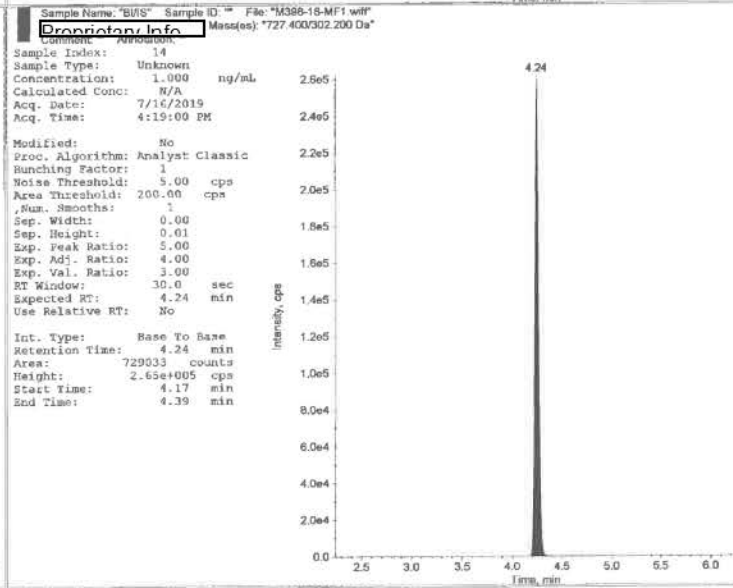
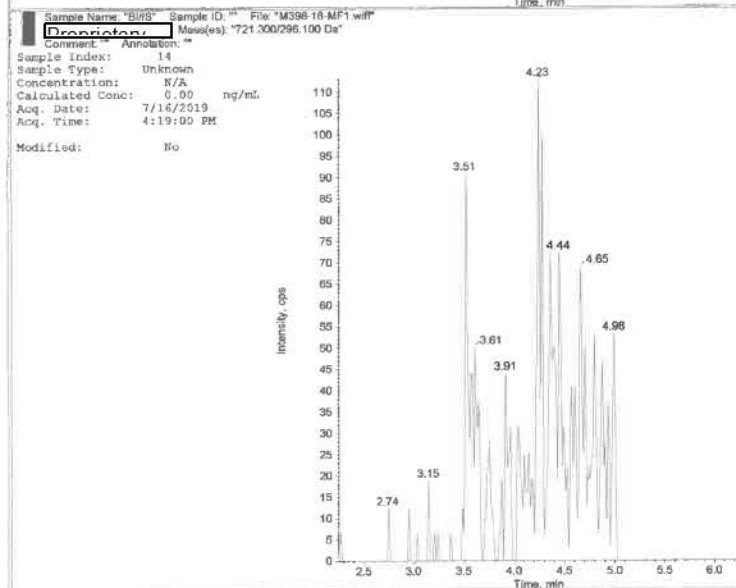
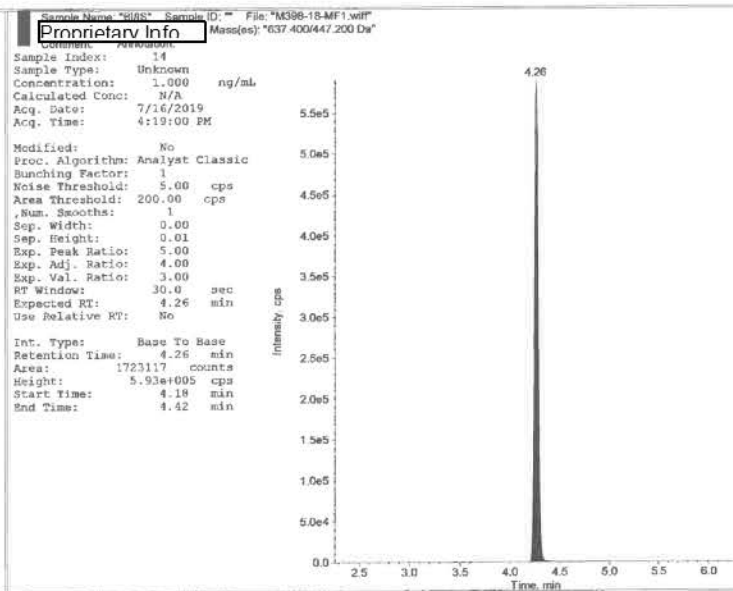
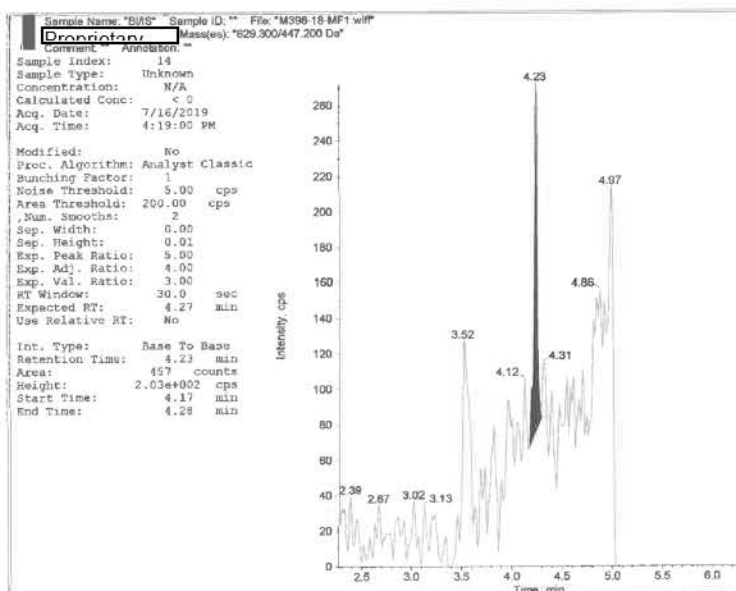


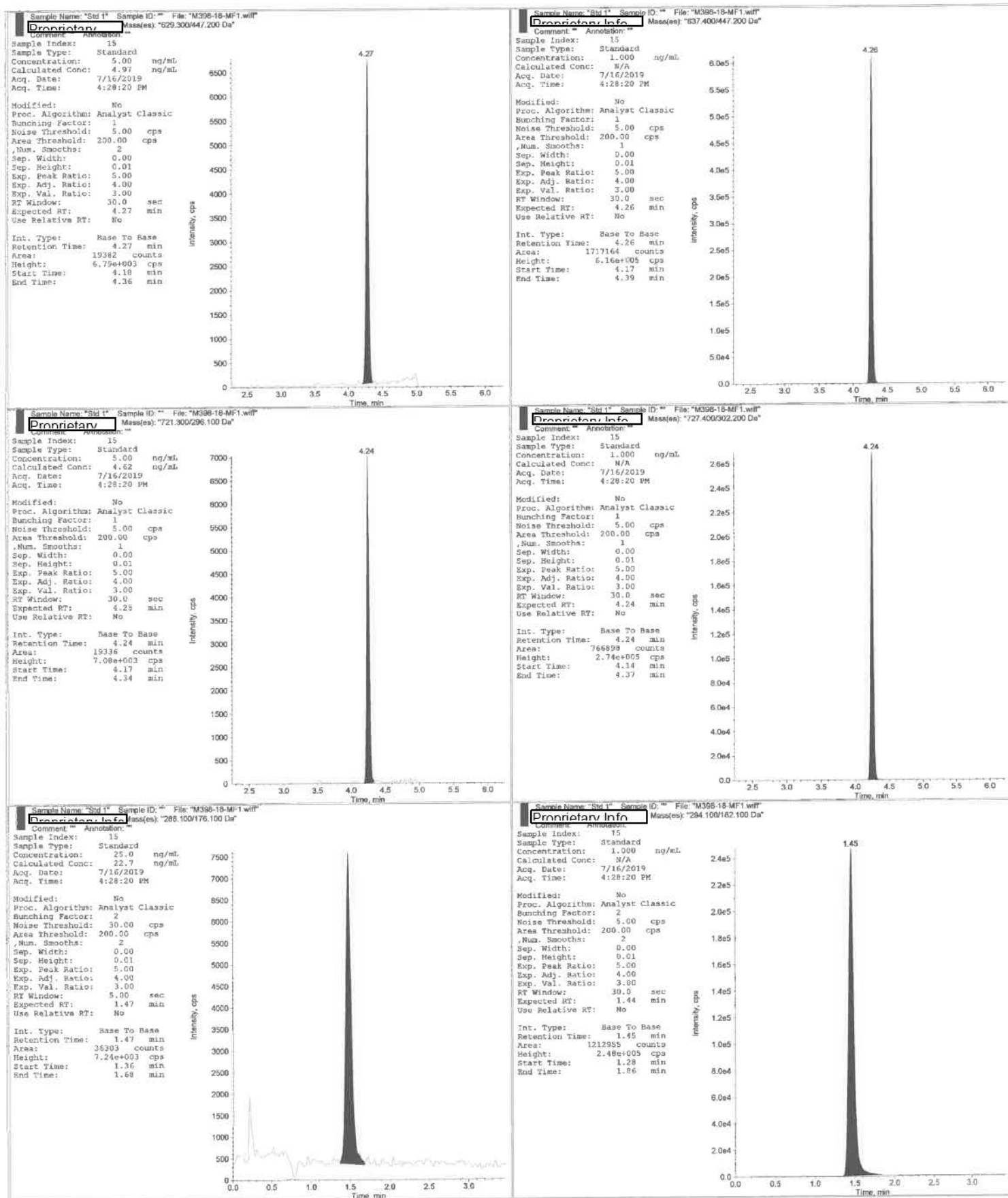


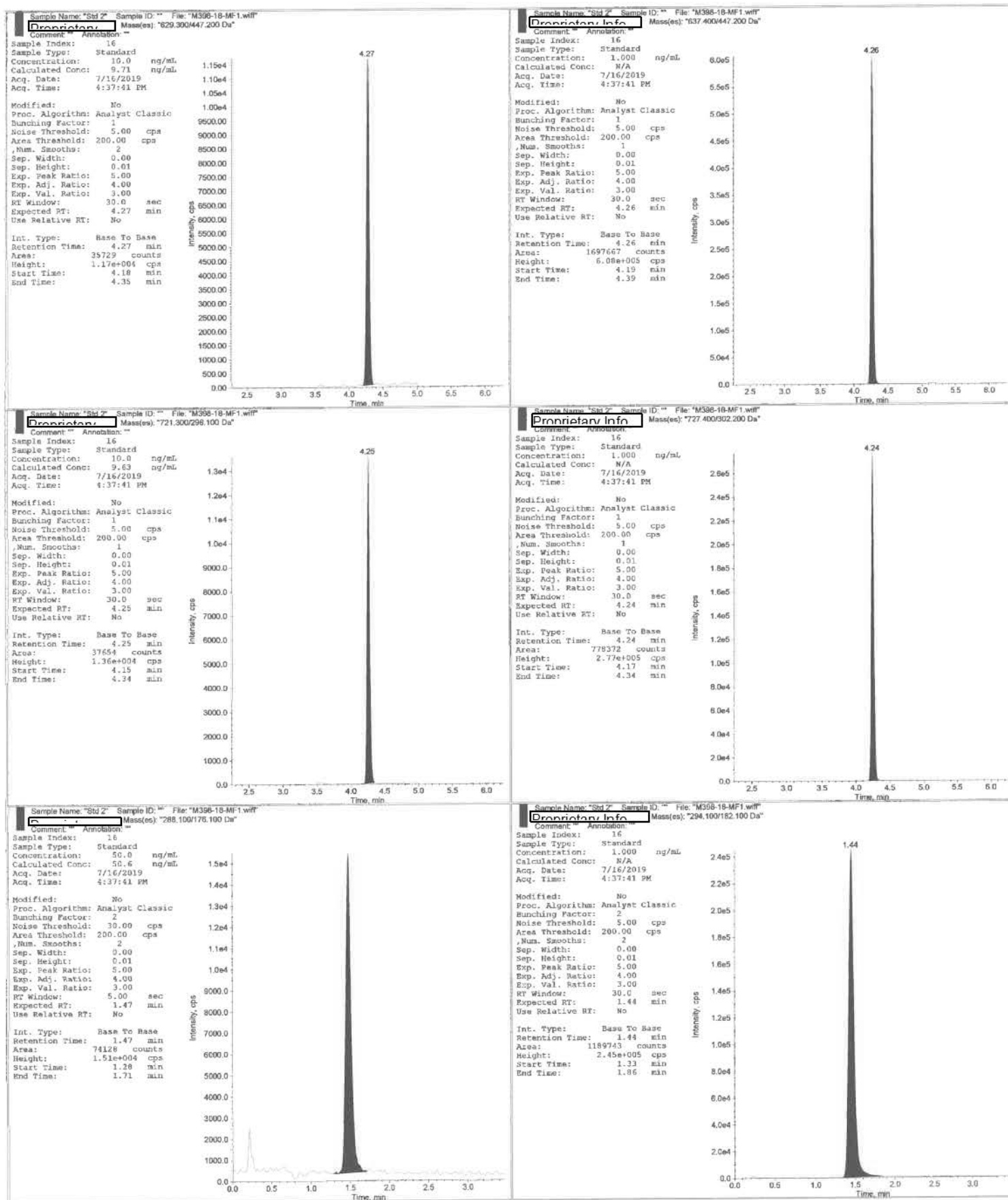




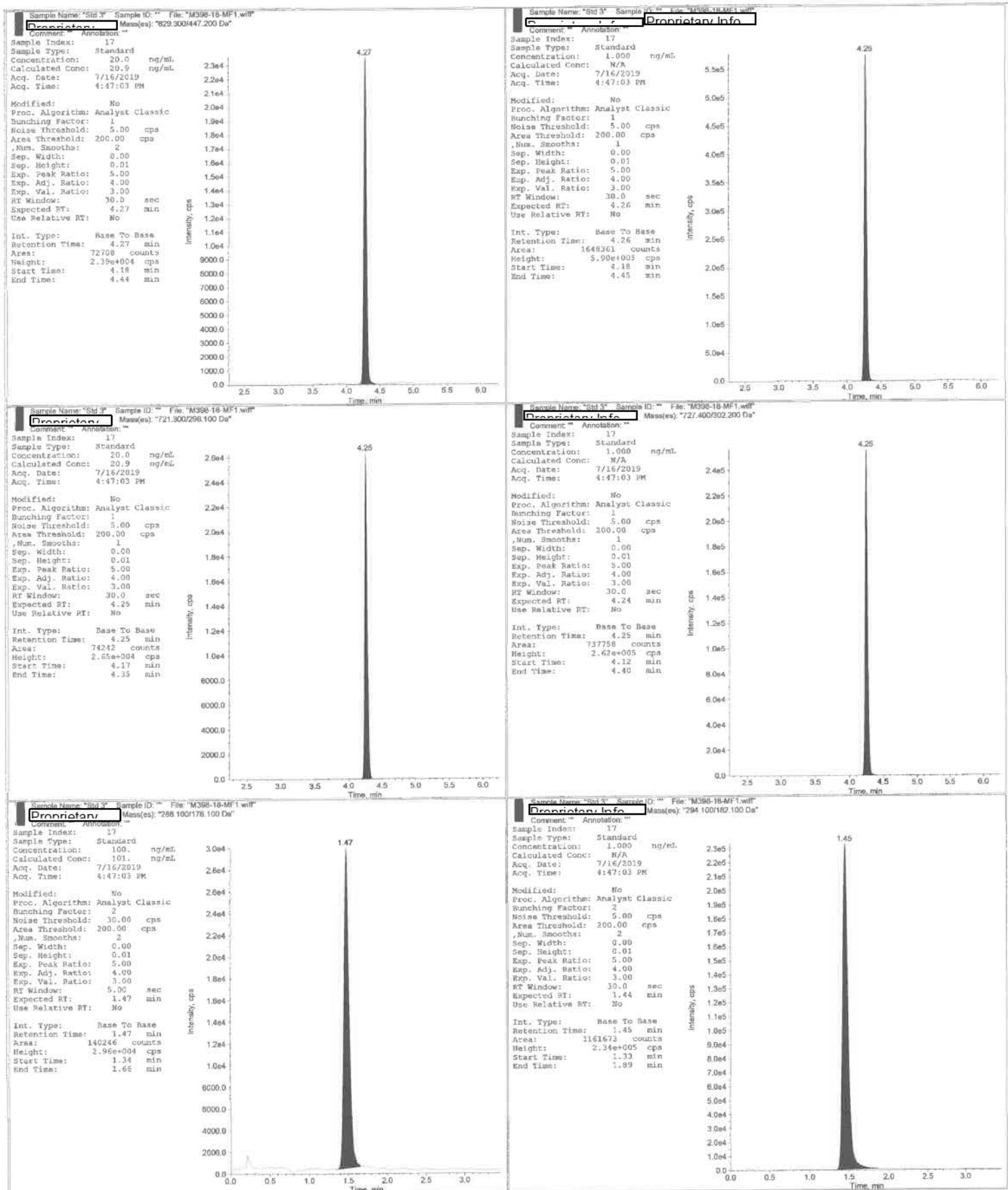




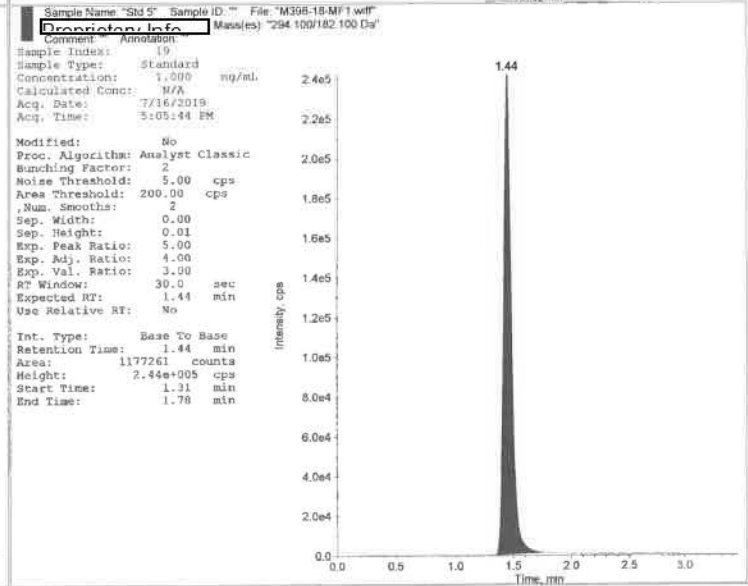
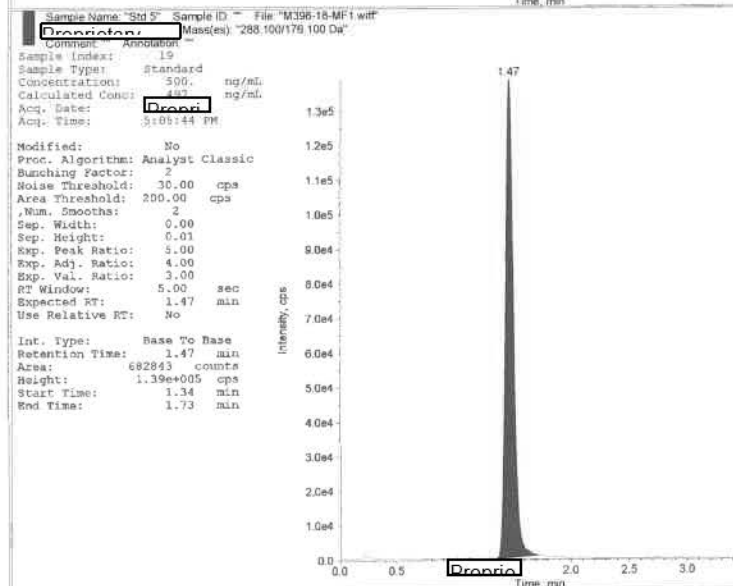
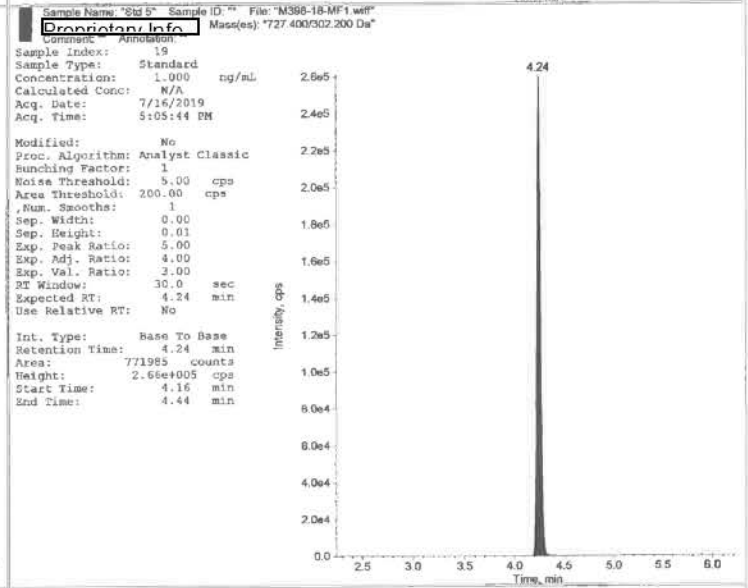
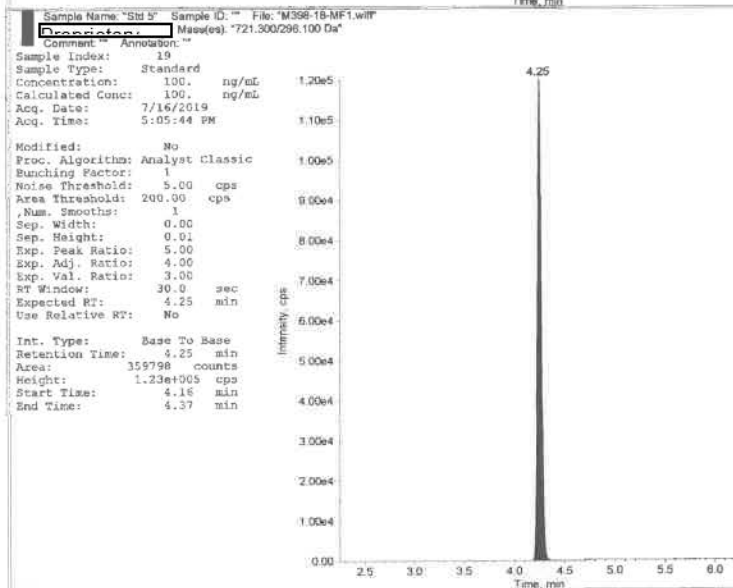
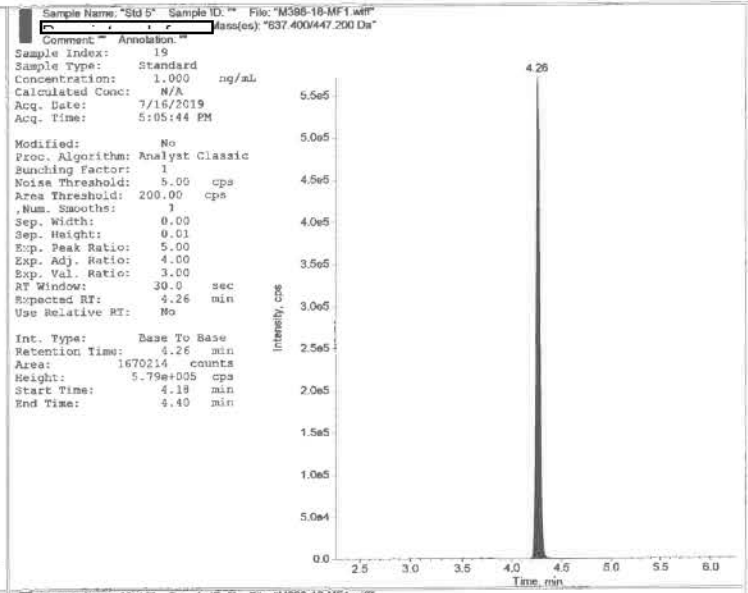
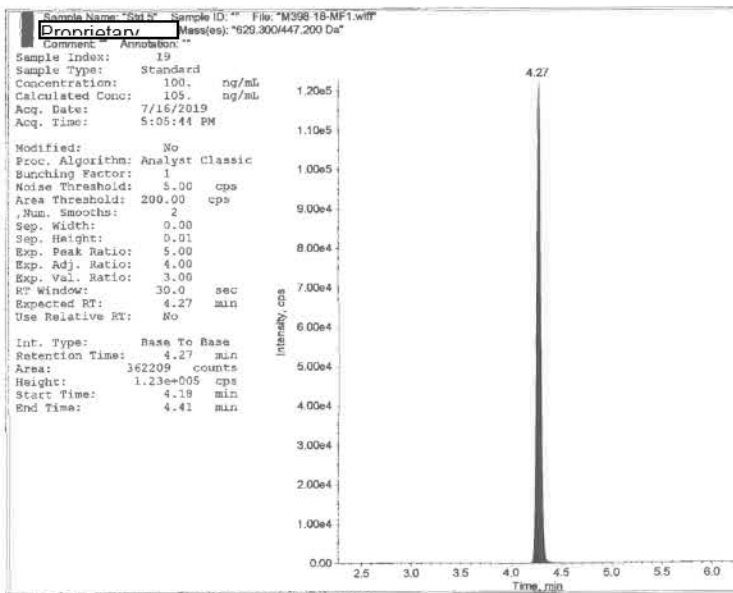


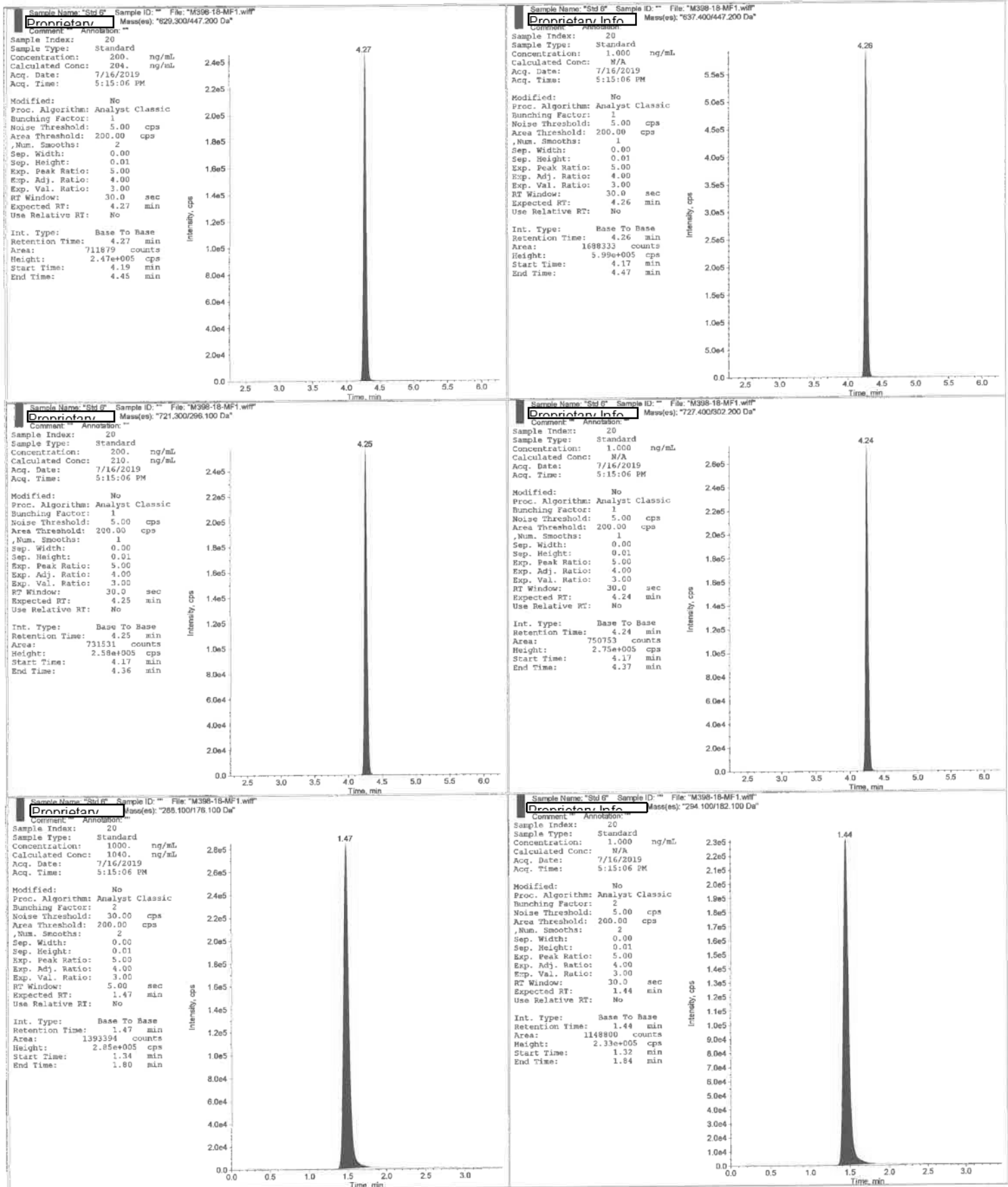


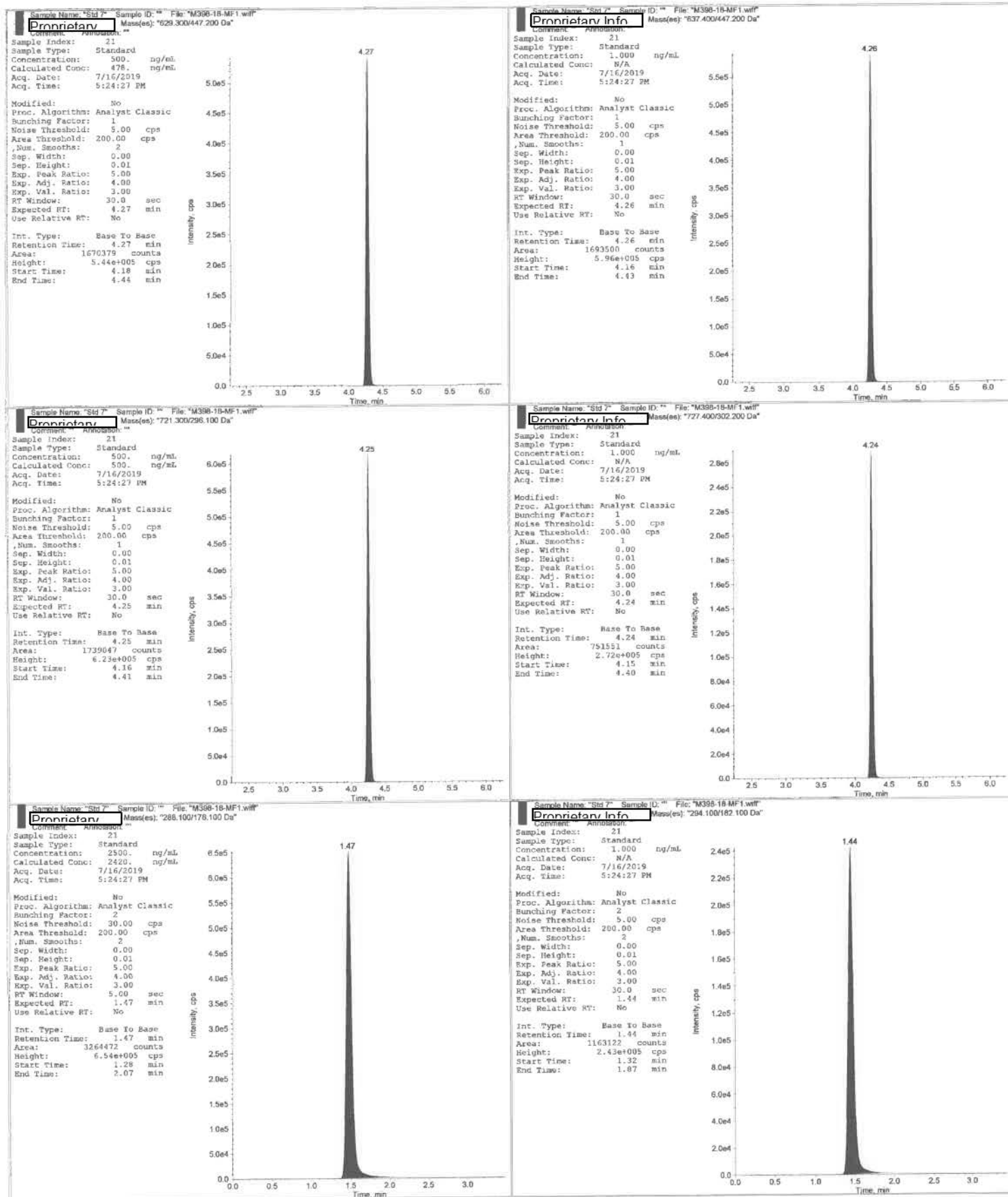
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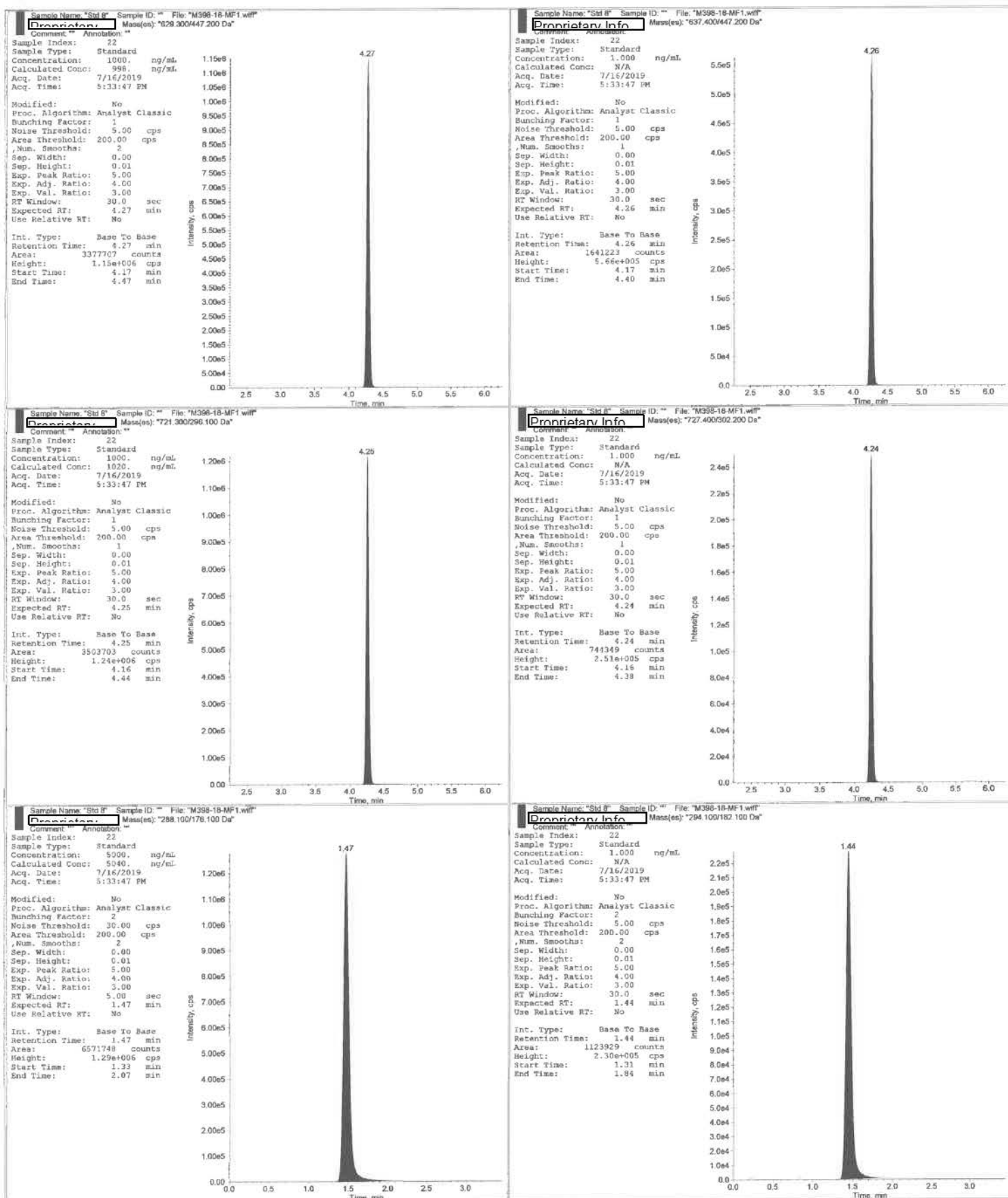


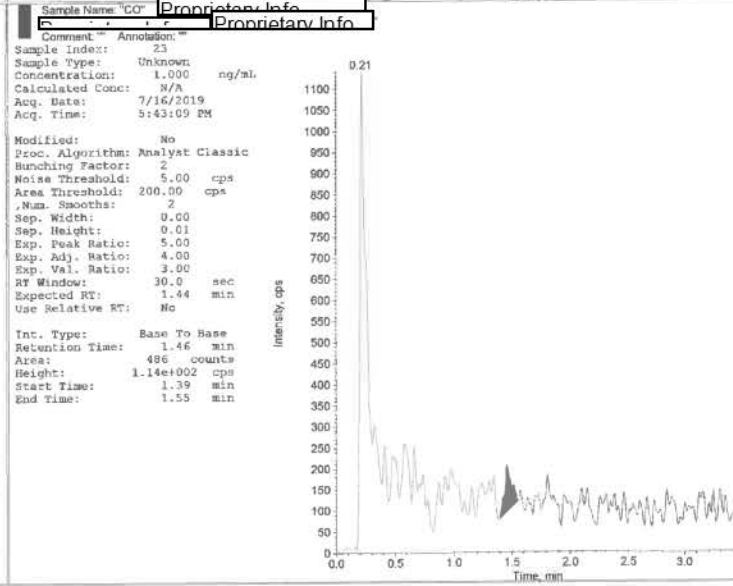
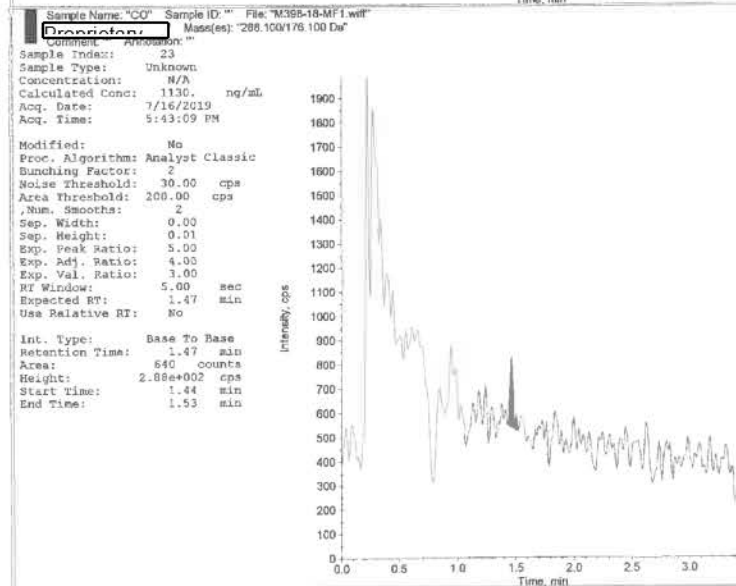
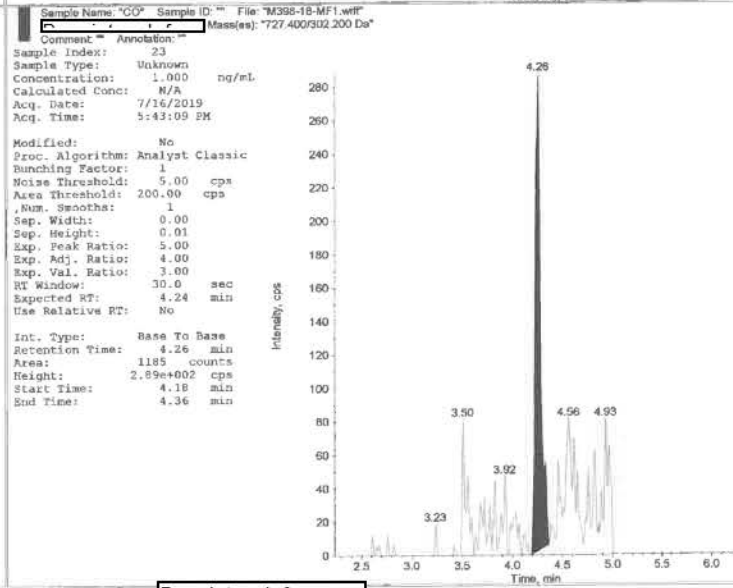
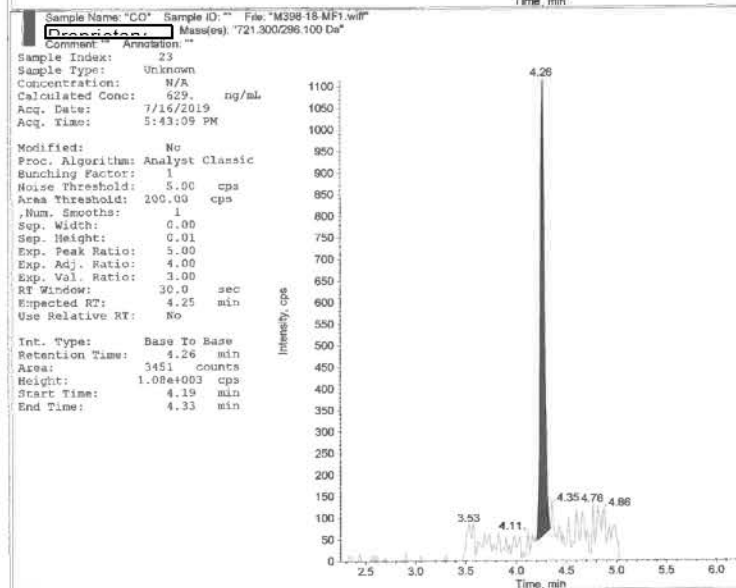
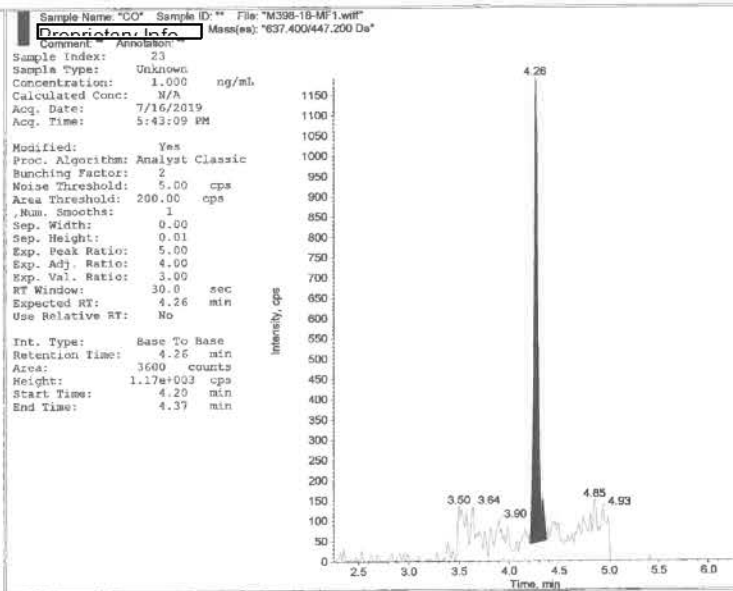
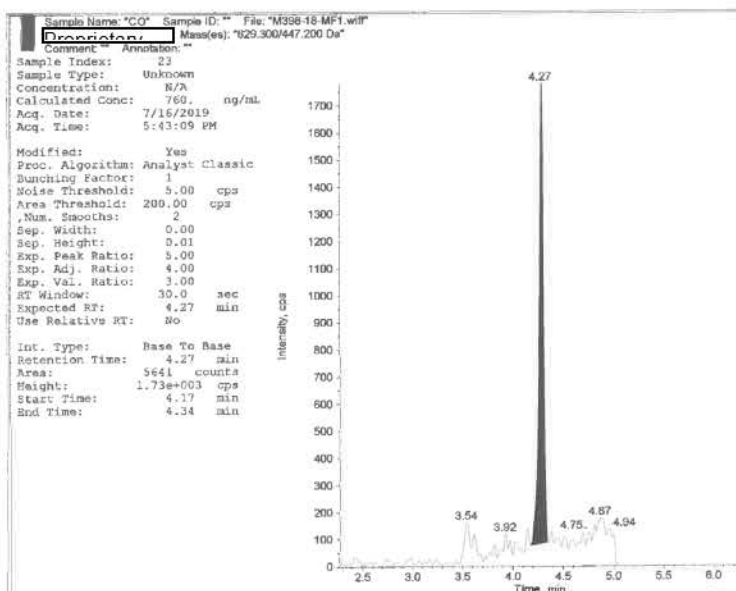


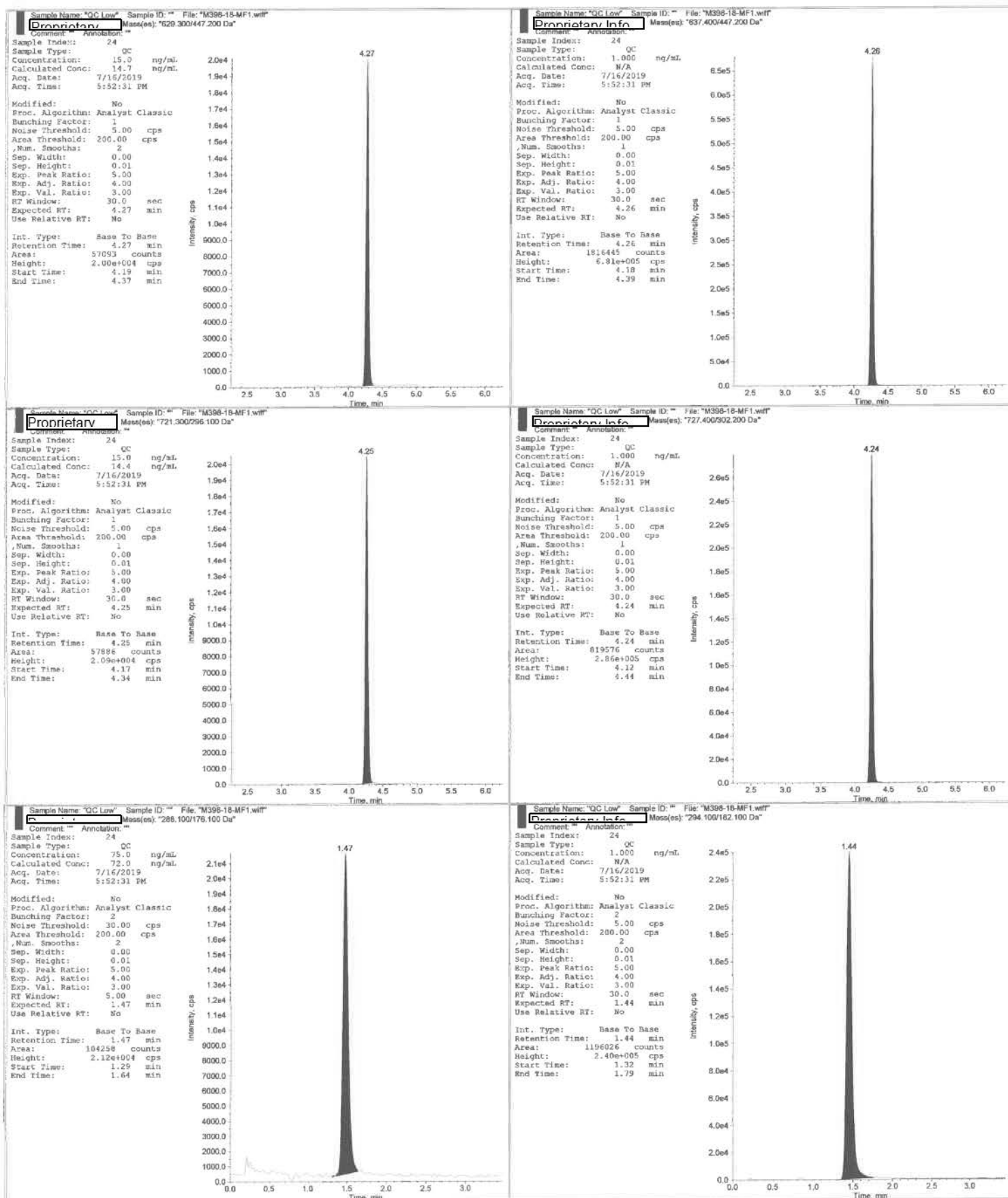


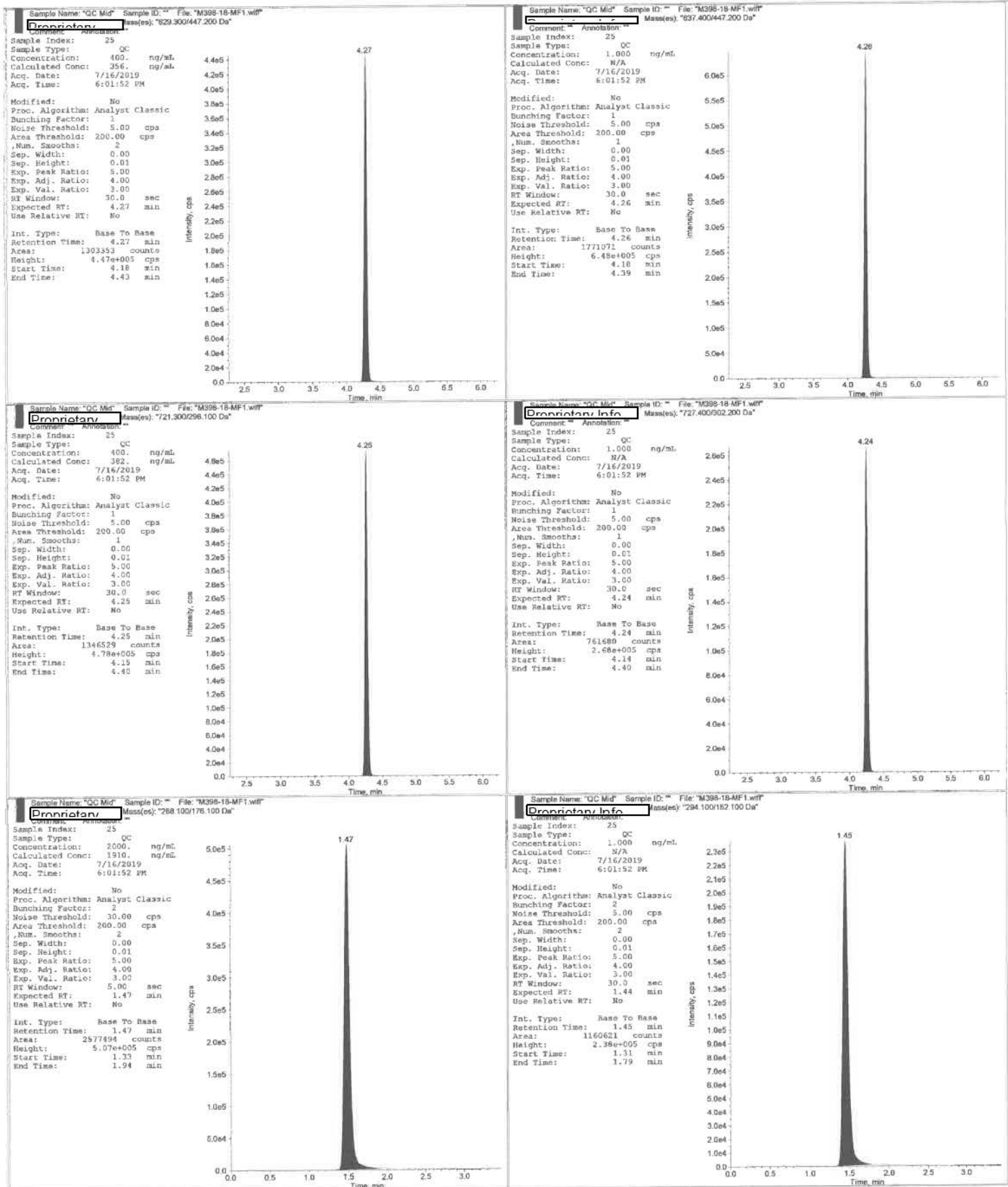


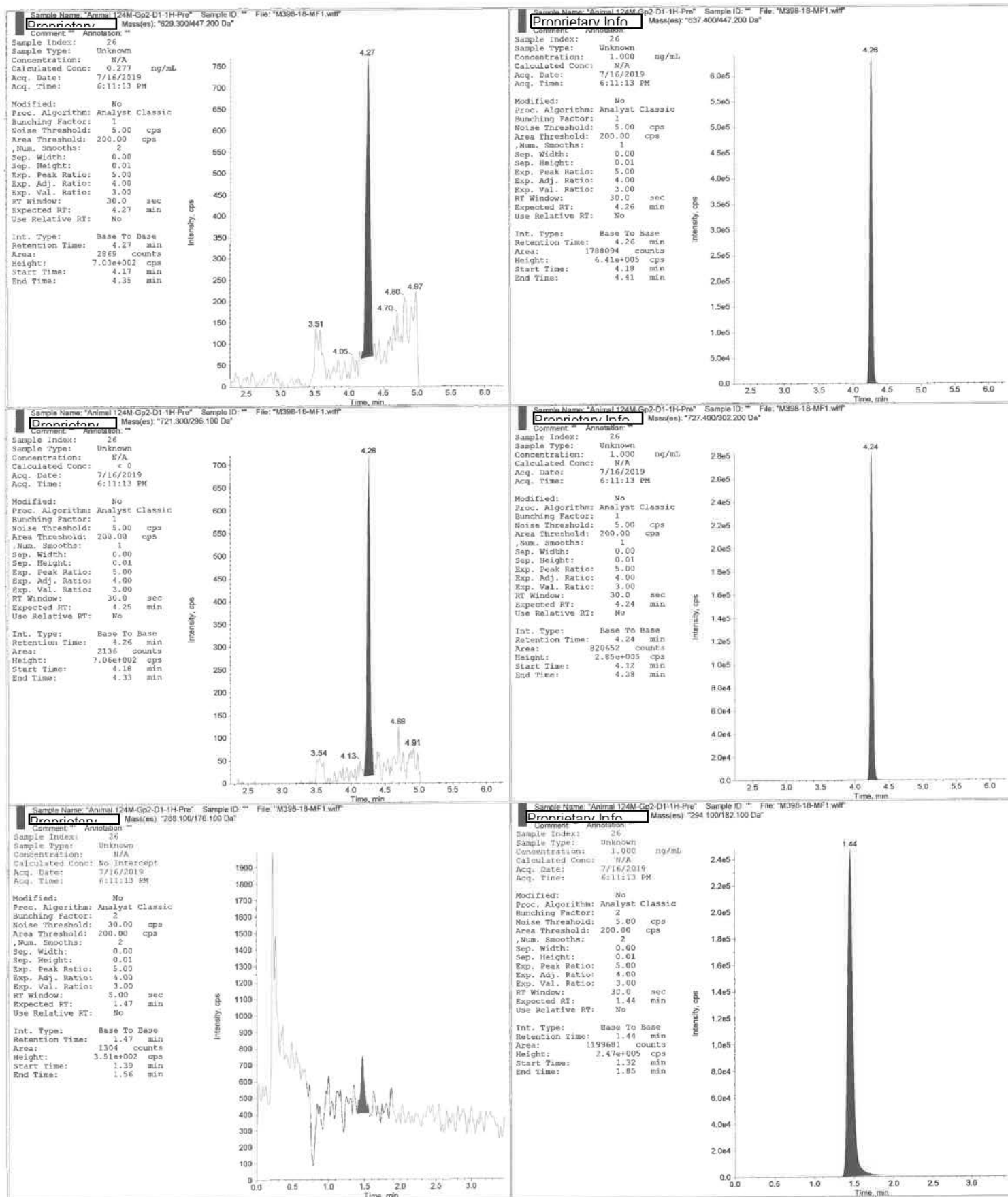
Results Path: D:\Analyst Data\Projects\M398-18\Results\M398-18-MF1-Final.rdb

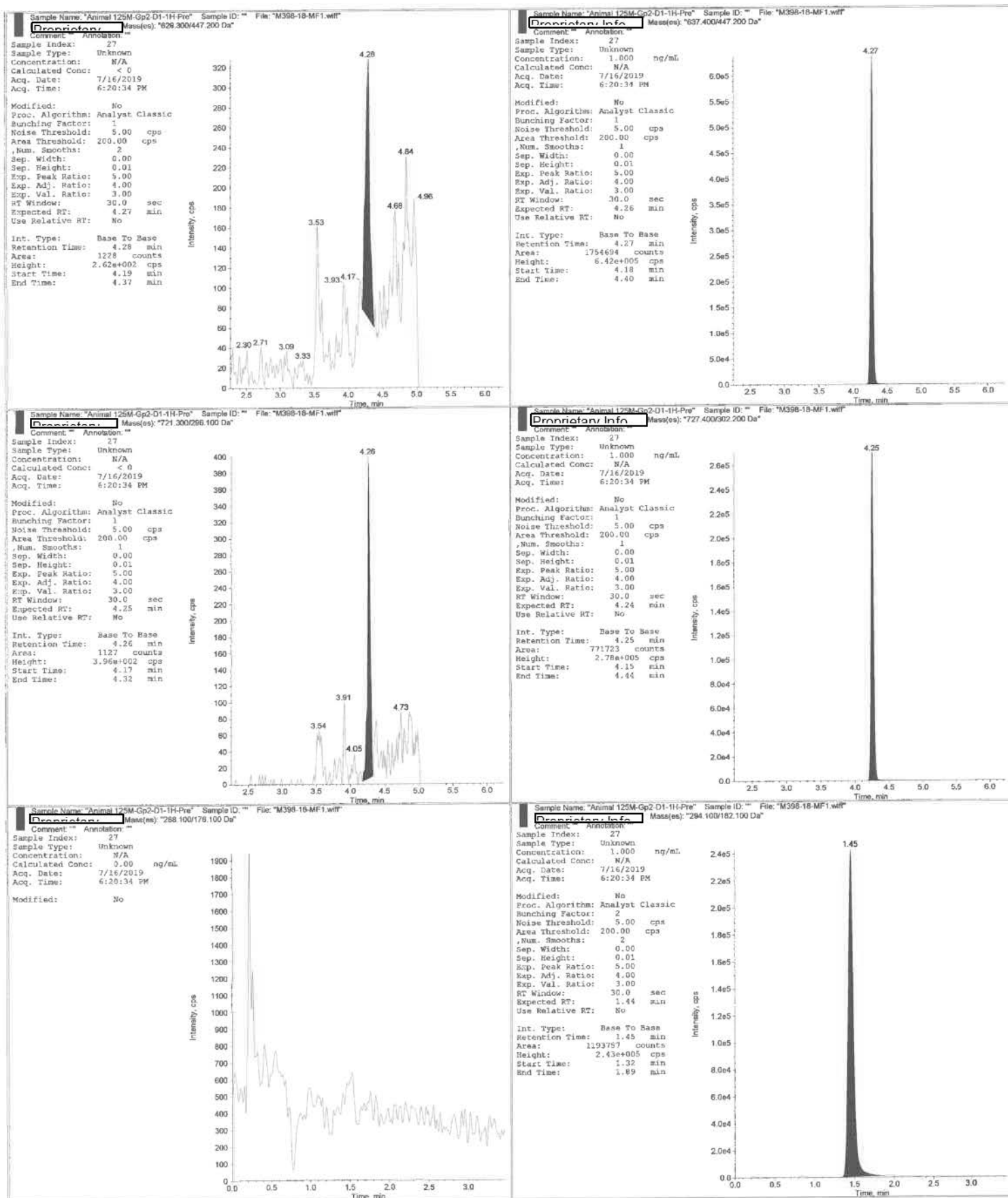


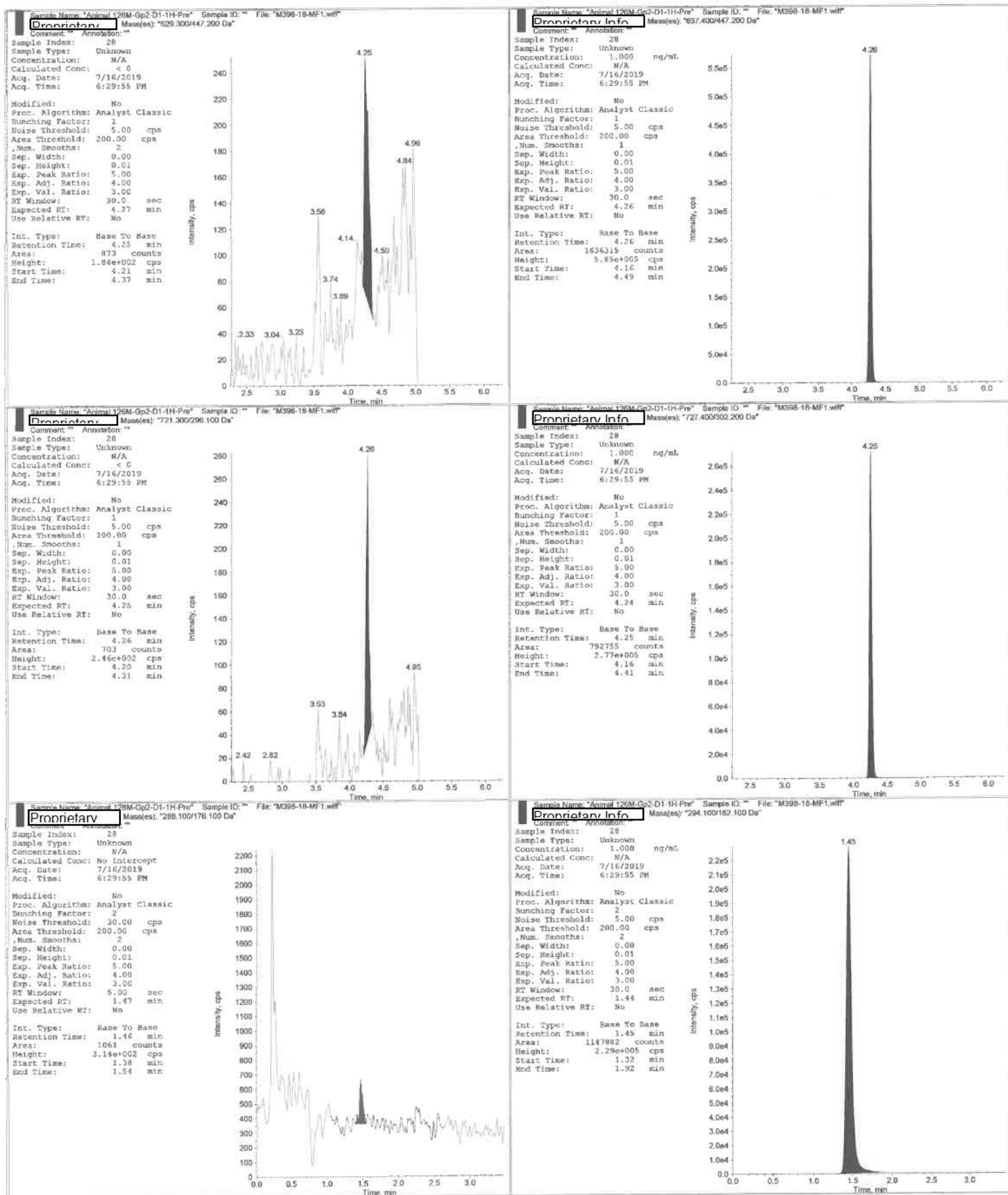




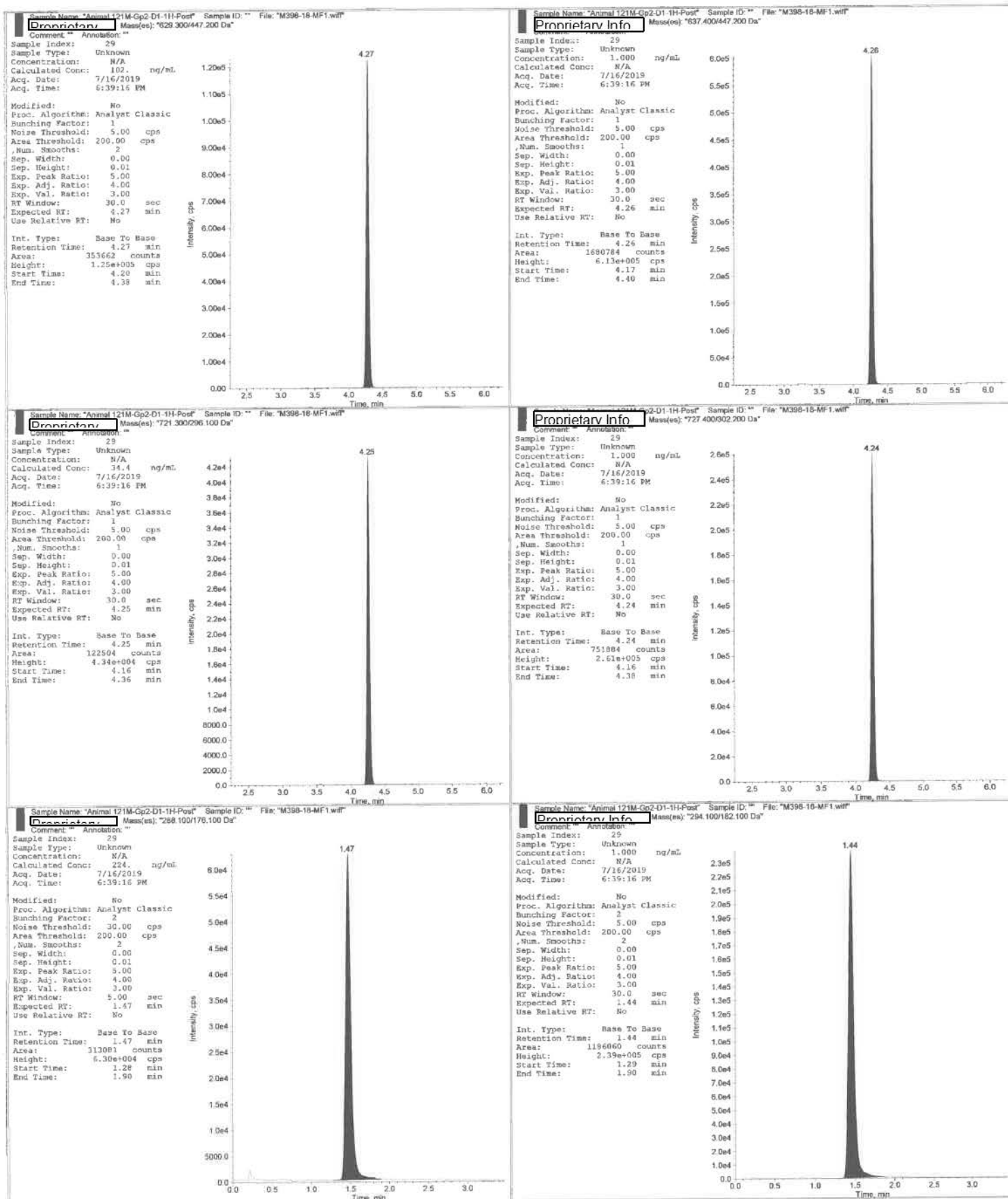




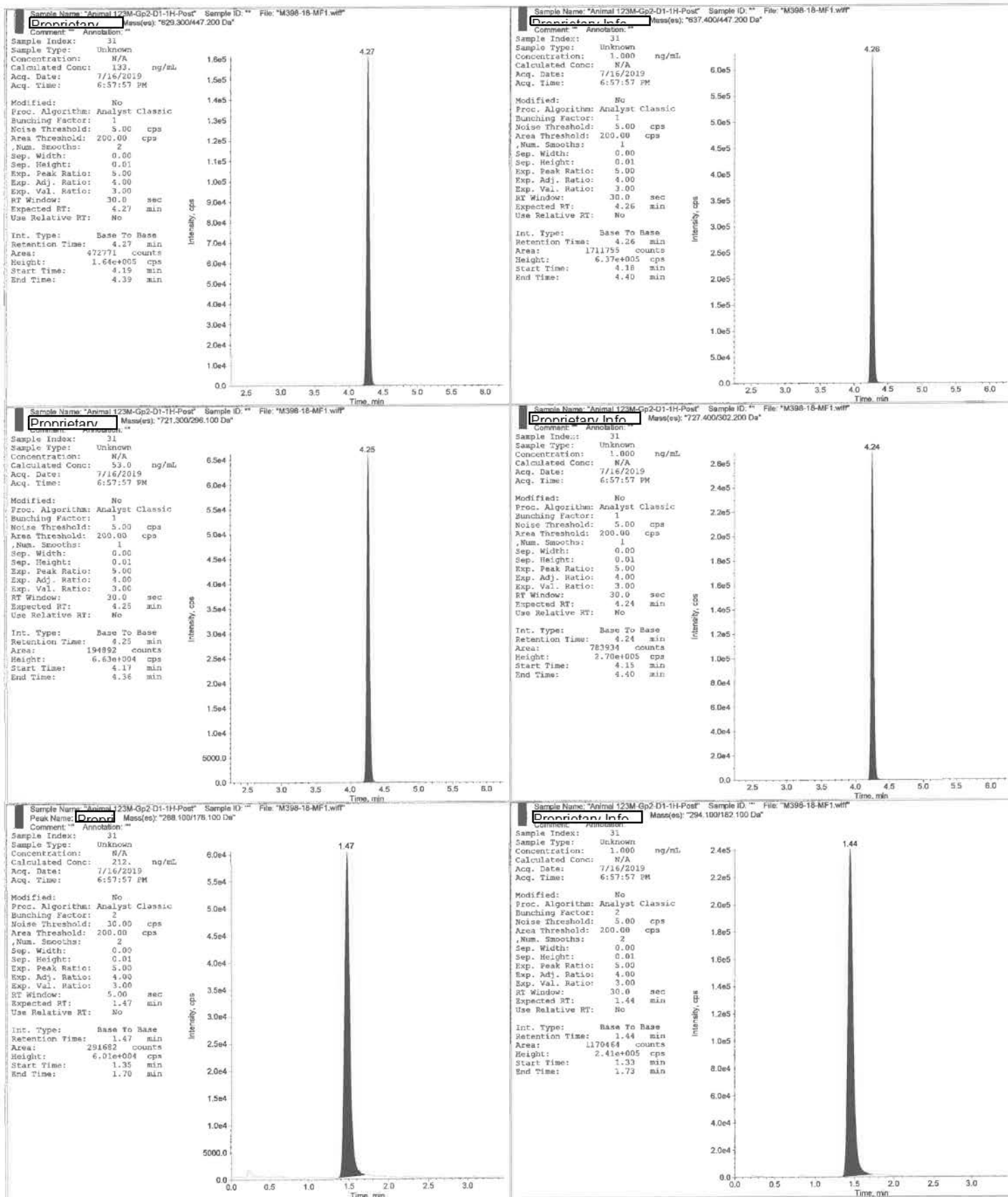


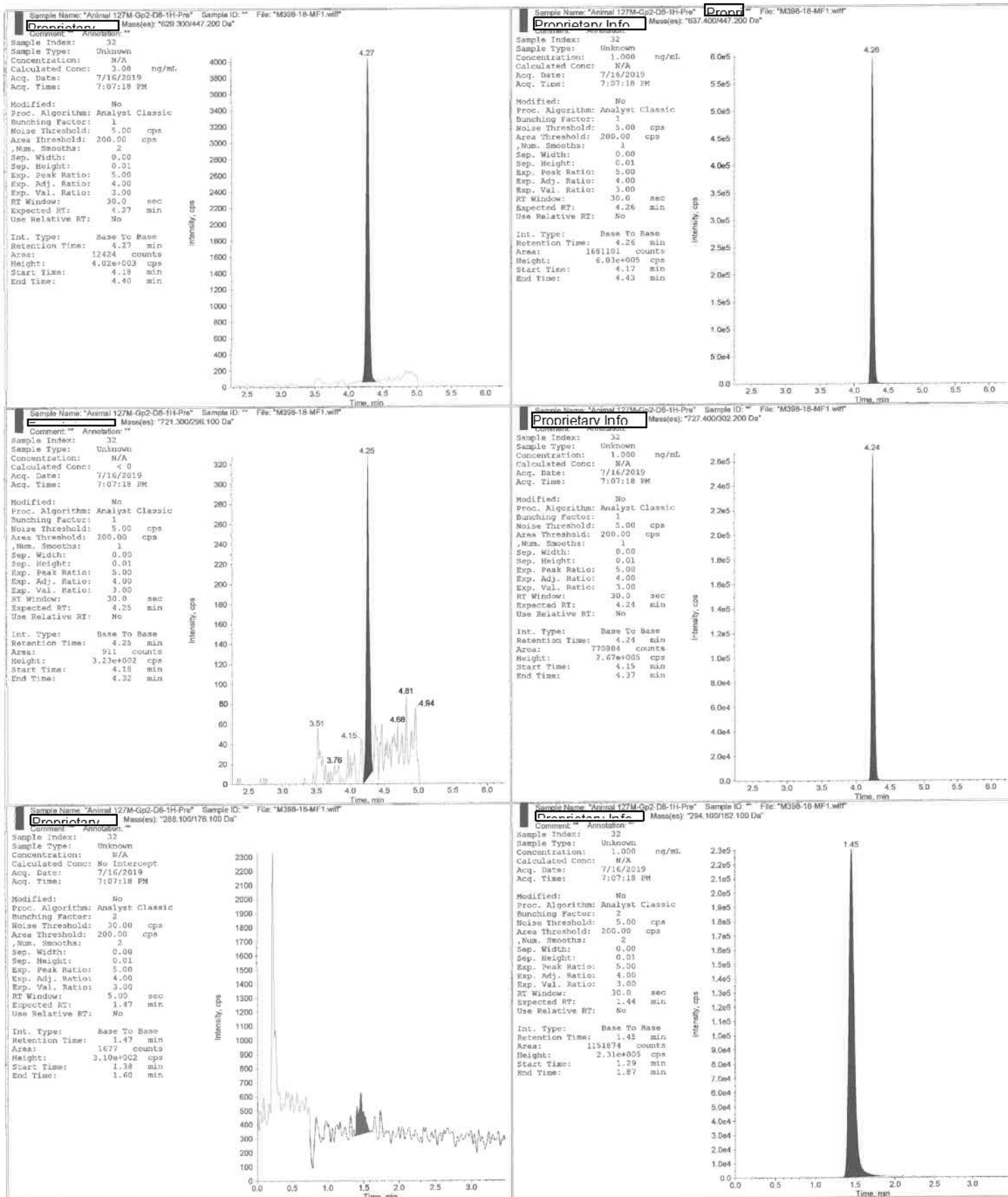


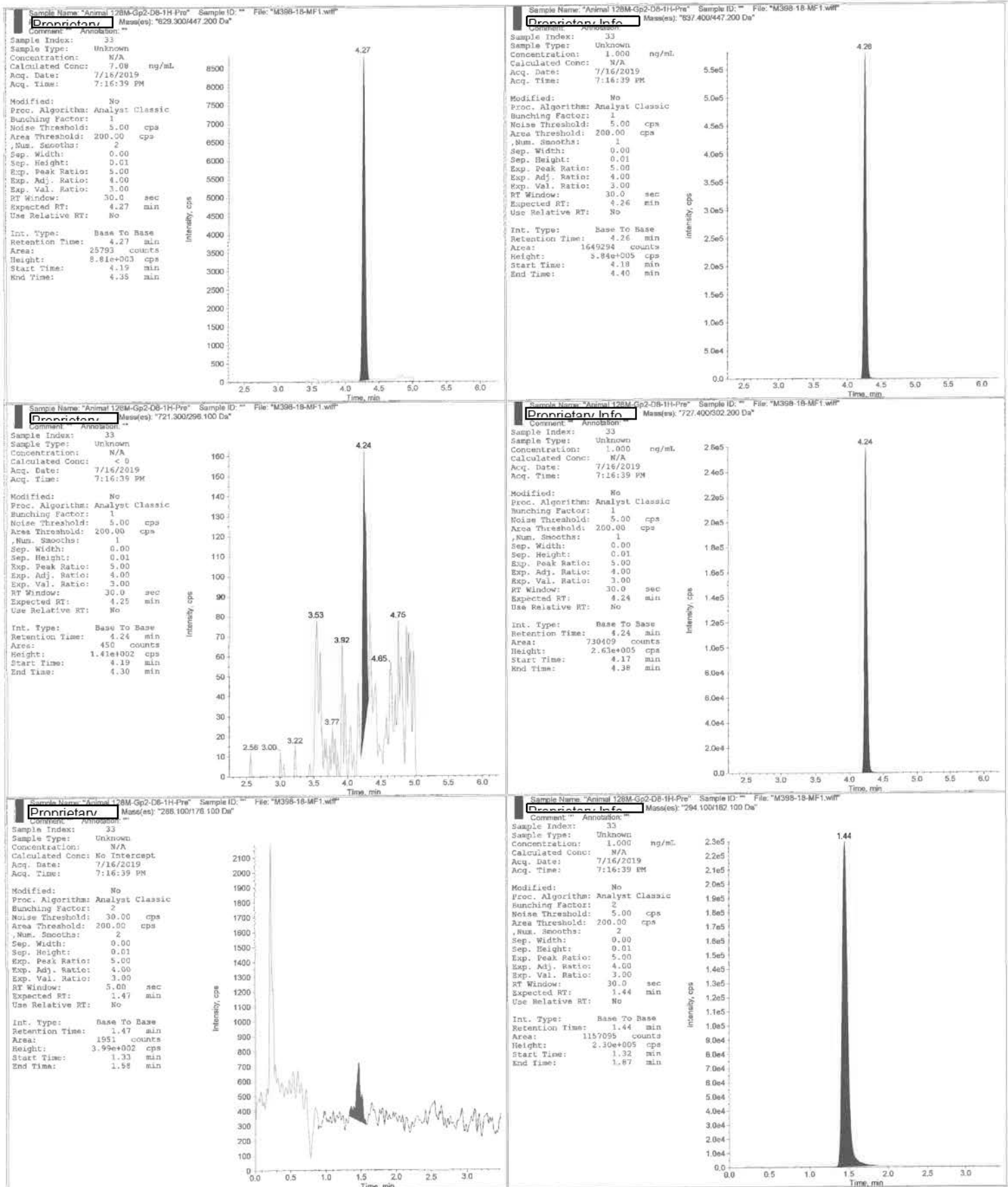
Results Path: D:\Analyst Data\Projects\M398-18\Results\M398-18-MF1-Final.rdb

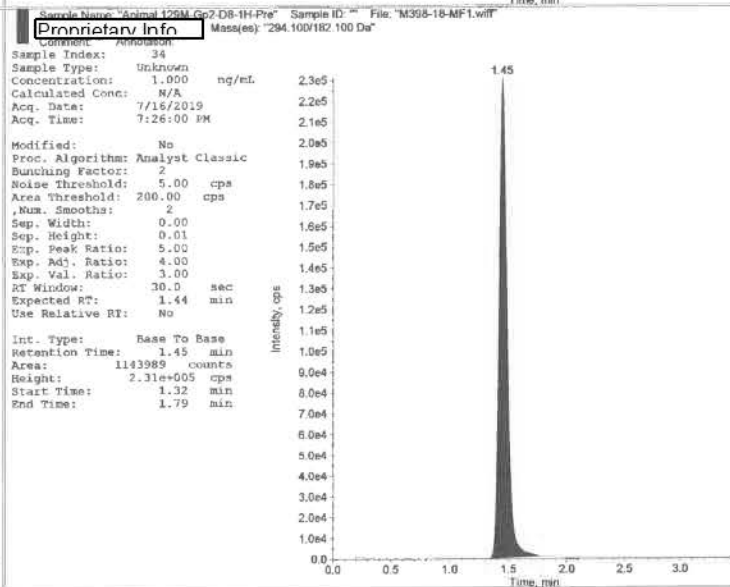
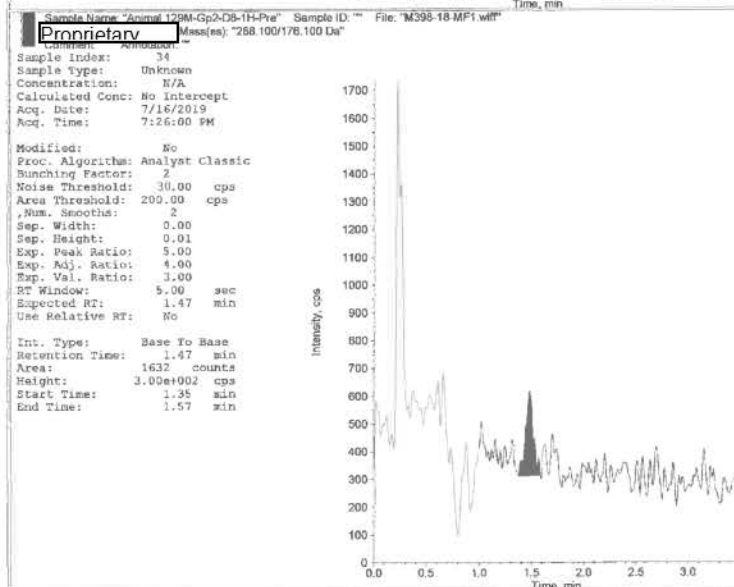
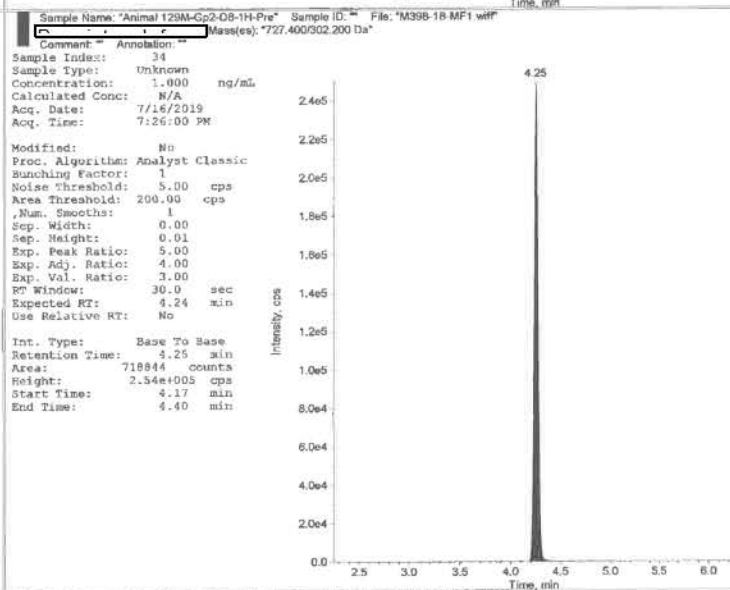
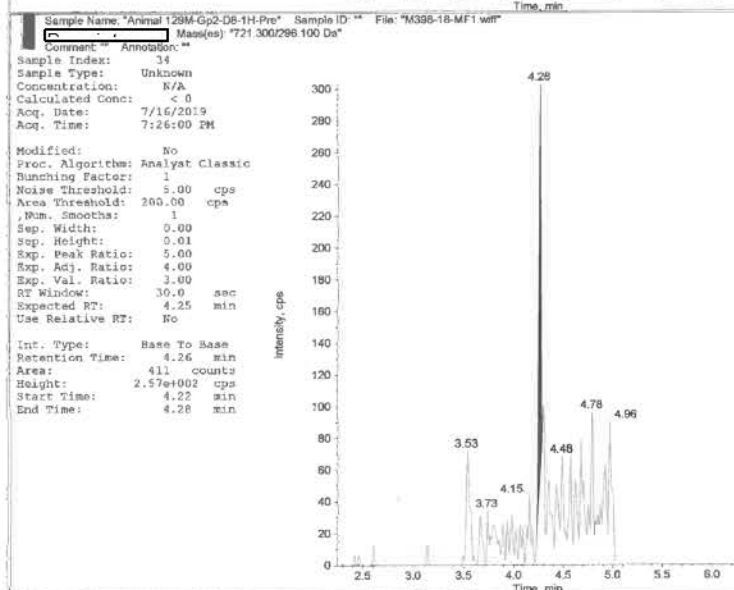
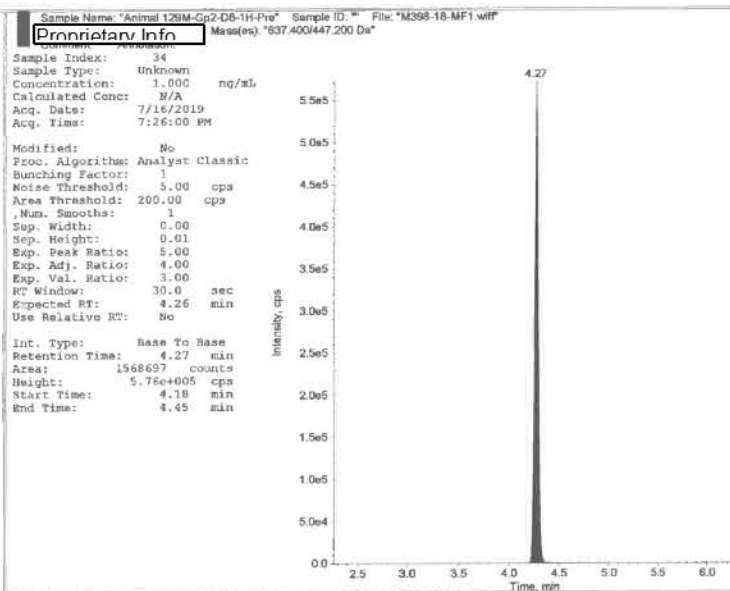
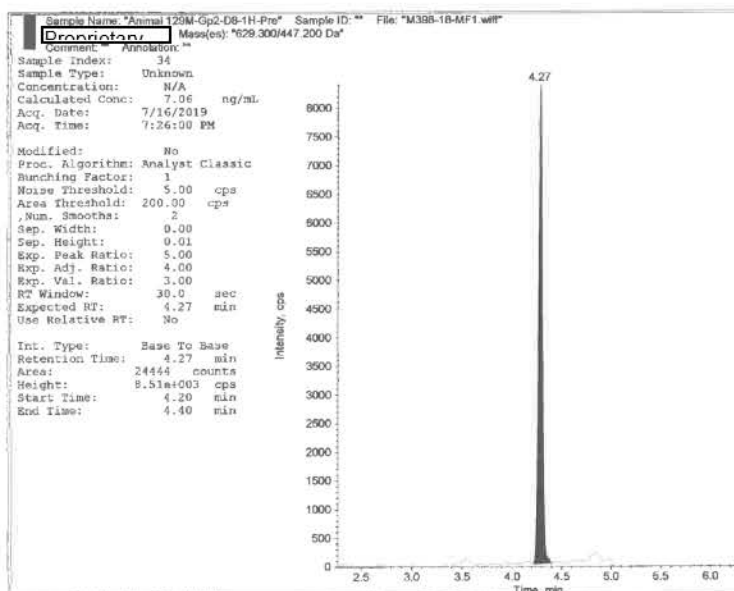


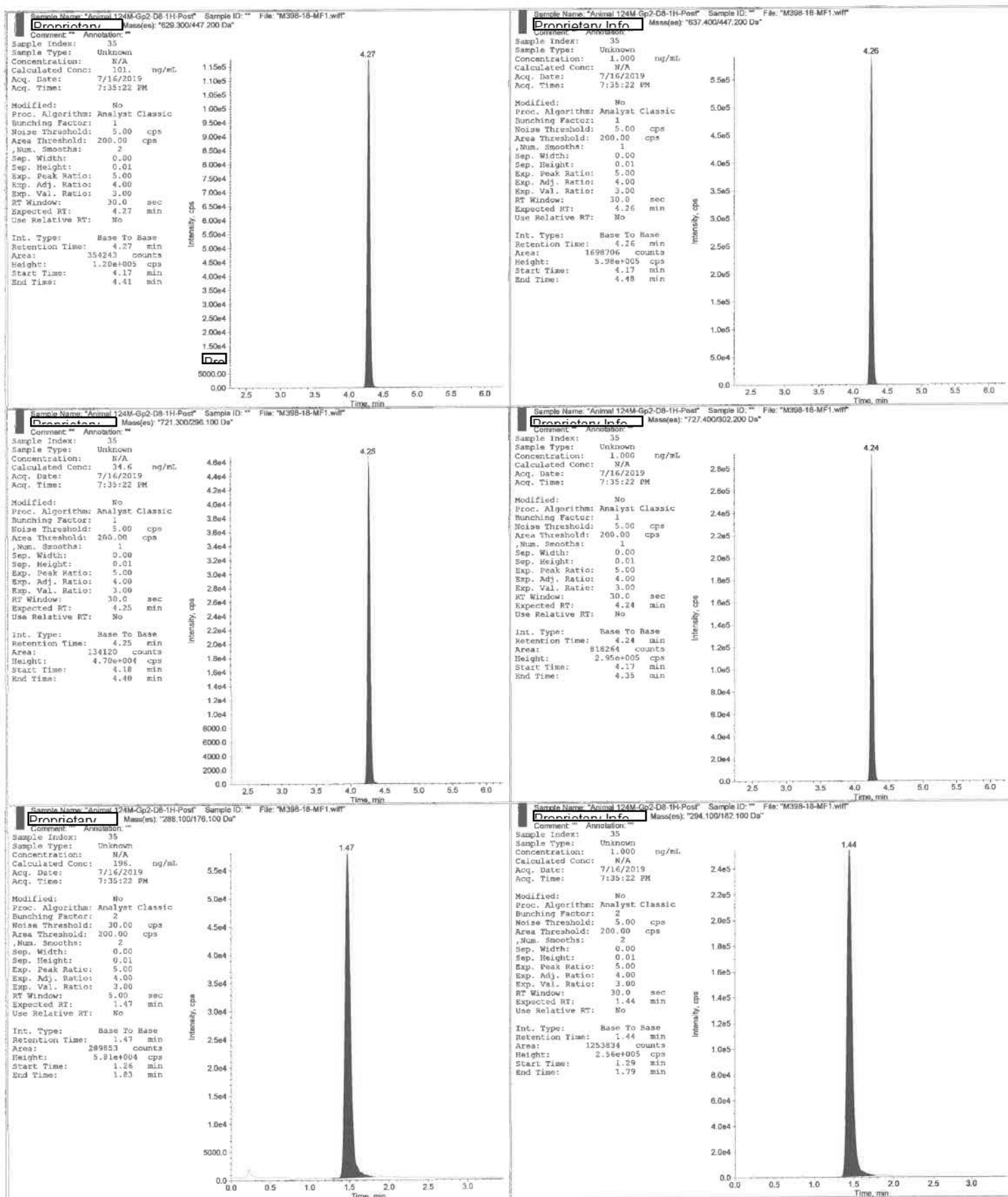


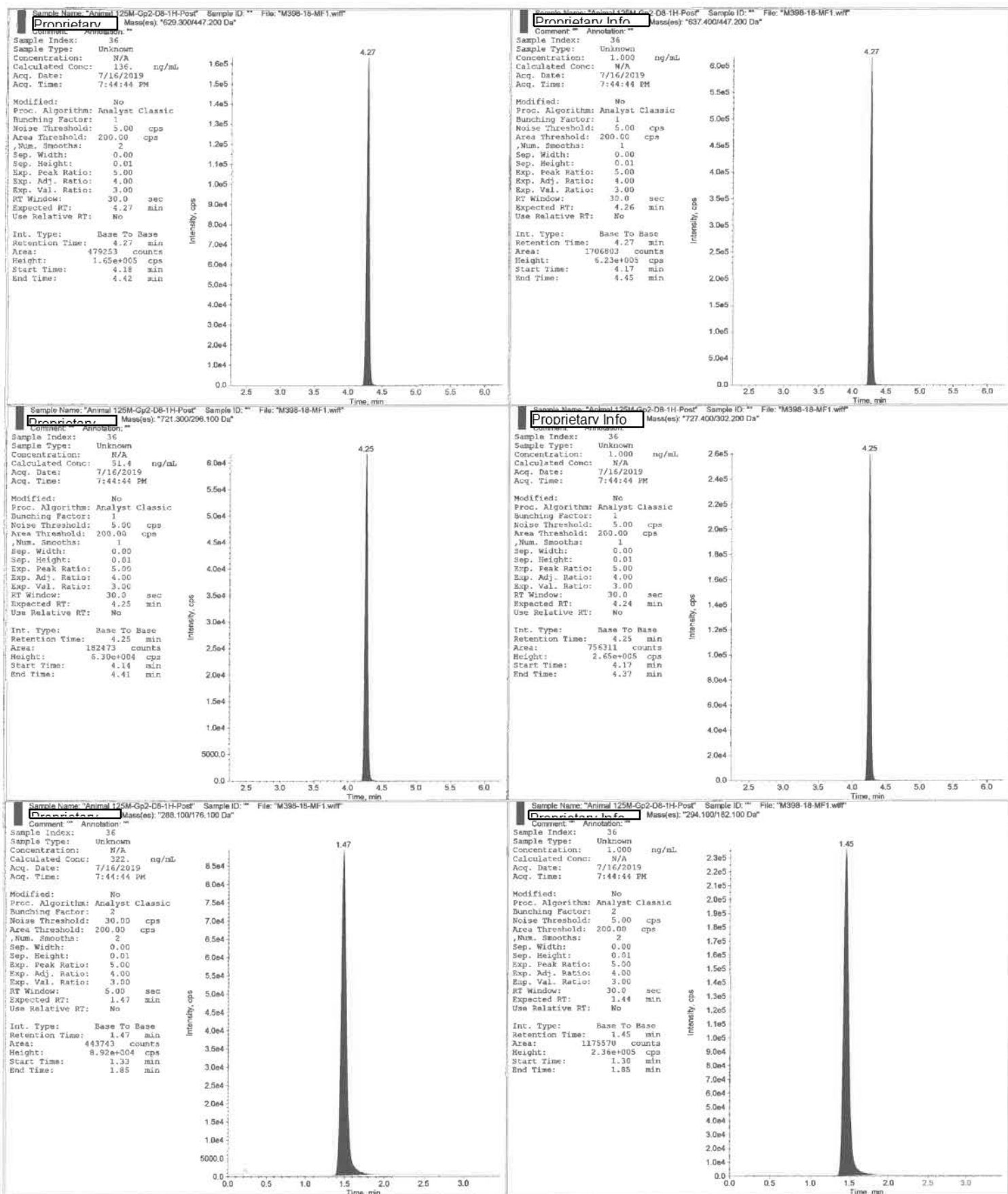


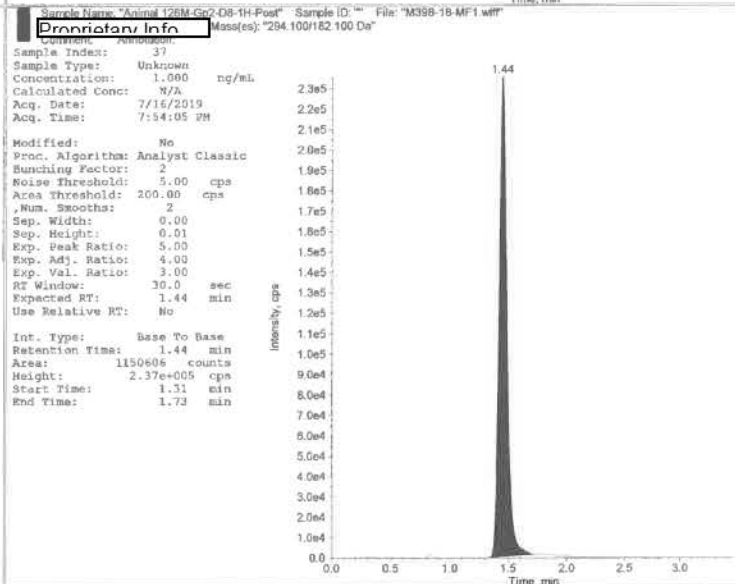
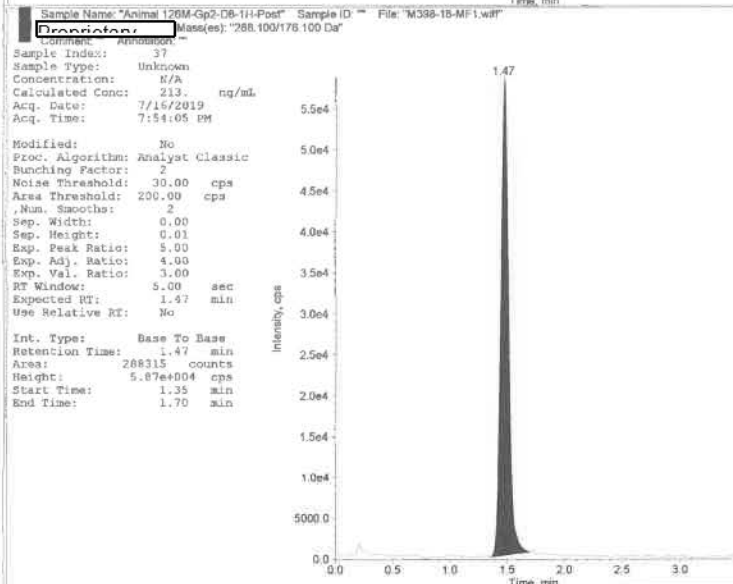
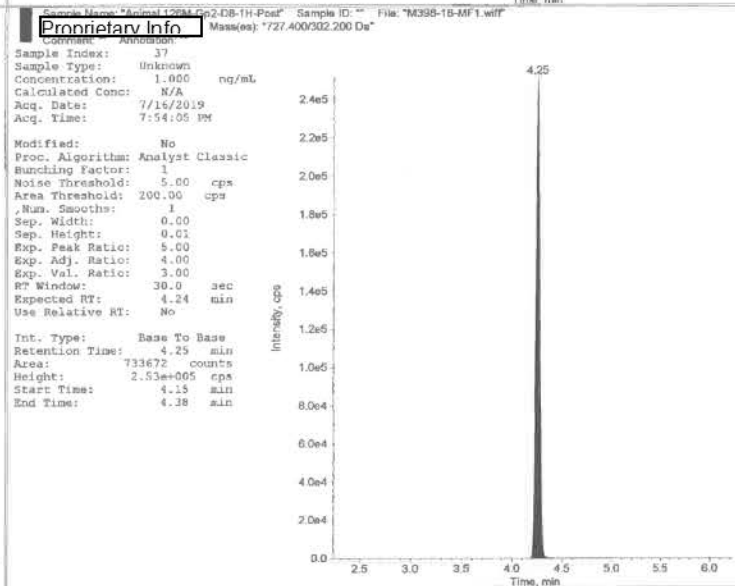
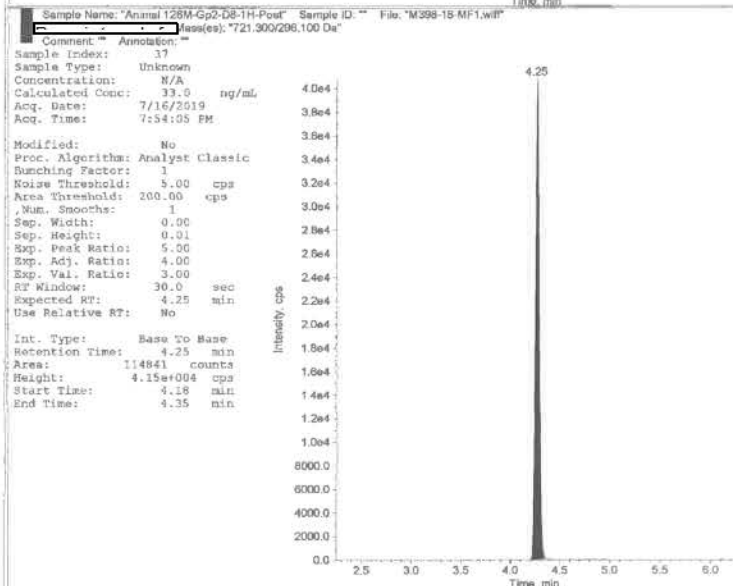
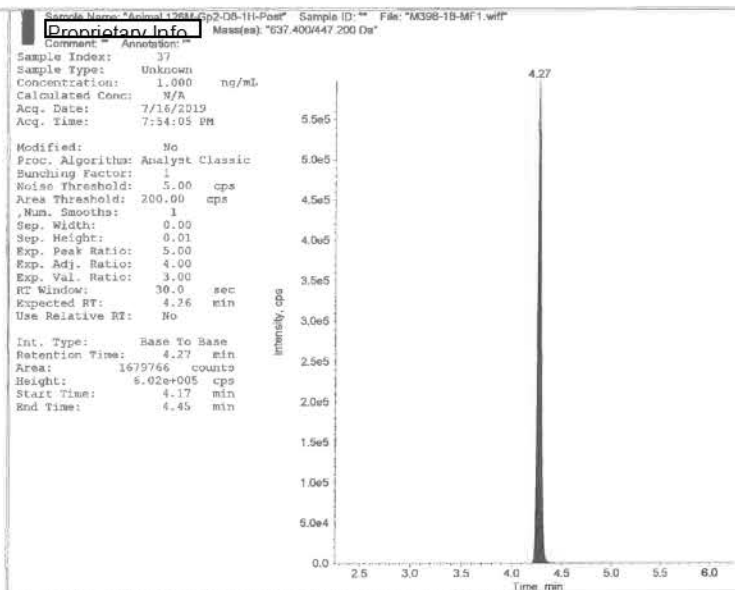
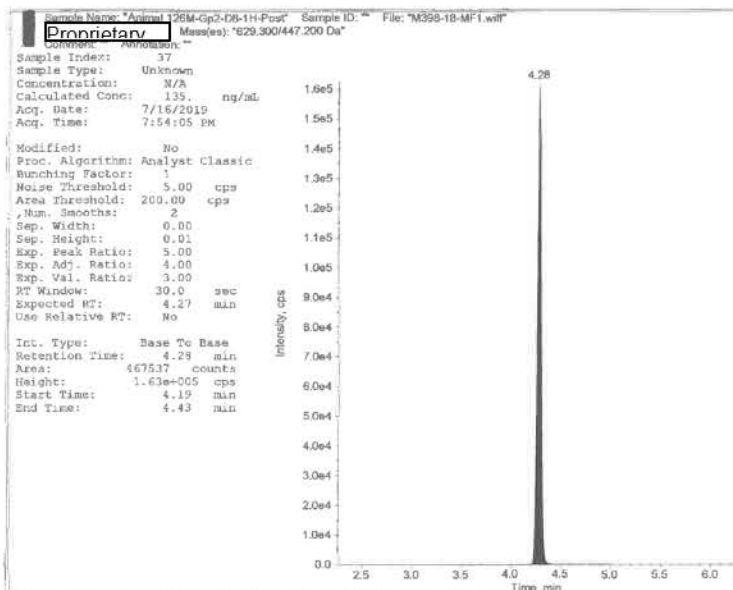












Results Path: D:\Analyst Data\Projects\M398-18\Results\M398-18-MF1-Final.rdb

Sample Name: "Animal 127M-Gp2-D15-1H-Pre" Sample ID: "" File: "M398-18-MF1.wif"

Comment: "Proprietary" Annotation: ""

Sample Index: 38

Sample Type: Unknown

Concentration: N/A

Calculated Conc: 8.09 ng/mL

Acq. Date: 7/16/2019

Acq. Time: 8:03:26 PM

Modified: No

Proc. Algorithm: Analyst Classic

Bunching Factor: 1

Noise Threshold: 5.00 cps

Area Threshold: 200.00 cps

Num. Smoother: 2

Sep. Width: 0.00

Sep. Height: 0.01

Exp. Peak Ratio: 5.00

Exp. Adj. Ratio: 4.00

Exp. Val. Ratio: 3.00

RT Window: 30.0 sec

Expected RT: 4.27 min

Use Relative RT: No

Int. Type: Base To Base

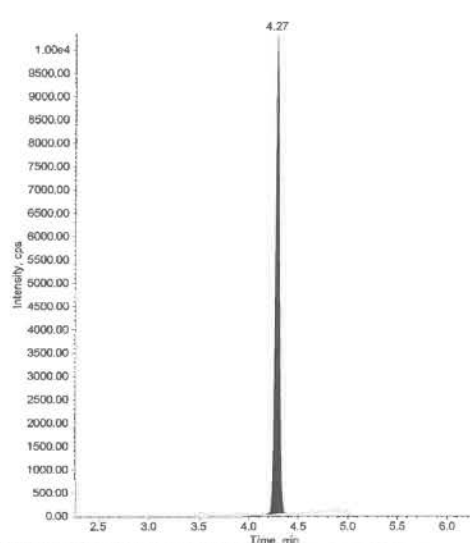
Retention Time: 4.27 min

Area: 29615 counts

Height: 1.03e+004 cps

Start Time: 4.17 min

End Time: 4.37 min



Sample Name: "Animal 127M-Gp2-D15-1H-Pre" Sample ID: "" File: "M398-18-MF1.wif"

Comment: "Proprietary" Annotation: ""

Sample Index: 38

Sample Type: Unknown

Concentration: 1.000 ng/mL

Calculated Conc: N/A

Acq. Date: 7/16/2019

Acq. Time: 8:03:26 PM

Modified: No

Proc. Algorithm: Analyst Classic

Bunching Factor: 1

Noise Threshold: 5.00 cps

Area Threshold: 200.00 cps

Num. Smoother: 1

Sep. Width: 0.00

Sep. Height: 0.01

Exp. Peak Ratio: 5.00

Exp. Adj. Ratio: 4.00

Exp. Val. Ratio: 3.00

RT Window: 30.0 sec

Expected RT: 4.26 min

Use Relative RT: No

Int. Type: Base To Base

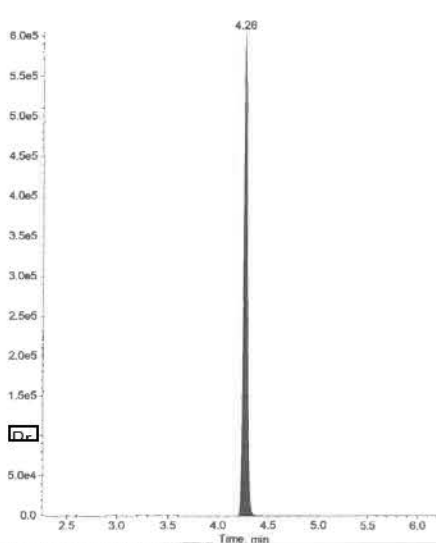
Retention Time: 4.26 min

Area: 1672398 counts

Height: 6.08e+005 cps

Start Time: 4.17 min

End Time: 4.40 min



Sample Name: "Animal 127M-Gp2-D15-1H-Pre" Sample ID: "" File: "M398-18-MF1.wif"

Comment: "Proprietary" Annotation: ""

Sample Index: 38

Sample Type: Unknown

Concentration: N/A

Calculated Conc: < 0

Acq. Date: 7/16/2019

Acq. Time: 8:03:26 PM

Modified: No

Proc. Algorithm: Analyst Classic

Bunching Factor: 1

Noise Threshold: 5.00 cps

Area Threshold: 200.00 cps

Num. Smoother: 1

Sep. Width: 0.00

Sep. Height: 0.01

Exp. Peak Ratio: 5.00

Exp. Adj. Ratio: 4.00

Exp. Val. Ratio: 3.00

RT Window: 30.0 sec

Expected RT: 4.25 min

Use Relative RT: No

Int. Type: Base To Base

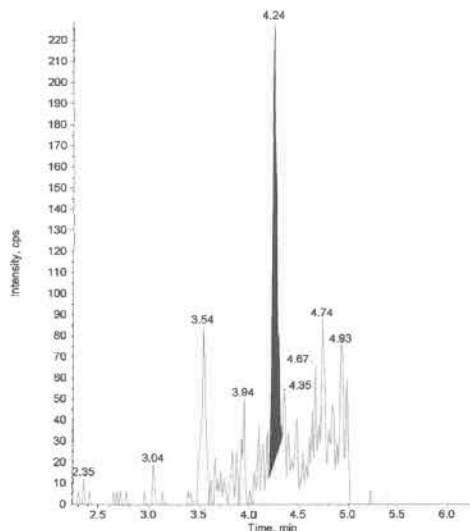
Retention Time: 4.24 min

Area: 622 counts

Height: 2.12e+002 cps

Start Time: 4.20 min

End Time: 4.33 min



Sample Name: "Animal 127M-Gp2-D15-1H-Pre" Sample ID: "" File: "M398-18-MF1.wif"

Comment: "Proprietary" Annotation: ""

Sample Index: 38

Sample Type: Unknown

Concentration: 1.000 ng/mL

Calculated Conc: N/A

Acq. Date: 7/16/2019

Acq. Time: 8:03:26 PM

Modified: No

Proc. Algorithm: Analyst Classic

Bunching Factor: 1

Noise Threshold: 5.00 cps

Area Threshold: 200.00 cps

Num. Smoother: 1

Sep. Width: 0.00

Sep. Height: 0.01

Exp. Peak Ratio: 5.00

Exp. Adj. Ratio: 4.00

Exp. Val. Ratio: 3.00

RT Window: 30.0 sec

Expected RT: 4.24 min

Use Relative RT: No

Int. Type: Base To Base

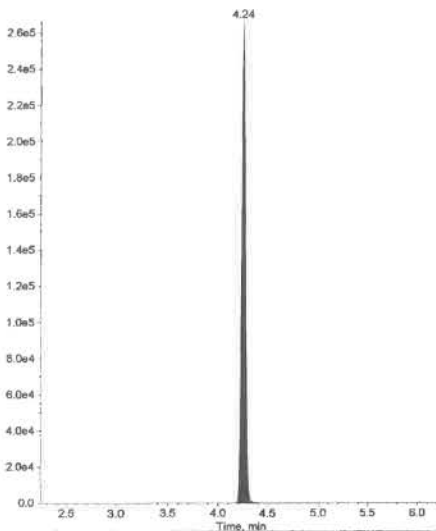
Retention Time: 4.24 min

Area: 777241 counts

Height: 2.67e+005 cps

Start Time: 4.11 min

End Time: 4.43 min



Sample Name: "Animal 127M-Gp2-D15-1H-Pre" Sample ID: "" File: "M398-18-MF1.wif"

Comment: "Proprietary" Annotation: ""

Sample Index: 38

Sample Type: Unknown

Concentration: N/A

Calculated Conc: No Intercept

Acq. Date: 7/16/2019

Acq. Time: 8:03:26 PM

Modified: No

Proc. Algorithm: Analyst Classic

Bunching Factor: 2

Noise Threshold: 30.00 cps

Area Threshold: 200.00 cps

Num. Smoother: 2

Sep. Width: 0.00

Sep. Height: 0.01

Exp. Peak Ratio: 5.00

Exp. Adj. Ratio: 4.00

Exp. Val. Ratio: 3.00

RT Window: 5.00 sec

Expected RT: 1.47 min

Use Relative RT: No

Int. Type: Base To Base

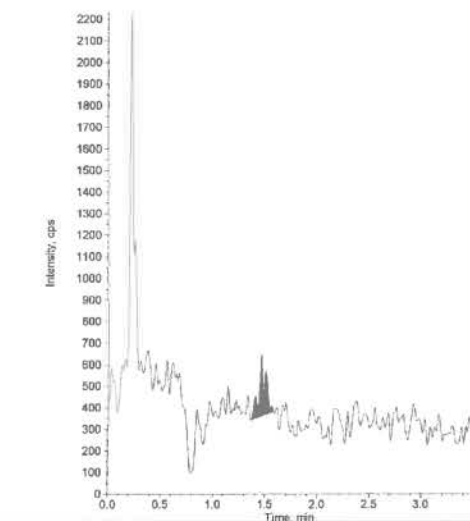
Retention Time: 1.46 min

Area: 1350 counts

Height: 2.85e+002 cps

Start Time: 1.35 min

End Time: 1.57 min



Sample Name: "Animal 127M-Gp2-D15-1H-Pre" Sample ID: "" File: "M398-18-MF1.wif"

Comment: "Proprietary" Annotation: ""

Sample Index: 38

Sample Type: Unknown

Concentration: 1.000 ng/mL

Calculated Conc: N/A

Acq. Date: 7/16/2019

Acq. Time: 8:03:26 PM

Modified: No

Proc. Algorithm: Analyst Classic

Bunching Factor: 2

Noise Threshold: 5.00 cps

Area Threshold: 200.00 cps

Num. Smoother: 2

Sep. Width: 0.00

Sep. Height: 0.01

Exp. Peak Ratio: 5.00

Exp. Adj. Ratio: 4.00

Exp. Val. Ratio: 3.00

RT Window: 30.0 sec

Expected RT: 1.44 min

Use Relative RT: No

Int. Type: Base To Base

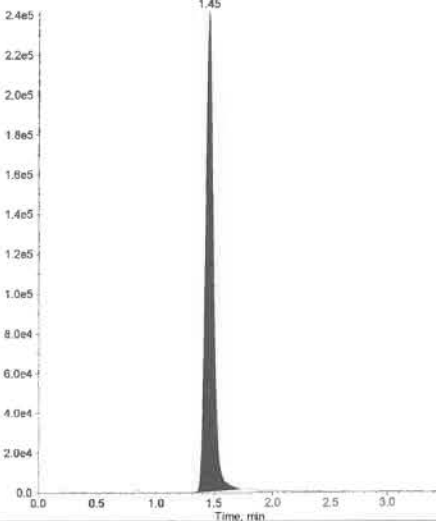
Retention Time: 1.45 min

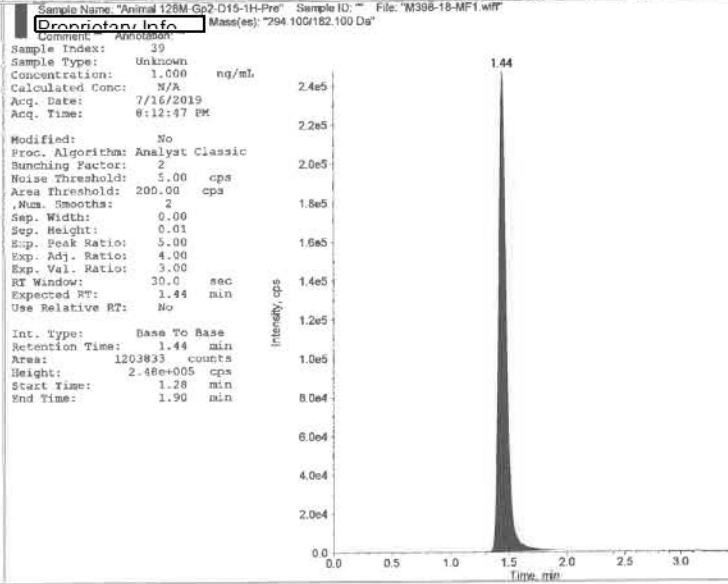
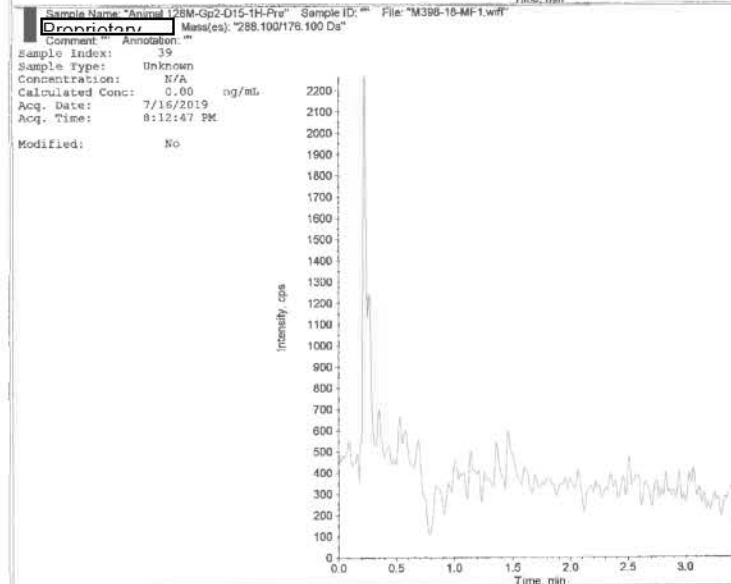
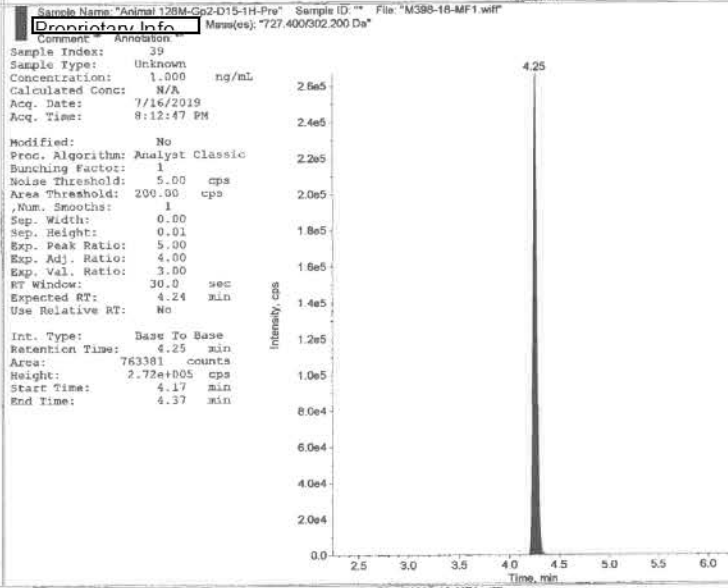
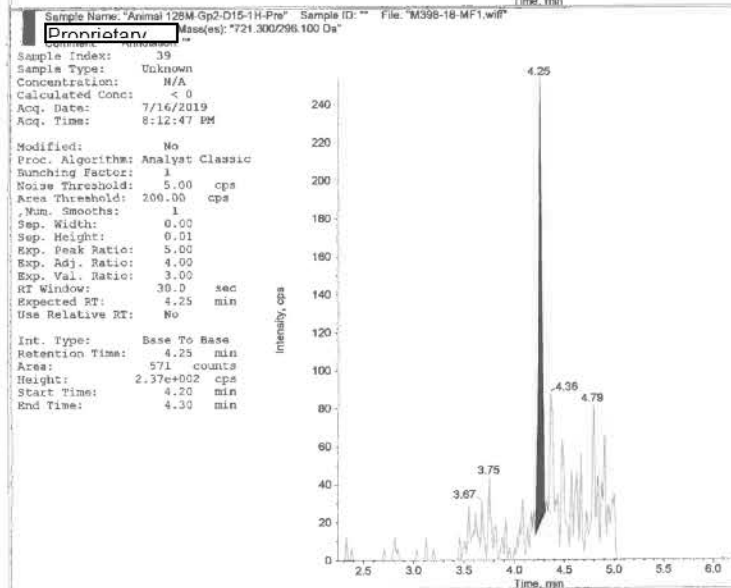
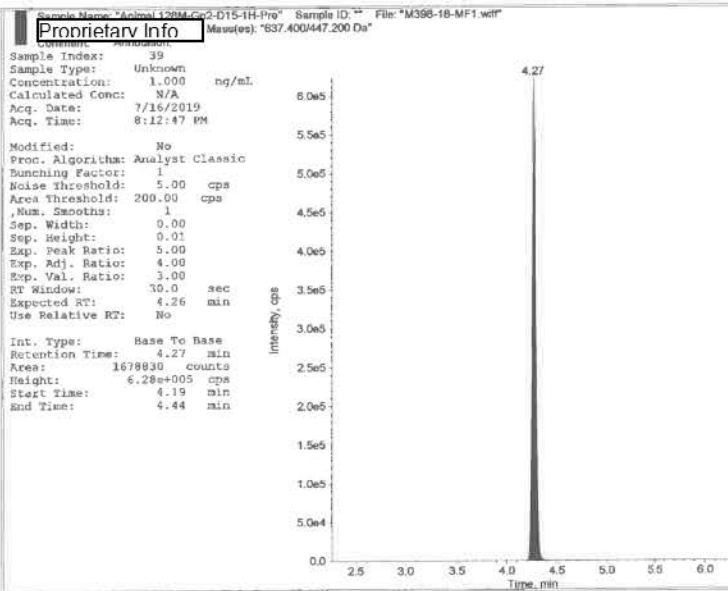
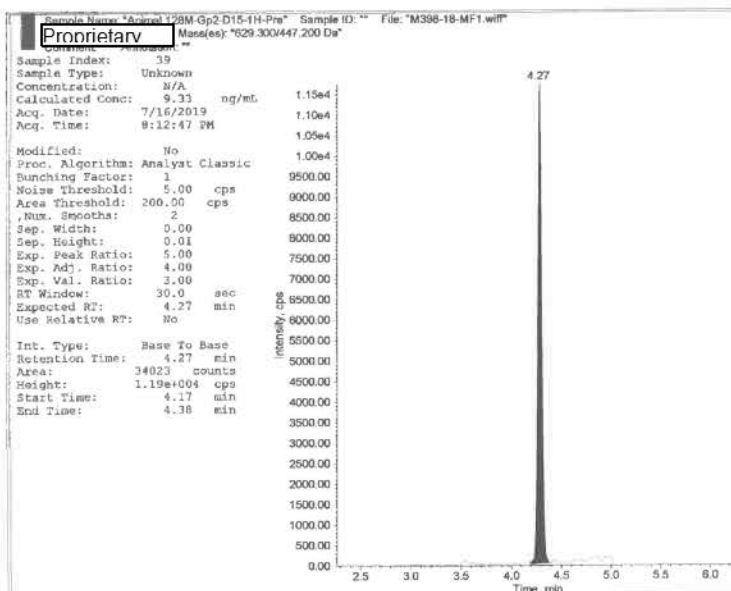
Area: 1167860 counts

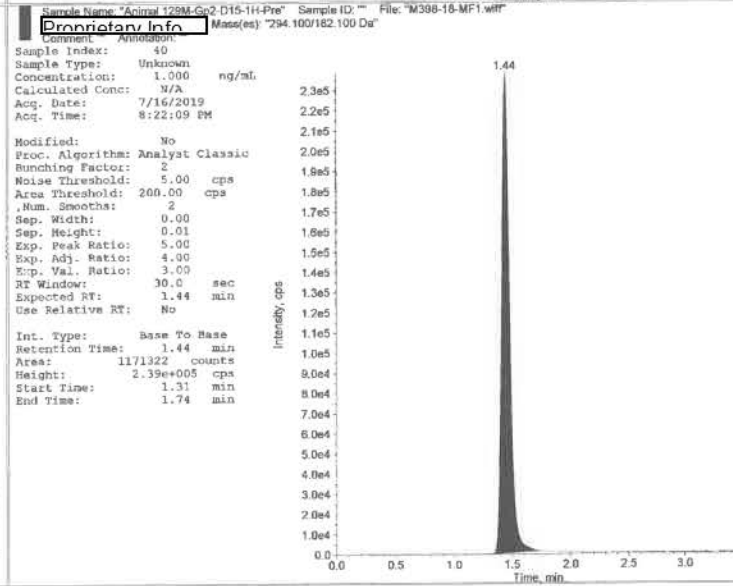
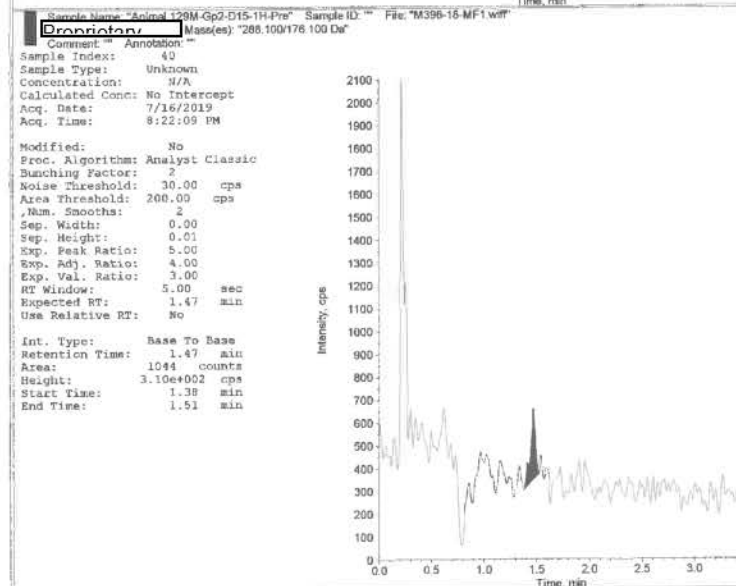
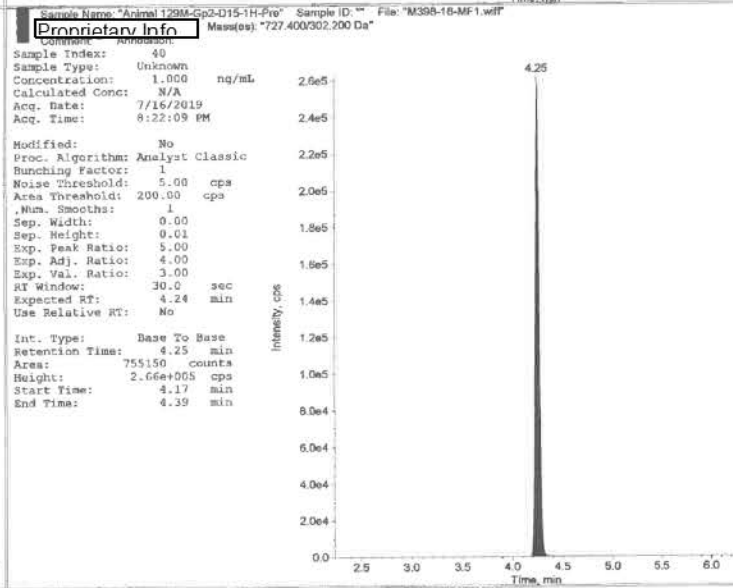
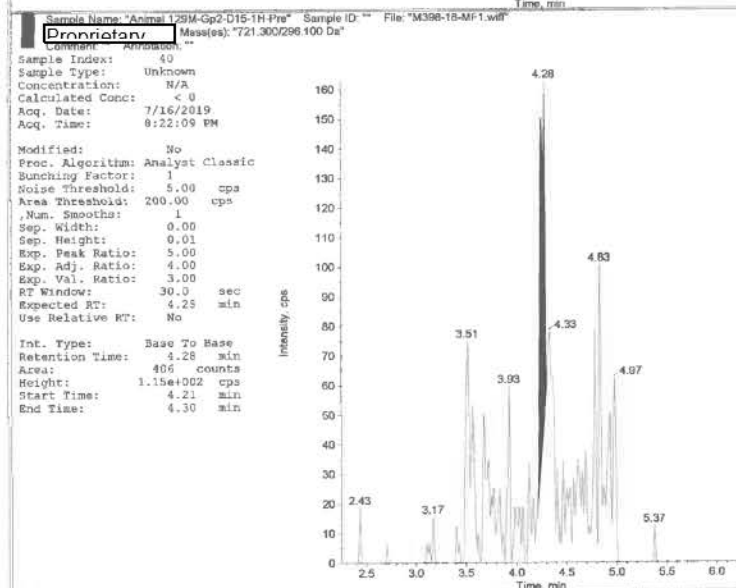
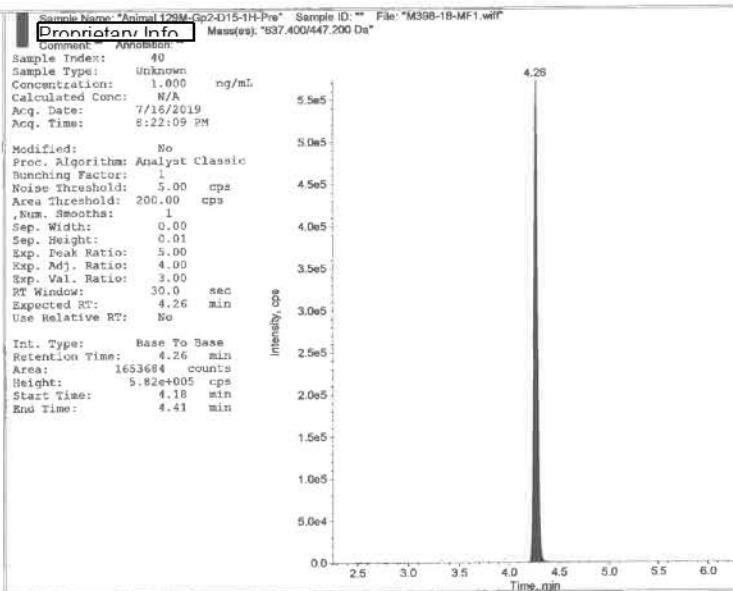
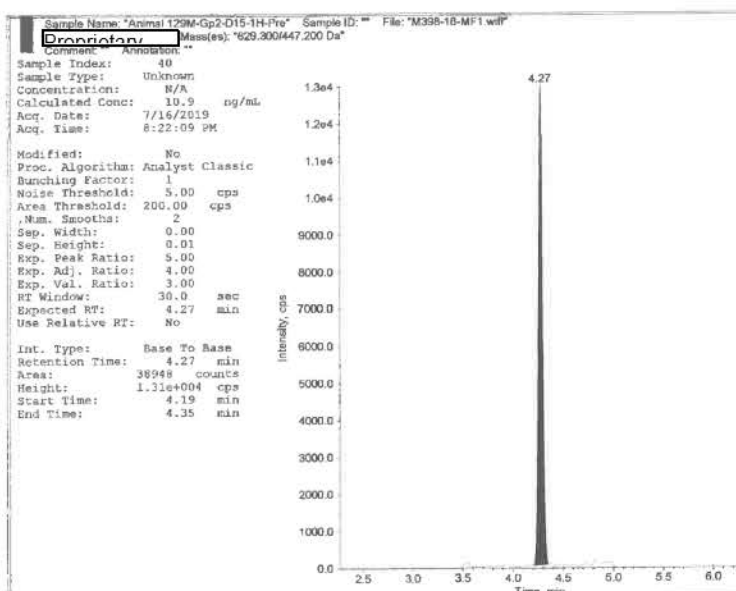
Height: 2.43e+005 cps

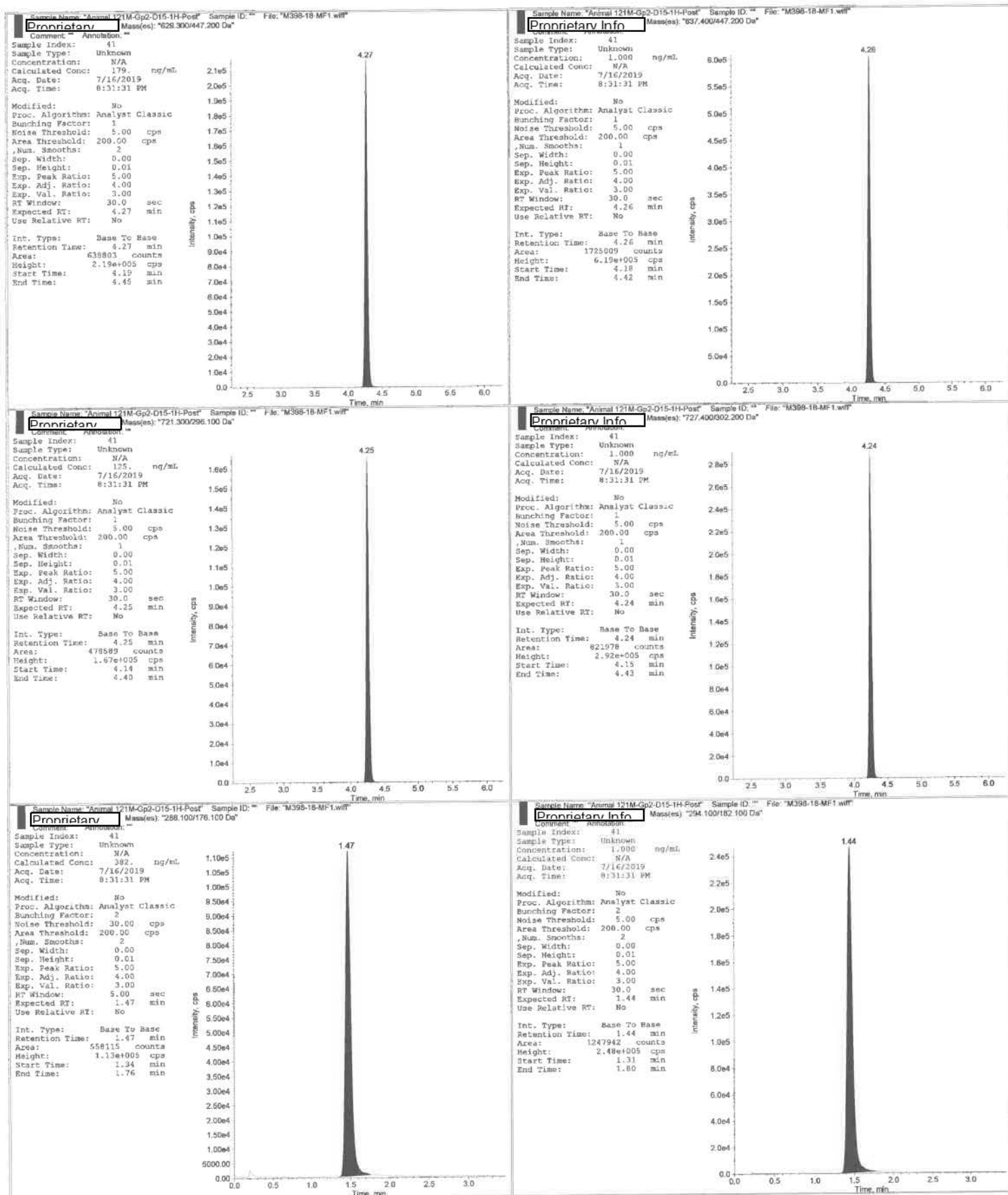
Start Time: 1.32 min

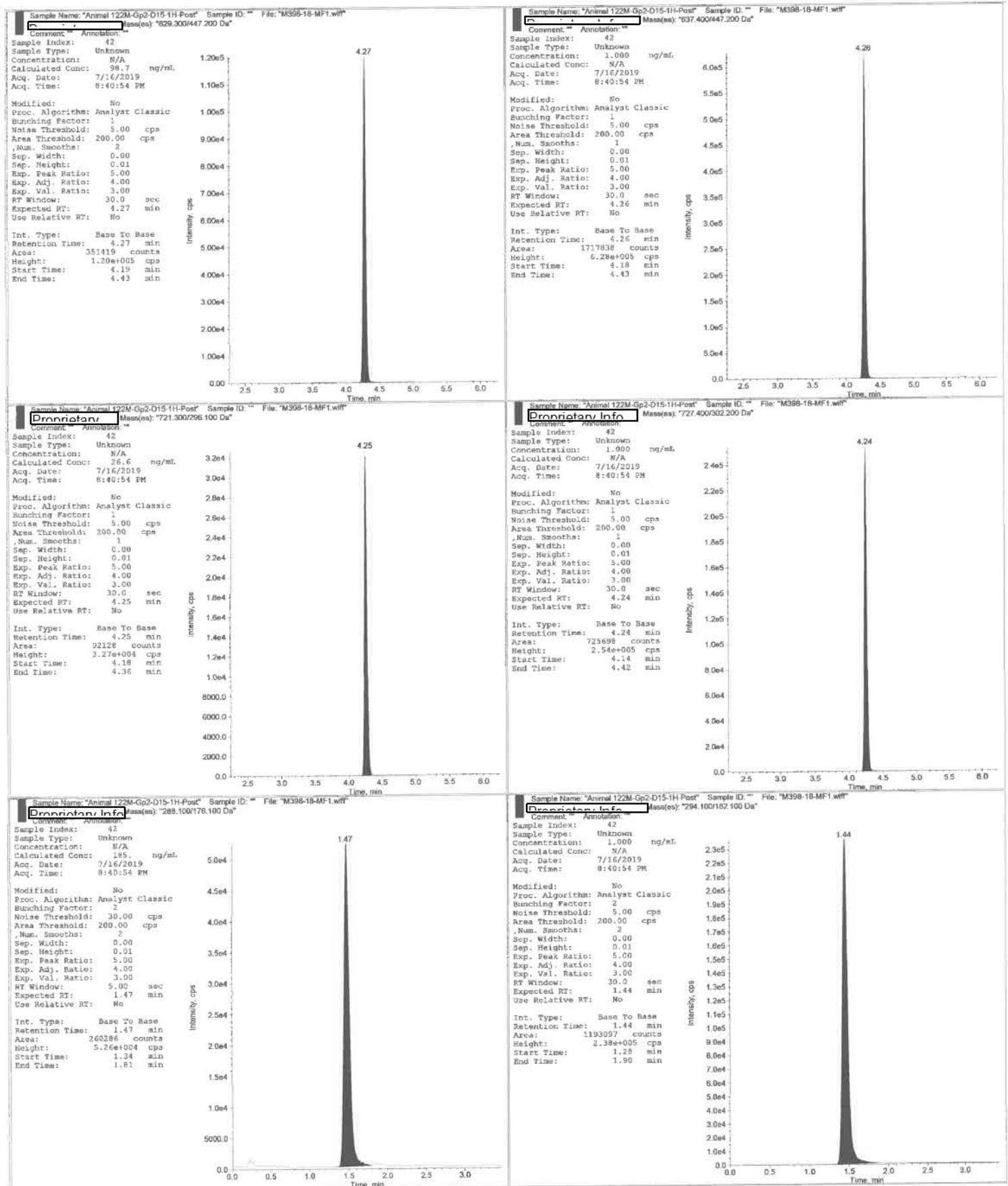
End Time: 1.73 min

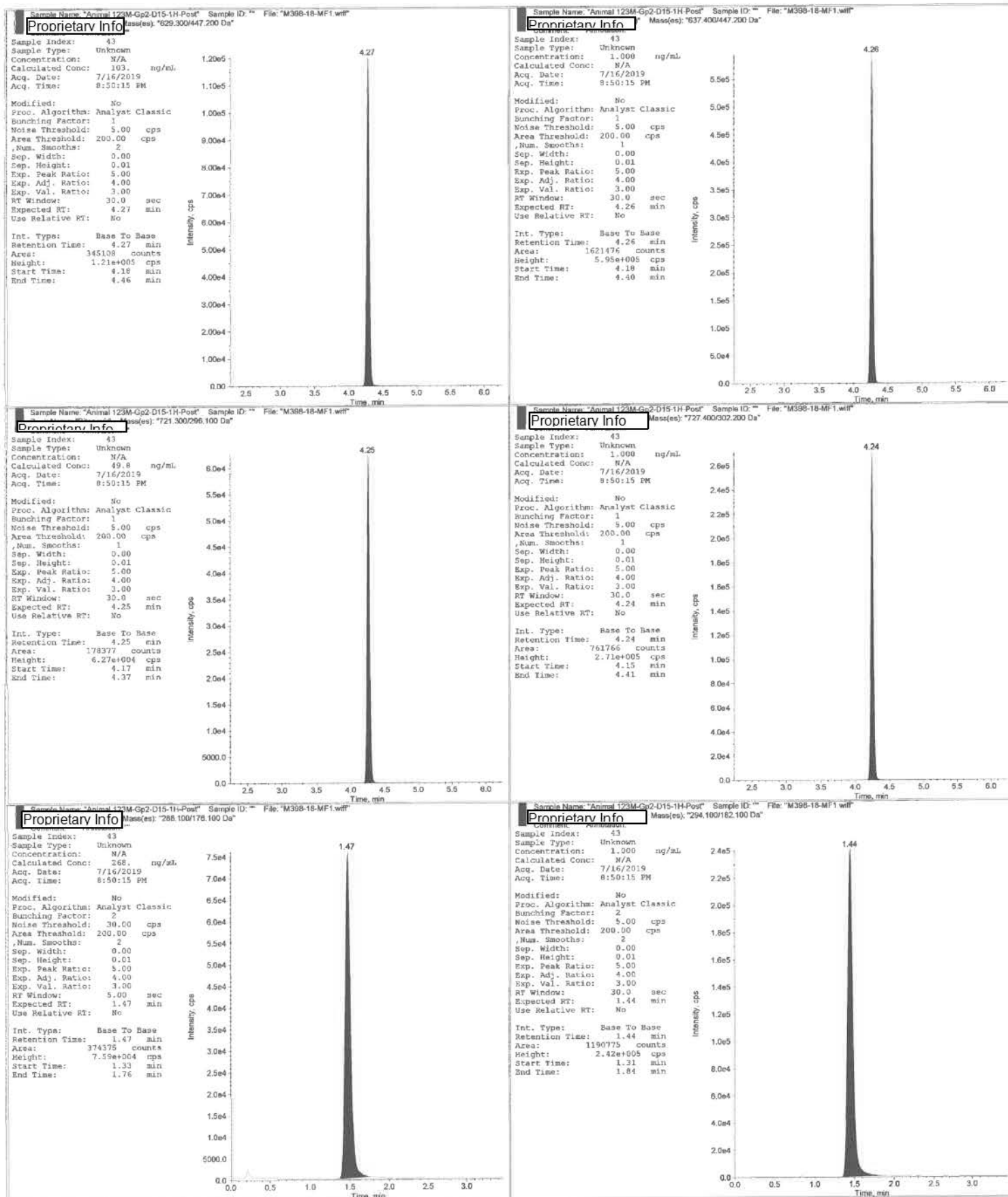


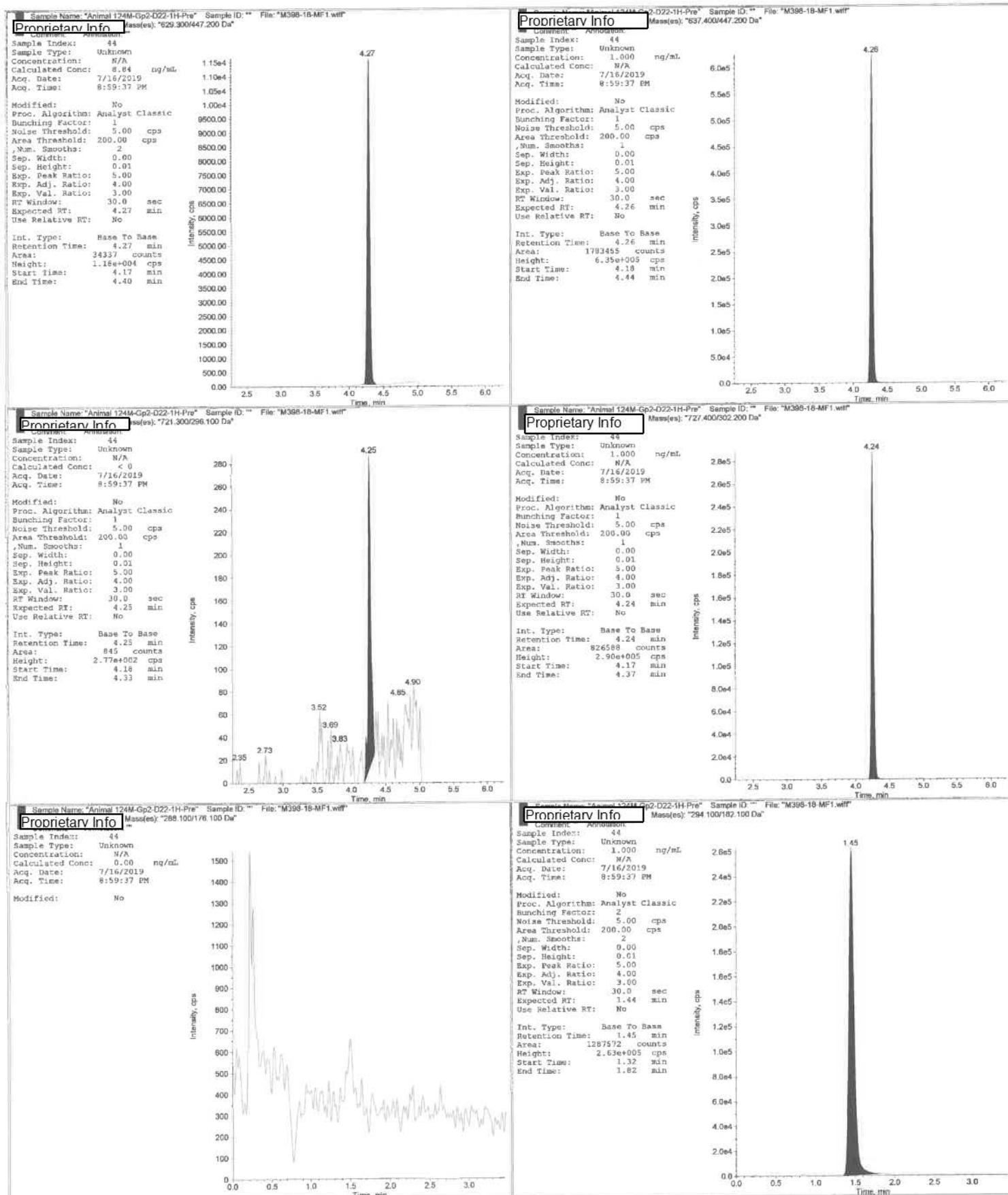


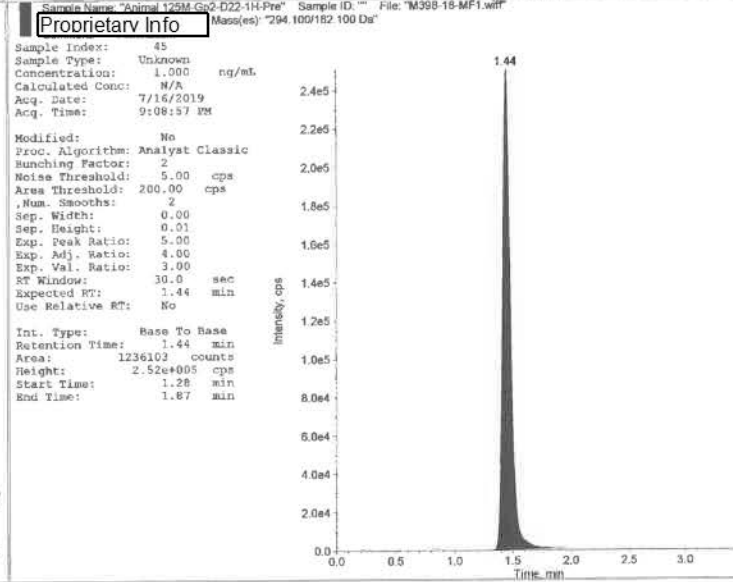
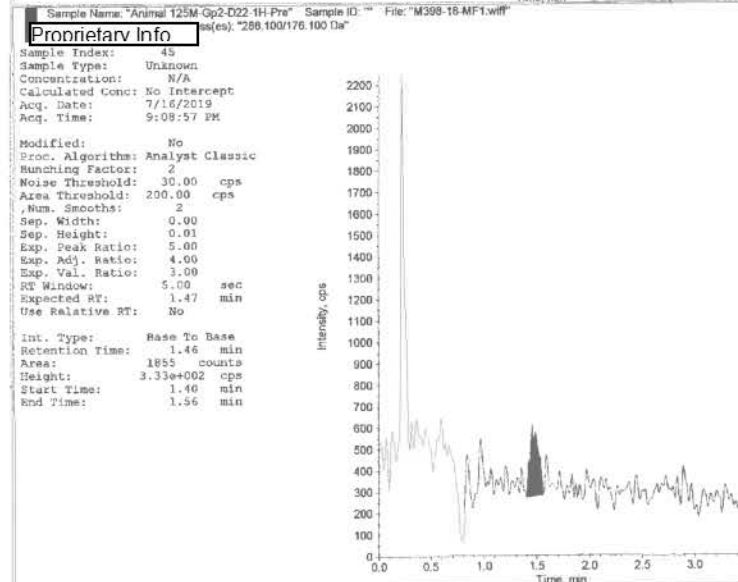
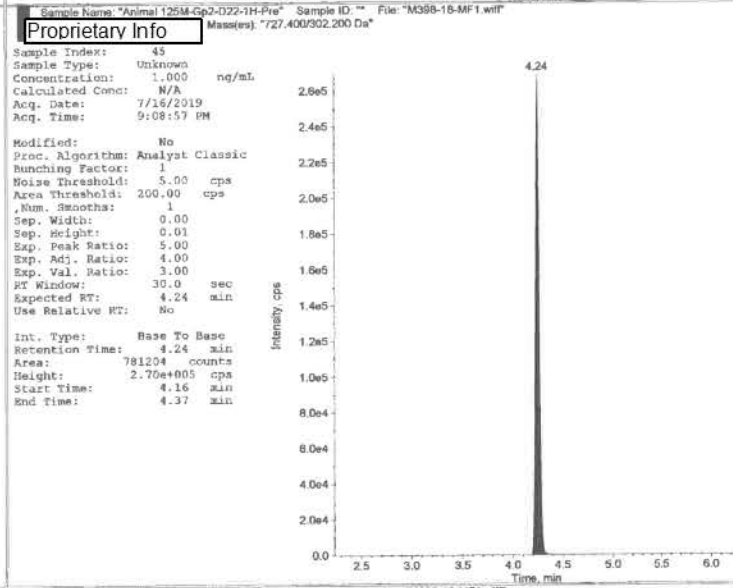
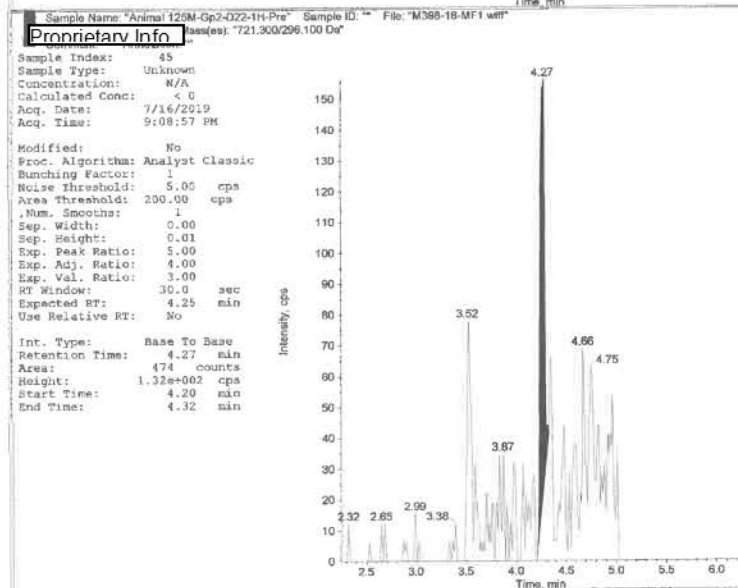
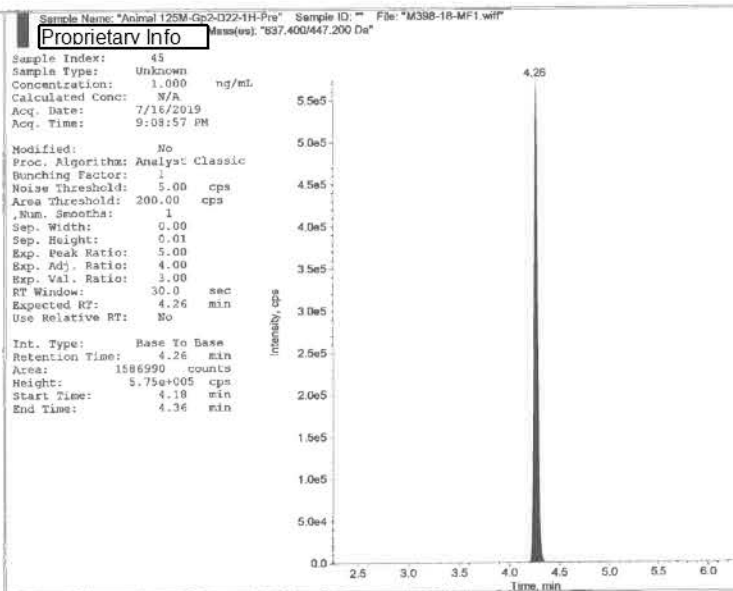
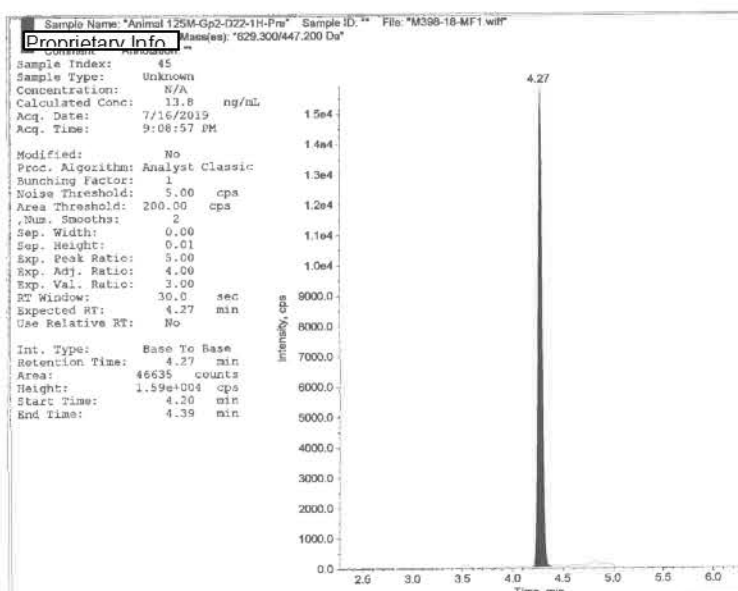


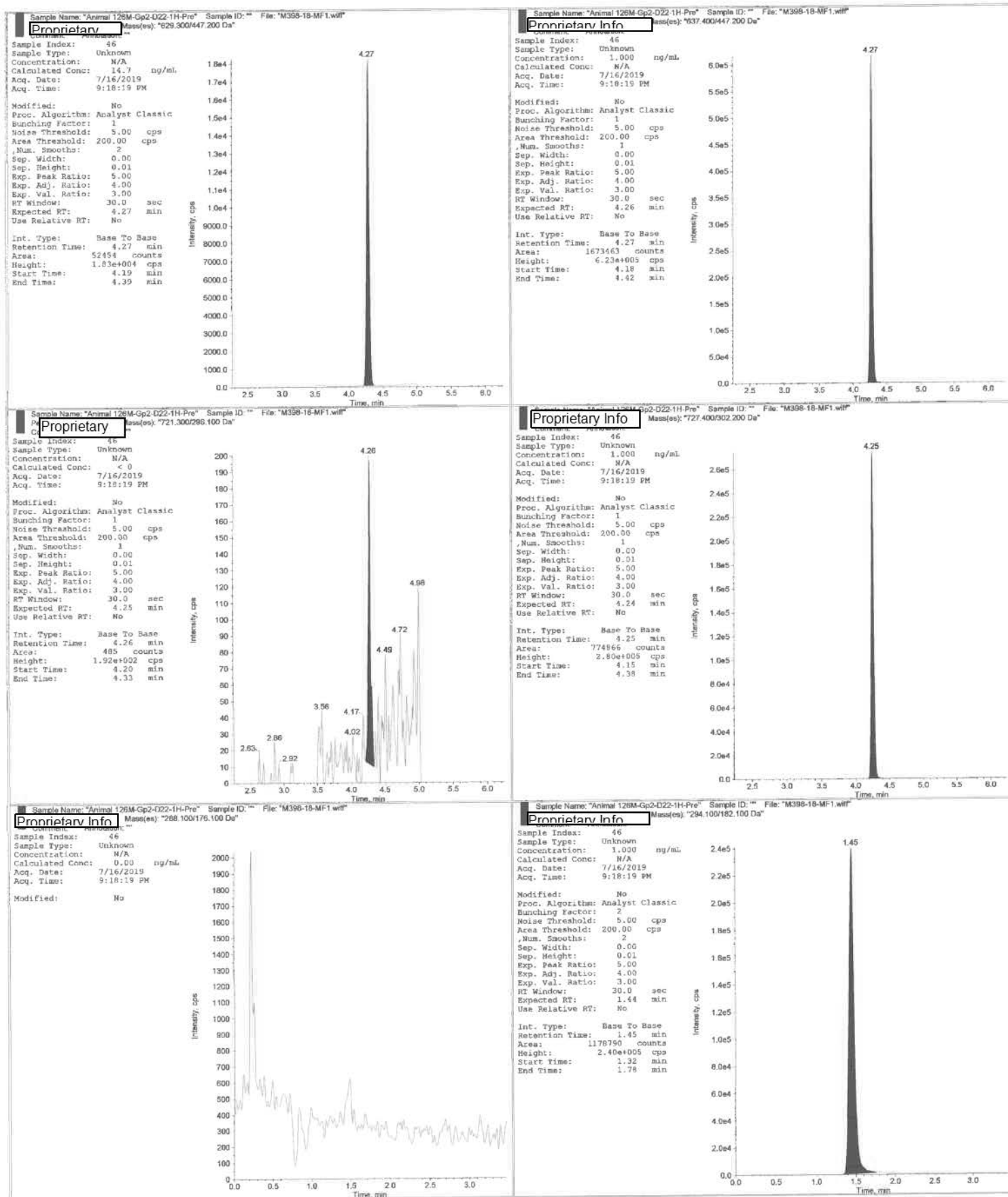


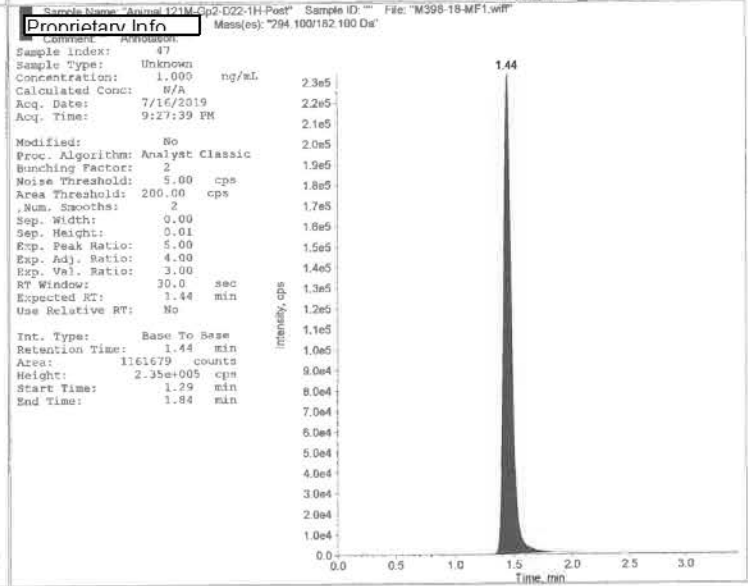
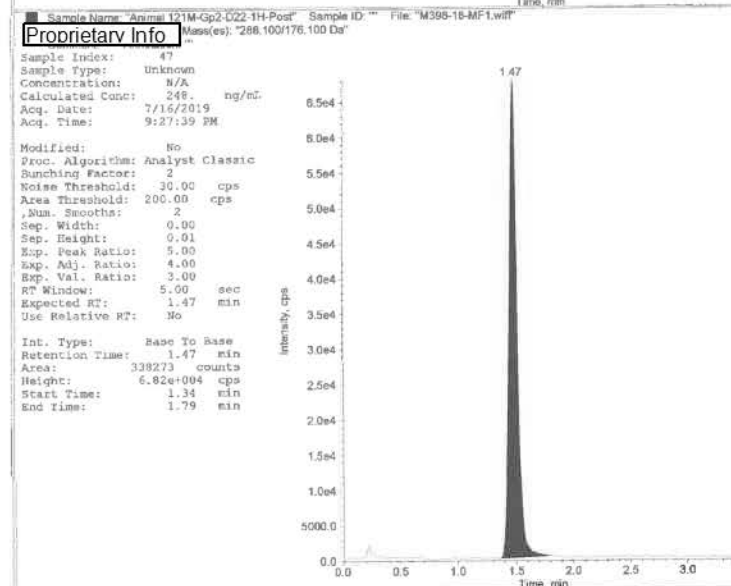
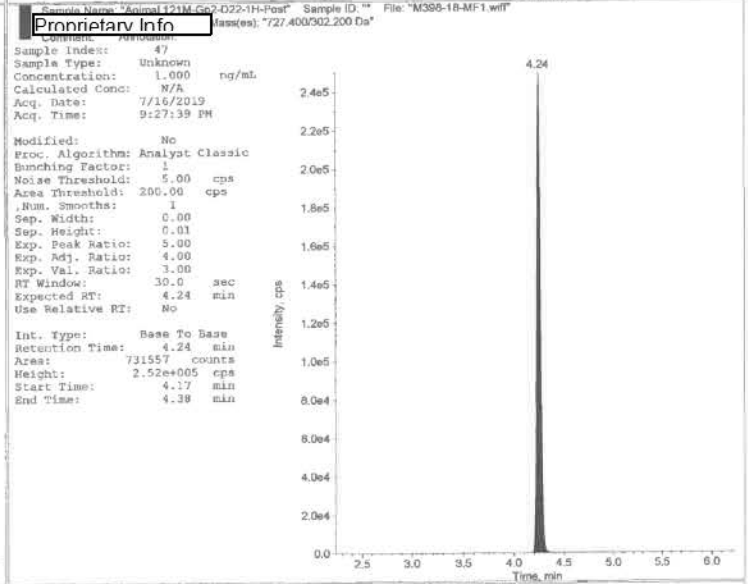
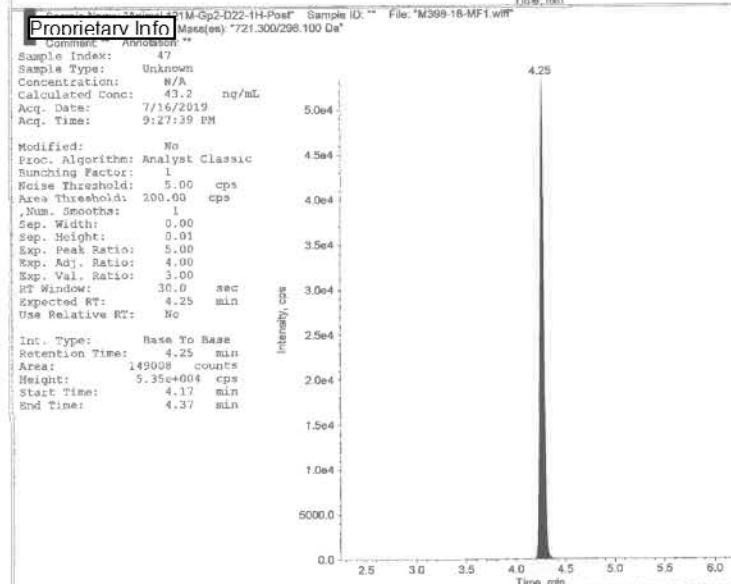
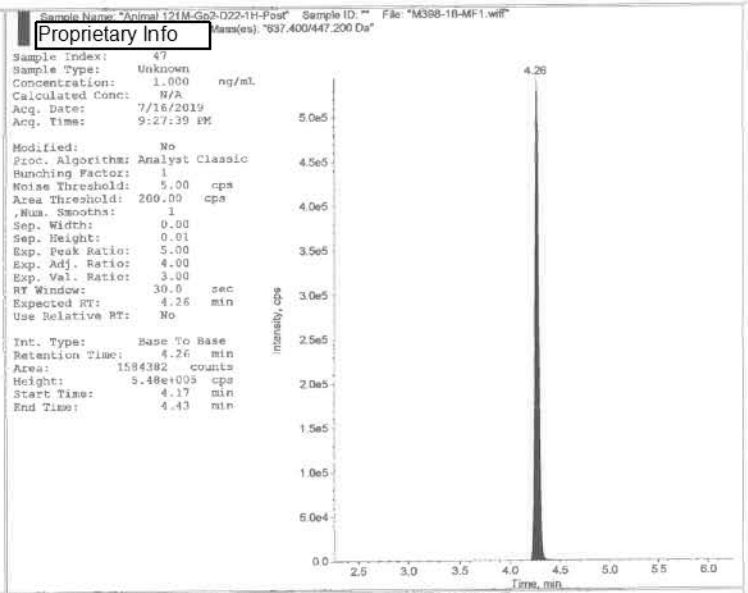
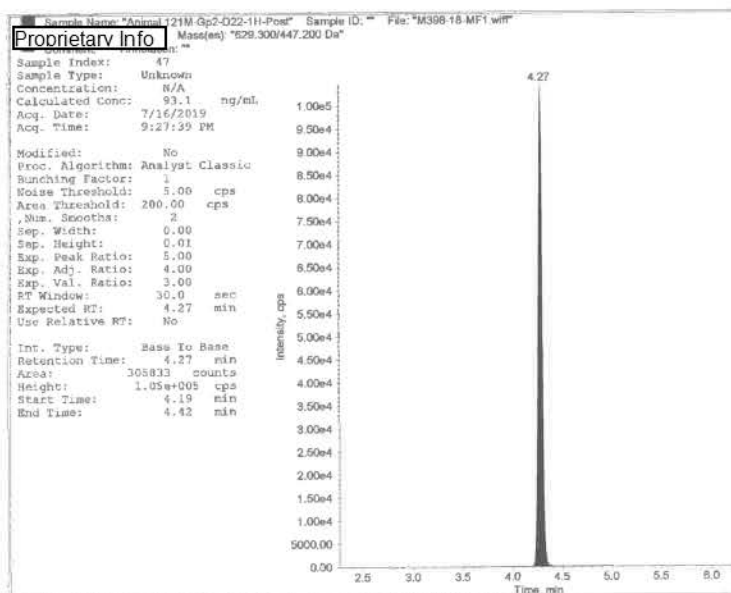


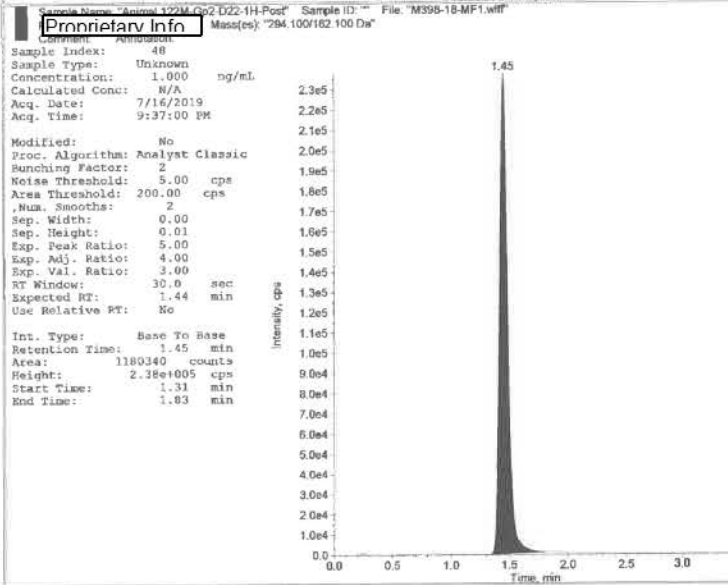
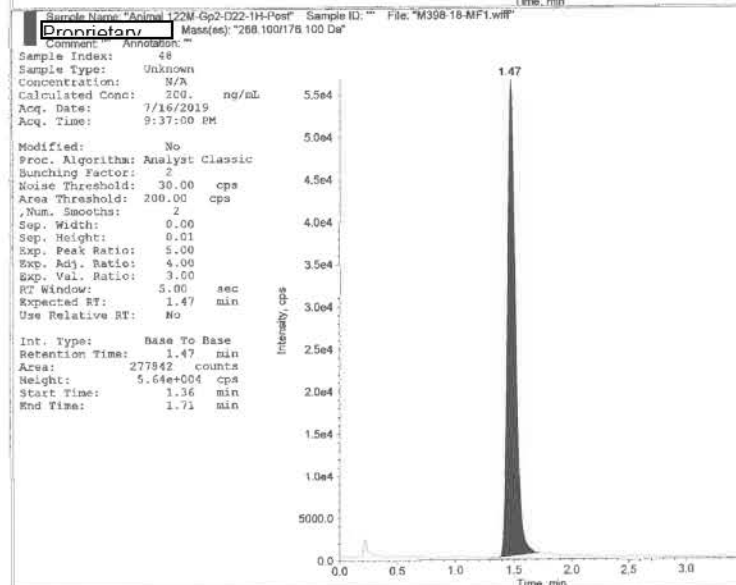
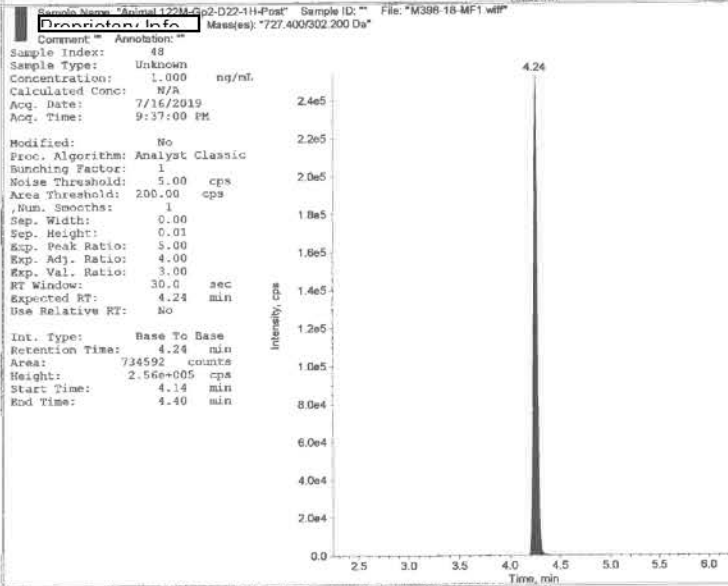
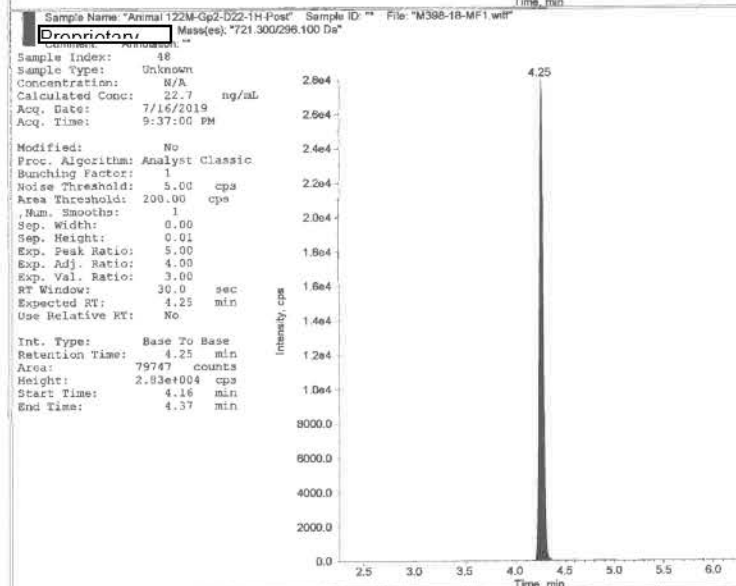
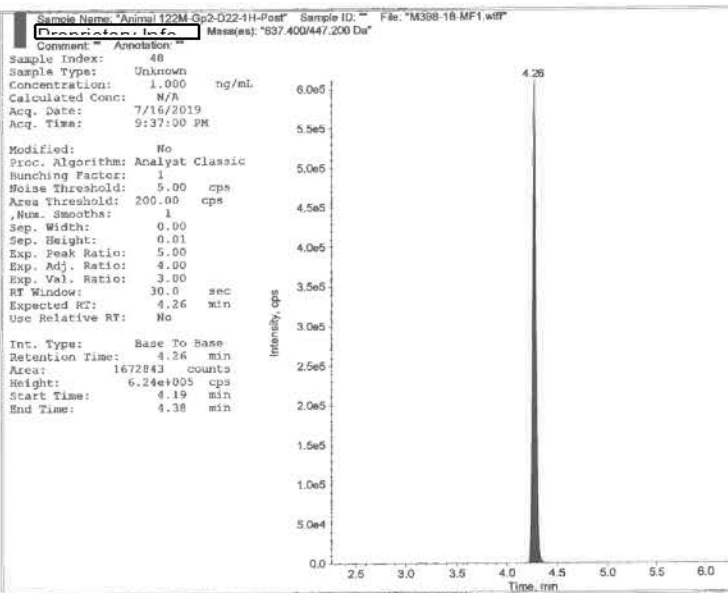
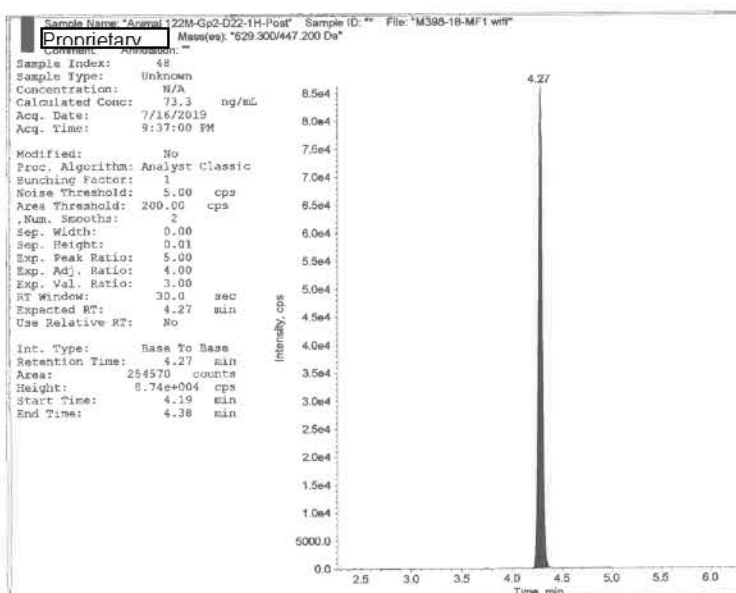


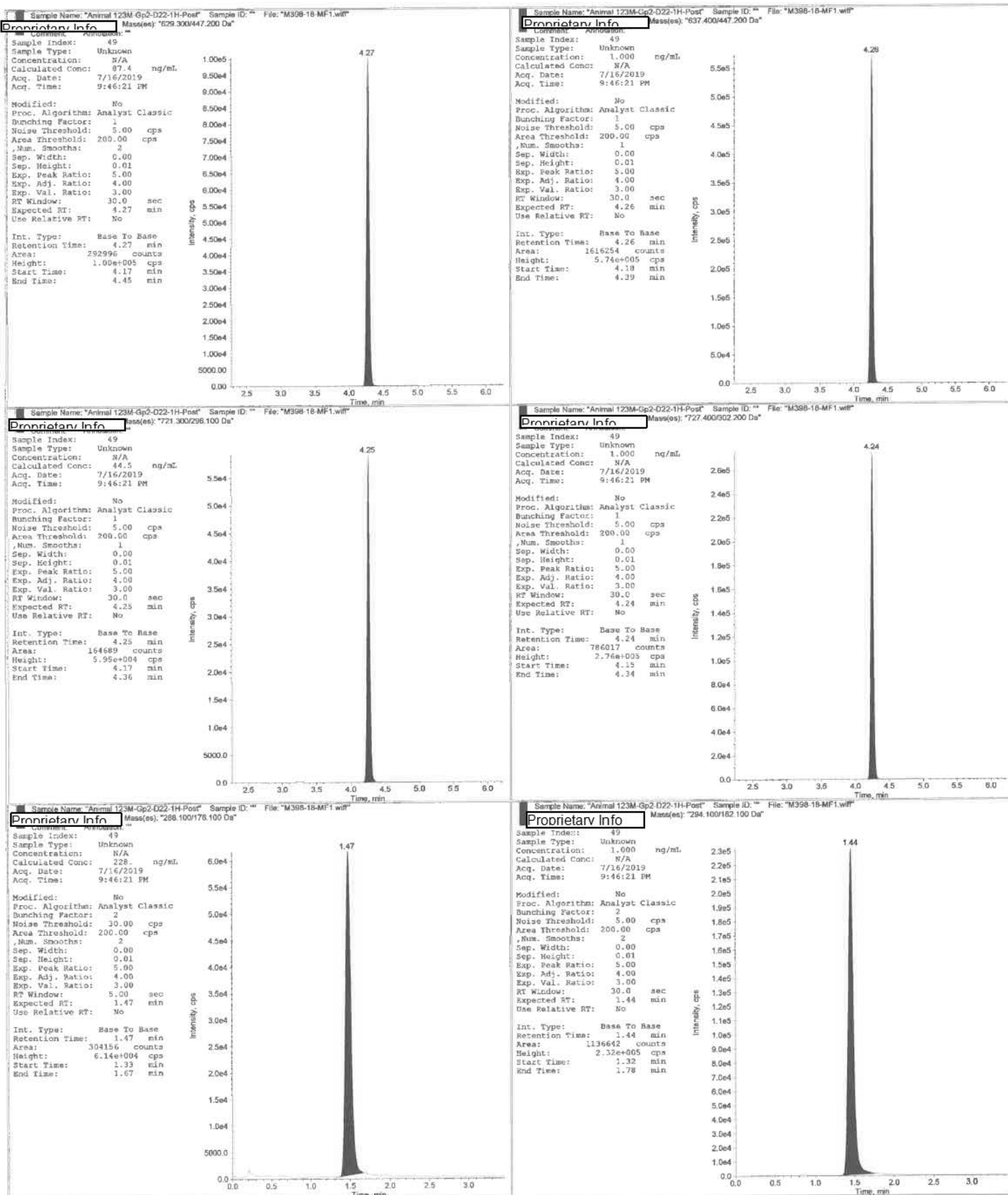


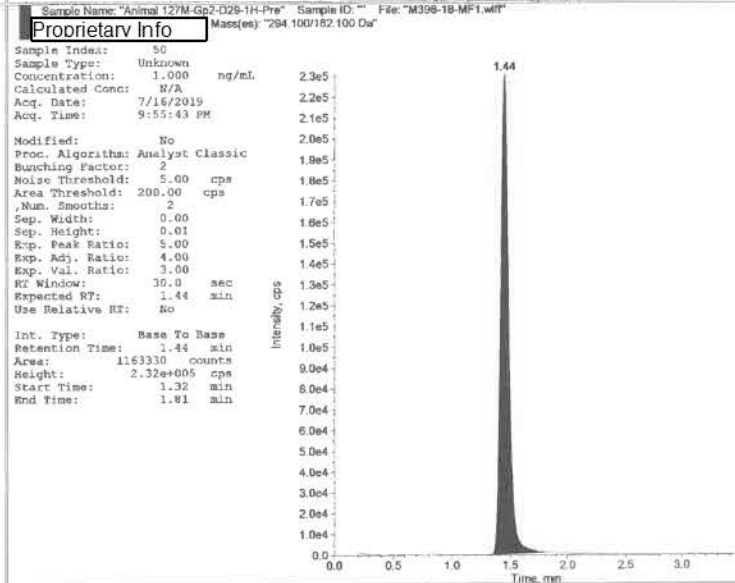
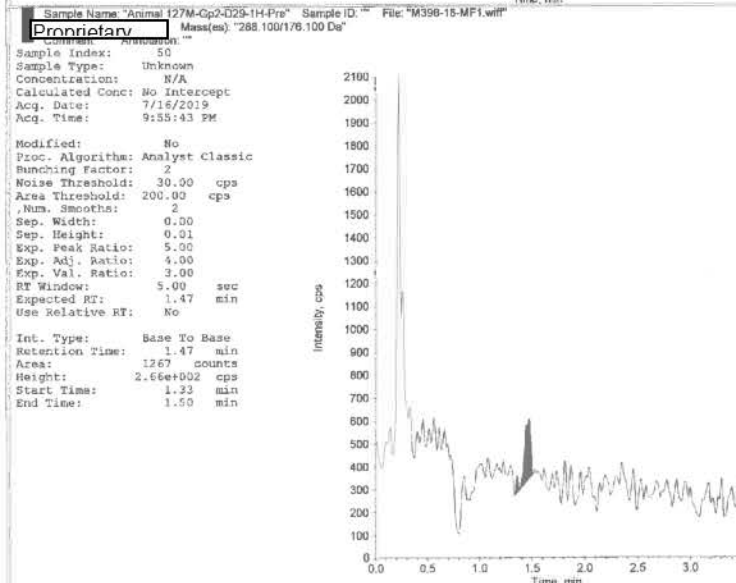
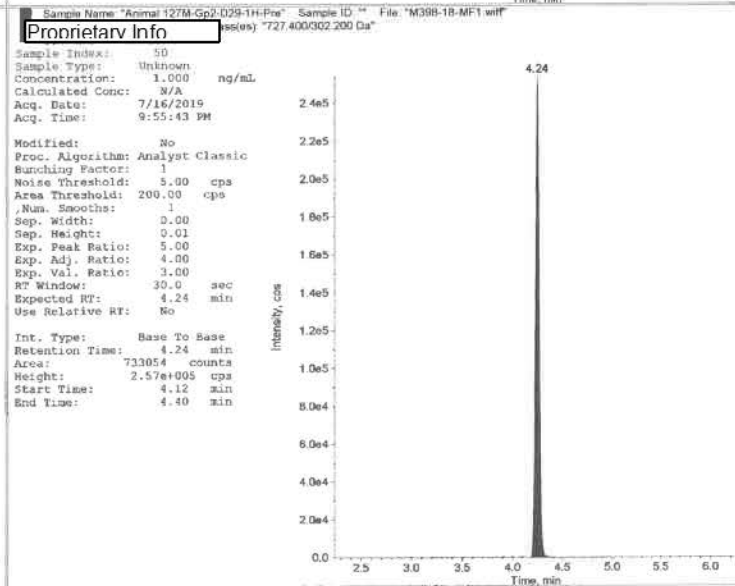
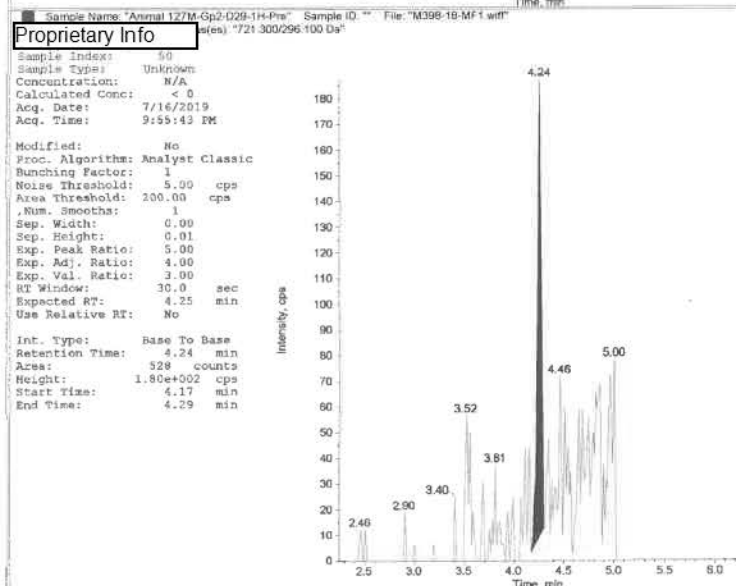
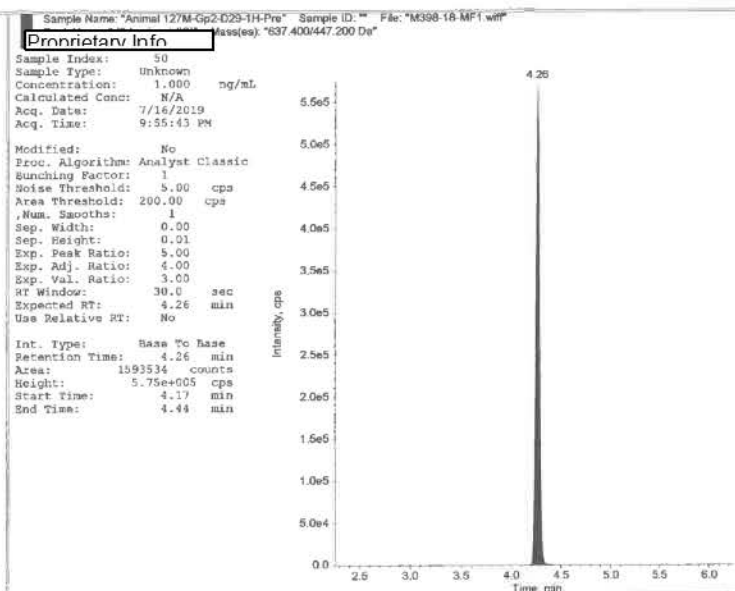
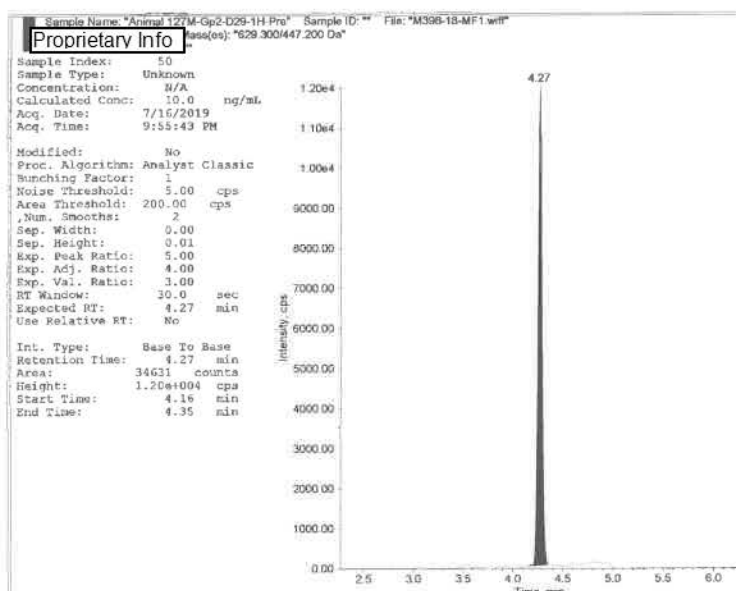


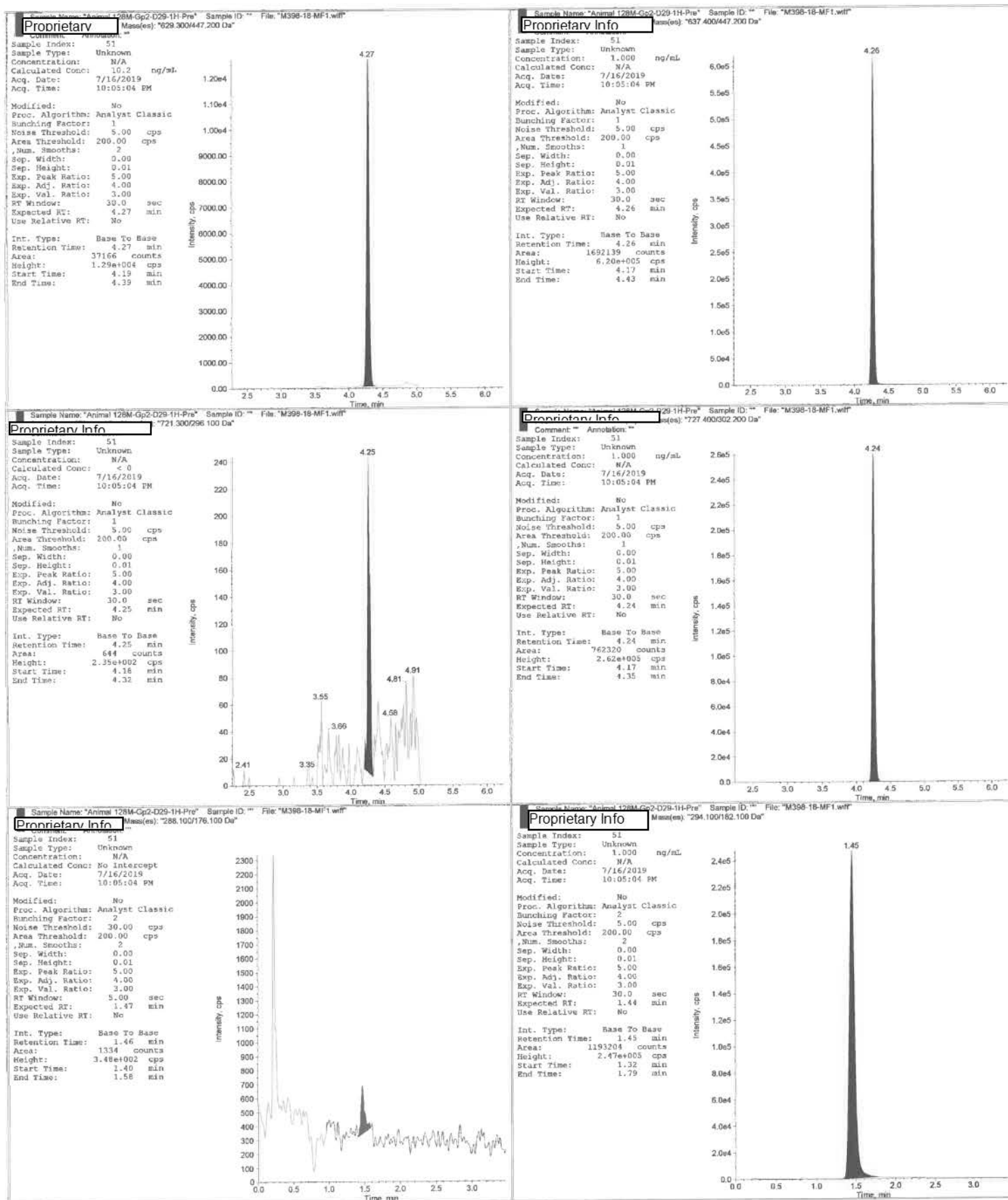


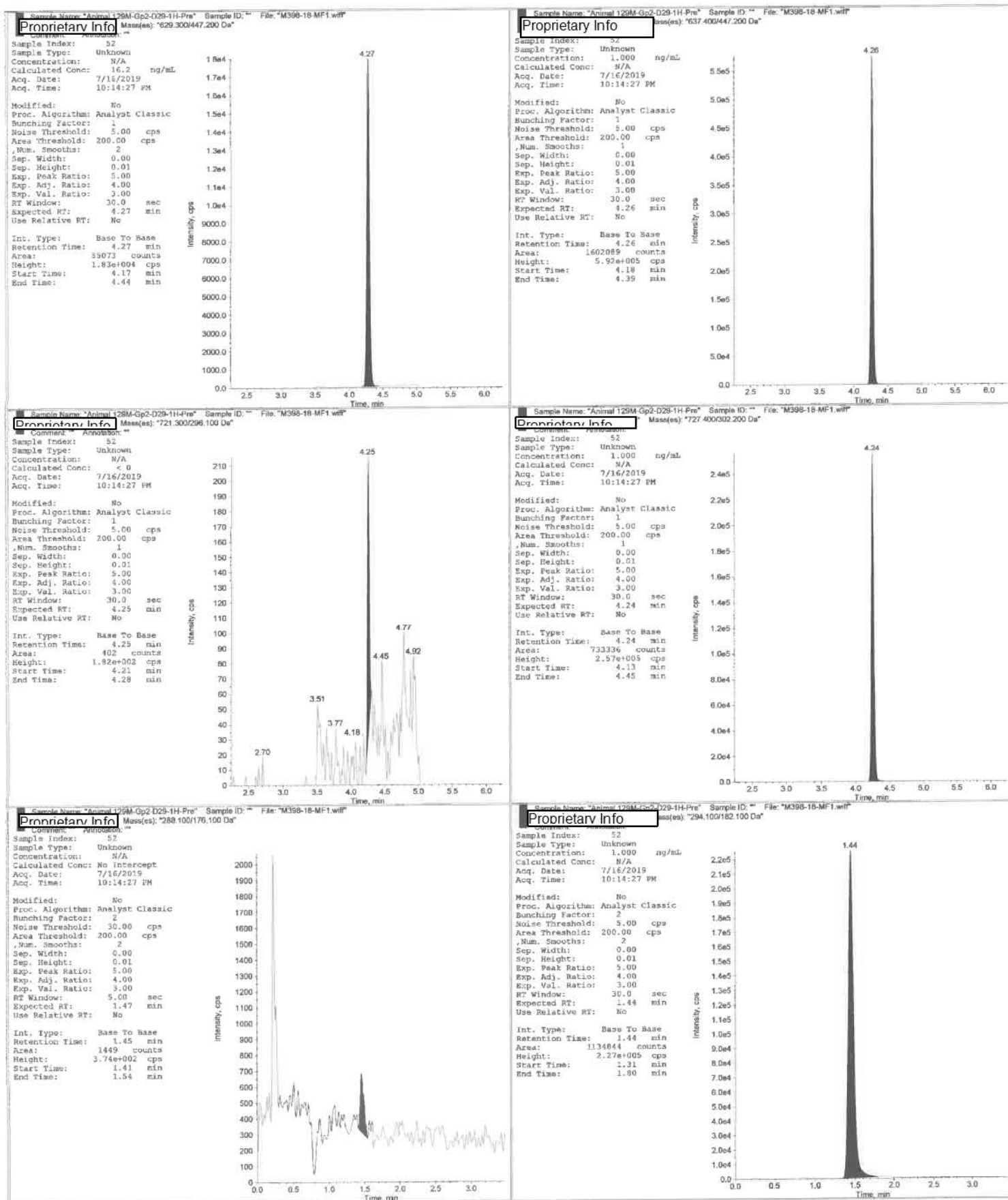


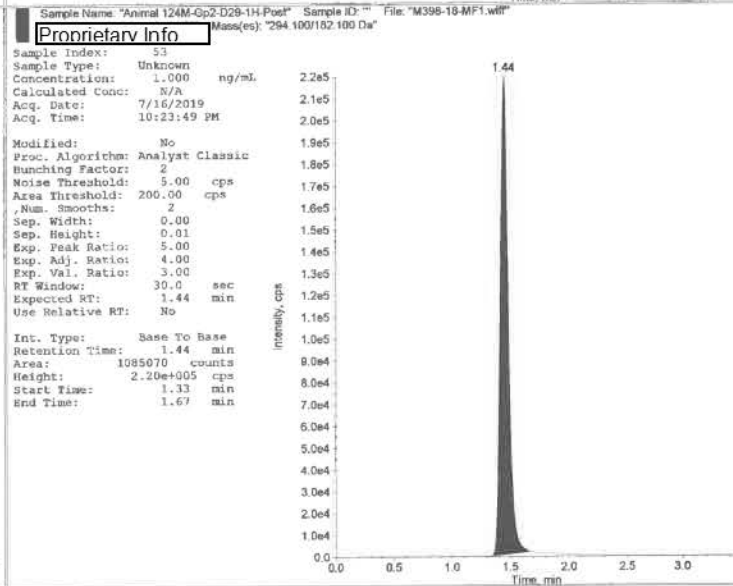
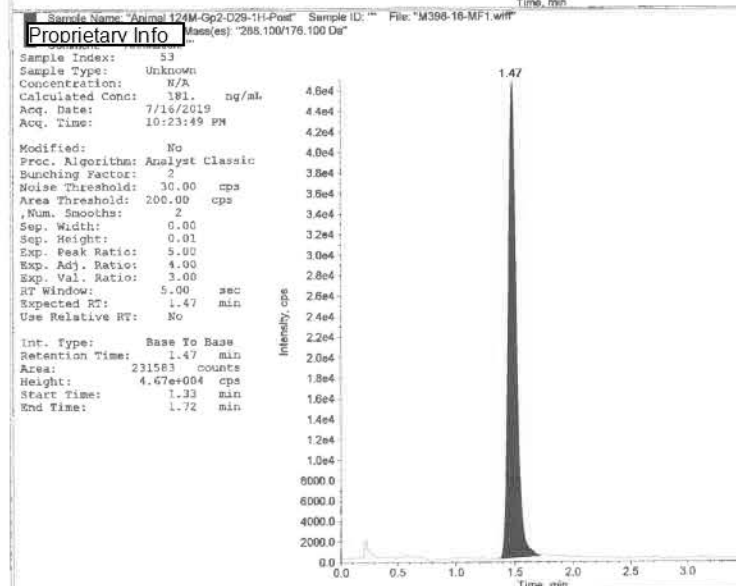
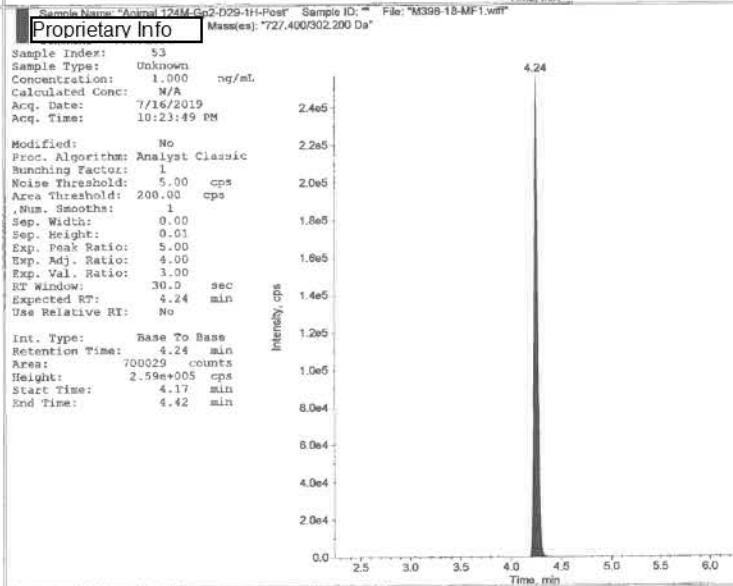
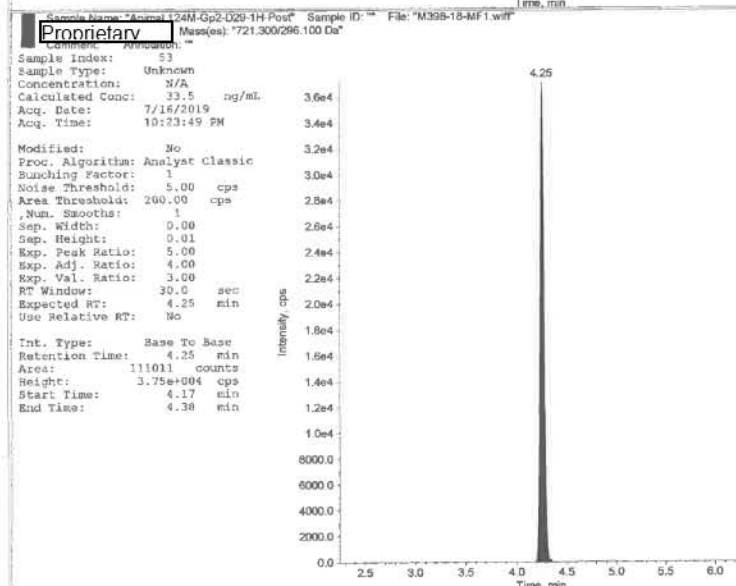
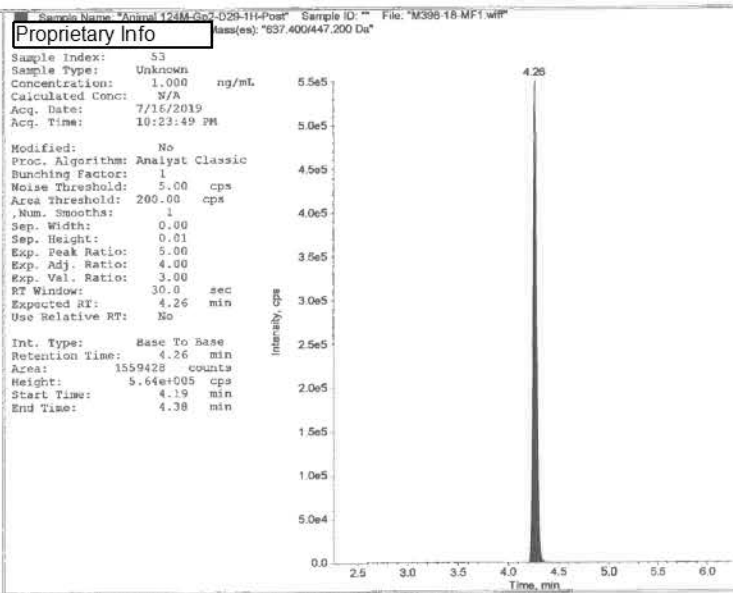
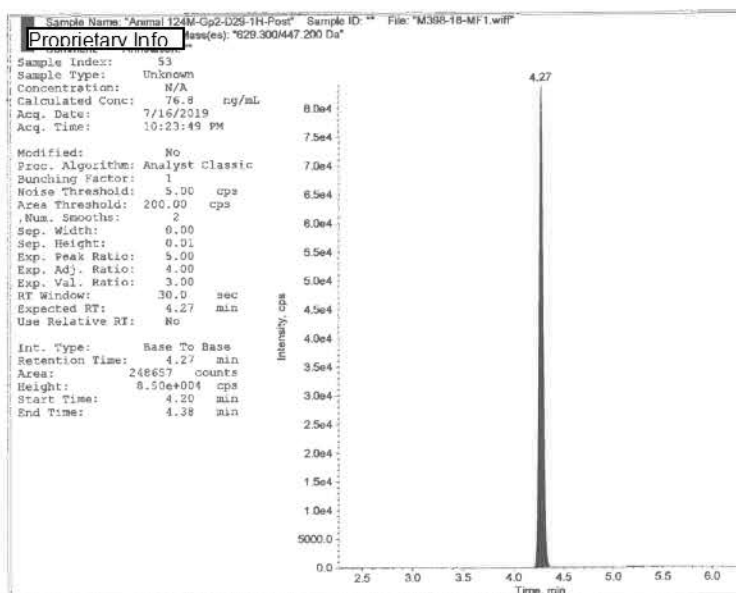


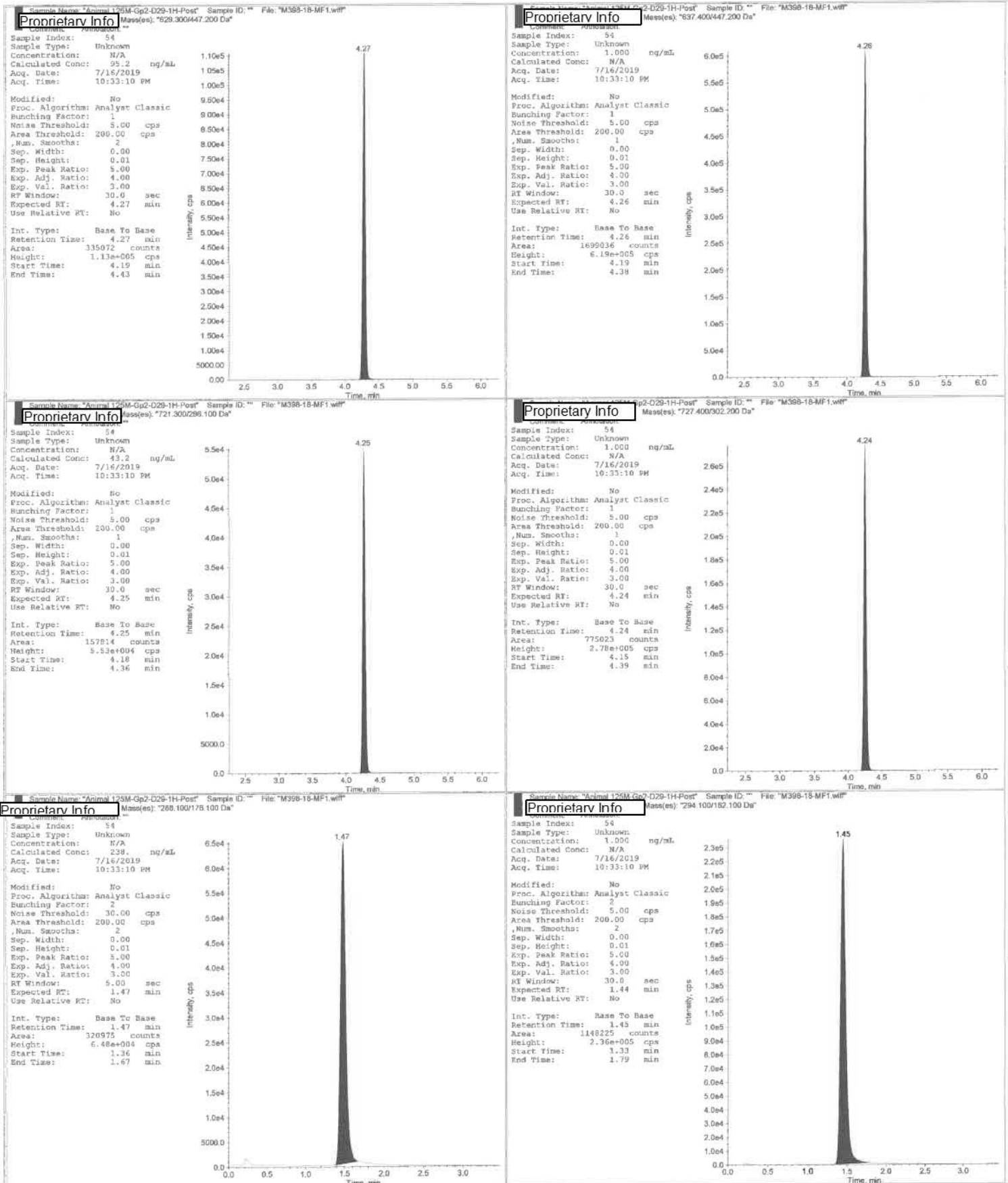


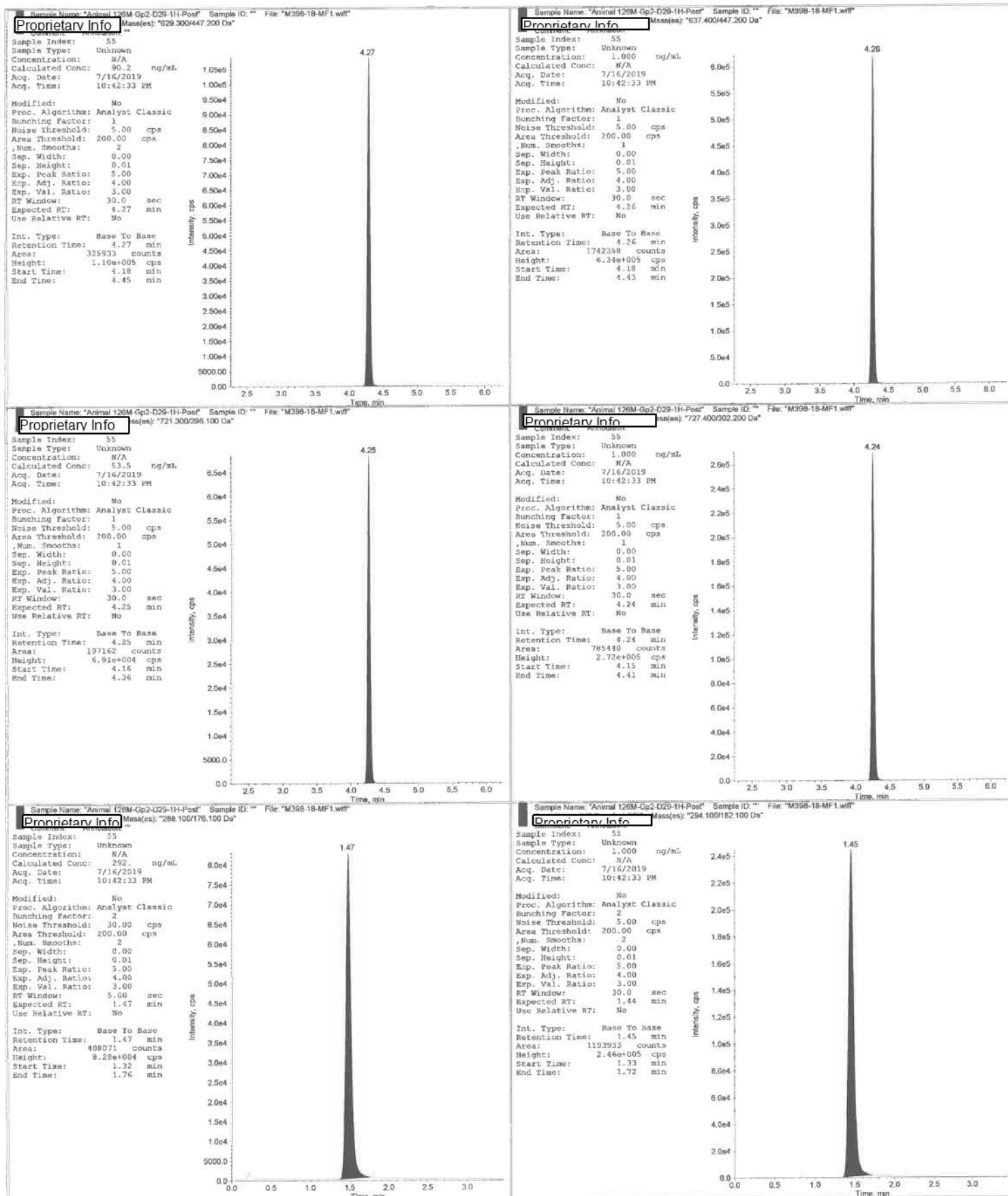


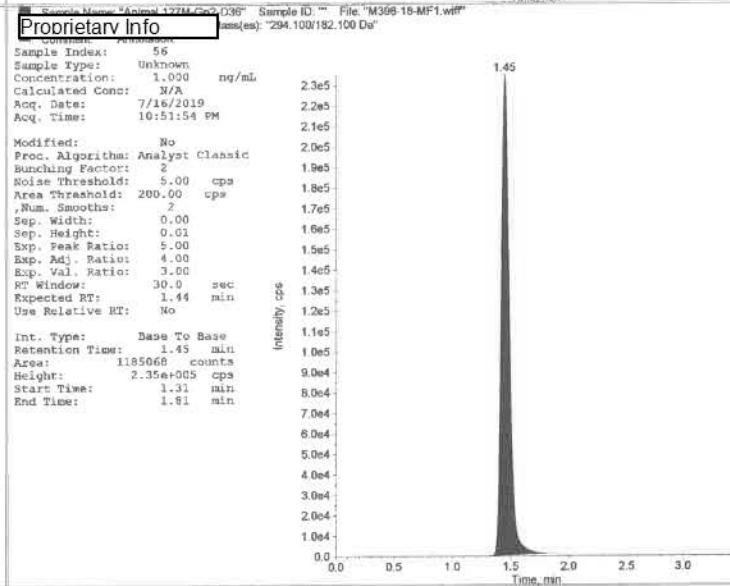
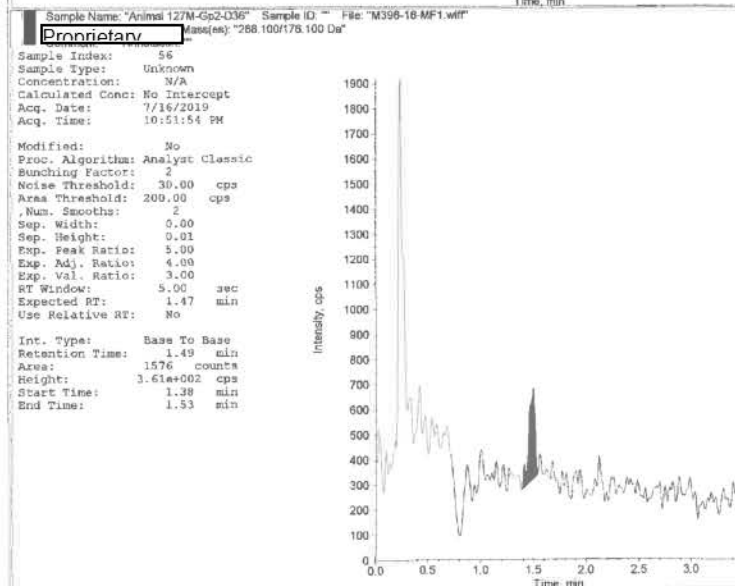
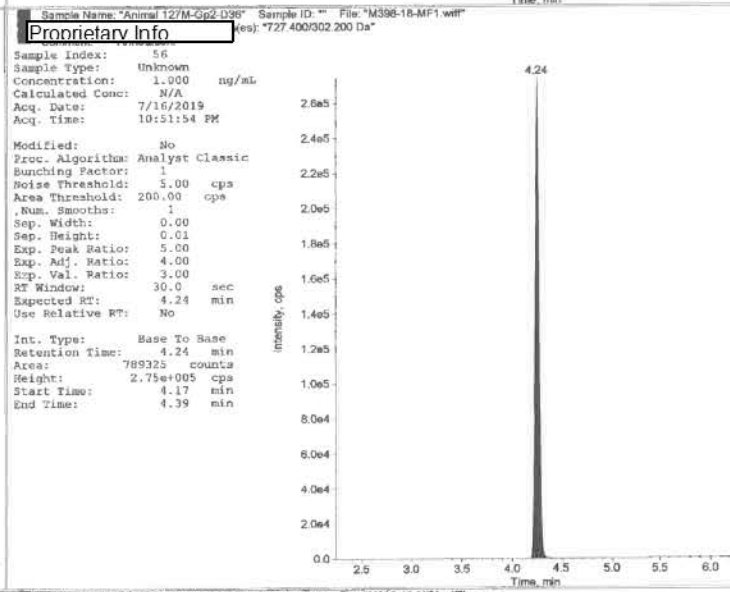
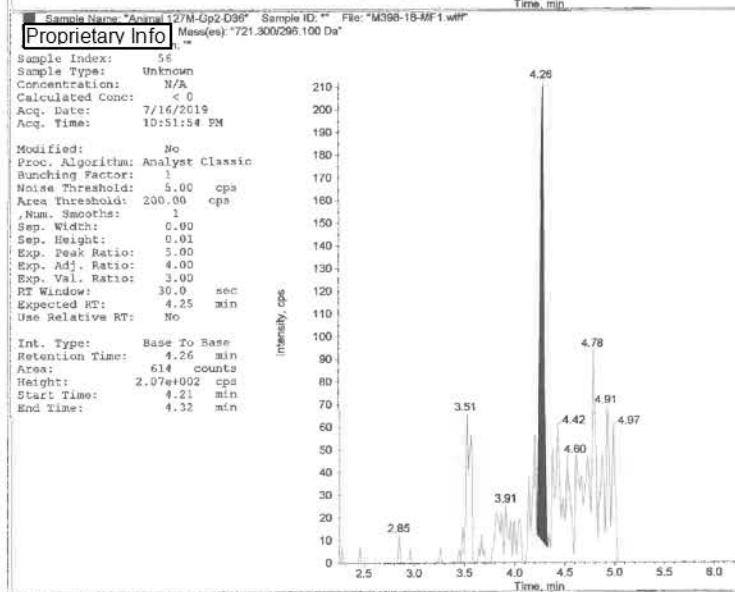
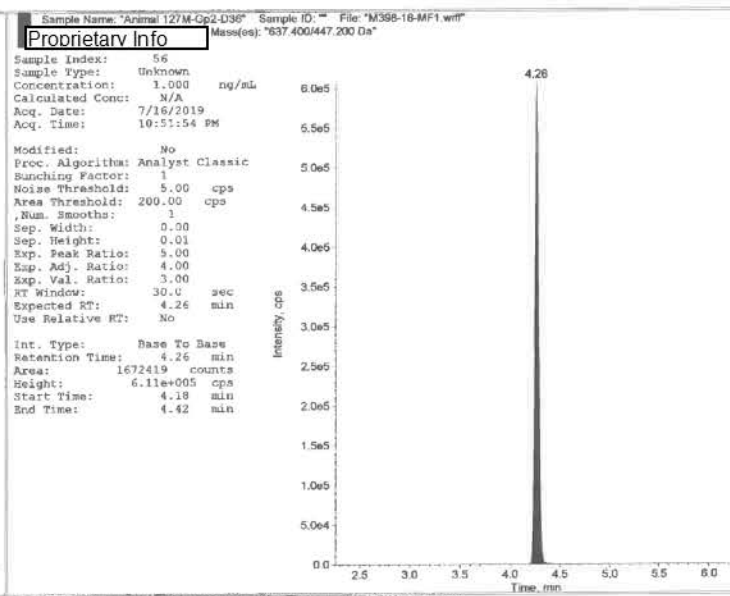
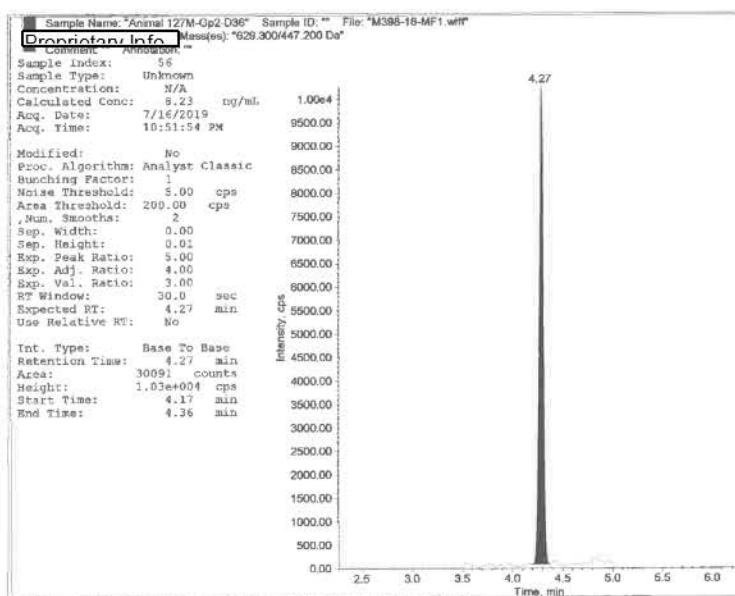


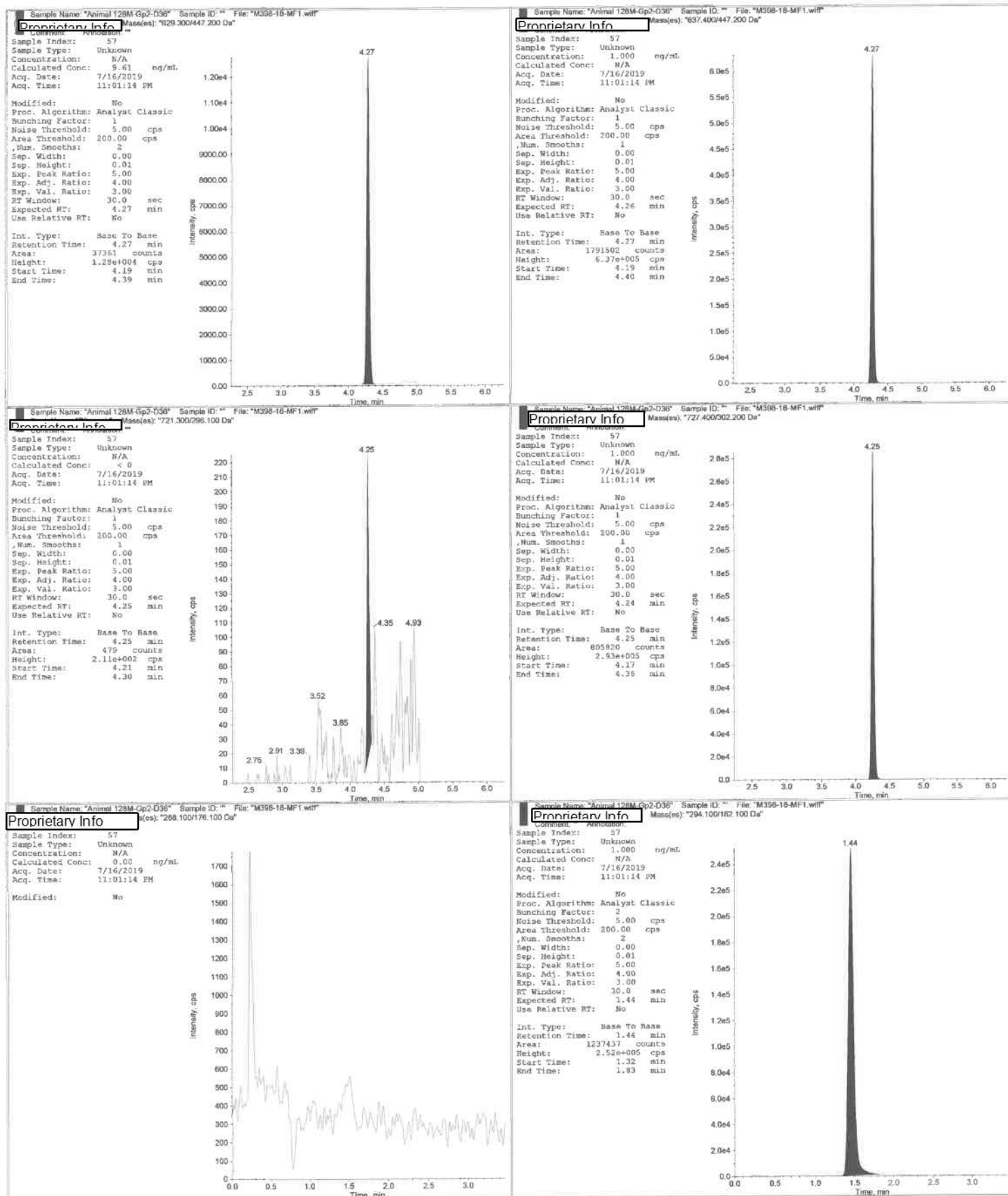


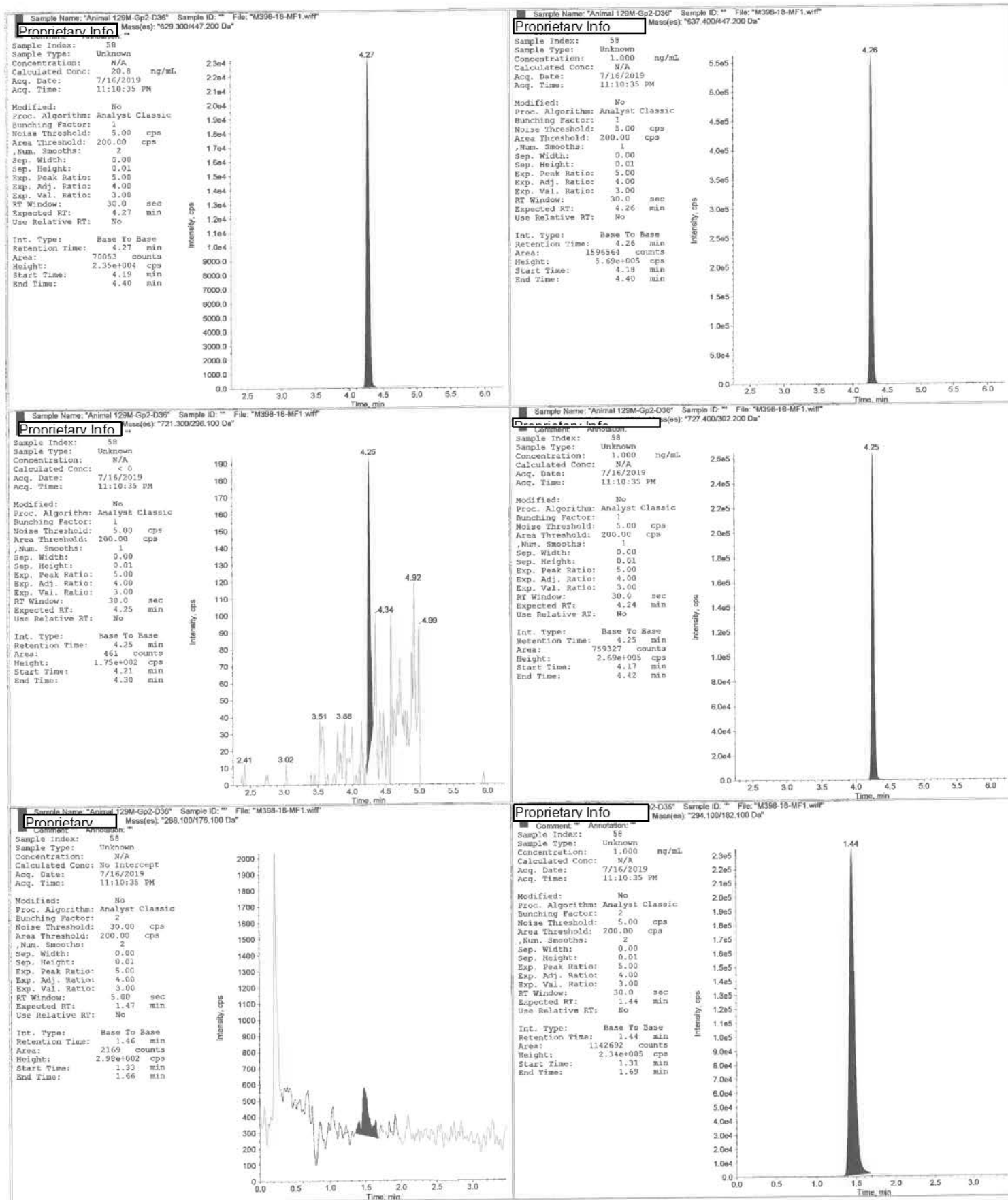










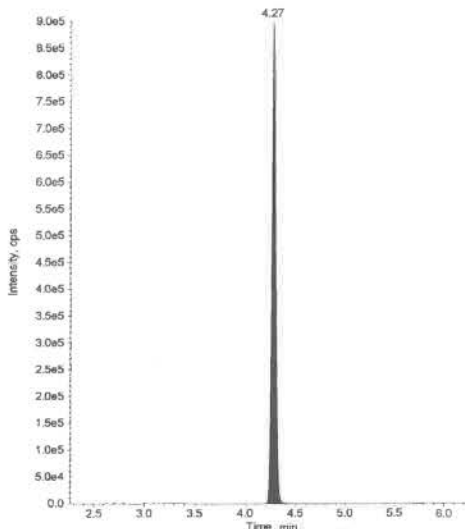


Sample Name: "QC High" Sample ID: " " File: "M398-18-MF1.wiff"
Mass(es): "629.300/447.200 Da"

Sample Index: 59
Sample Type: QC
Concentration: 800. ng/mL
Calculated Conc: 801. ng/mL
Acq. Date: 7/16/2019
Acq. Time: 11:19:56 PM

Modified: No
Proc. Algorithm: Analyst Classic
Bunching Factor: 1
Noise Threshold: 5.00 cps
Area Threshold: 200.00 cps
Num. Smoother: 2
Sep. Width: 0.00
Sep. Height: 0.01
Exp. Peak Ratio: 5.00
Exp. Adj. Ratio: 4.00
Exp. Val. Ratio: 3.00
RT Window: 30.0 sec
Expected RT: 4.27 min
Use Relative RT: No

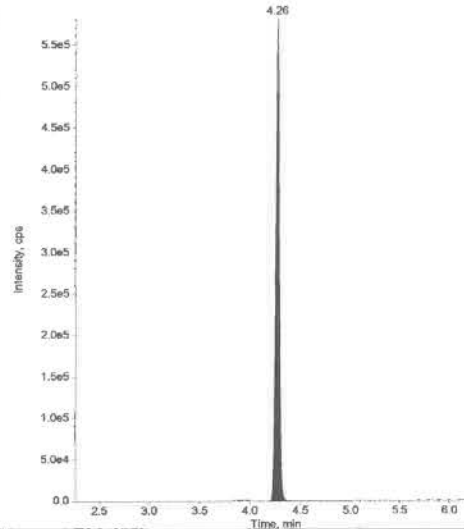
Int. Type: Base To Base
Retention Time: 4.27 min
Area: 2664440 counts
Height: 9.15e+005 cps
Start Time: 4.19 min
End Time: 4.45 min



Sample Index: 59
Sample Type: QC
Concentration: 1.000 ng/mL
Calculated Conc: N/A
Acq. Date: 7/16/2019
Acq. Time: 11:19:56 PM

Modified: No
Proc. Algorithm: Analyst Classic
Bunching Factor: 1
Noise Threshold: 5.00 cps
Area Threshold: 200.00 cps
Num. Smoother: 1
Sep. Width: 0.00
Sep. Height: 0.01
Exp. Peak Ratio: 5.00
Exp. Adj. Ratio: 4.00
Exp. Val. Ratio: 3.00
RT Window: 30.0 sec
Expected RT: 4.26 min
Use Relative RT: No

Int. Type: Base To Base
Retention Time: 4.26 min
Area: 1613186 counts
Height: 5.92e+005 cps
Start Time: 4.19 min
End Time: 4.39 min

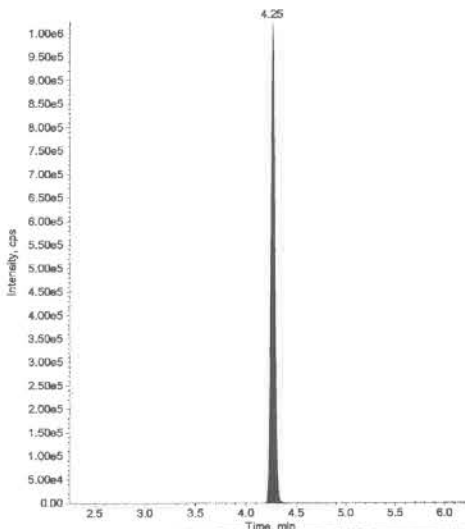


Sample Name: "QC High" Sample ID: " " File: "M398-18-MF1.wiff"
Mass(es): "721.300/299.100 Da"

Sample Index: 59
Sample Type: QC
Concentration: 800. ng/mL
Calculated Conc: 782. ng/mL
Acq. Date: 7/16/2019
Acq. Time: 11:19:56 PM

Modified: No
Proc. Algorithm: Analyst Classic
Bunching Factor: 1
Noise Threshold: 5.00 cps
Area Threshold: 200.00 cps
Num. Smoother: 1
Sep. Width: 0.00
Sep. Height: 0.01
Exp. Peak Ratio: 5.00
Exp. Adj. Ratio: 4.00
Exp. Val. Ratio: 3.00
RT Window: 30.0 sec
Expected RT: 4.25 min
Use Relative RT: No

Int. Type: Base To Base
Retention Time: 4.25 min
Area: 2932218 counts
Height: 1.03e+006 cps
Start Time: 4.17 min
End Time: 4.41 min

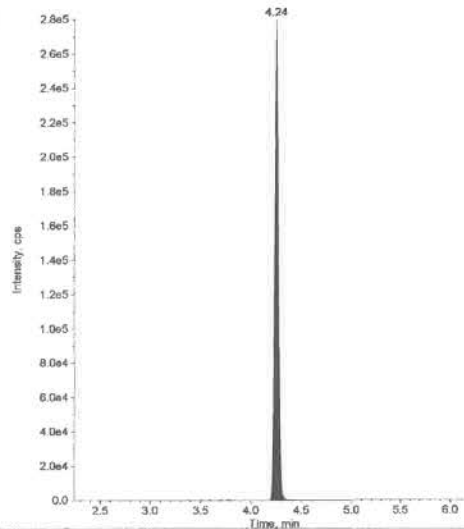


Sample Name: "QC High" Sample ID: " " File: "M398-18-MF1.wiff"
Mass(es): "727.400/302.200 Da"

Sample Index: 59
Sample Type: QC
Concentration: 1.000 ng/mL
Calculated Conc: N/A
Acq. Date: 7/16/2019
Acq. Time: 11:19:56 PM

Modified: No
Proc. Algorithm: Analyst Classic
Bunching Factor: 1
Noise Threshold: 5.00 cps
Area Threshold: 200.00 cps
Num. Smoother: 1
Sep. Width: 0.00
Sep. Height: 0.01
Exp. Peak Ratio: 5.00
Exp. Adj. Ratio: 4.00
Exp. Val. Ratio: 3.00
RT Window: 30.0 sec
Expected RT: 4.24 min
Use Relative RT: No

Int. Type: Base To Base
Retention Time: 4.24 min
Area: 810721 counts
Height: 2.83e+005 cps
Start Time: 4.15 min
End Time: 4.40 min

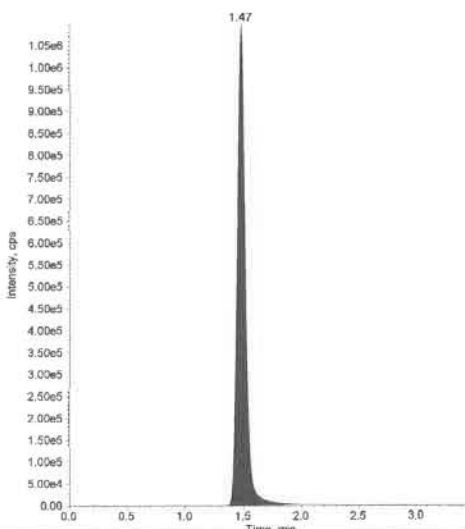


Sample Name: "QC High" Sample ID: " " File: "M398-18-MF1.wiff"
Mass(es): "288.100/176.100 Da"

Sample Index: 59
Sample Type: QC
Concentration: 4000. ng/mL
Calculated Conc: 3800. ng/mL
Acq. Date: 7/16/2019
Acq. Time: 11:19:56 PM

Modified: No
Proc. Algorithm: Analyst Classic
Bunching Factor: 2
Noise Threshold: 30.00 cps
Area Threshold: 200.00 cps
Num. Smoother: 2
Sep. Width: 0.00
Sep. Height: 0.01
Exp. Peak Ratio: 5.00
Exp. Adj. Ratio: 4.00
Exp. Val. Ratio: 3.00
RT Window: 5.00 sec
Expected RT: 1.47 min
Use Relative RT: No

Int. Type: Base To Base
Retention Time: 1.47 min
Area: 5450935 counts
Height: 1.10e+006 cps
Start Time: 1.33 min
End Time: 2.01 min

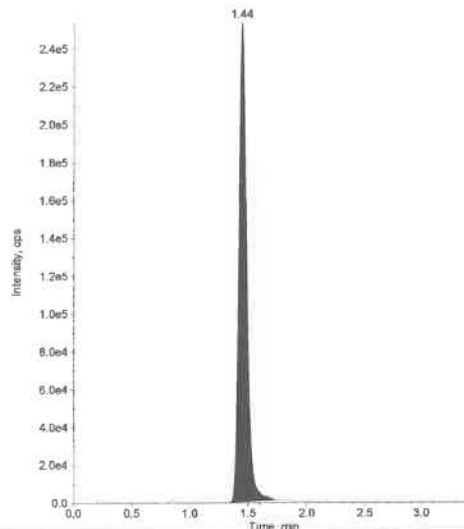


Sample Name: "QC High" Sample ID: " " File: "M398-18-MF1.wiff"
Mass(es): "294.100/182.100 Da"

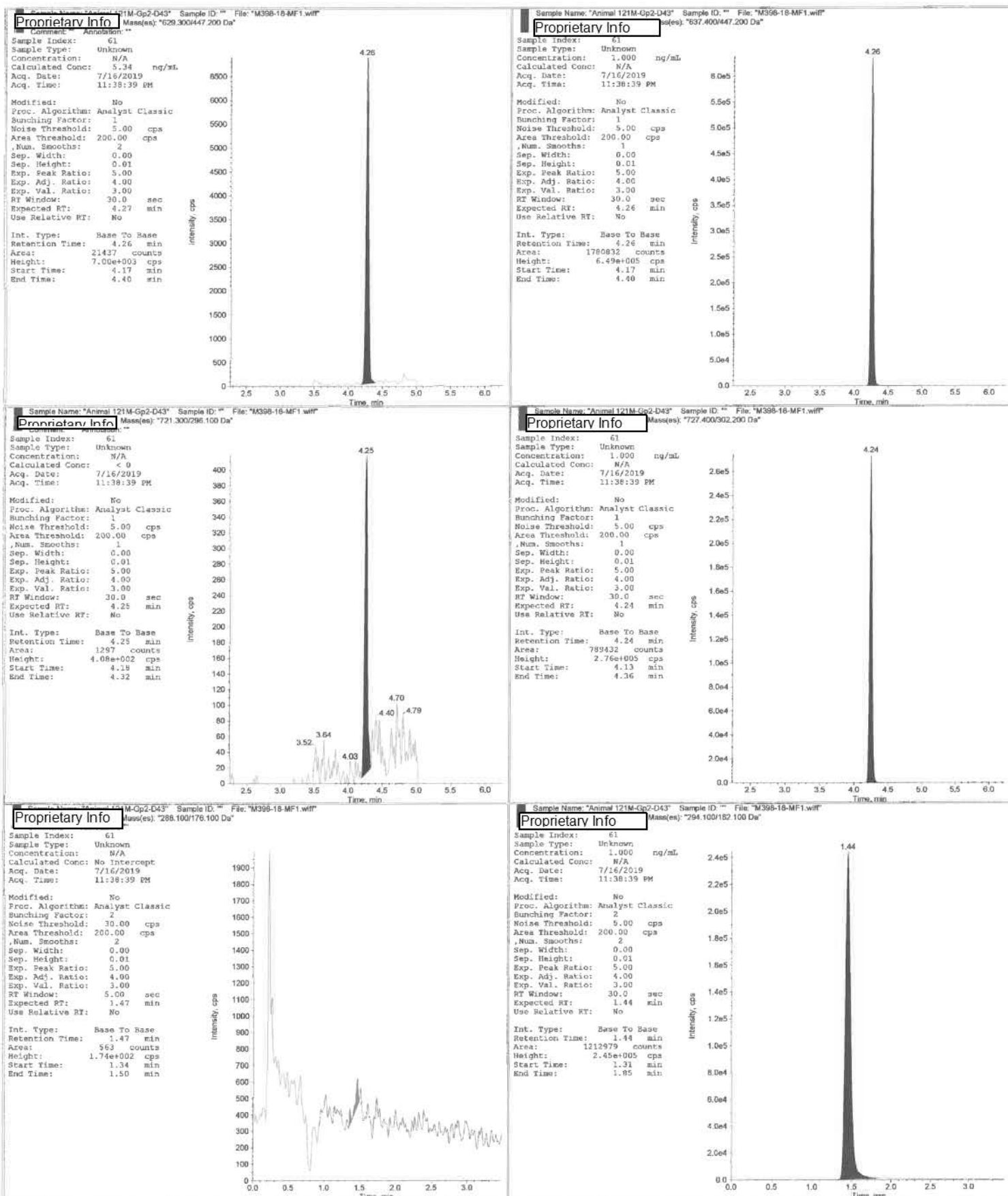
Sample Index: 59
Sample Type: QC
Concentration: 1.000 ng/mL
Calculated Conc: N/A
Acq. Date: 7/16/2019
Acq. Time: 11:19:56 PM

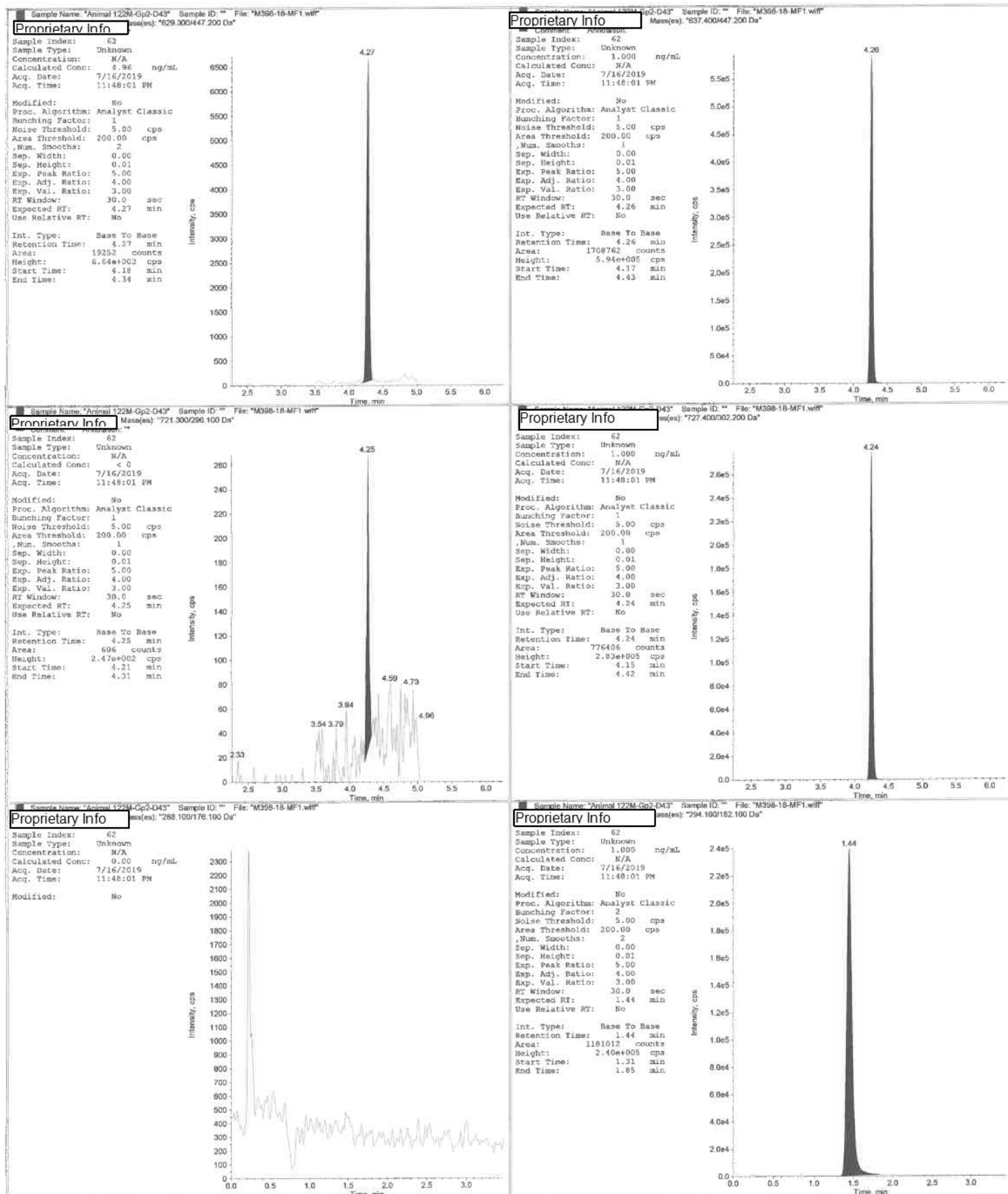
Modified: No
Proc. Algorithm: Analyst Classic
Bunching Factor: 2
Noise Threshold: 5.00 cps
Area Threshold: 200.00 cps
Num. Smoother: 2
Sep. Width: 0.00
Sep. Height: 0.01
Exp. Peak Ratio: 5.00
Exp. Adj. Ratio: 4.00
Exp. Val. Ratio: 3.00
RT Window: 30.0 sec
Expected RT: 1.44 min
Use Relative RT: No

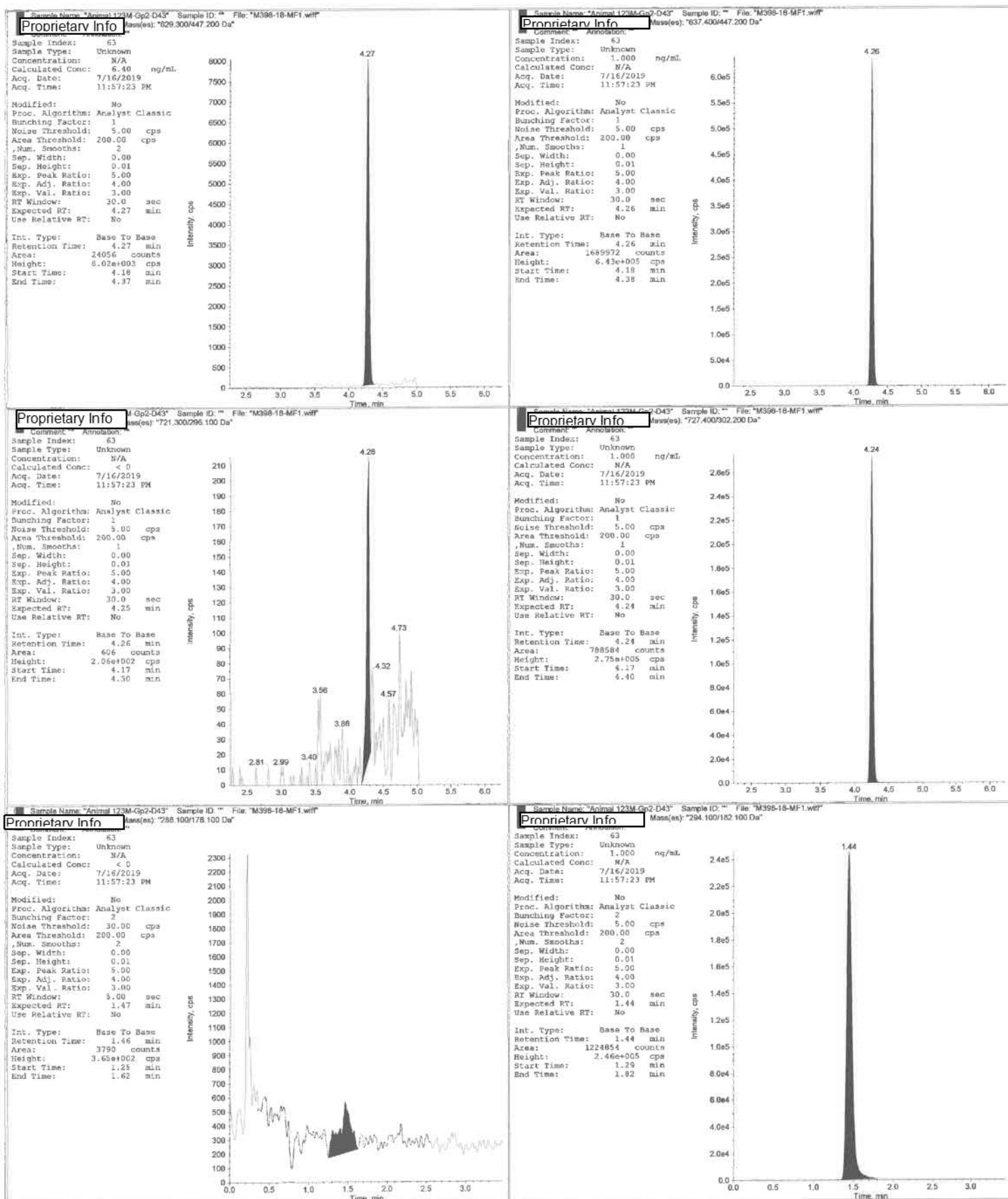
Int. Type: Base To Base
Retention Time: 1.44 min
Area: 1235885 counts
Height: 2.55e+005 cps
Start Time: 1.33 min
End Time: 1.75 min

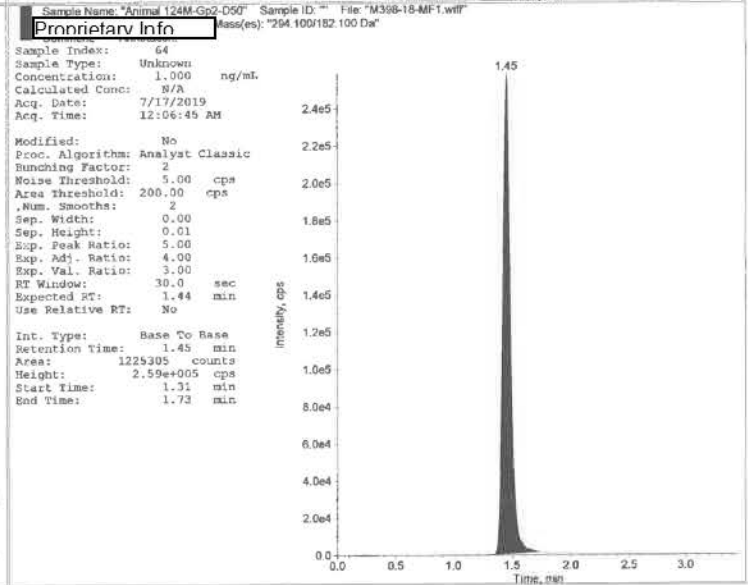
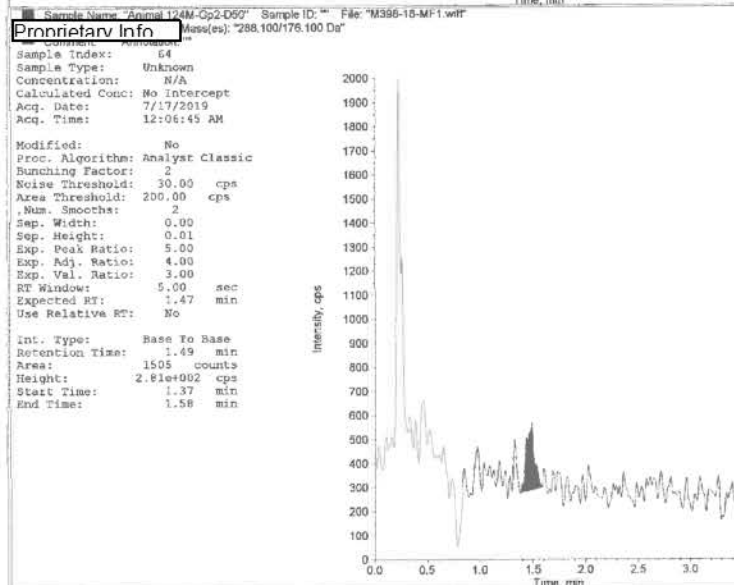
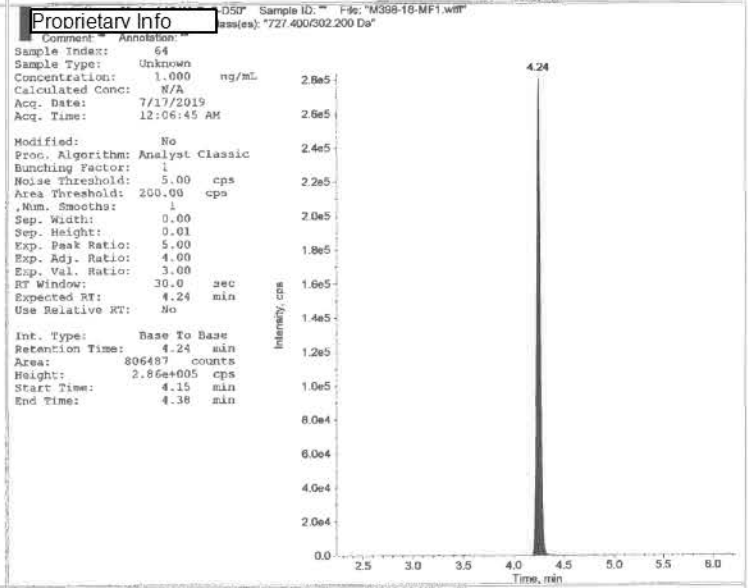
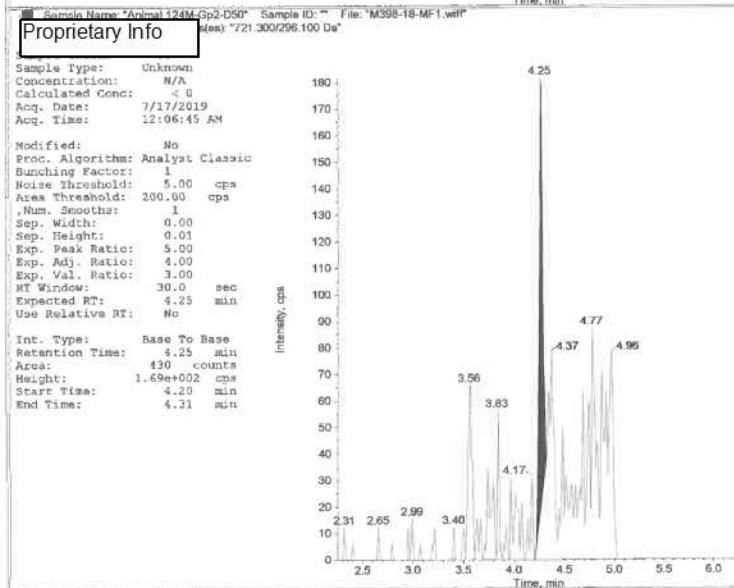
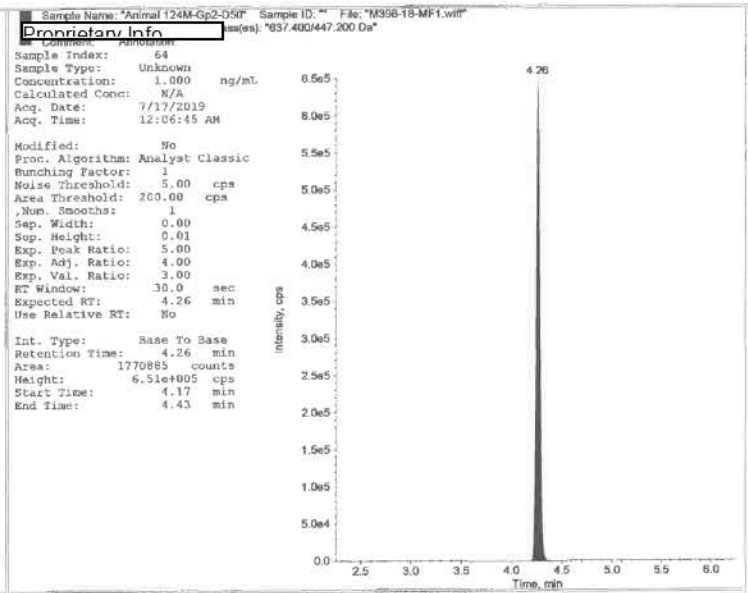
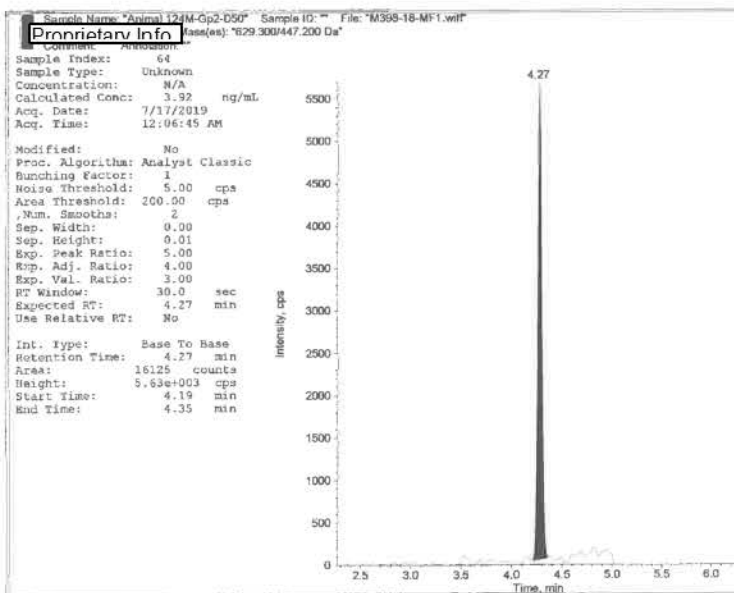


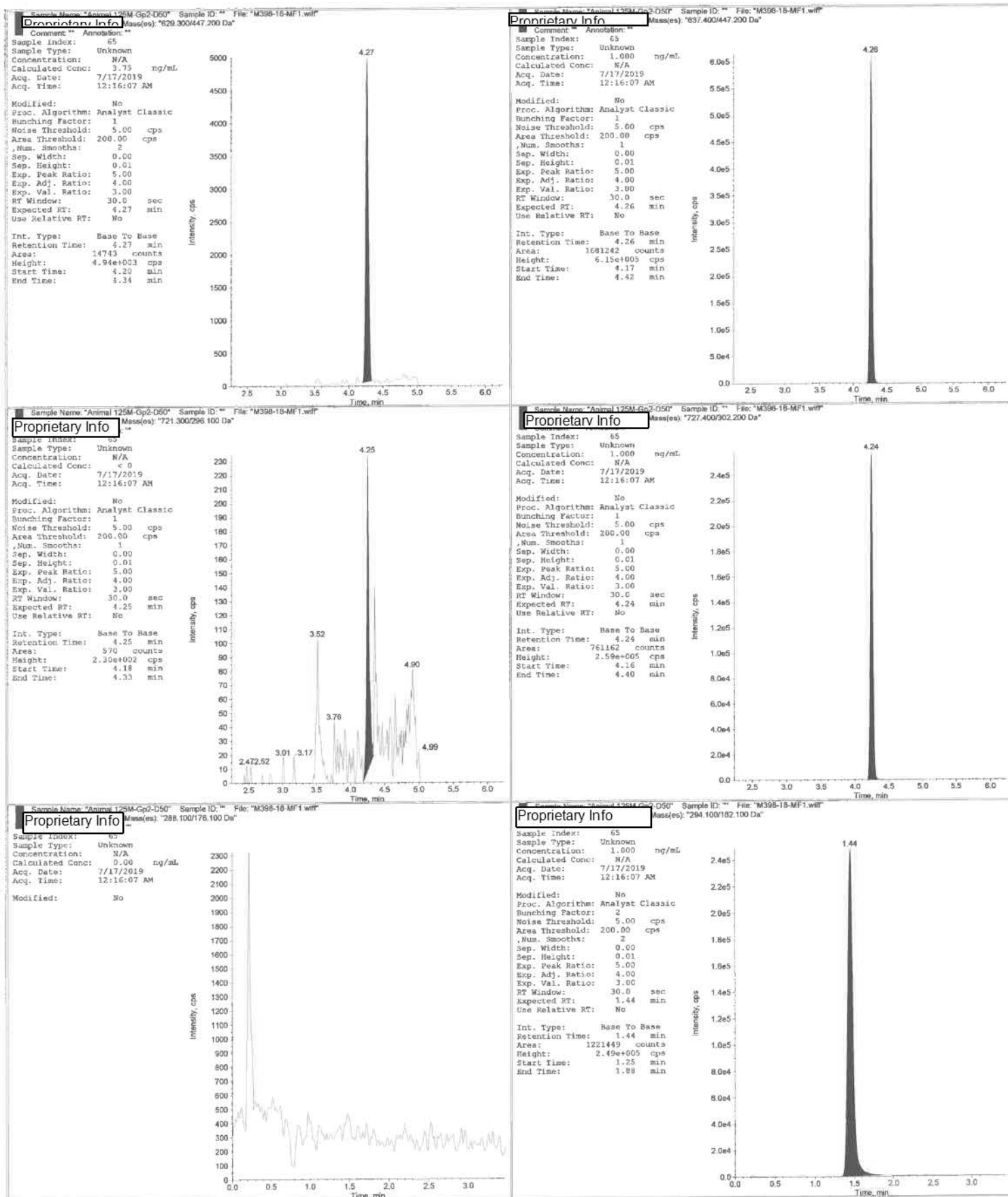


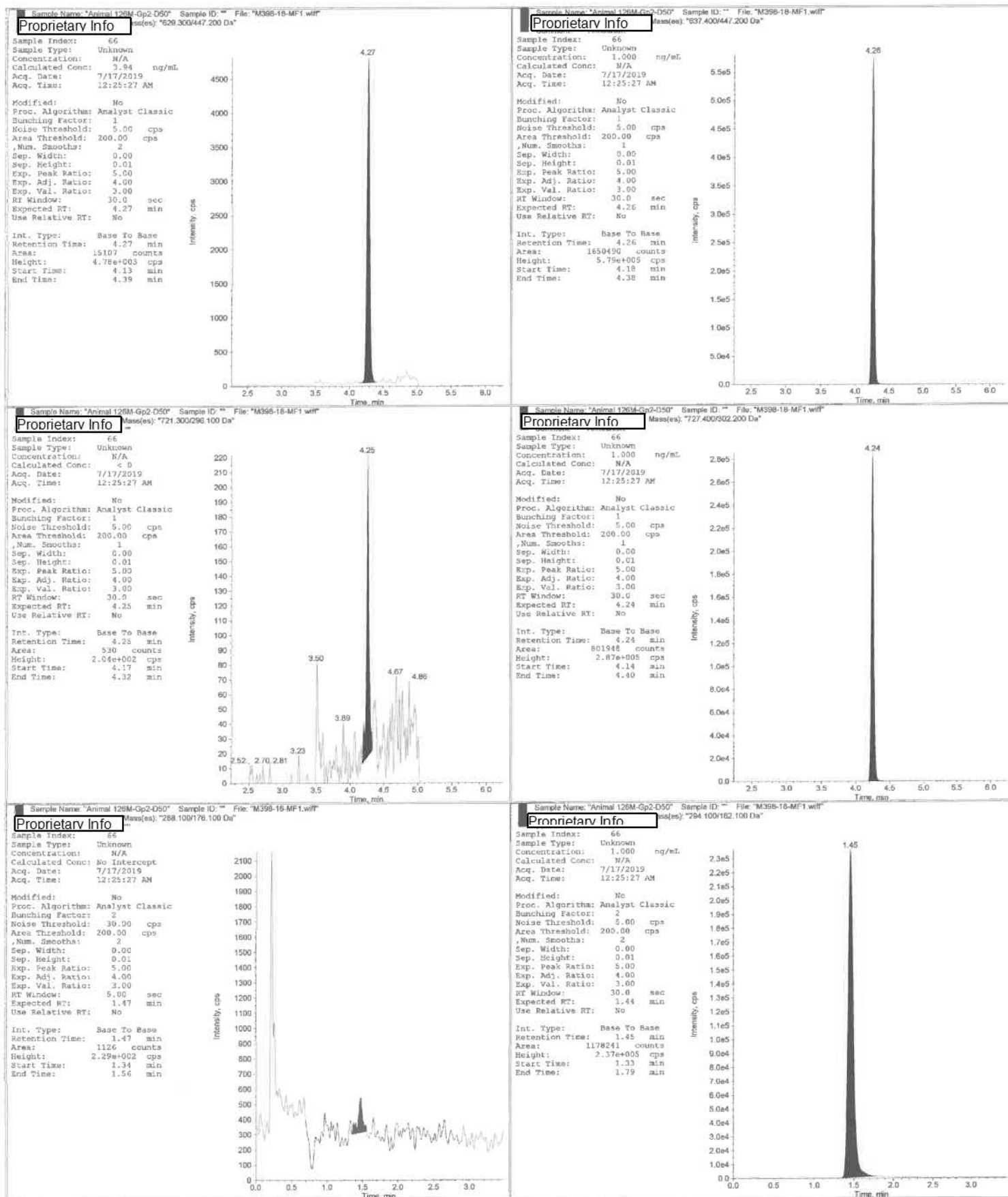


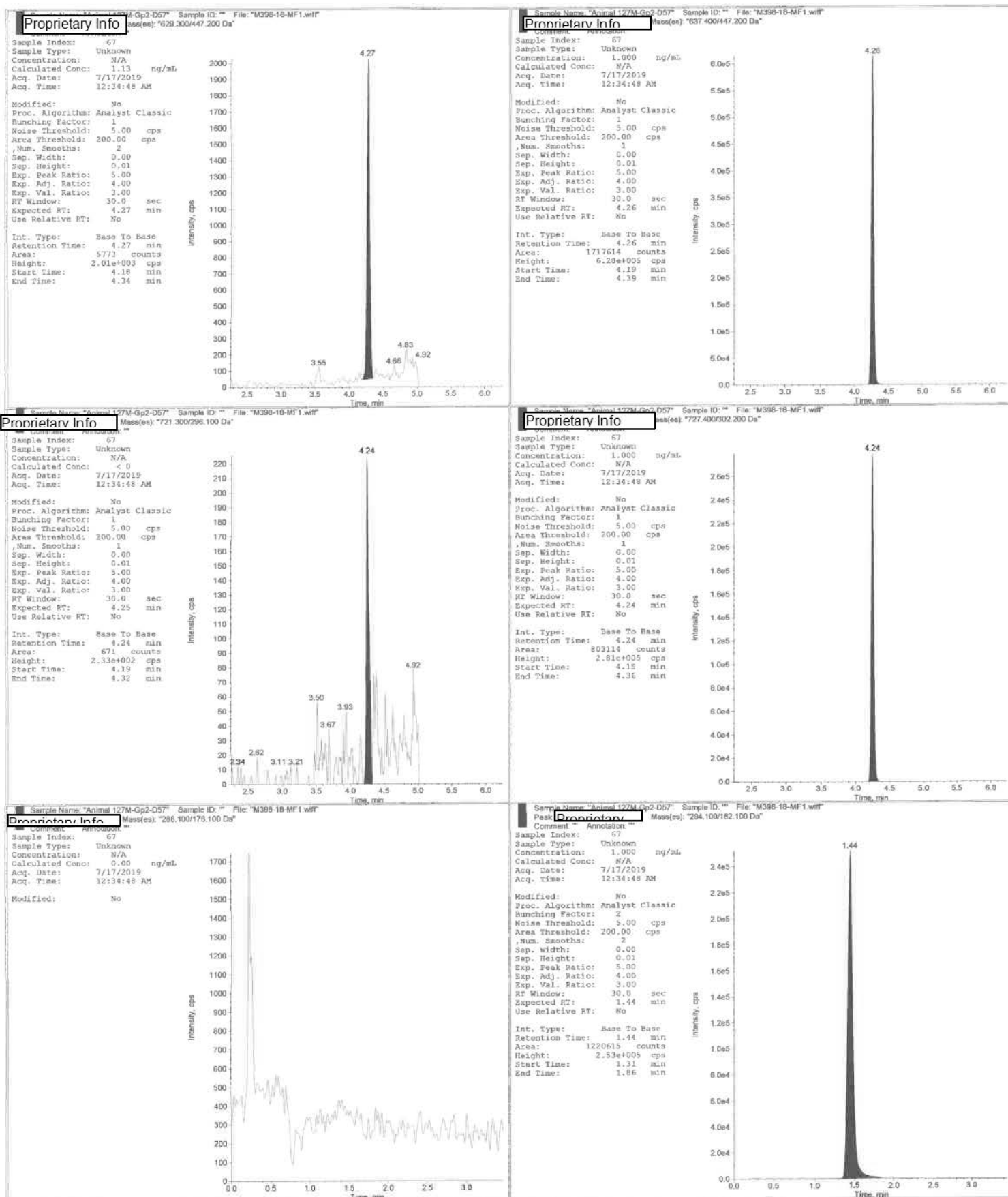


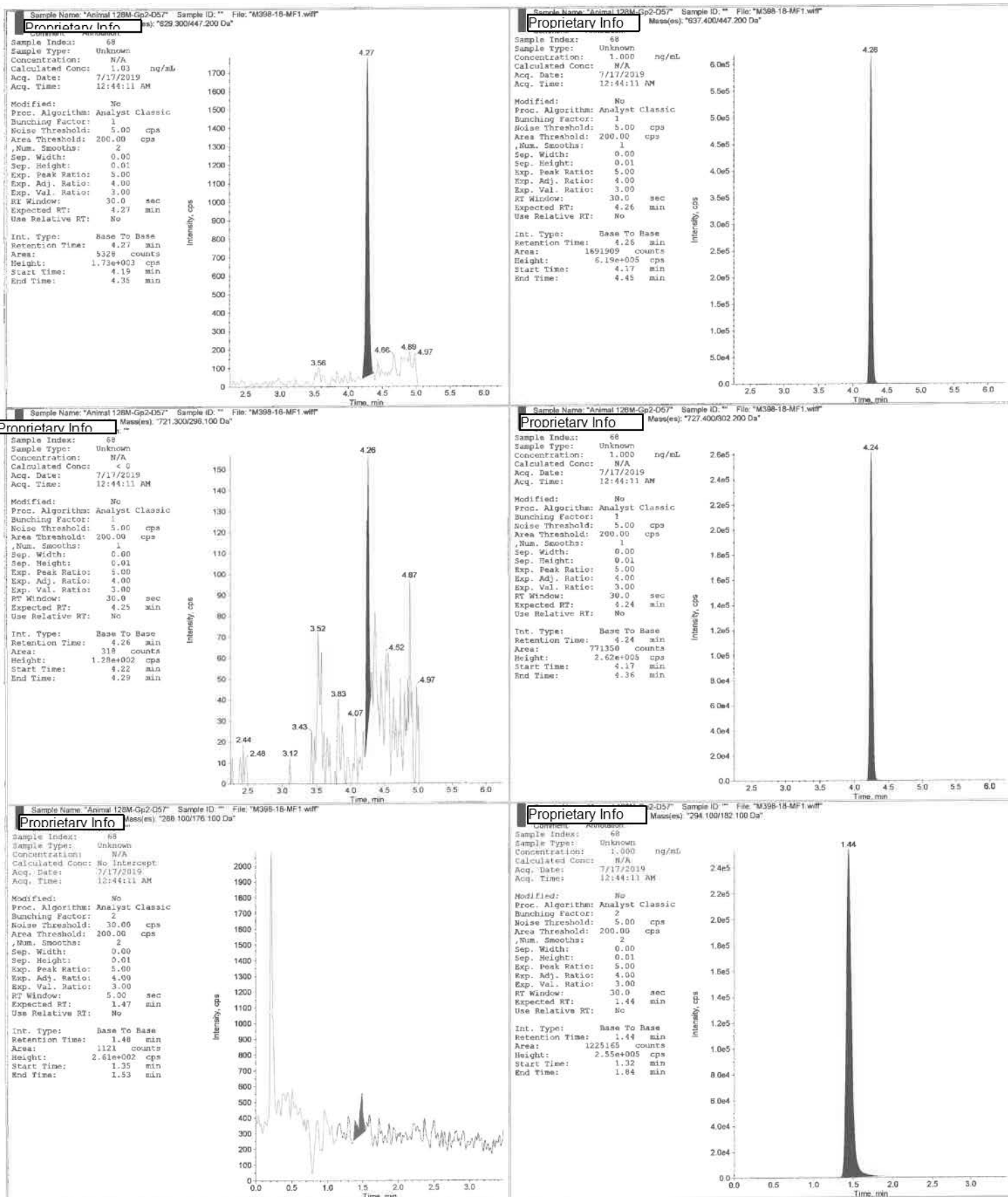


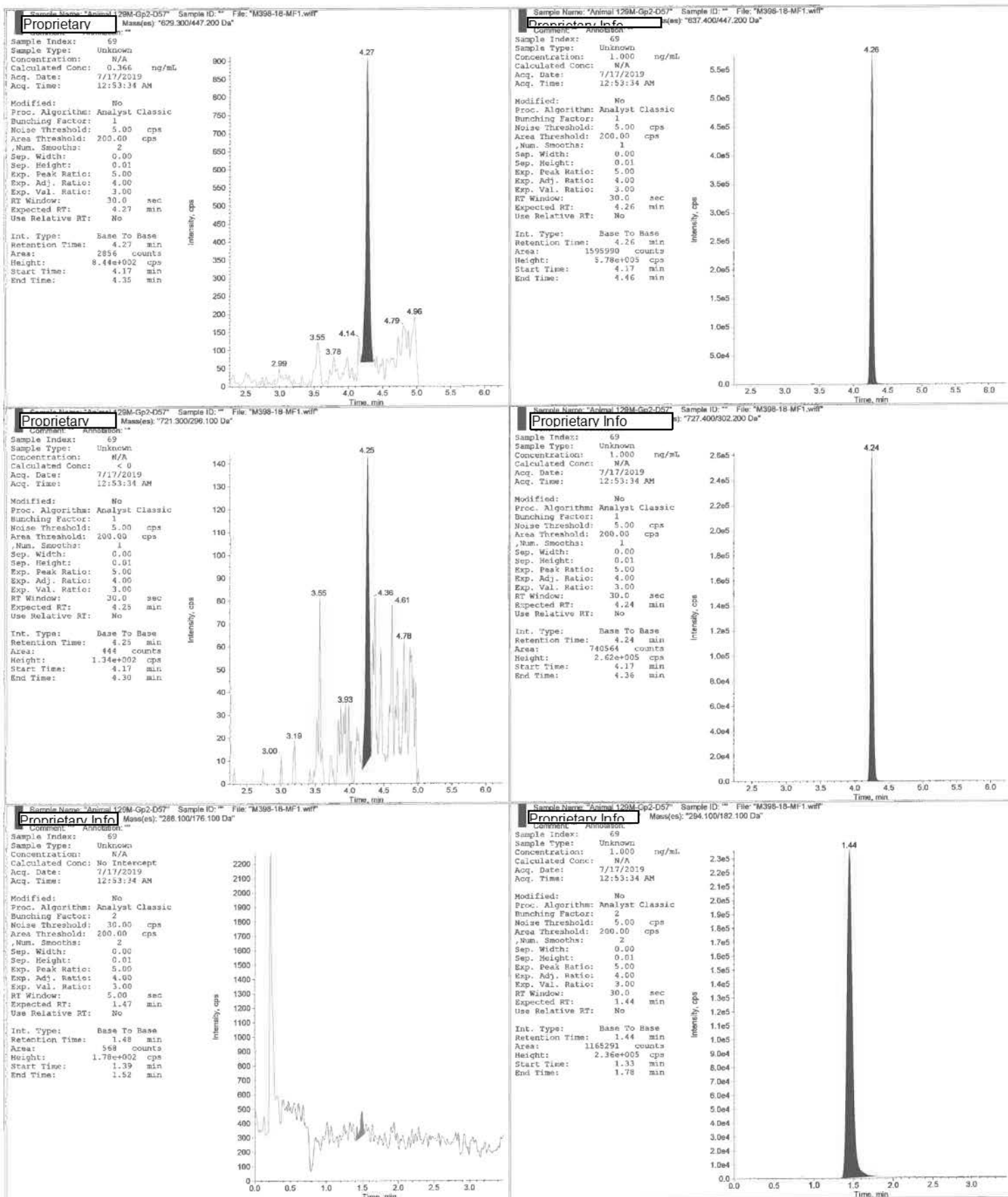


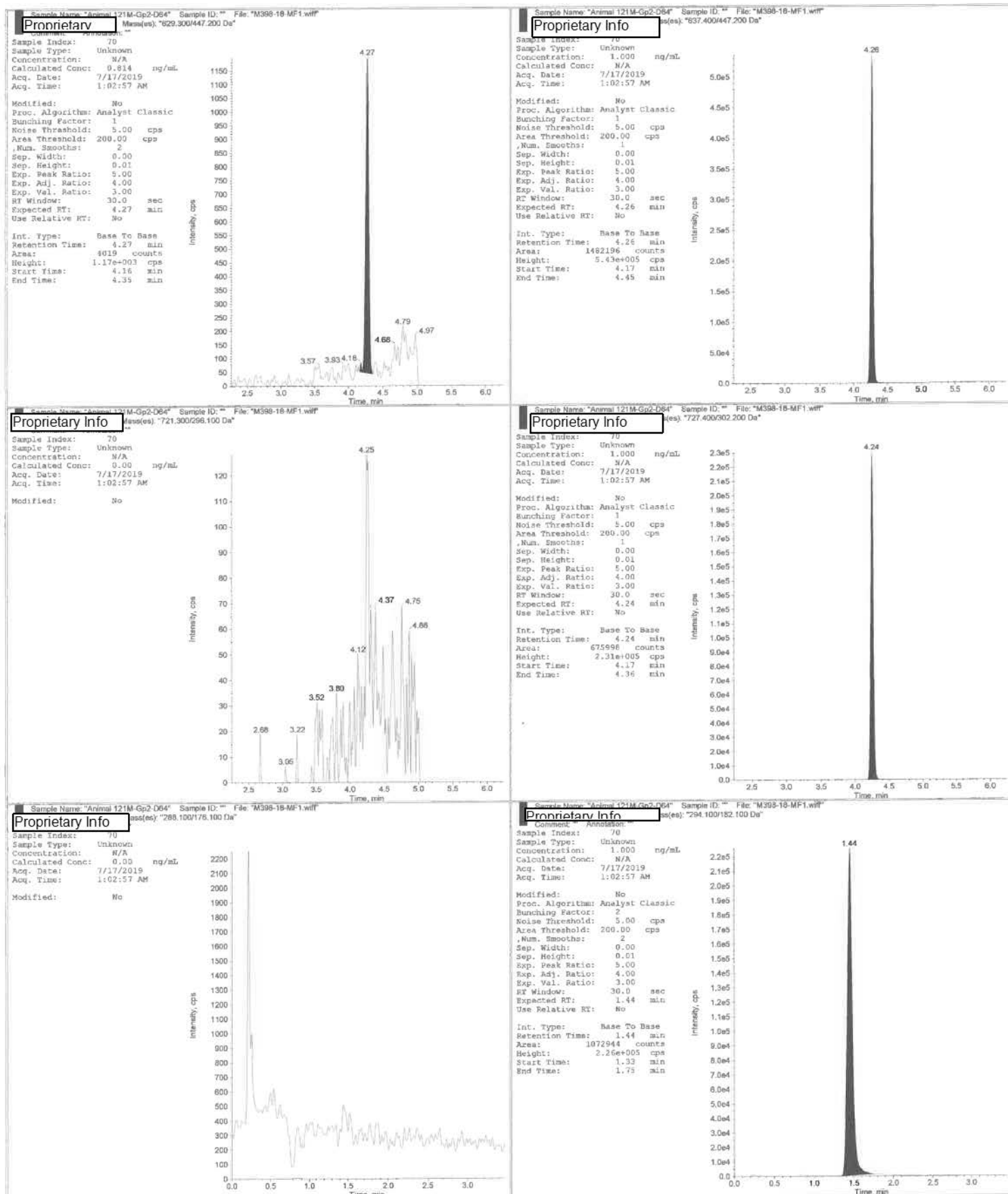


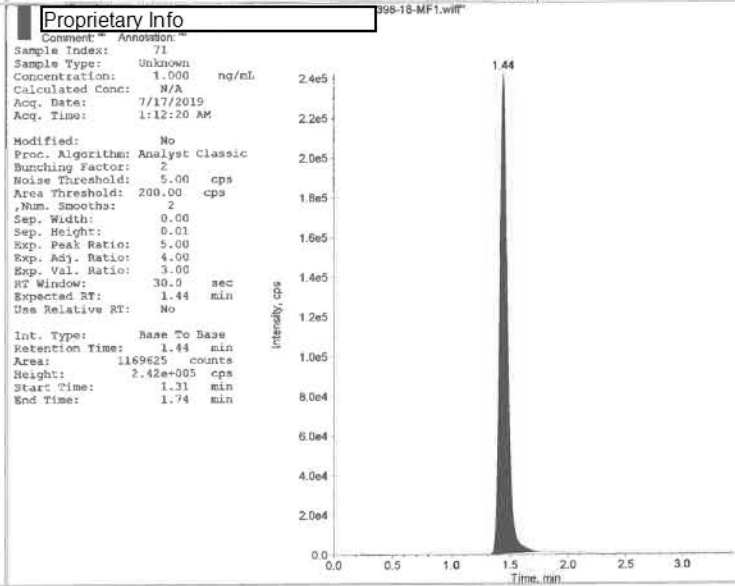
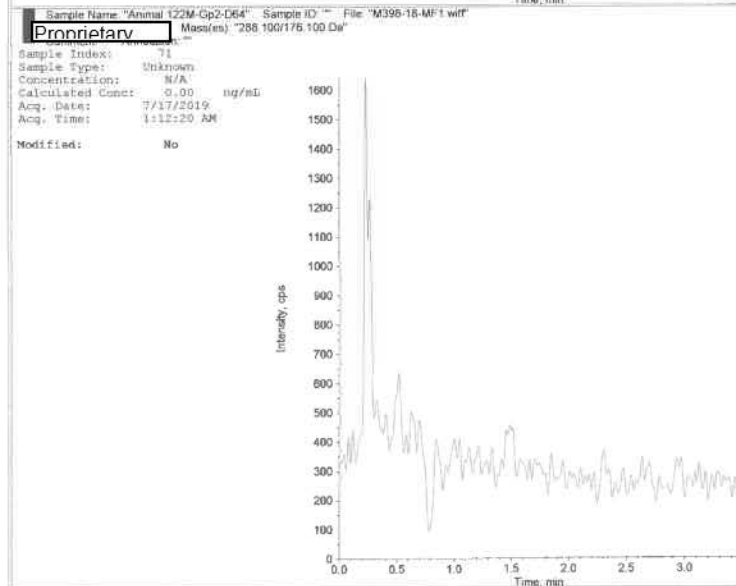
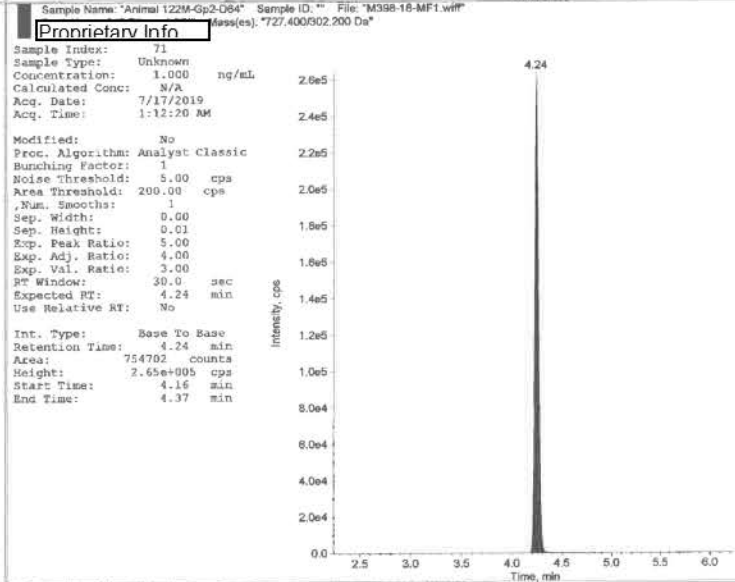
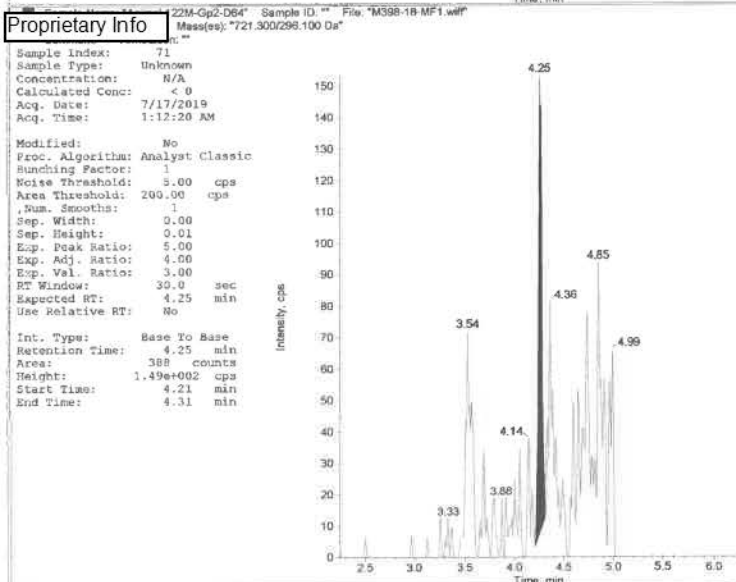
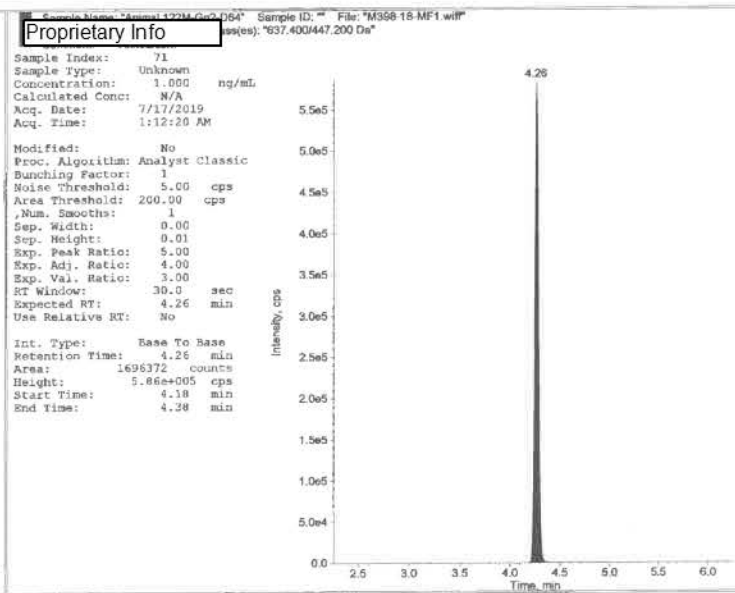
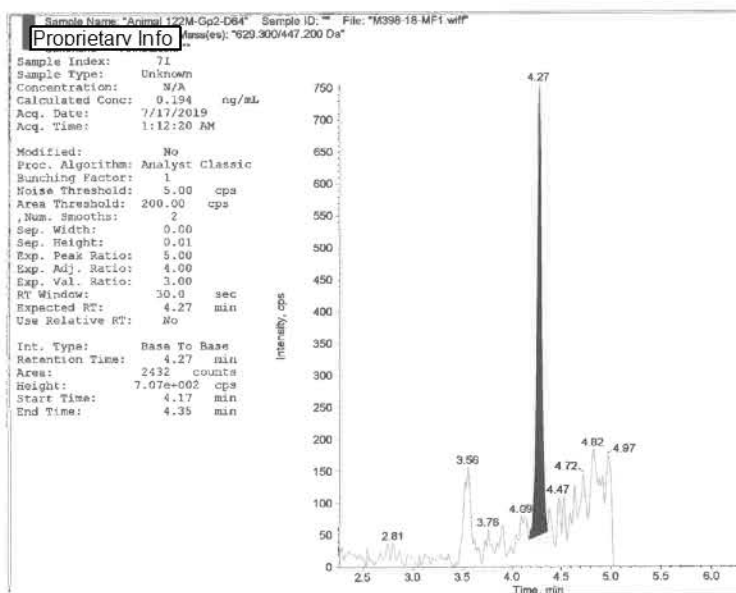


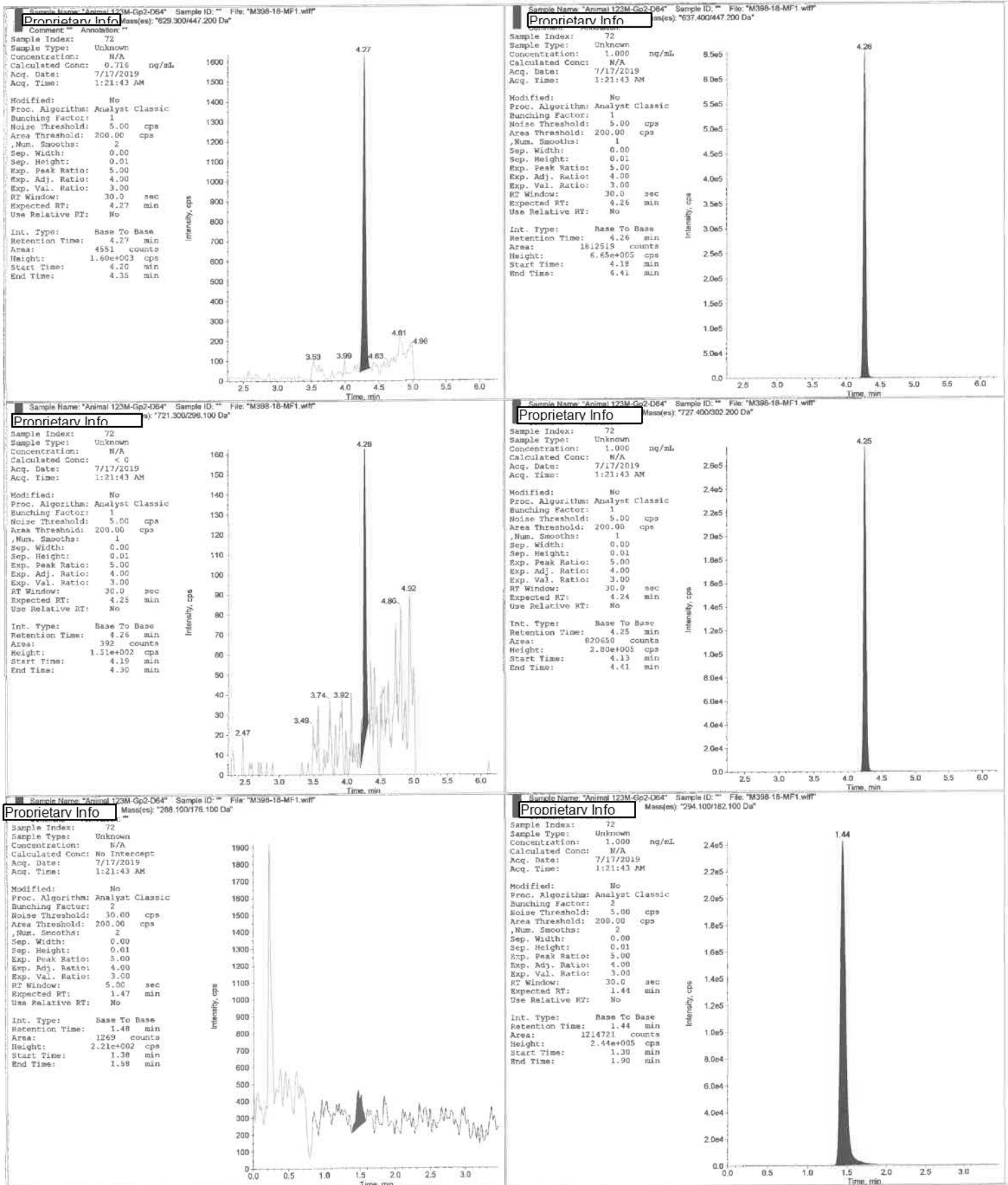


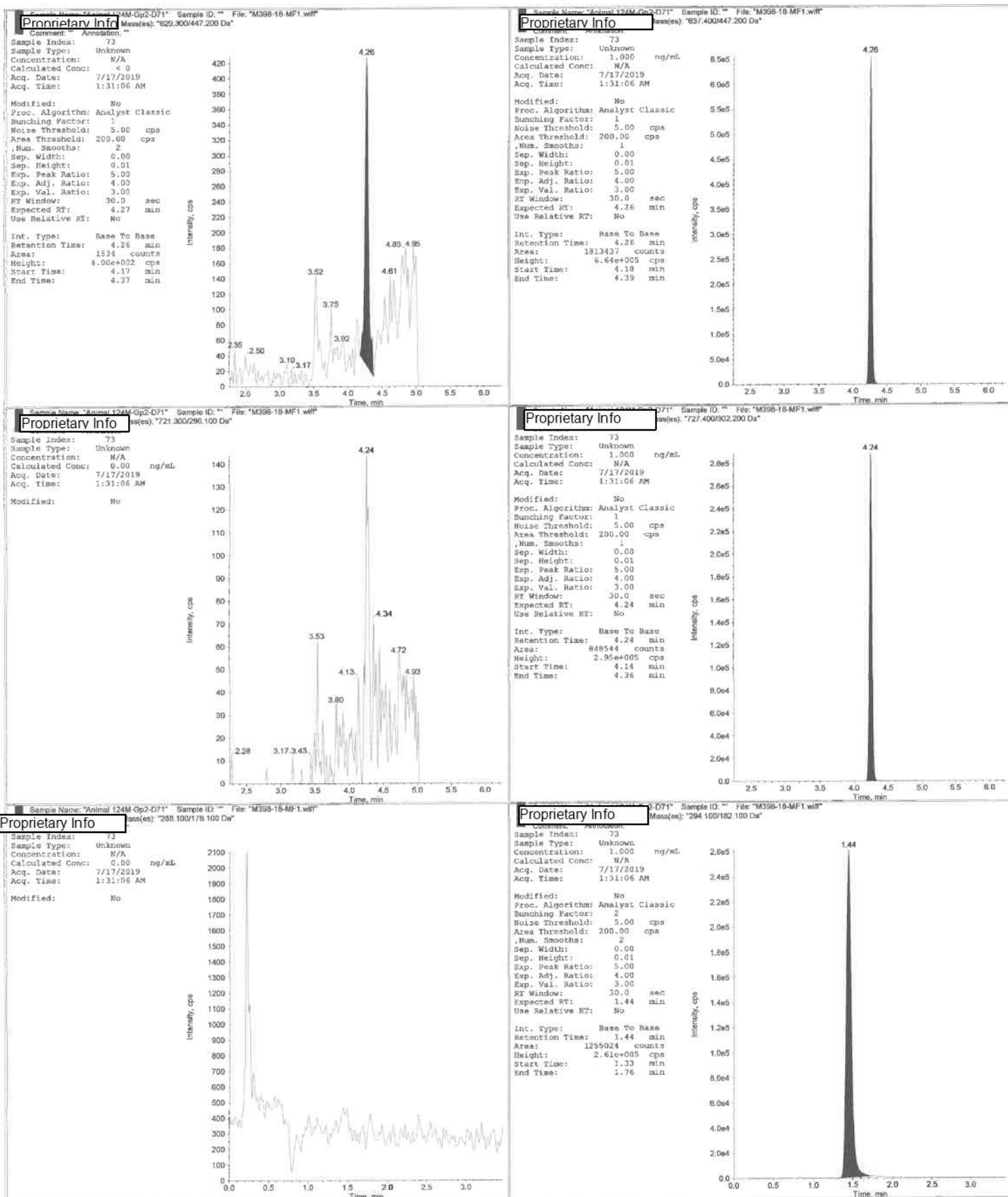


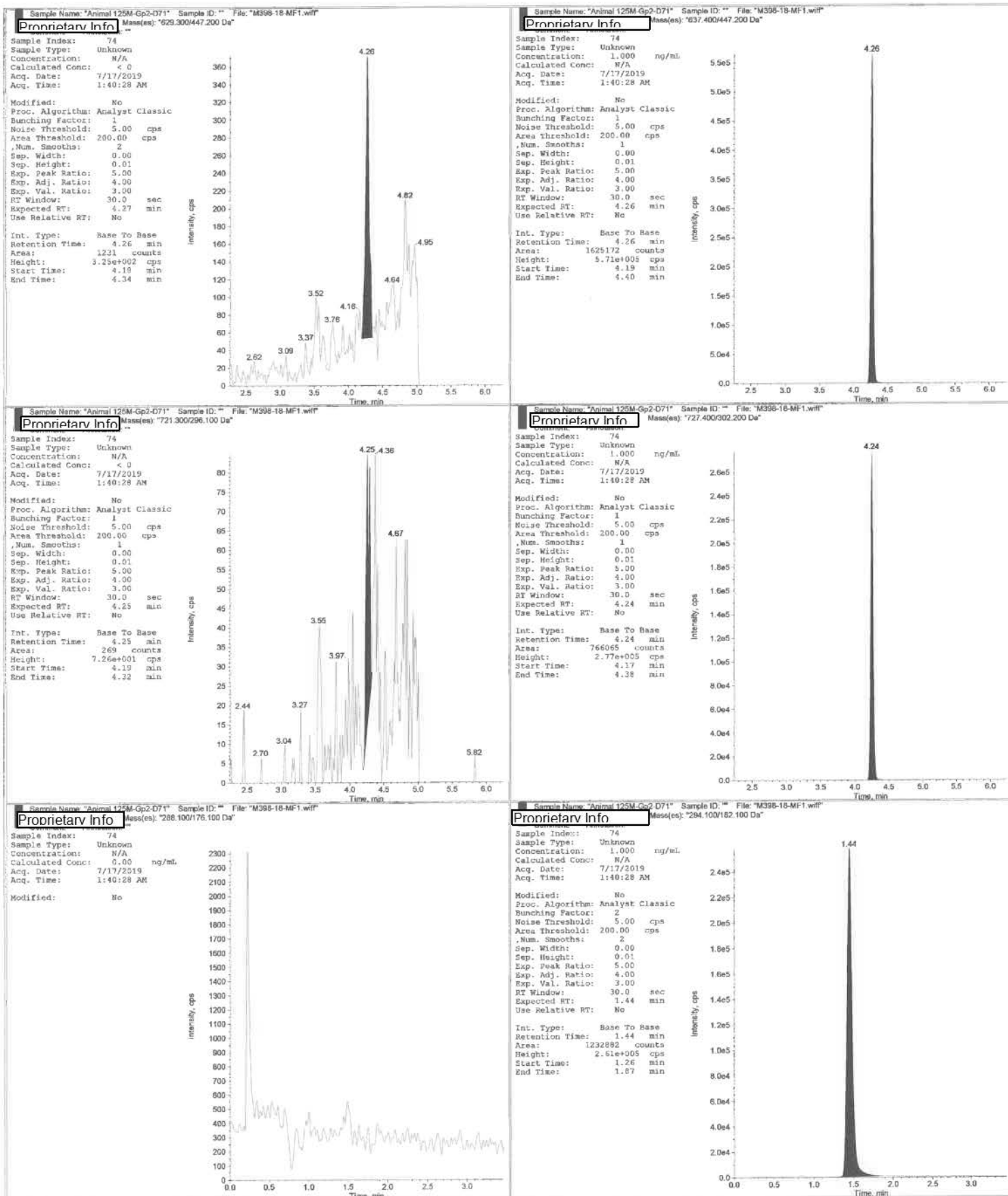


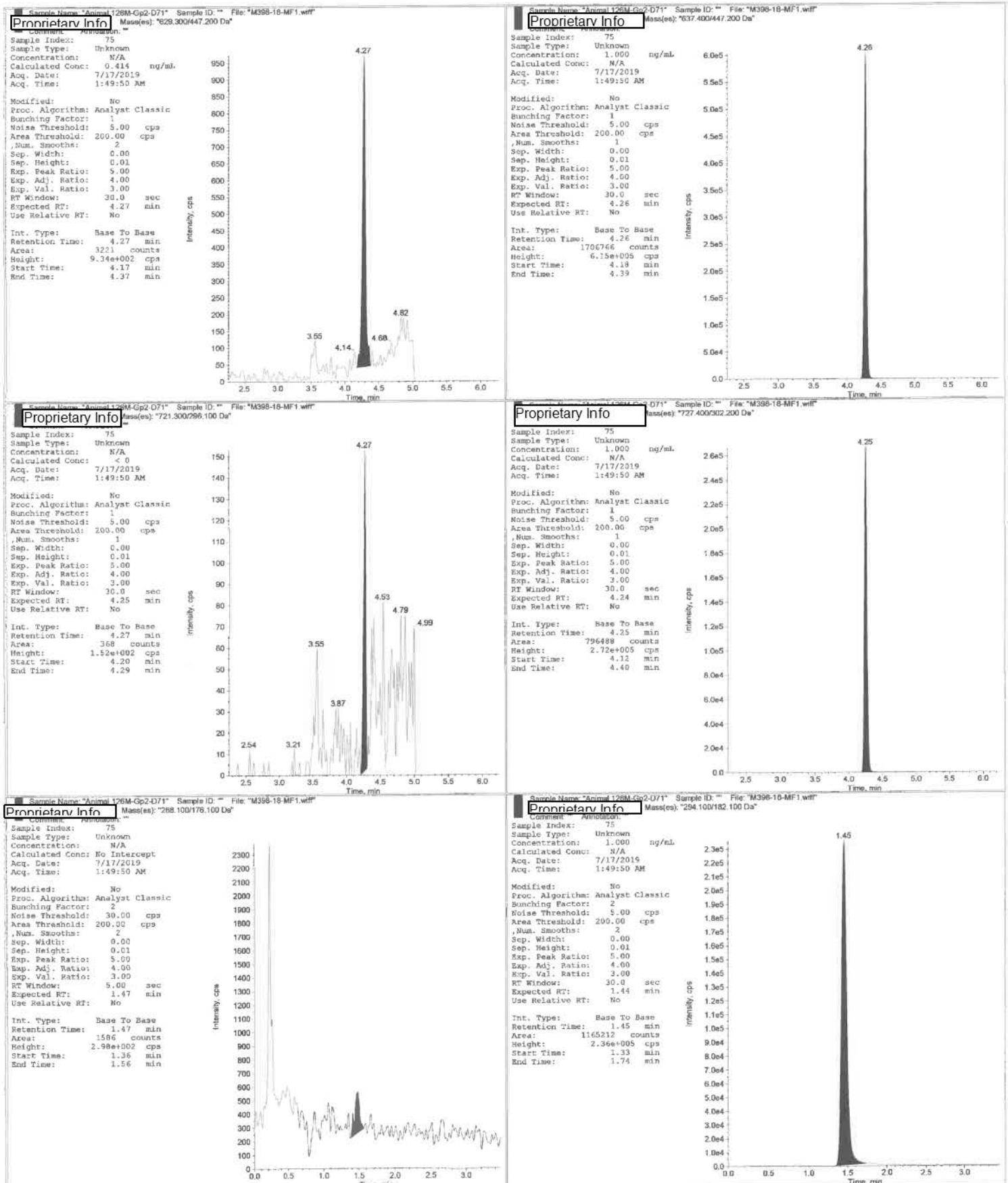


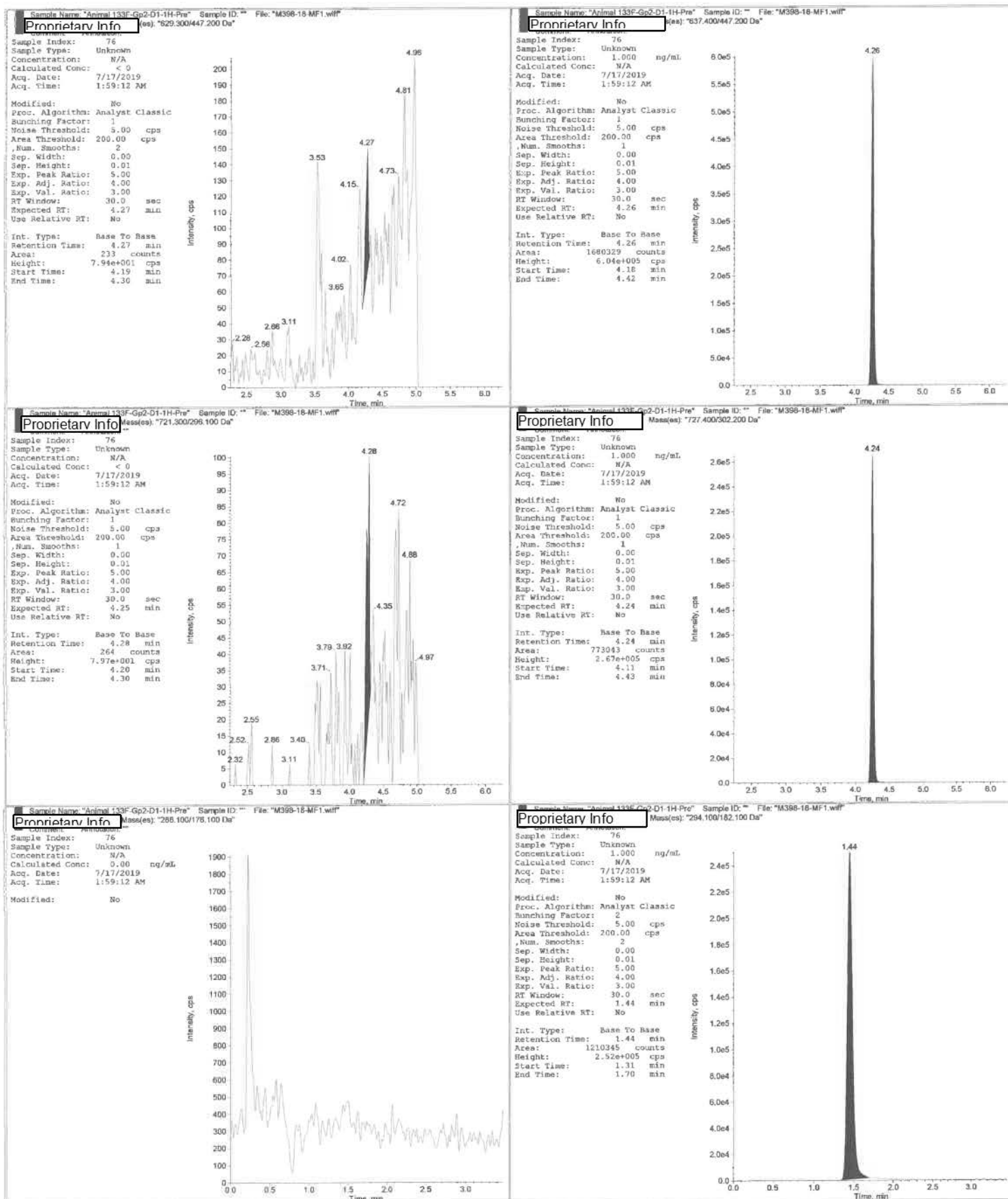


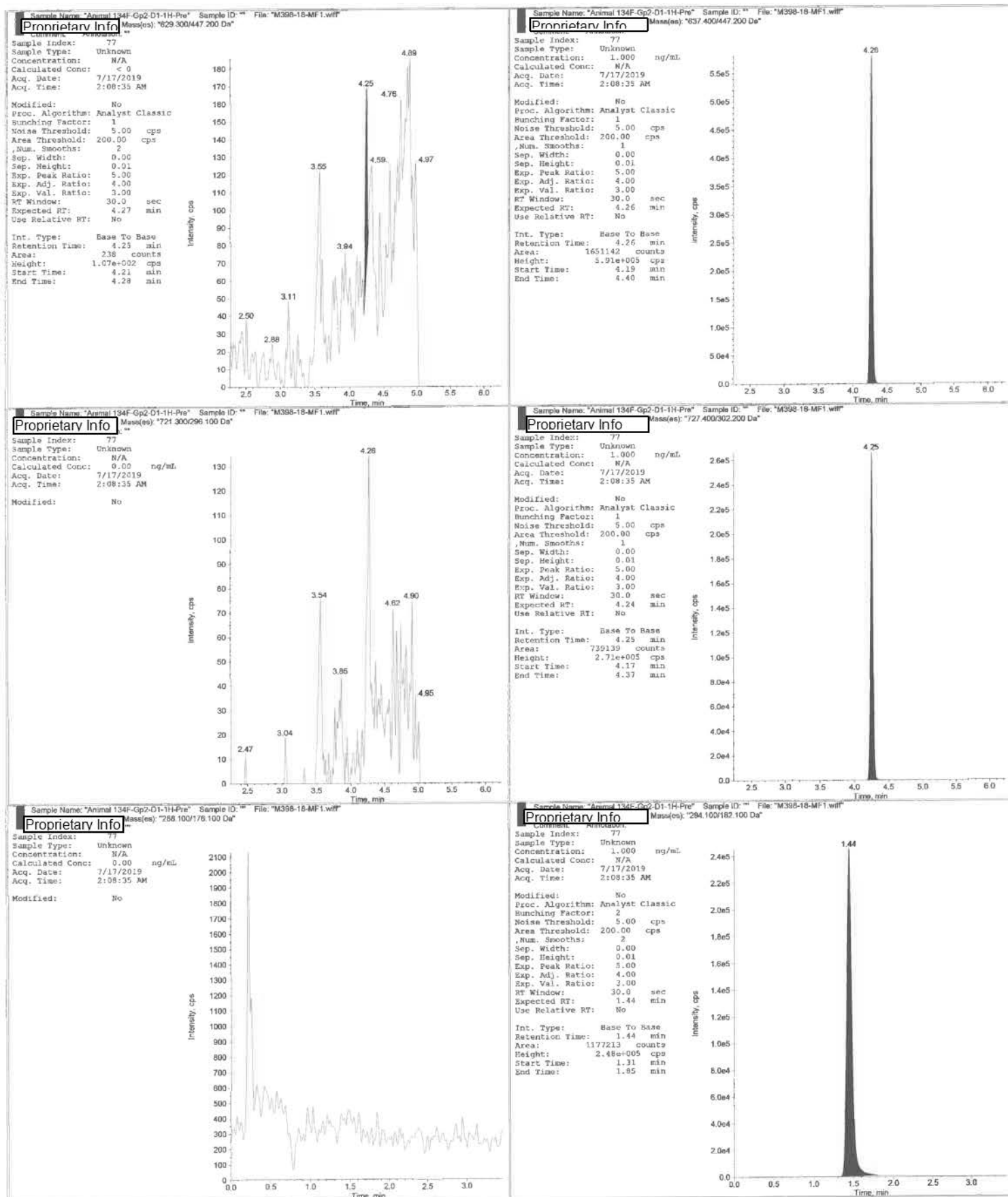


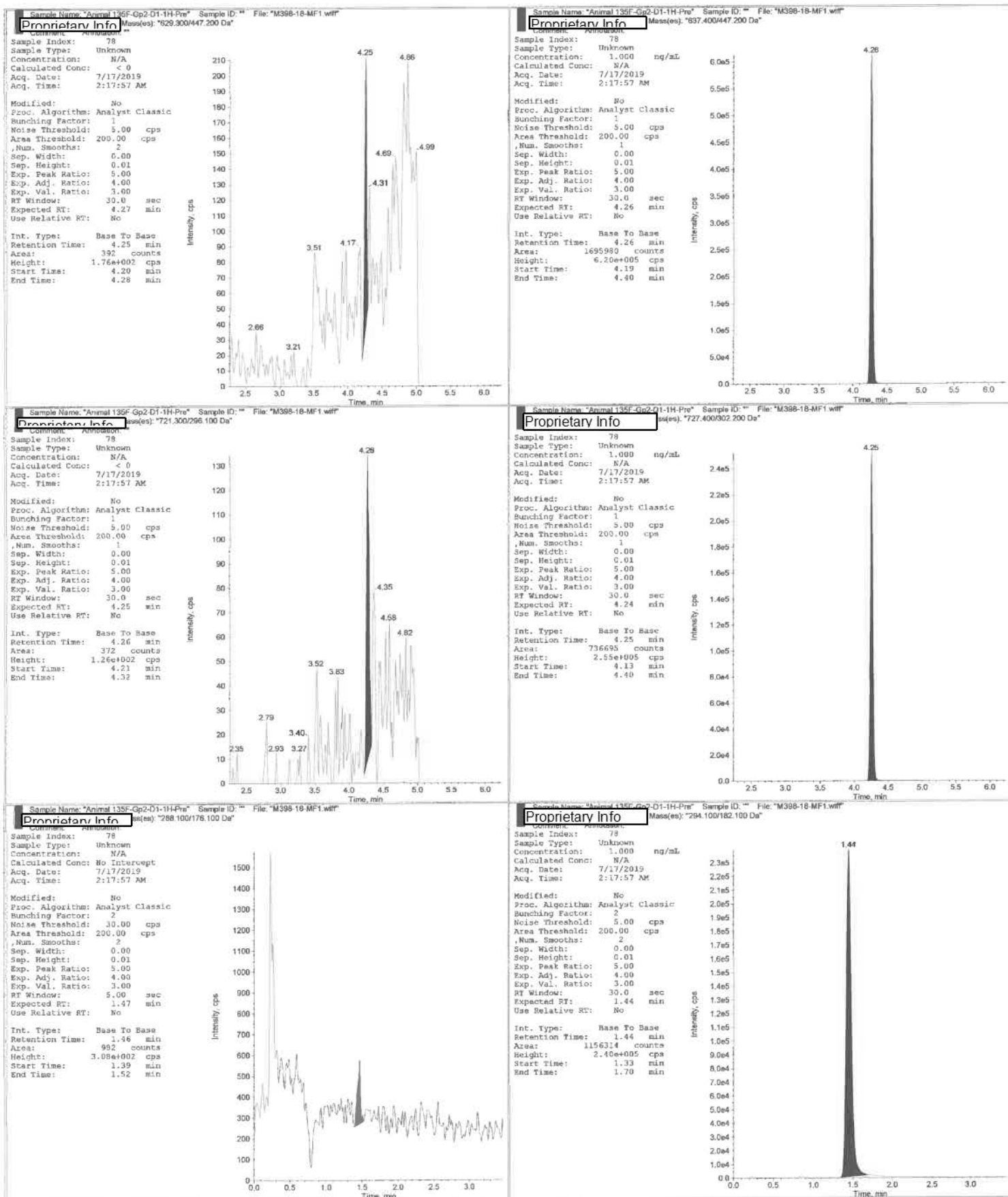






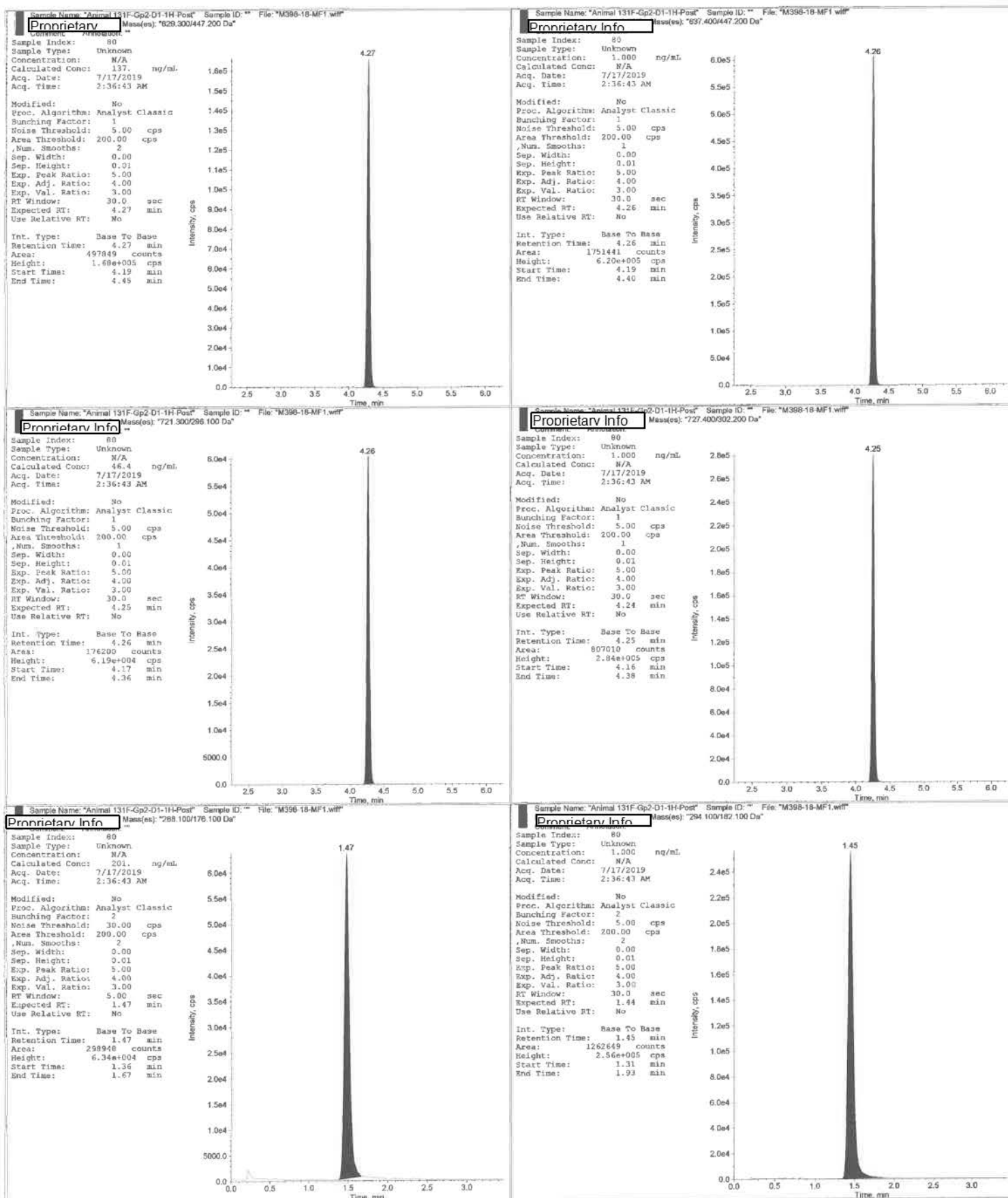


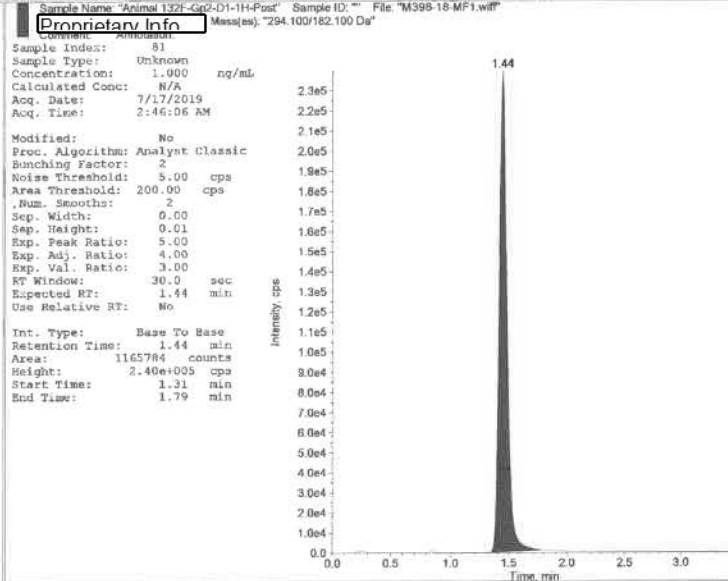
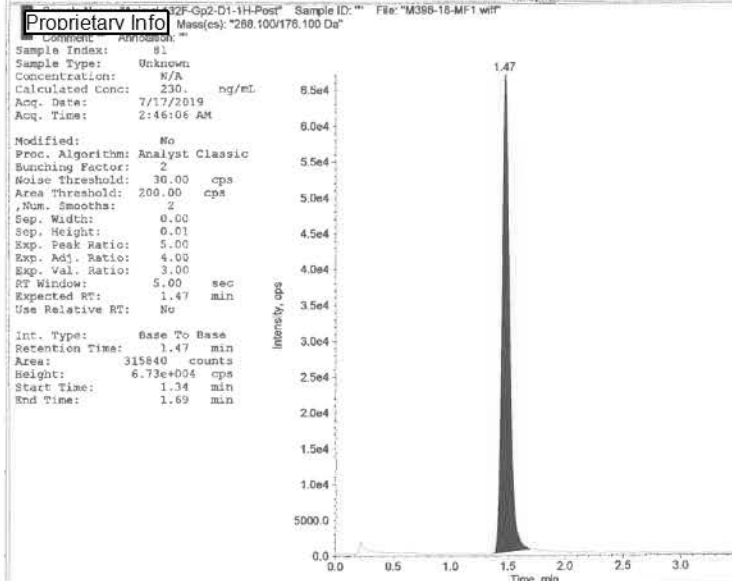
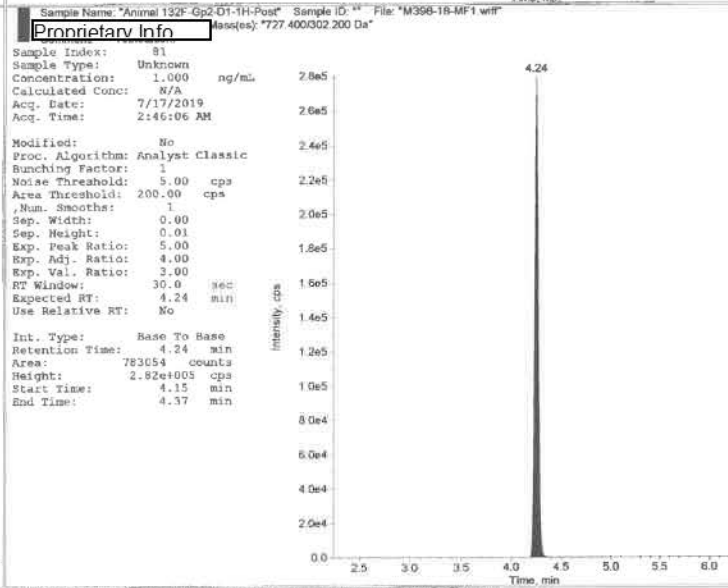
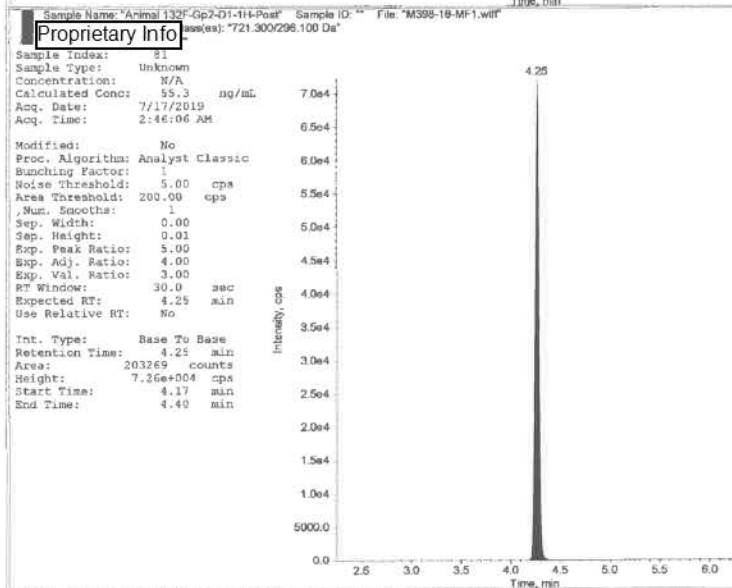
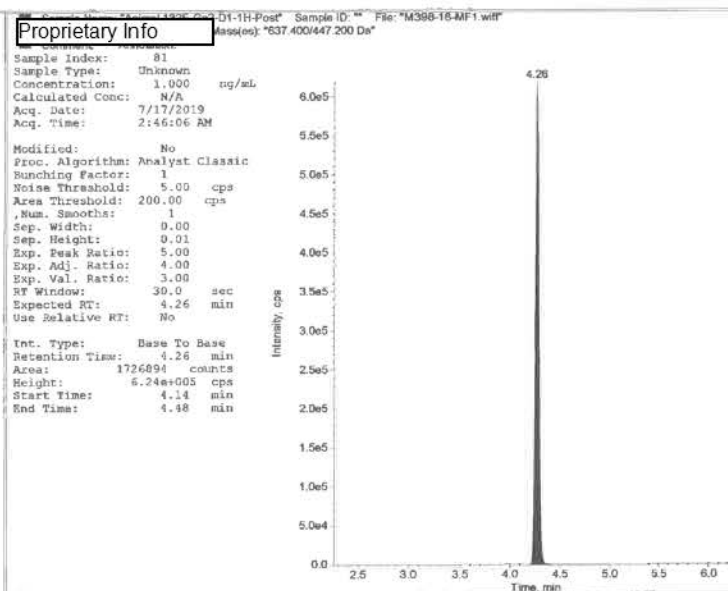
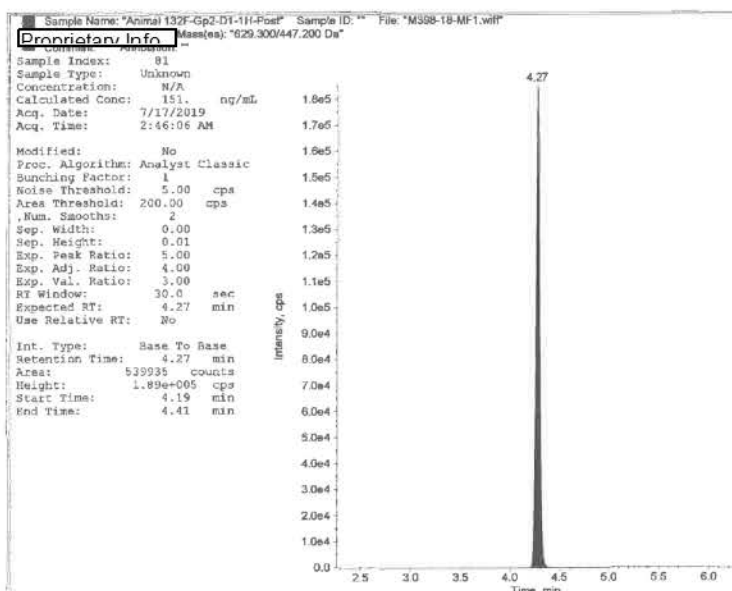


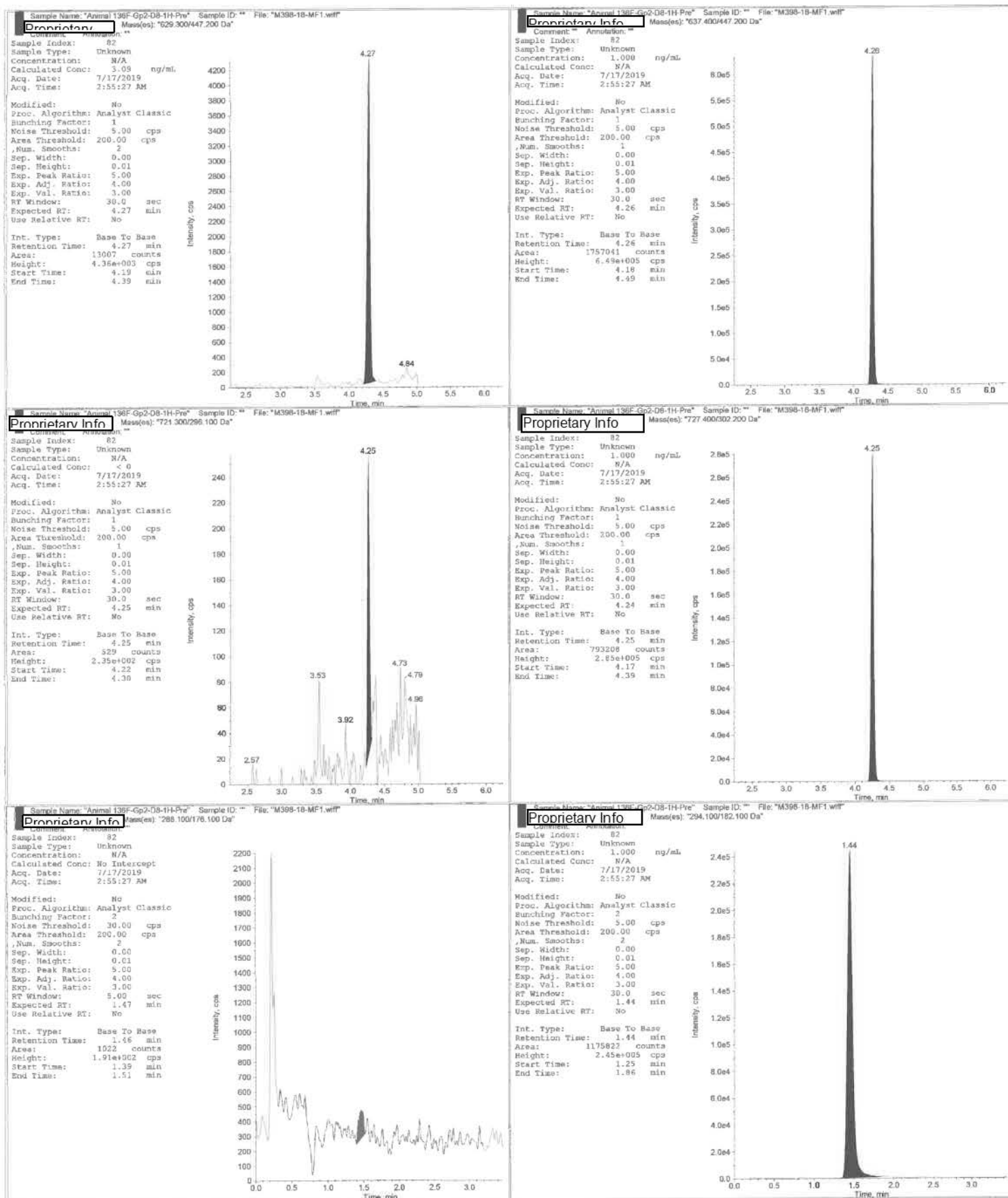


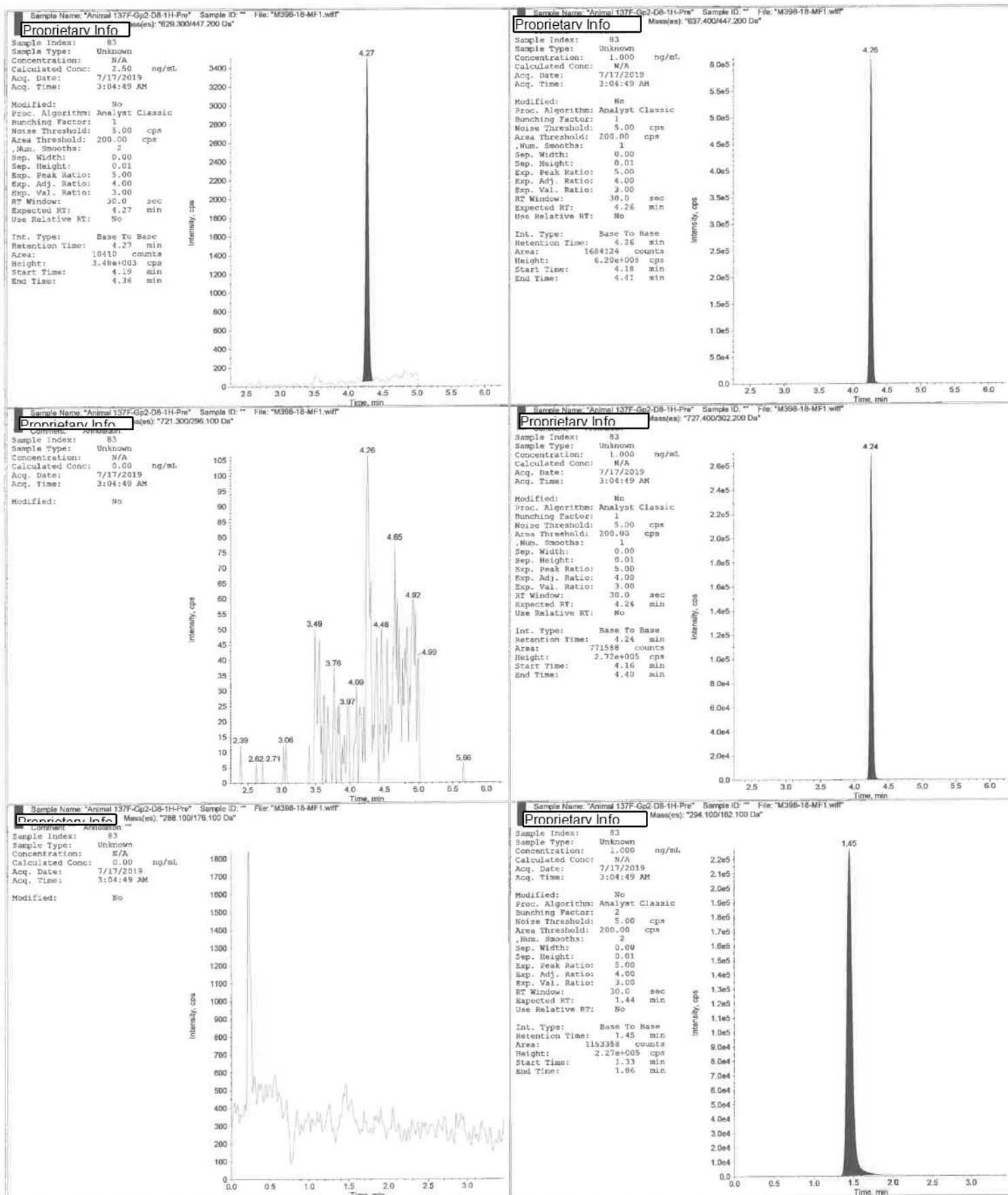


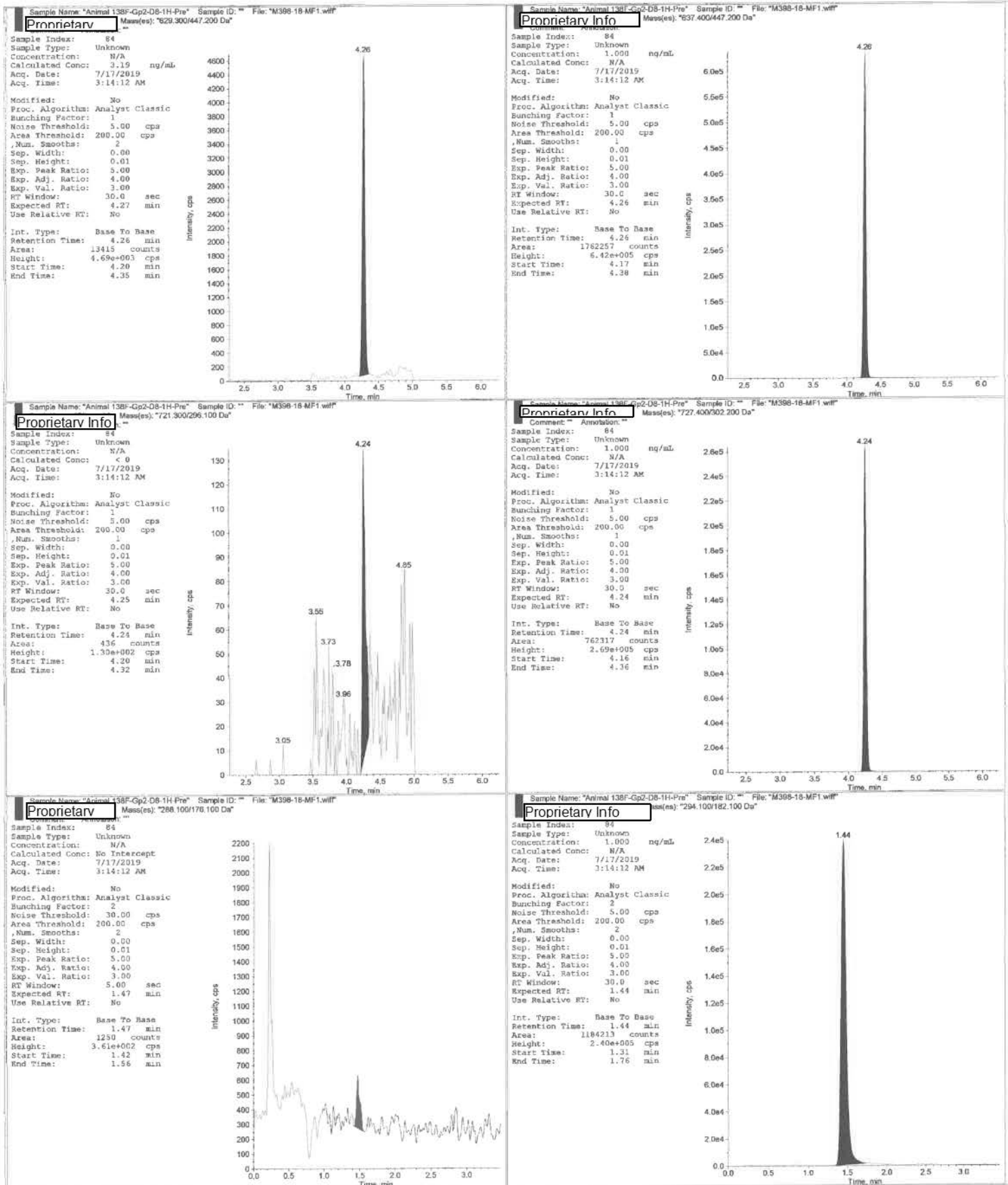
Results Path: D:\Analyst Data\Projects\M398-18\Results\M398-18-MF1-Final.rdb









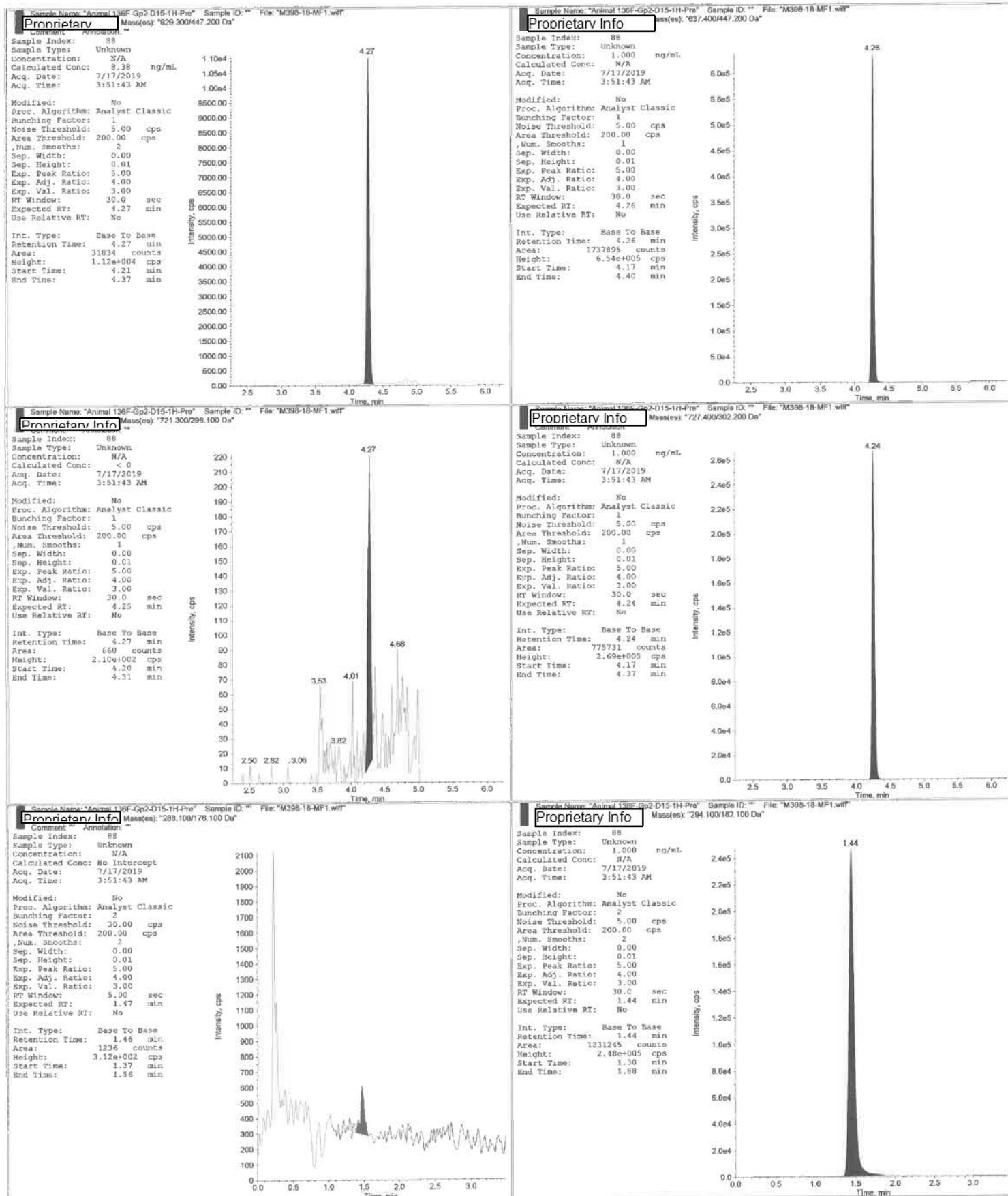


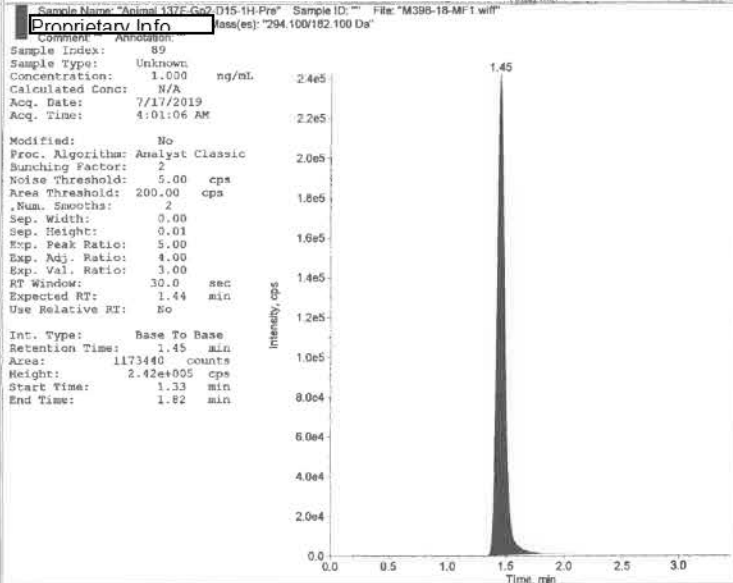
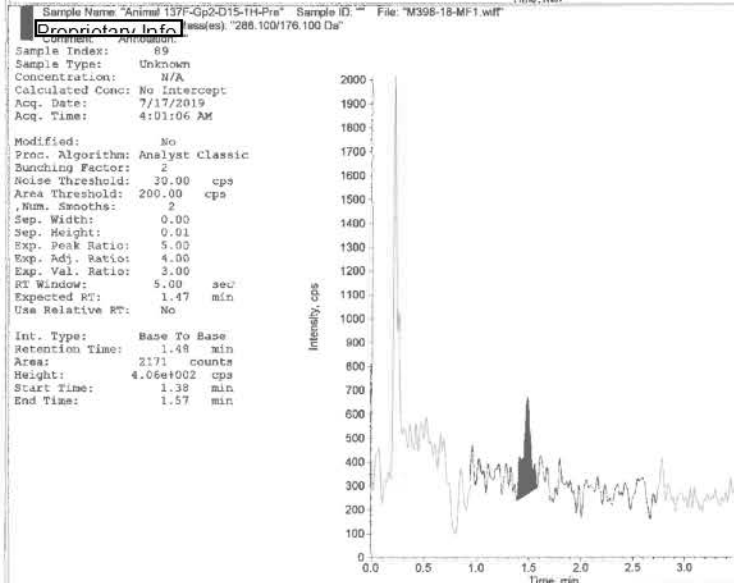
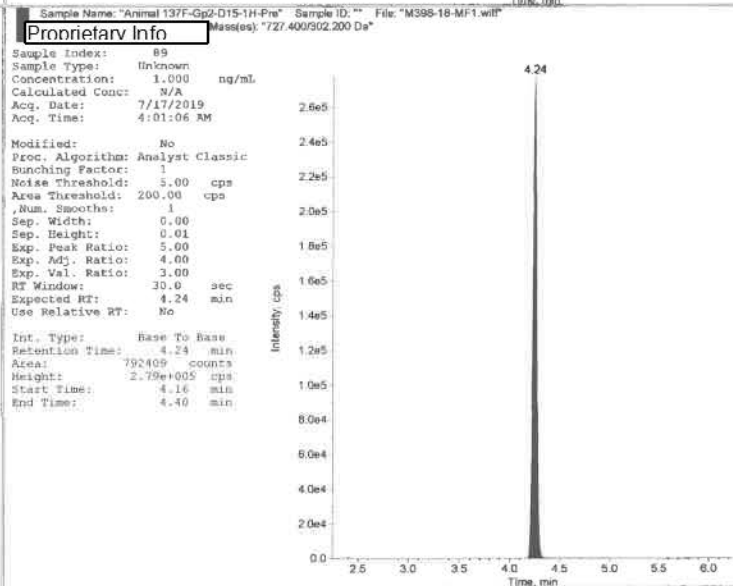
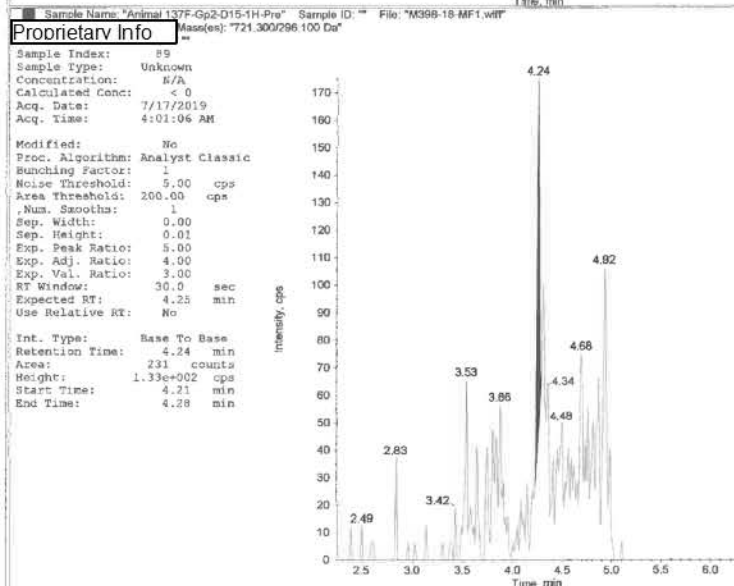
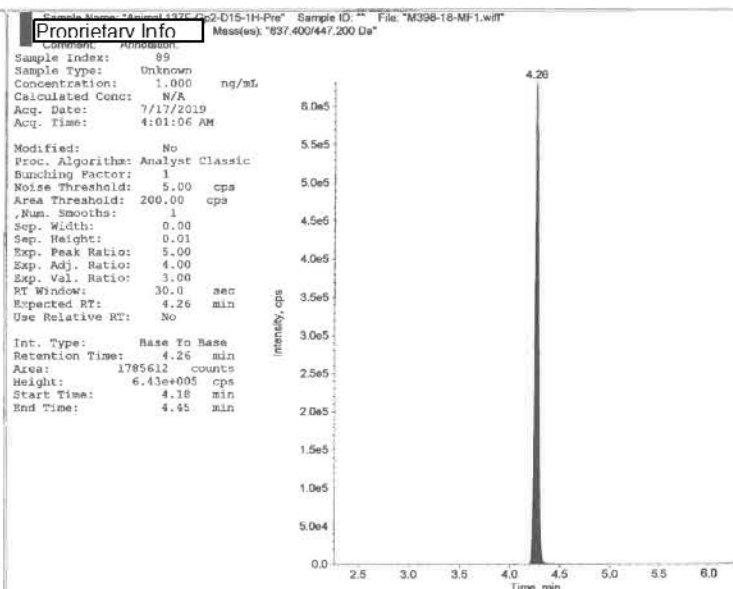
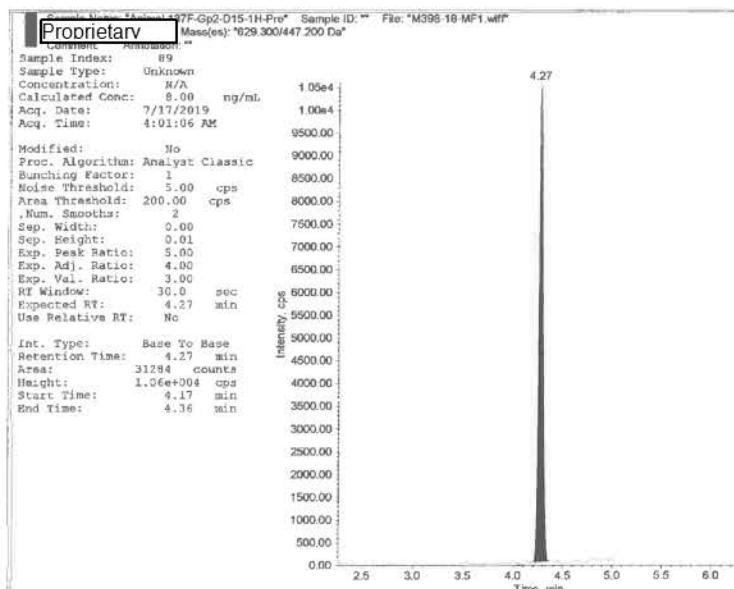
Results Path: D:\Analyst Data\Projects\M398-18\Results\M398-18-MF1-Final.rdb

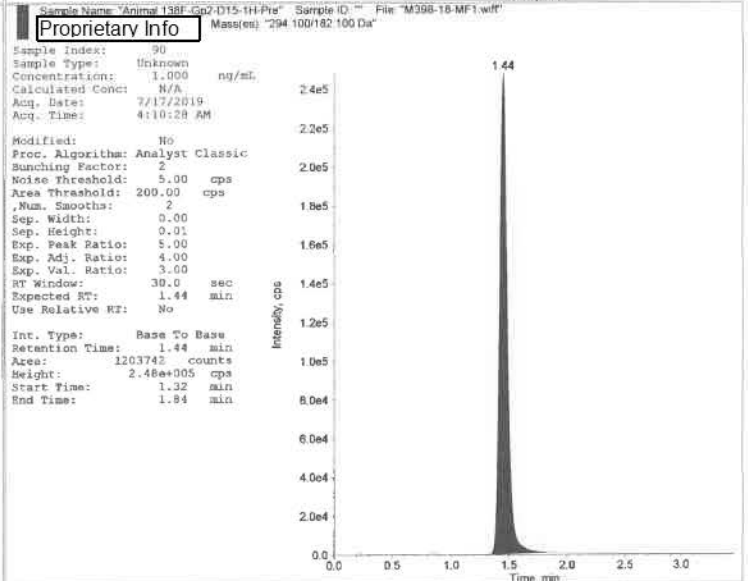
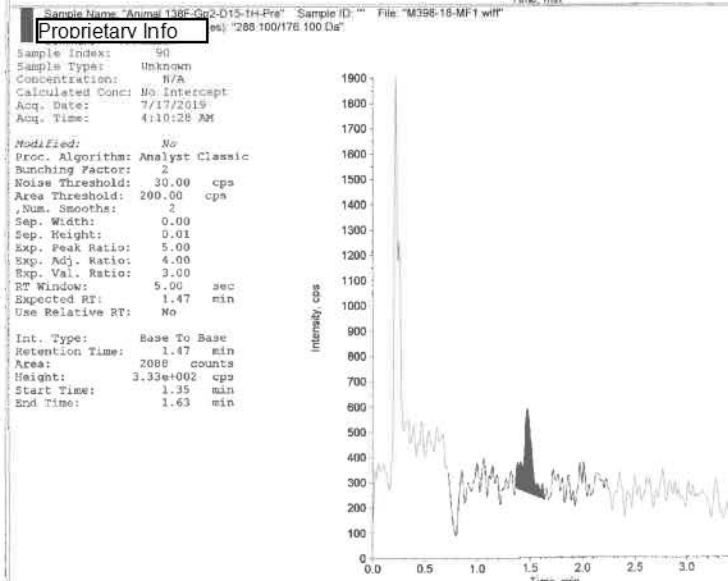
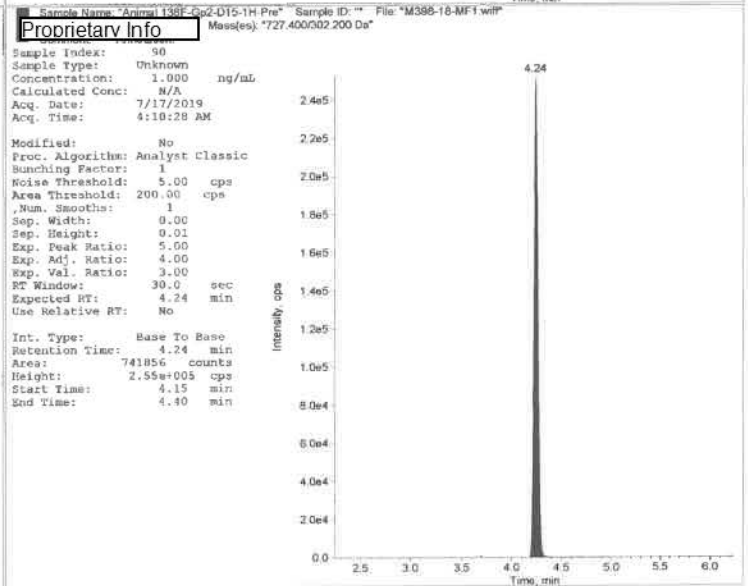
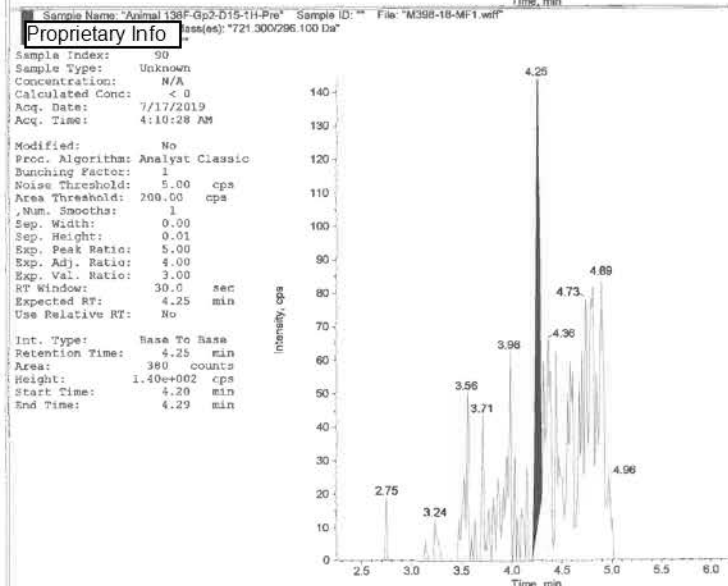
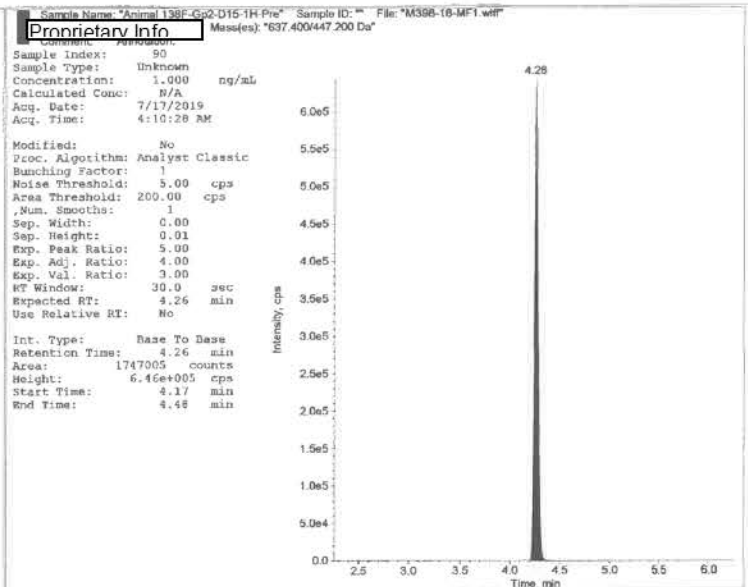
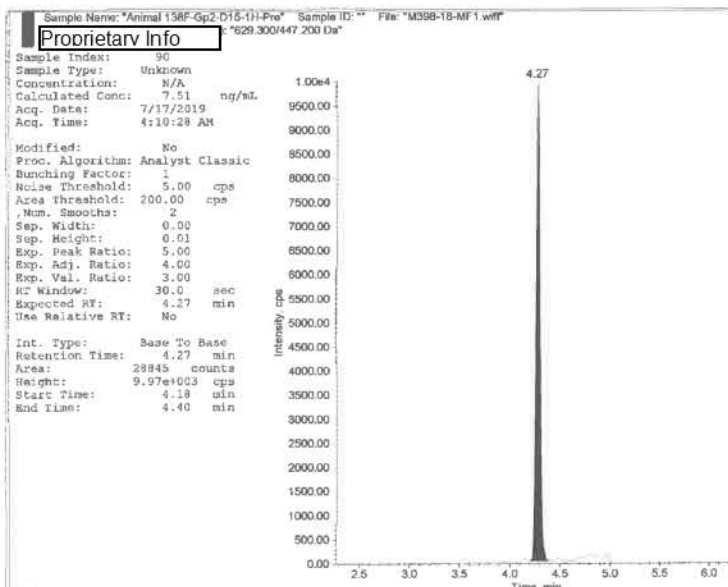


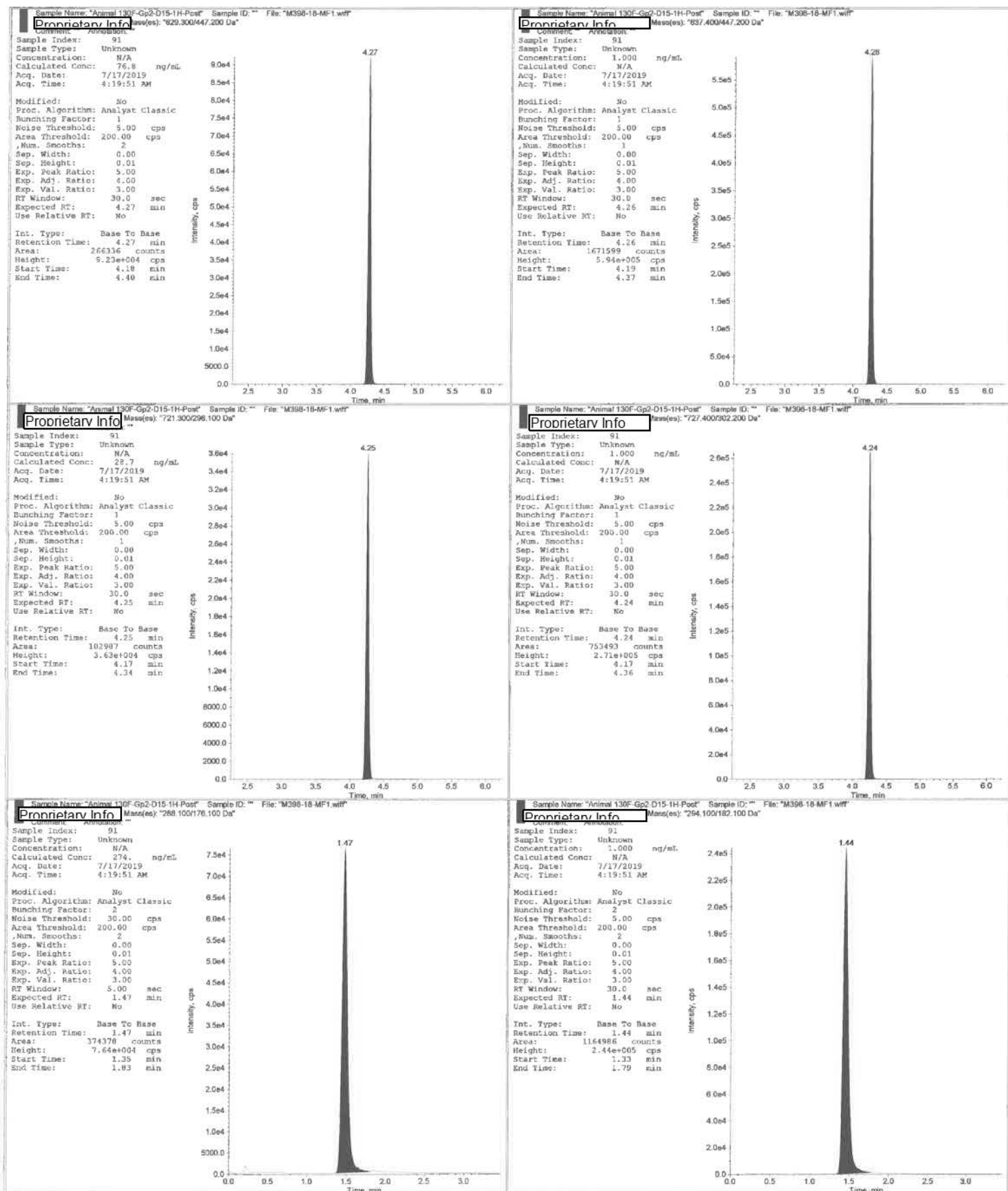


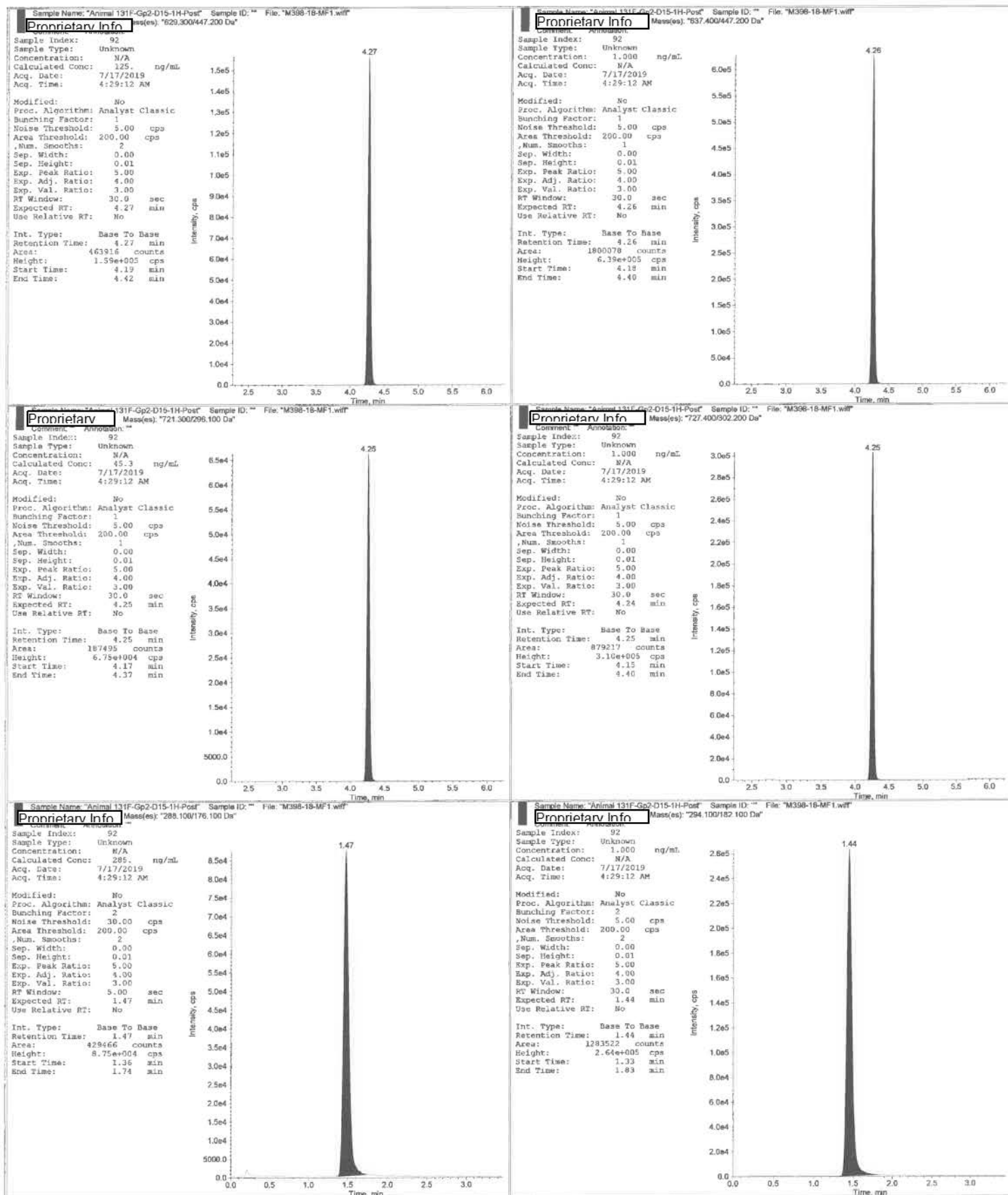


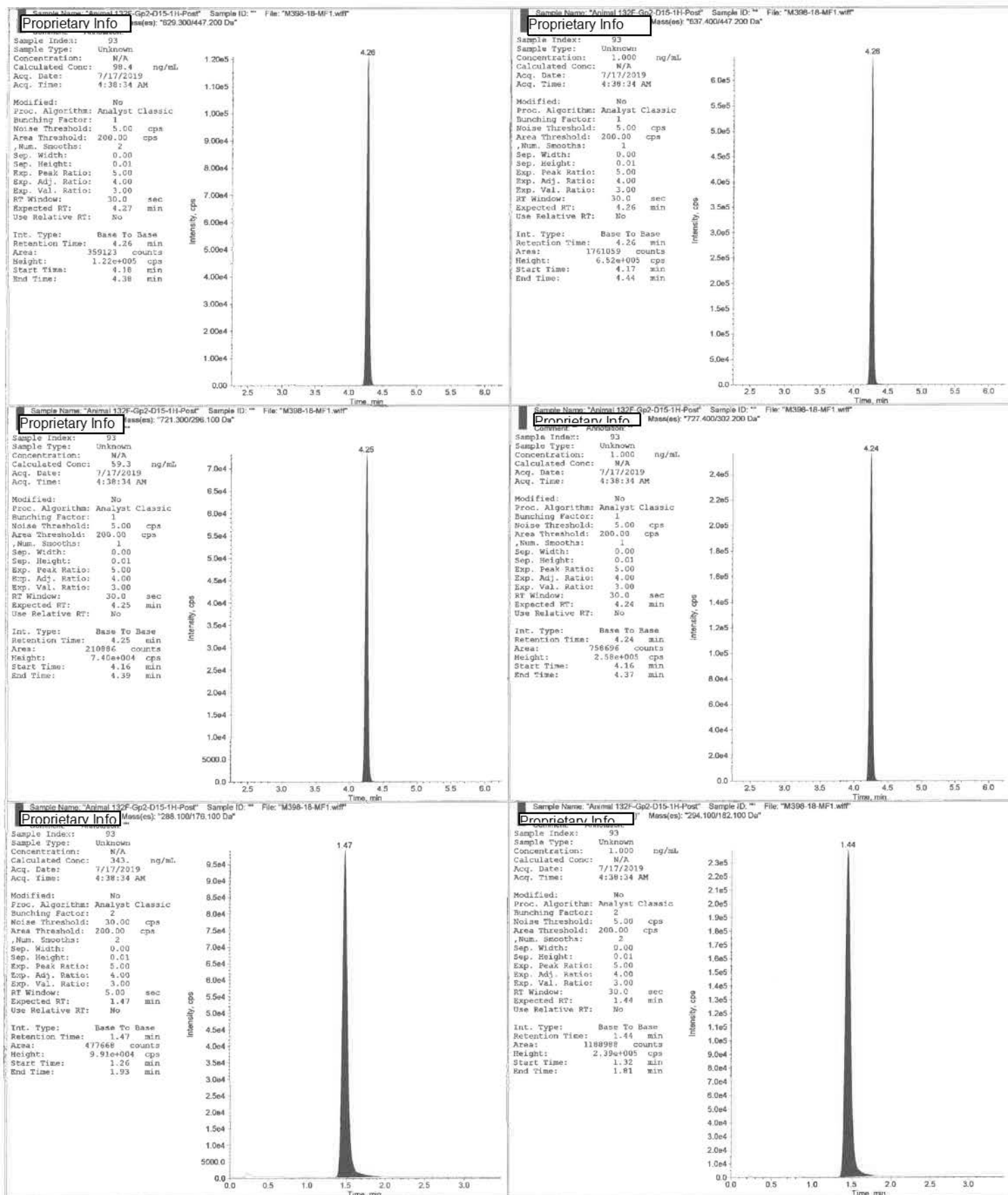


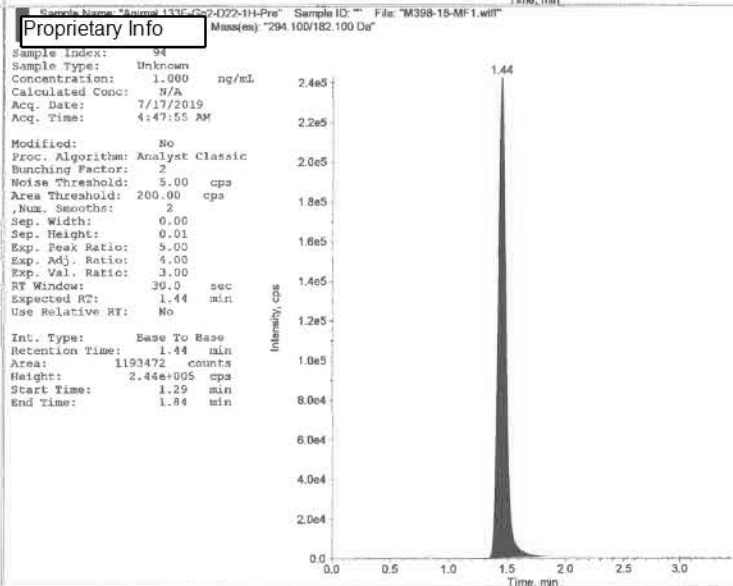
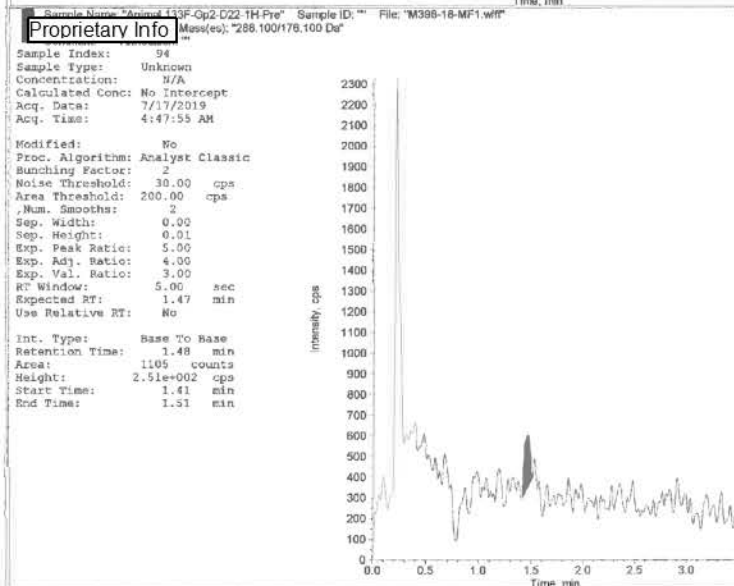
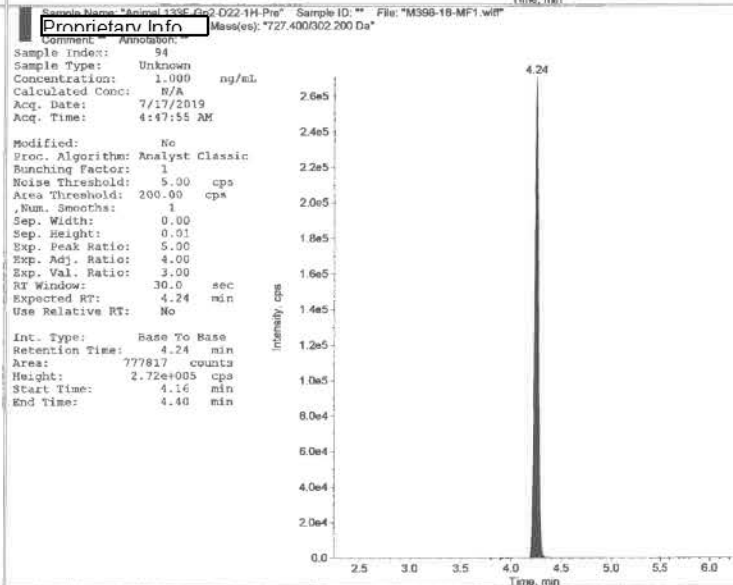
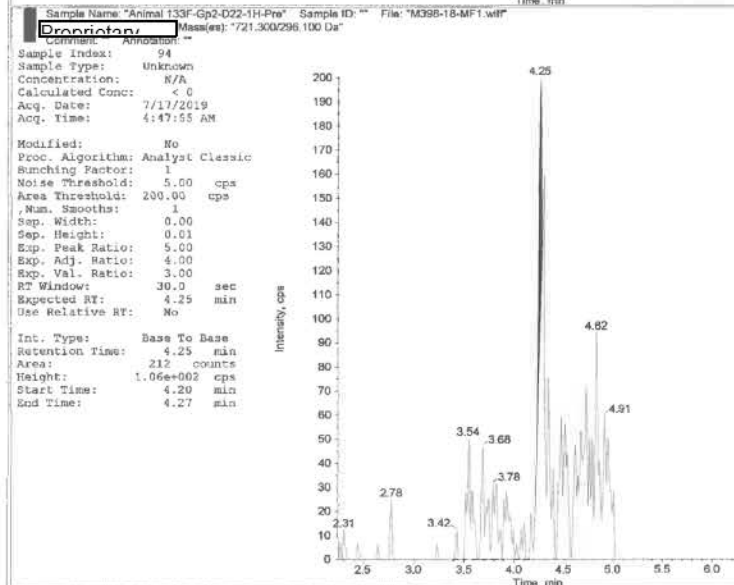
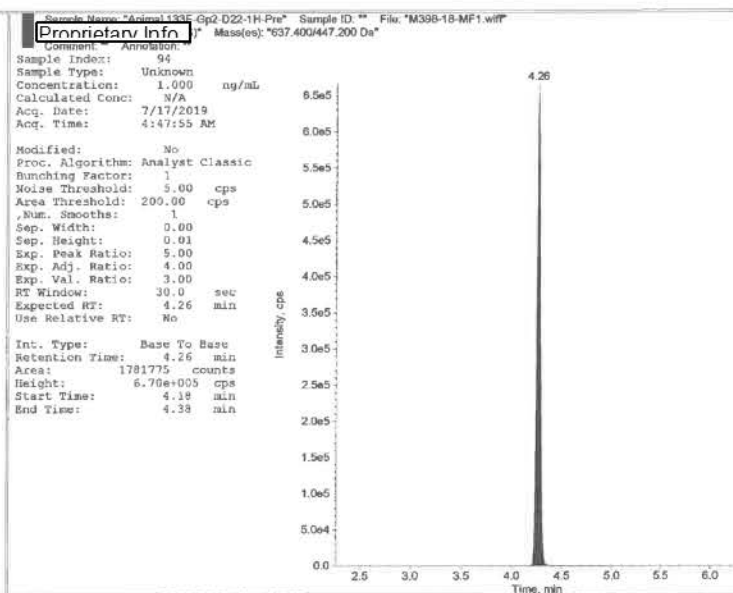
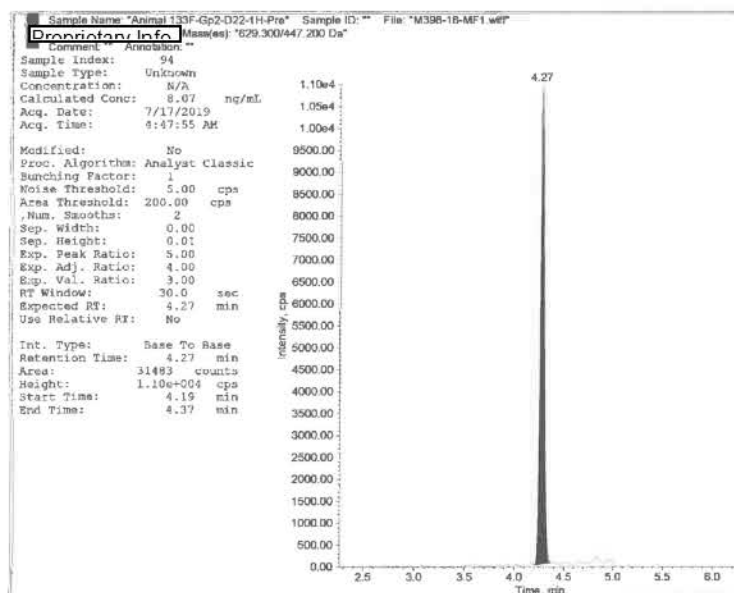


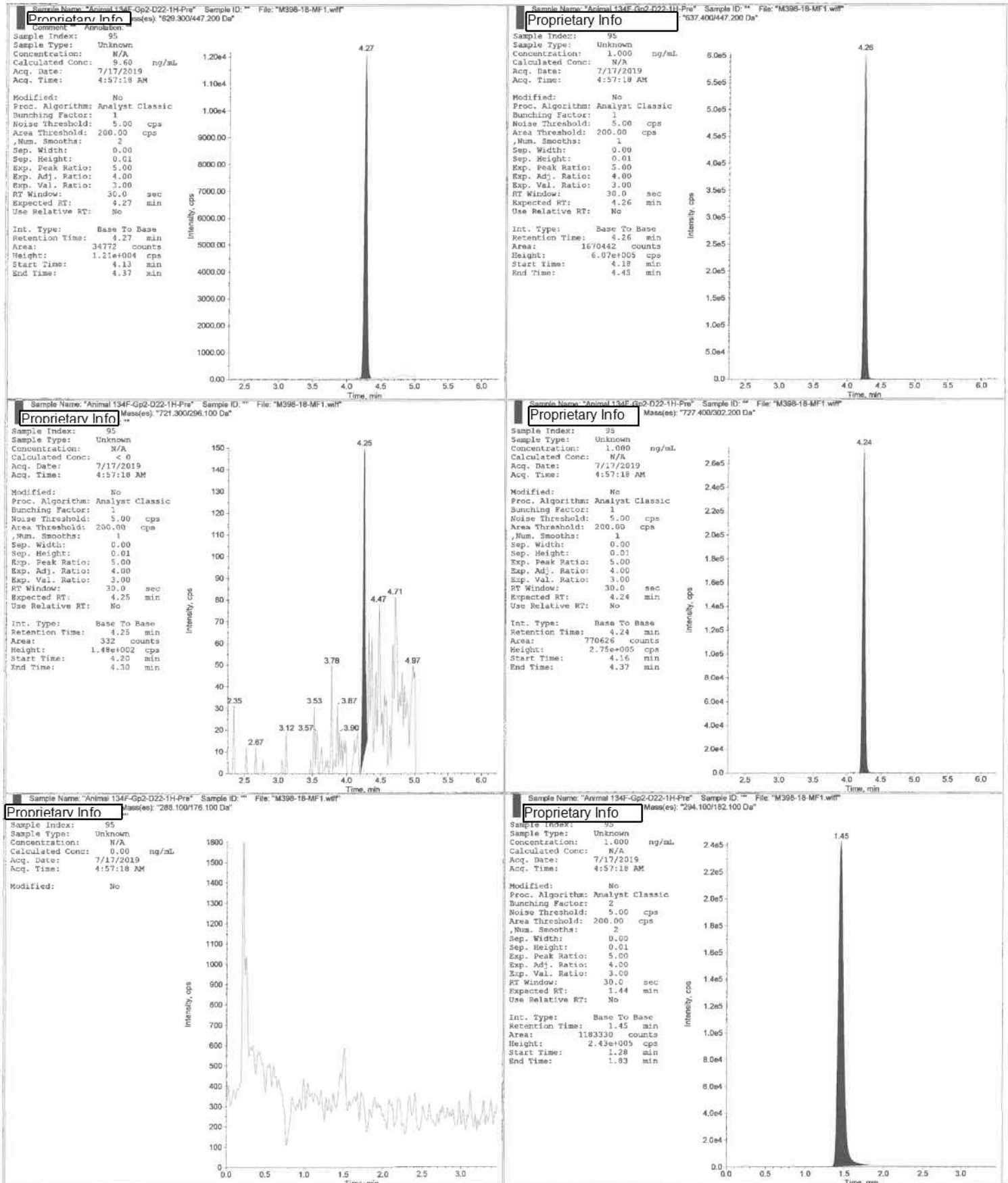


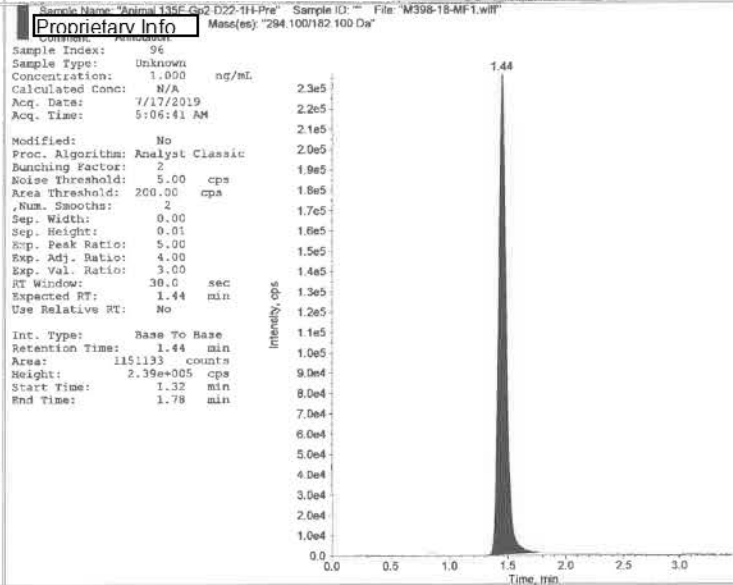
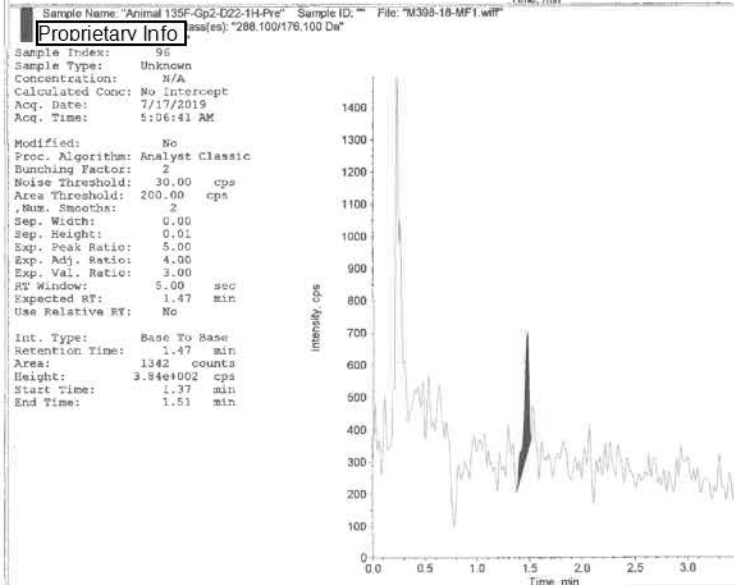
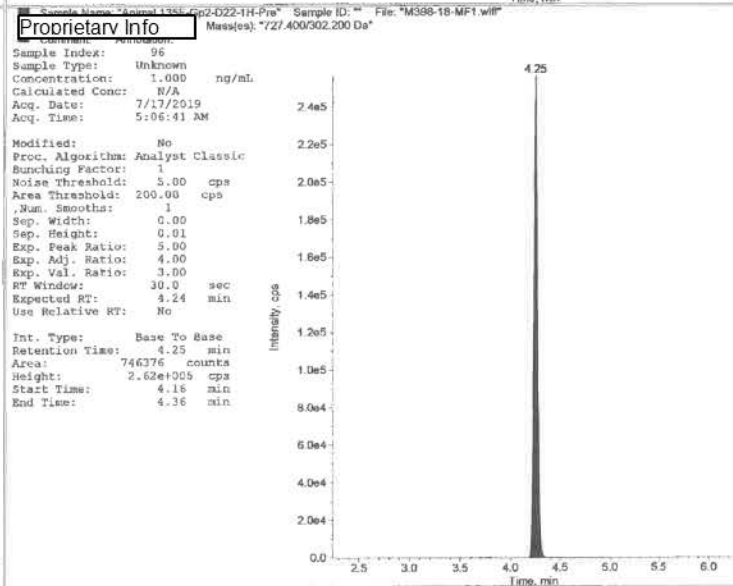
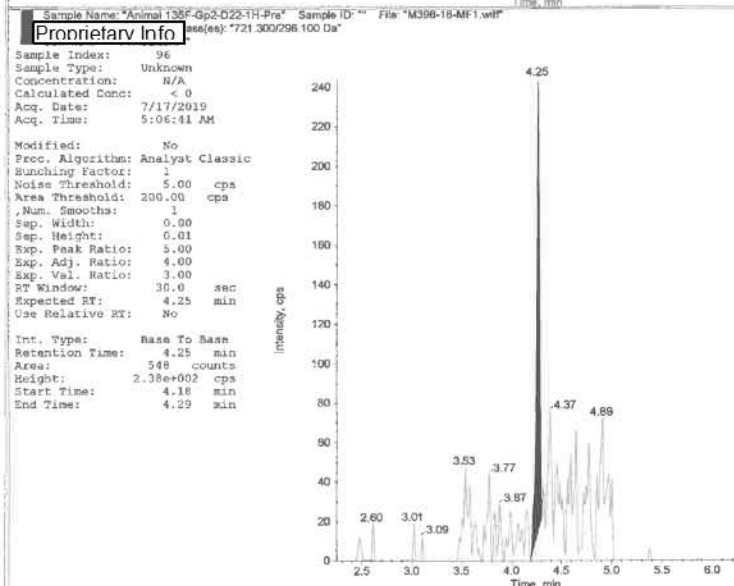
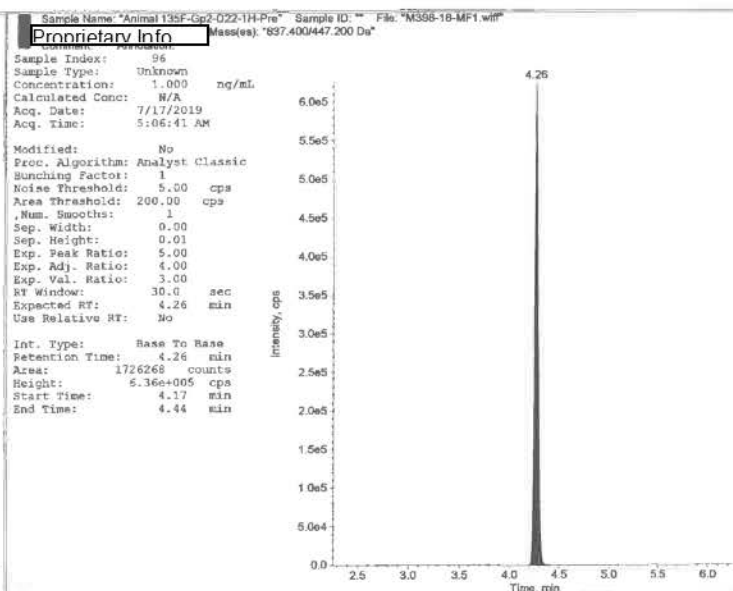
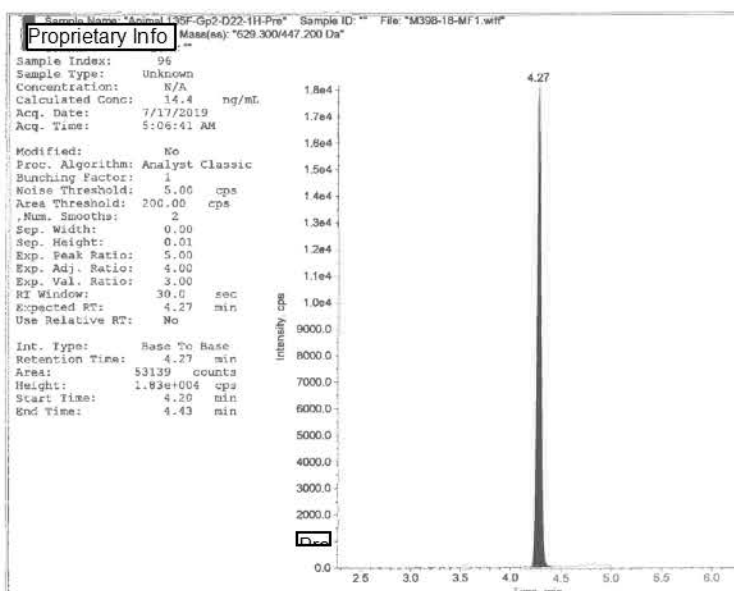


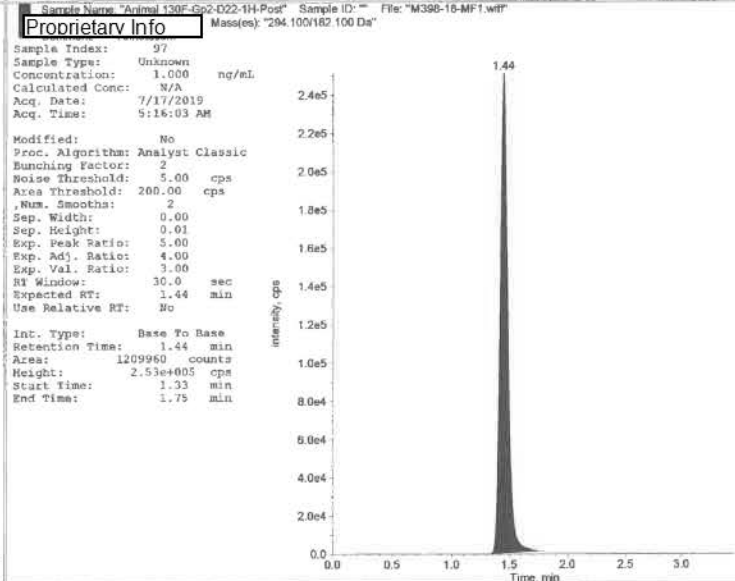
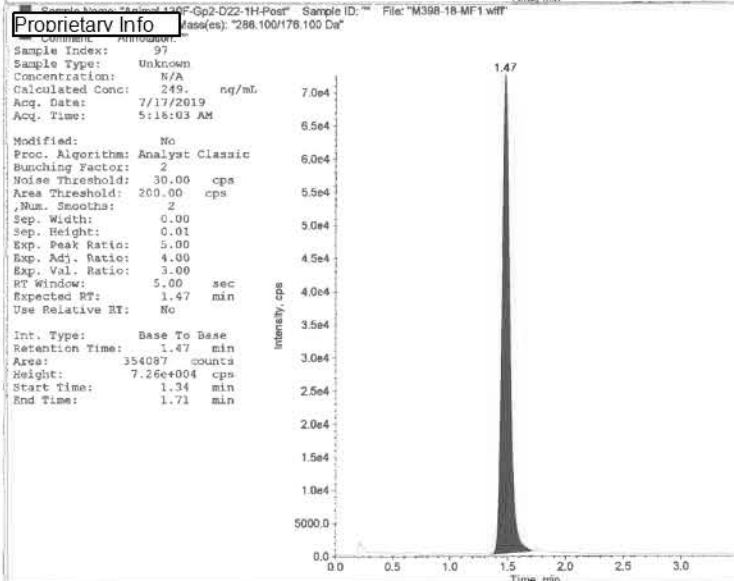
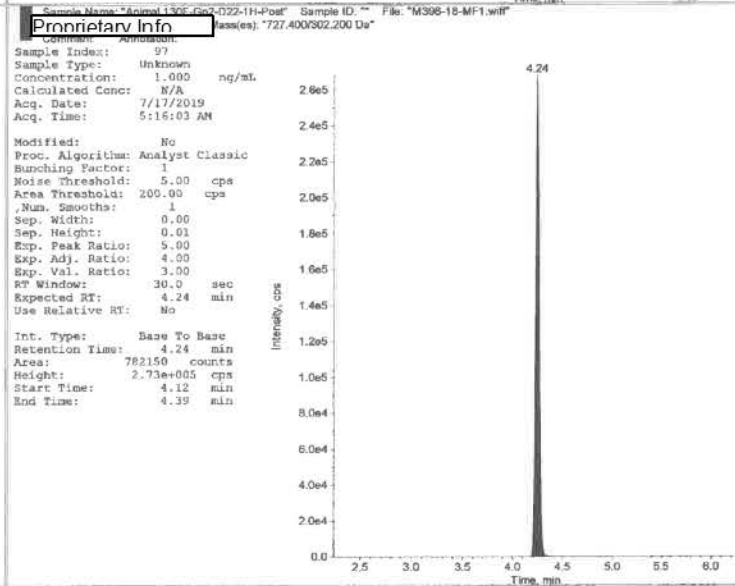
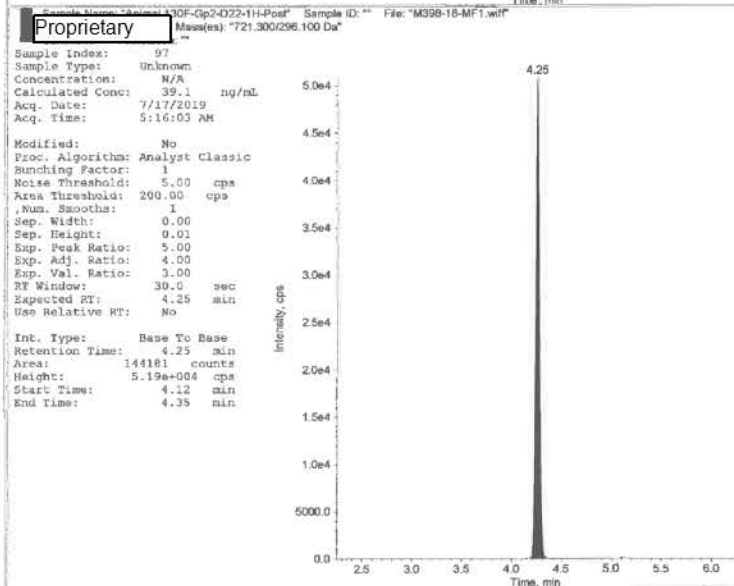
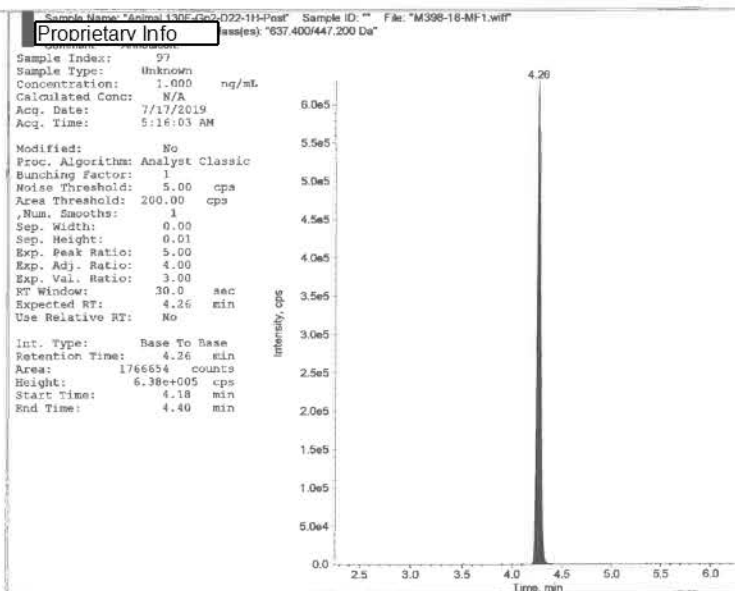
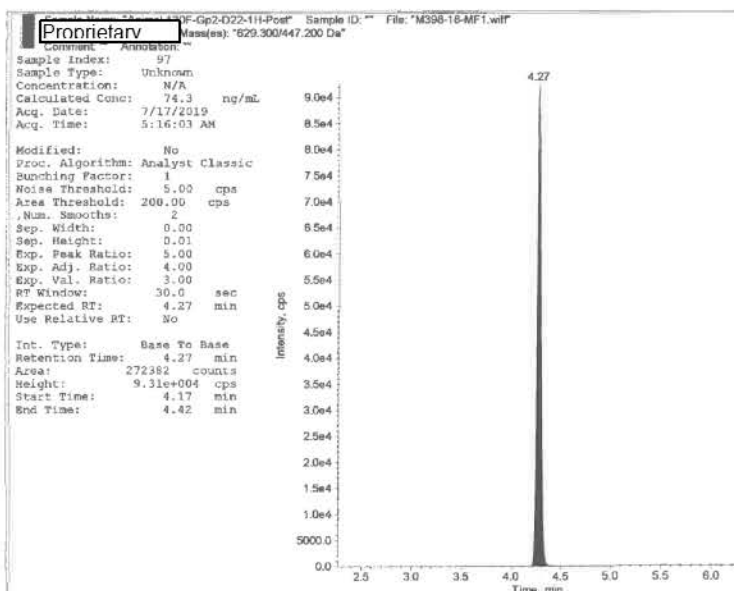






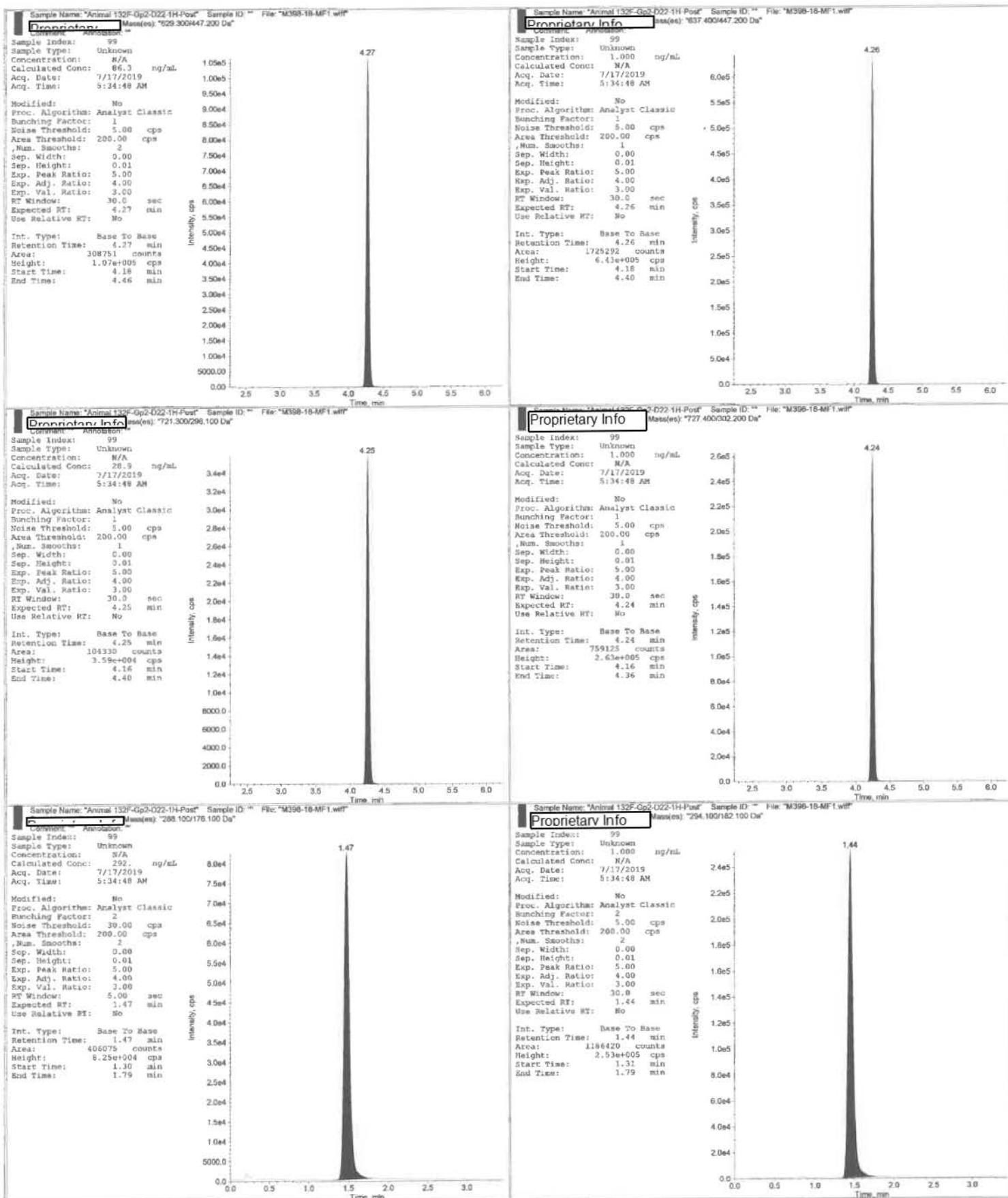


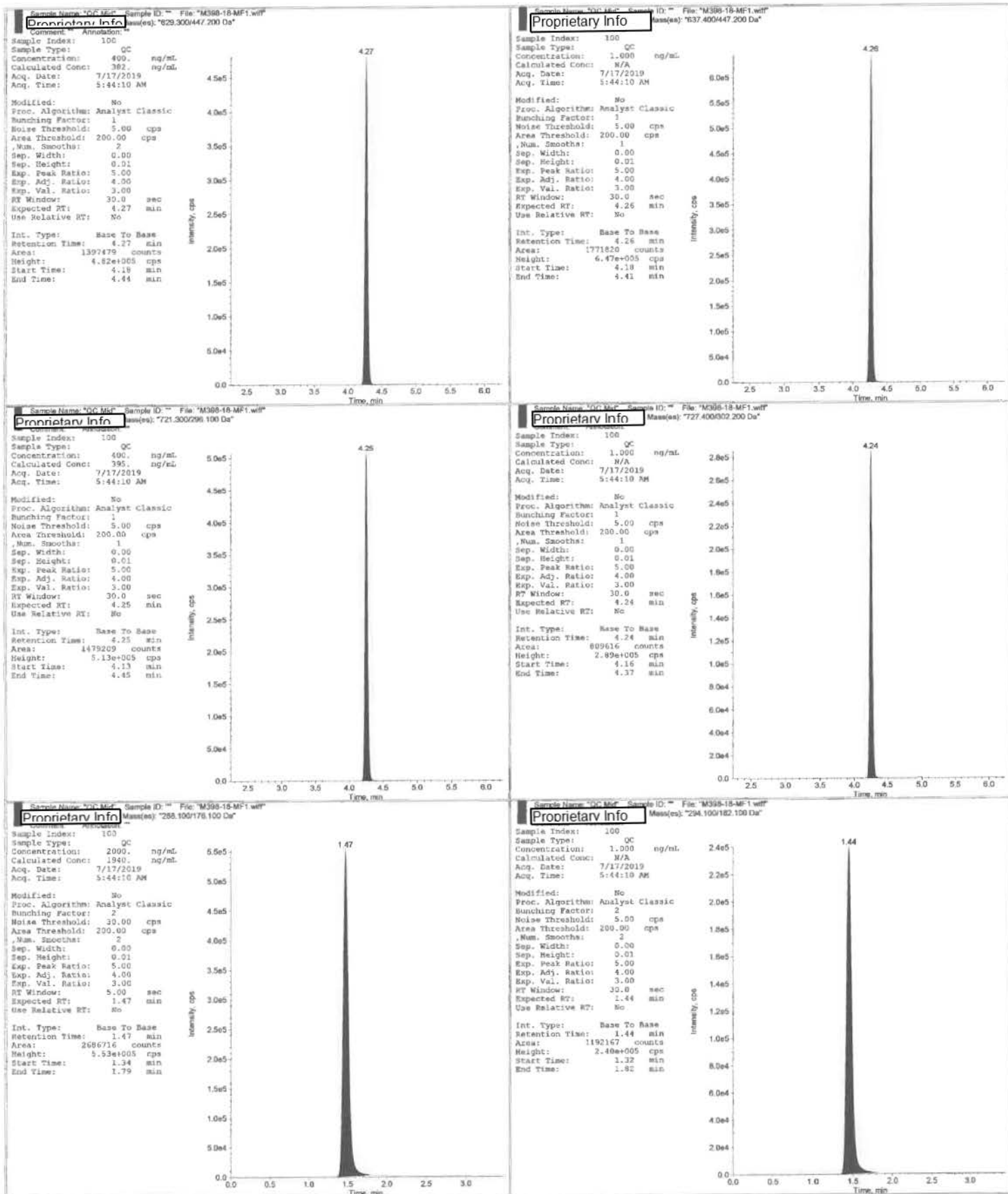




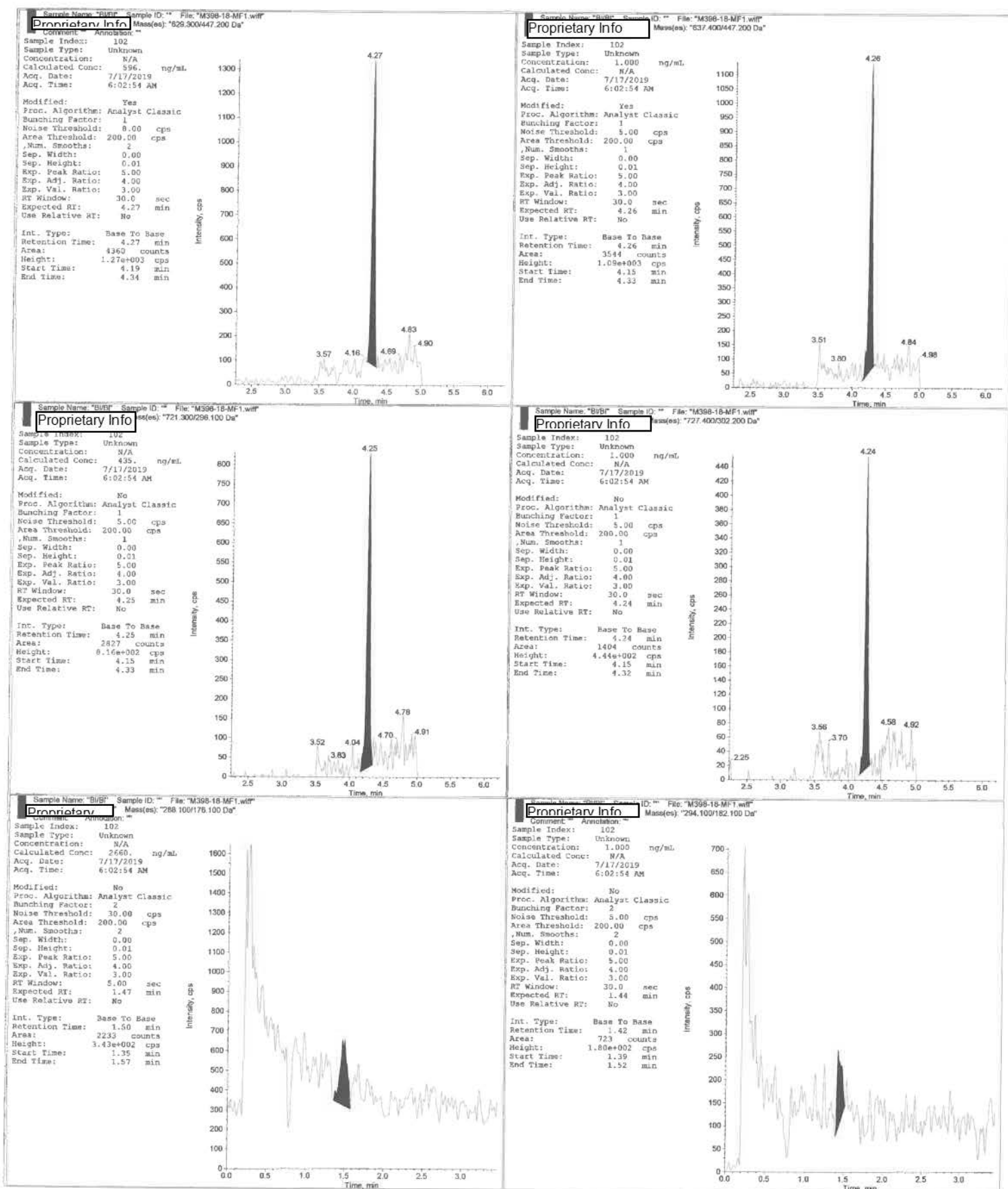
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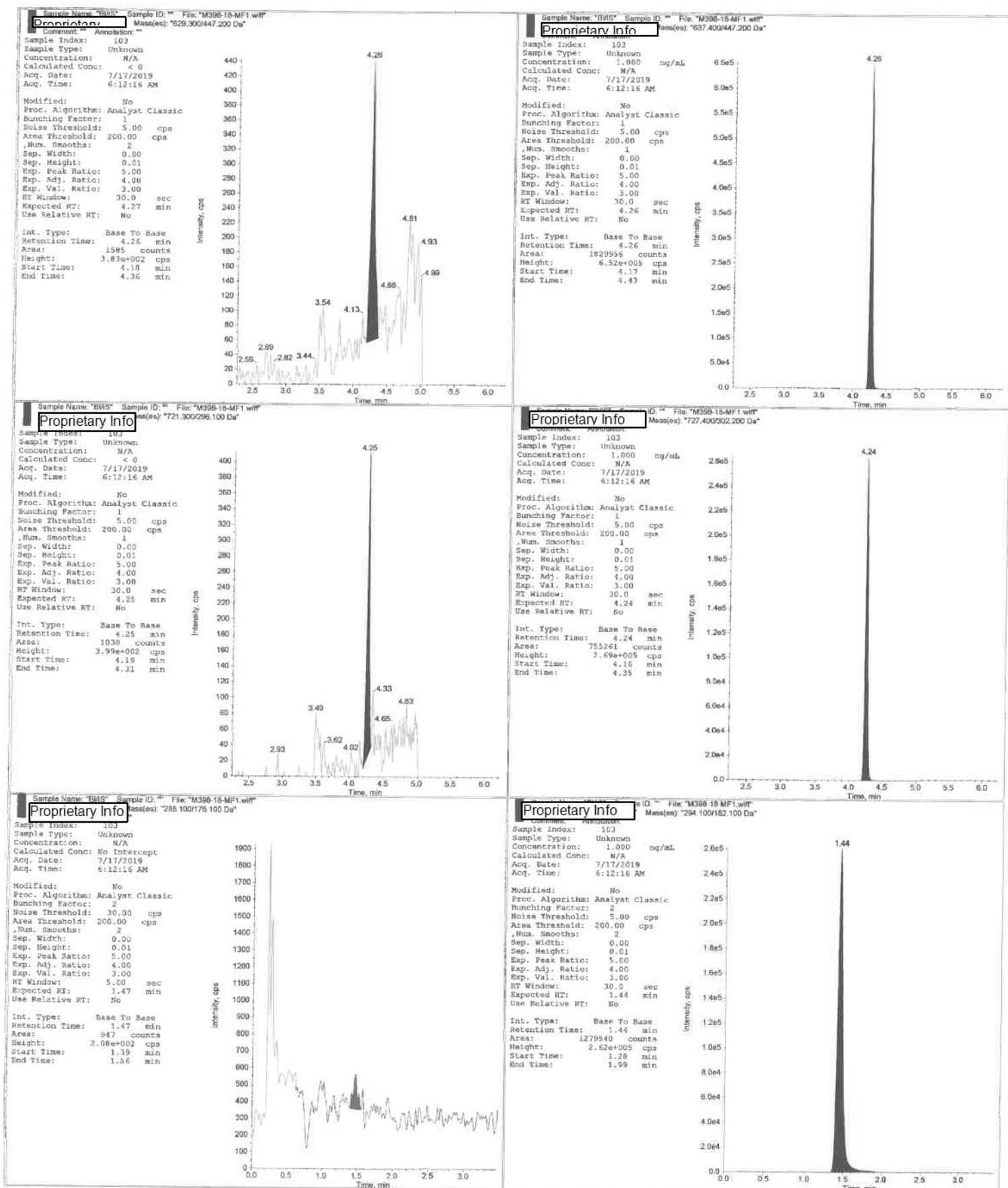








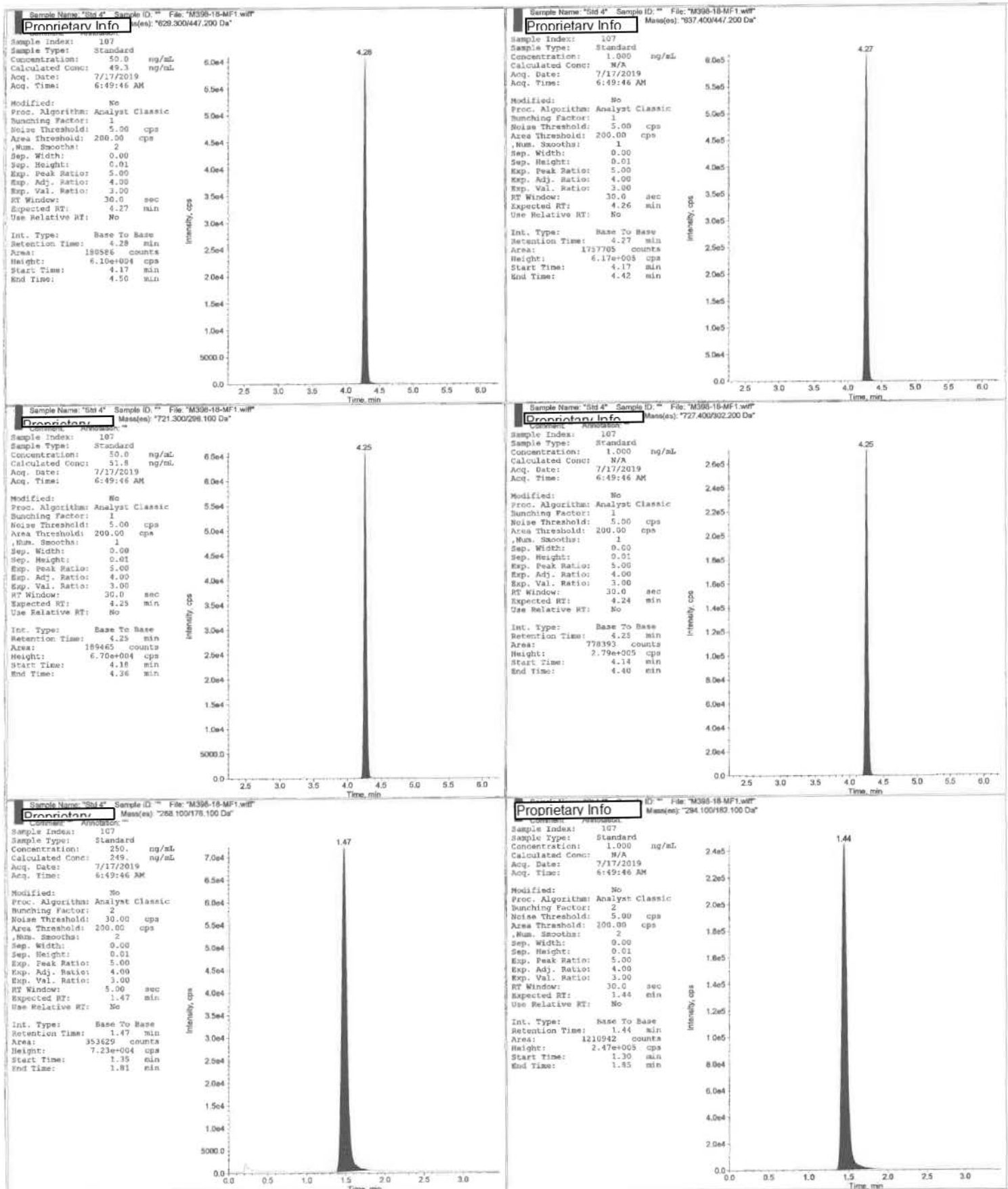




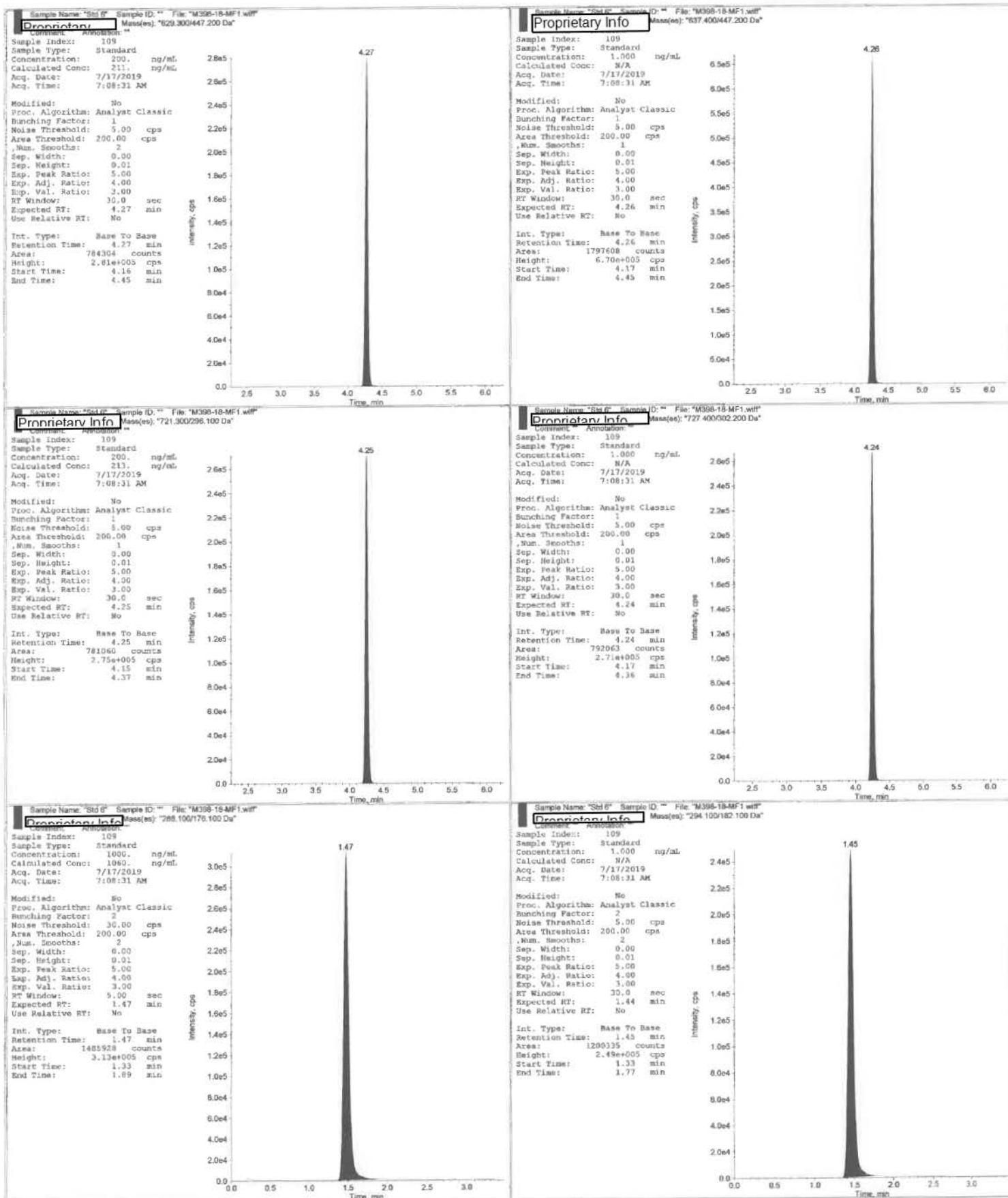


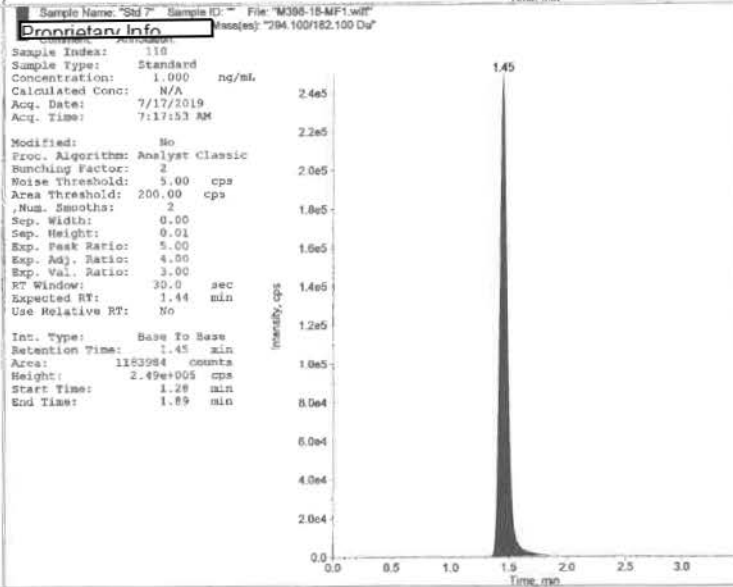
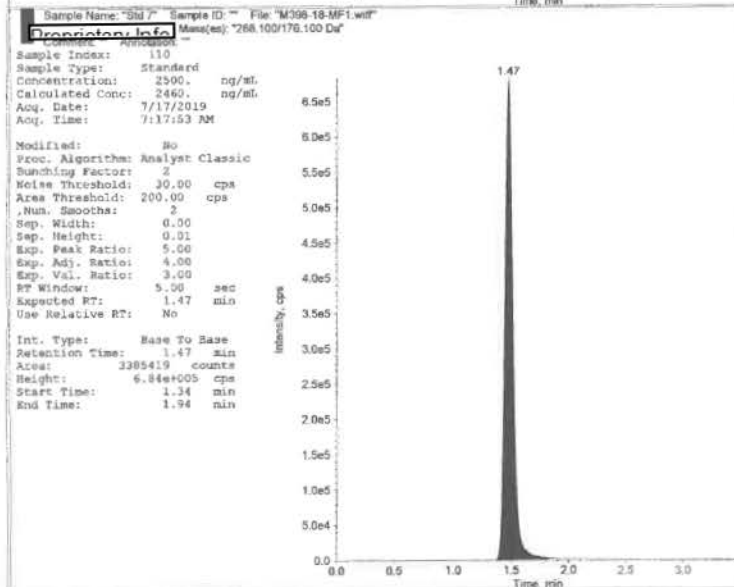
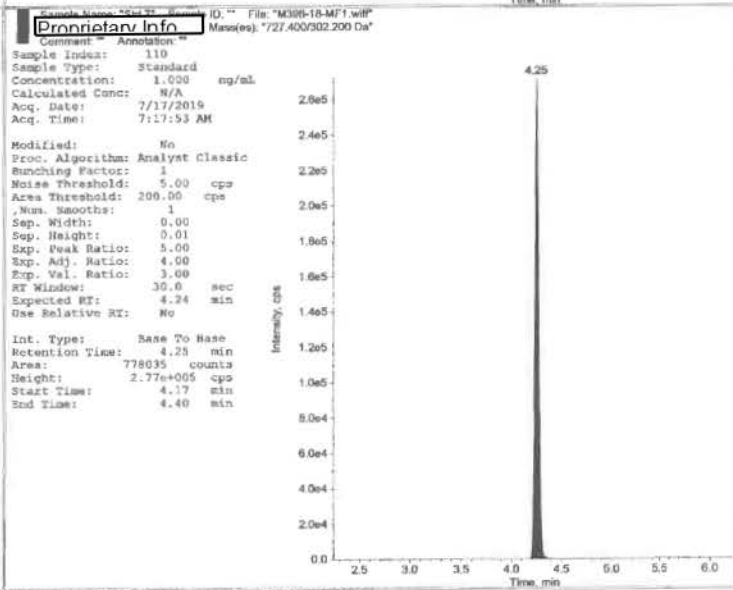
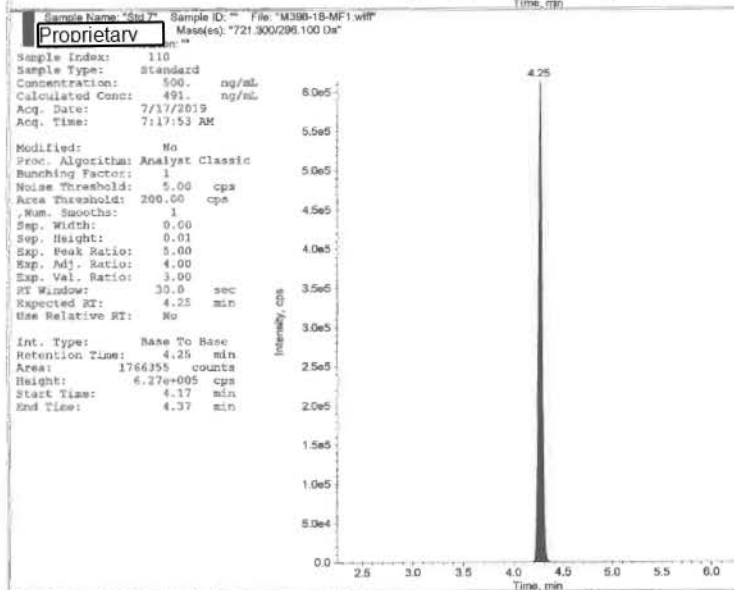
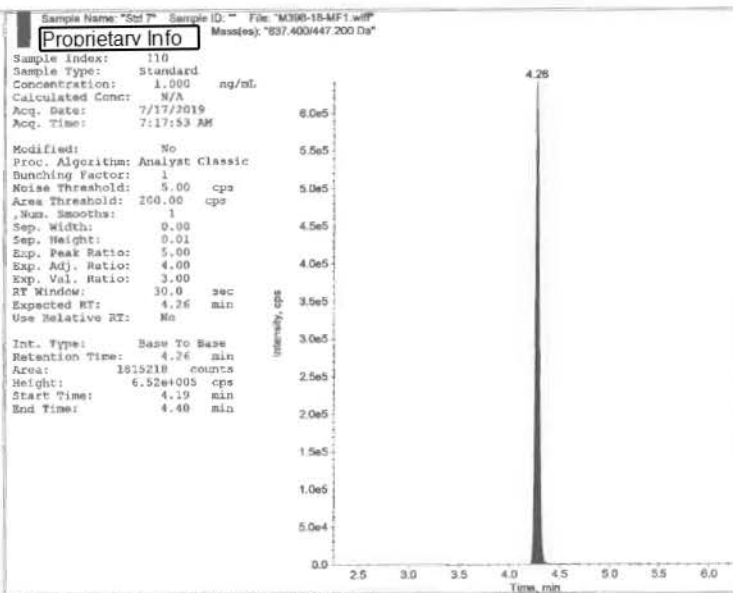
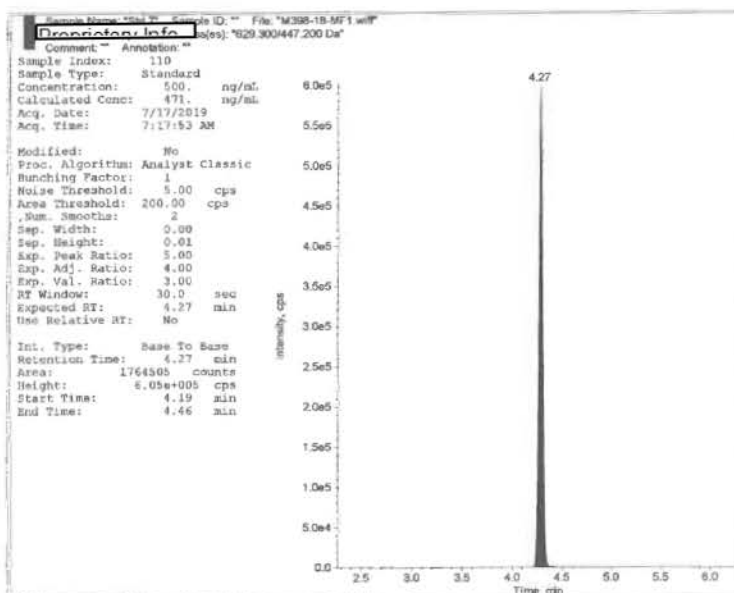


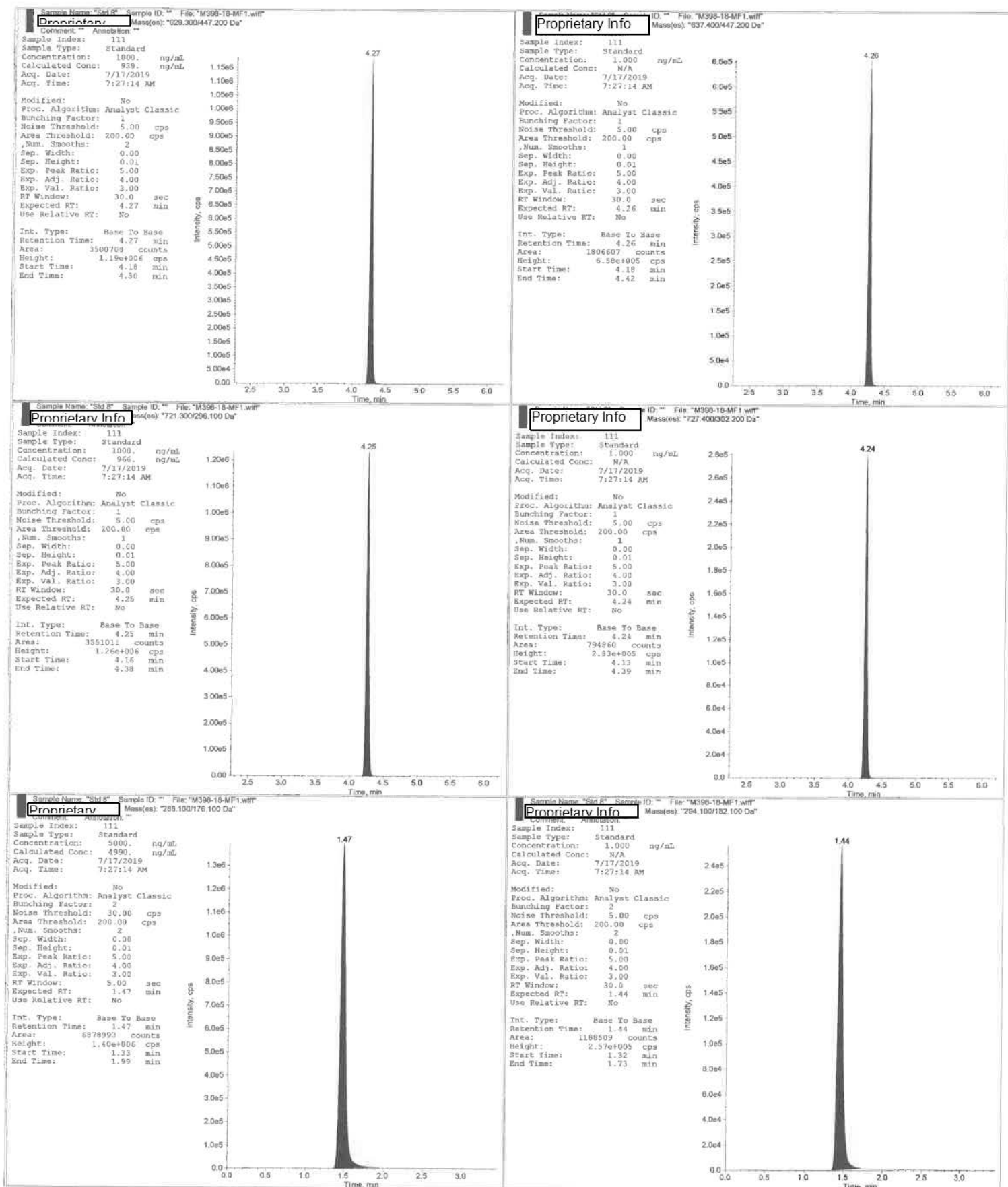


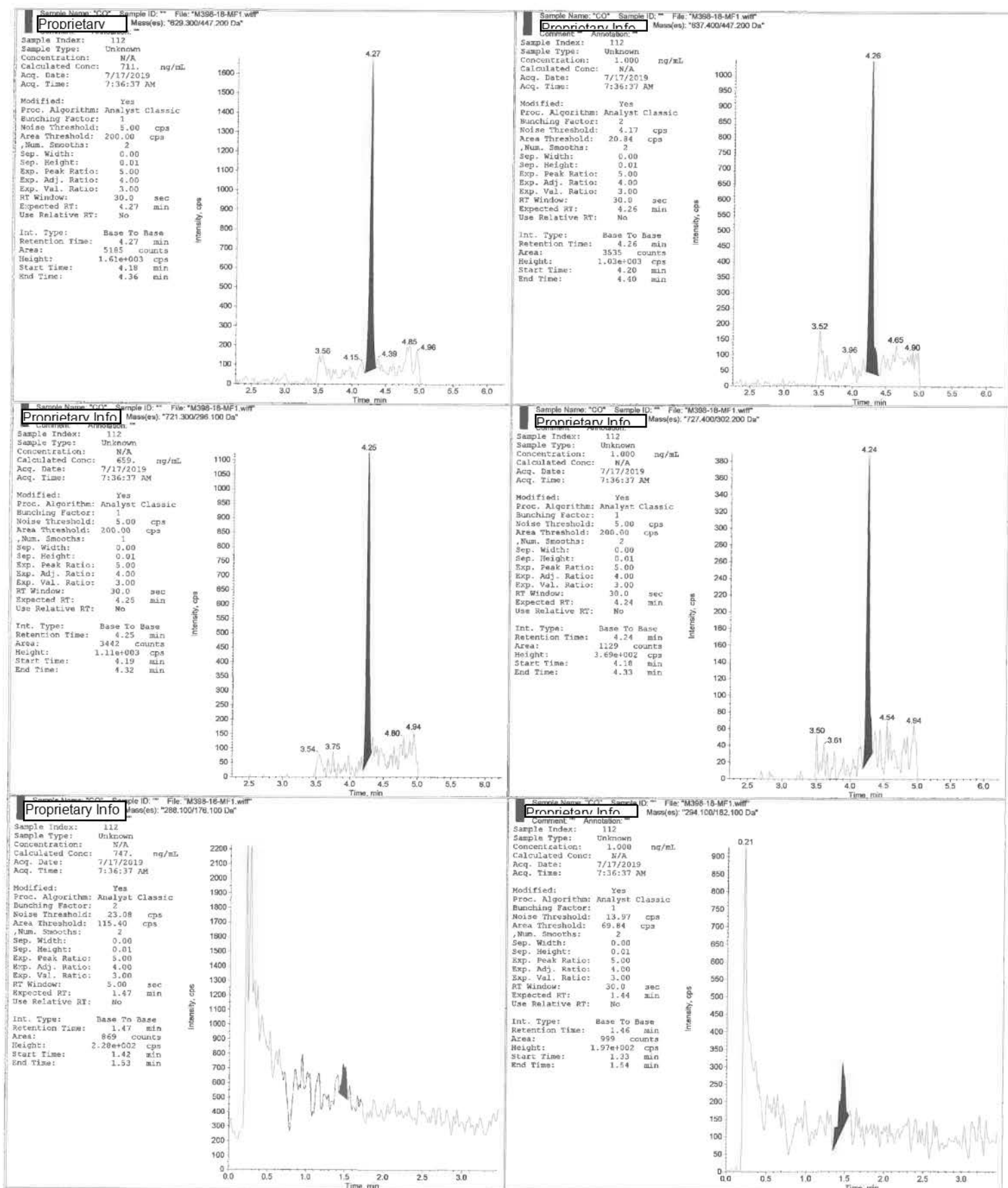


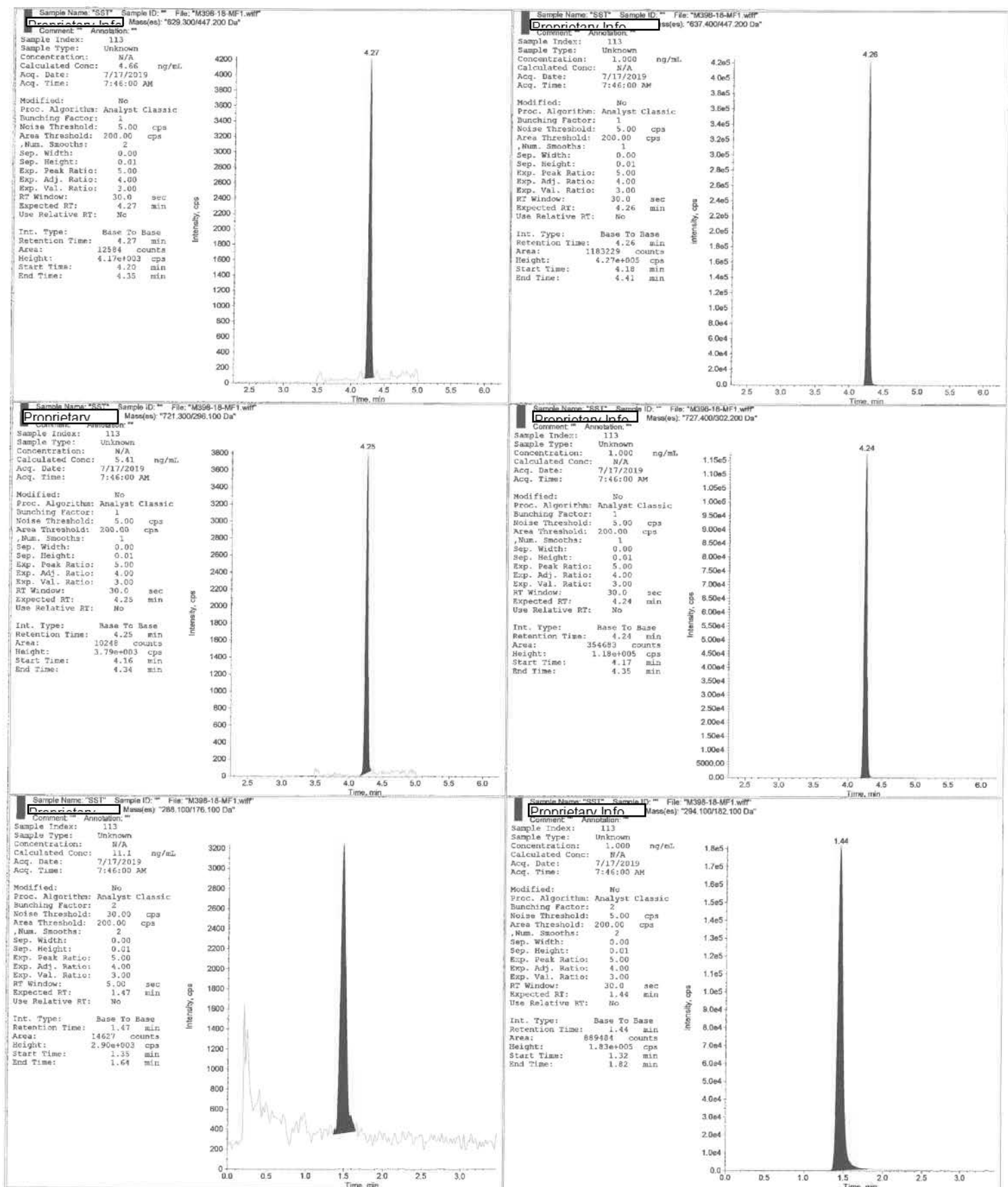












GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Appendix H
TOXICOKINETICS

Written by:

Redacted by agreement

11-11-19

Date

Approved by:

11-7-19

Date

SRI International
Biosciences Division

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

I. METHODS

Adult male and female Sprague Dawley rats (3/sex) were administered weekly subcutaneous (sc) doses of [Proprietary] [Prop] a formulation of lopinavir [Proprieta] [Proprietary] [Proprieta] and [Proprietary] [Proprieta] for 5 weeks. Individual test compound doses were as follows: [Propri] at 1.5 mg/kg (Group 2), 15 mg/kg (Group 3) and 30 mg/kg (Group 4); [Propri] at 0.8625 mg/kg (Group 2), 8.625 mg/kg (Group 3) and 17.25 mg/kg (Group 4); and [Propri] at 0.4125 mg/kg (Group 2), 4.125 mg/kg (Group 3) and 8.25 mg/kg (Group 4). Blood samples for toxicokinetic (TK) analysis were collected from the TK satellite animals at 1 hr predose and 1 hr postdose on dose administration days (Days 1, 8, 15, 22 and 29). Additional samples were collected at a single time point on Days 36, 43, 50, 57, 64 and 71.

TK data analysis was performed on the measurable plasma concentrations of each test compound from Appendix G (Bioanalytical Chemistry). The plasma concentration data of each test compound were analyzed using Phoenix[®] WinNonlin[®] (version 6.3) software to perform non-compartmental and sparse sampling analyses. Individual animal plasma concentrations at each actual time of blood collection were used in TK data analysis. The dose administered in each dose group was entered into the program as mg/kg and, as a result, no additional corrections for individual body weights of the animals were necessary. Plasma concentration data were not available after Day 15 for Animal #163, as it was sacrificed in moribund condition on Day 17.

Plasma concentrations that were less than the lower limit of quantitation (LLOQ of 5.00 ng/ml for [Propri] and [Propri] and 25.00 ng/ml for [Proprie] of the bioanalytical assay were not included in TK data analysis. Mean plasma concentrations that were less than the LLOQ of each compound were assigned a value of 2.00 ng/ml only to illustrate apparent troughs in the concentration vs. time profiles. The following TK parameters were determined for each test compound in [Proprietary] [Pro] using the administration of the first dose on Day 1 as time zero: overall apparent maximal plasma concentration (C_{max}) and area under the plasma concentration time curve up to the last blood collection time (AUC_{last}).

II. RESULTS

A. Plasma Drug Levels

The time-course of plasma concentrations of [Propri] [Propri] and [Propri] is shown in Figures 1 to 3, respectively. Measurable concentrations of [Propri] were obtained even after 5 weeks of dose administration up to Day 43 in the low dose group (Group 2) and up to Day 71 in the mid and high-dose groups (Groups 3 and 4) (Figure 1). [Propri] levels were less than the LLOQ at all times after 5 weeks of dose administration in both sexes in the low dose group (Group 2) and in males in the mid dose group (Group 3), with measurable concentrations obtained on Day 36 in females in the mid dose group (Group 3) and in both sexes in the high dose group (Group 4) (Figure 2). [Propri] levels were less than the LLOQ at all times after the 5-week dose administration schedule at all blood collection times, except in one male Day 36 (Figure 3).

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
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B. Toxicokinetic Parameters

The toxicokinetic parameters [Propri] [Propri] and [Propri] are presented in Table H-1. The overall group C_{max} based on administration of the first dose was 127, 449 and 565 ng/ml (males) and 177, 956 and 1,185 ng/ml (females) for [Propri] 278, 3,147 and 6,163 ng/ml (males) and 302, 3,517 and 6,157 ng/ml (females) for [Propri] and 67.1, 292 and 284 ng/ml (males) and 60.2, 694 and 855 ng/ml (females) for [Propri] in Groups 2, 3 and 4, respectively. Corresponding mean AUC_{last} was 2,123, 9,848, and 16,021 day*ng/ml (males) and 2,564, 14,450 and 19,619 day*ng/ml (females) for [Propri] 6,733, 74,233, 135,384 day*ng/ml (males) and 7,659, 83,216 and 145,541 day*ng/ml (females) for [Propri] and 1,290, 5,365 and 5,160 day*ng/ml (males) and 1,109, 8,871 and 6,883 day*ng/ml (females) for [Propri] in Groups 2, 3, and 4, respectively (Table H-1).

The rank order of AUC_{last} between the three compounds was [Propri] >> [Propri] > [Propri] at the dose ranges administered. Plasma exposure of [Propri] and [Propri] increased disproportionately with dose increments from Group 2 to Groups 3 and 4, while that of [Propri] was more dose proportionate. The group AUC_{last} of [Propri] in Group 4 was ~8-fold greater than the AUC_{last} in Group 2, for a 20-fold increment in dose from 1.5 to 30 mg/kg. The group AUC_{last} of [Propri] in Group 4 was ~4- to 6-fold greater than the AUC_{last} in Group 2, for a 20-fold increment in dose from 0.4125 to 8.25 mg/kg (Table H-1).

No major sex differences were noted in the plasma exposure of all three test compounds, except for 50% and 70% greater AUC_{last} in females when compared with males, in Group 3 for [Propri] and [Propri] respectively (Table H-1).

III. CONCLUSION

Toxicokinetic data analysis was performed on the measurable plasma concentrations of [Propri] [Propri] and [Propri] from weekly sc administration of [Proprietary] [Pro] for 5 weeks. Plasma exposure parameters (overall C_{max} and AUC_{last}) indicated a much greater exposure for [Propri] when compared with [Propri] and [Propri] in the dose ranges studied. There was a disproportionate increase in plasma exposure of [Propri] and [Propri] with dose increments from Group 2 to Group 4. No major sex differences were noted in the plasma exposure, except for a 50% and 70% greater AUC_{last} in females for [Propri] and [Propri] in Group 3, respectively.

GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Table H-1

Toxicokinetic Parameters of [Proprietary Info] [Proprietary] and [Proprietary] after Weekly SC Administration of [Proprietary Info] [Pro] for 5 weeks in Male and Female Sprague Dawley Rats

Compound	Group	Sex	Dose (mg/kg)	C _{max} ± SE (ng/ml)	AUC _{last} ± SE (day*ng/ml)
[Proprietary Info]					

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix I

INDIVIDUAL ANIMAL CLINICAL PATHOLOGY

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix I-1

INDIVIDUAL HEMATOLOGY

Page 2808 of 3822 to Page 2962 of 3822

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Key Page**General Footnotes**

Provantis version 10.1.0.1

"." indicates Not Applicable

Statistical significance indicated on a group with an N < 3 is not valid

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
White Blood Cells	White Blood Cells
Red Blood Cells	Red Blood Cells
Hemoglobin	Hemoglobin
Hematocrit	Hematocrit
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
RDW	Red Blood Cell Distribution Width
Platelet Count	Platelet Count
MeanPlatelet Volume	Mean Platelet Volume
Percent Neutrophils	Percent Neutrophils
Percent Lymphocytes	Percent Lymphocytes
Percent Monocytes	Percent Monocytes
Percent Eosinophils	Percent Eosinophils
Percent Basophils	Percent Basophils
Percent Band	Percent BAND
Percent Atyp Lymphocytes	Percent Atypical Lymphocytes
Neutrophils (Absolute)	Absolute Neutrophils
Lymphocytes (Absolute)	Absolute Lymphocytes
Monocytes (Absolute)	Absolute Monocytes
Eosinophils (Absolute)	Absolute Eosinophils
Basophils (Absolute)	Absolute Basophils
Band (Absolute)	Absolute BAND
Atyp Lymph (Absolute)	Atypical Lymphocytes (Absolute)

Key Page**Measurement Descriptions (Continued)**

<u>Headings Used</u>	<u>Description</u>
Percent Reticulocyte	Percent Reticulocytes
Reticulocyte (Absolute)	Absolute Reticulocytes

Unit Descriptions

<u>Headings Used</u>	<u>Description</u>
%	%
10^9/L	10^9/L
fL	fL
g/dL	g/dL
pg	pg
x10^3/uL	x10^3/uL
x10^6/uL	x10^6/uL

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>
White Blood Cells	Mean Standard Deviation Count (N)
Red Blood Cells	Mean Standard Deviation Count (N)
Hemoglobin	Mean Standard Deviation Count (N)

Key Page**Measurement/Statistics (Continued)**

<u>Measurement</u>	<u>Descriptive</u>
Hematocrit	Mean Standard Deviation Count (N)
MCV	Mean Standard Deviation Count (N)
MCH	Mean Standard Deviation Count (N)
MCHC	Mean Standard Deviation Count (N)
RDW	Mean Standard Deviation Count (N)
Platelet Count	Mean Standard Deviation Count (N)
MeanPlatelet Volume	Mean Standard Deviation Count (N)
Percent Neutrophils	Mean Standard Deviation Count (N)
Percent Lymphocytes	Mean Standard Deviation Count (N)

Key Page**Measurement/Statistics (Continued)**

<u>Measurement</u>	<u>Descriptive</u>
Percent Monocytes	Mean Standard Deviation Count (N)
Percent Eosinophils	Mean Standard Deviation Count (N)
Percent Basophils	Mean Standard Deviation Count (N)
Percent Band	Mean Count (N)
Percent Atyp Lymphocytes	Mean Count (N)
Neutrophils (Absolute)	Mean Standard Deviation Count (N)
Lymphocytes (Absolute)	Mean Standard Deviation Count (N)
Monocytes (Absolute)	Mean Standard Deviation Count (N)
Eosinophils (Absolute)	Mean Standard Deviation Count (N)
Basophils (Absolute)	Mean Standard Deviation Count (N)

Key Page**Measurement/Statistics (Continued)**

<u>Measurement</u>	<u>Descriptive</u>
Band (Absolute)	Mean Count (N)
Atyp Lymph (Absolute)	Mean Count (N)
Percent Reticulocyte	Mean Standard Deviation Count (N)
Reticulocyte (Absolute)	Mean Standard Deviation Count (N)

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Comment Abbreviations

RC = Result Comment

Individual Hematology

Proprietary Info

Proprietary Info

End of Print

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix I-2

INDIVIDUAL CLINICAL CHEMISTRY

Page 2970 of 3822 to Page 3116 of 3822

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Key Page**General Footnotes**

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"." indicates Not Applicable

Statistical significance indicated on a group with an N < 3 is not valid

Replacement Values

<u>Value</u>	<u>Description</u>
<0.15	<0.15
<0.17	<0.17

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
Blood Urea Nitrogen	Blood Urea Nitrogen
Creatinine	Creatinine
Glucose	Glucose
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
Alkaline Phosphatase	Alkaline Phosphatase
Total Bilirubin	Total Bilirubin
Sodium	Sodium
Potassium	Potassium
Chloride	Chloride
Calcium	Calcium
Phosphorus	Phosphorus
Total Protein	Total Protein
Albumin	Albumin
Globulin	Globulin
Alb/Glo Ratio	Albumin/Globulin Ratio
Cholesterol	Cholesterol
Triglyceride	Triglyceride

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with Propriet Pr in Sprague Dawley Rats

Key Page**Unit Descriptions**

<u>Headings Used</u>	<u>Description</u>
g/dL	g/dL
mg/dL	mg/dL
mmol/L	mmol/L
U/L	U/L

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>
Blood Urea Nitrogen	Mean Standard Deviation Count (N)
Creatinine	Mean Standard Deviation Count (N)
Glucose	Mean Standard Deviation Count (N)
AST	Mean Standard Deviation Count (N)
ALT	Mean Standard Deviation Count (N)
Alkaline Phosphatase	Mean Standard Deviation Count (N)
Total Bilirubin	Count (N)

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with Propriet Pr in Sprague Dawley Rats

Key Page**Measurement/Statistics (Continued)**

<u>Measurement</u>	<u>Descriptive</u>
Sodium	Mean Standard Deviation Count (N)
Potassium	Mean Standard Deviation Count (N)
Chloride	Mean Standard Deviation Count (N)
Calcium	Mean Standard Deviation Count (N)
Phosphorus	Mean Standard Deviation Count (N)
Total Protein	Mean Standard Deviation Count (N)
Albumin	Mean Standard Deviation Count (N)
Globulin	Mean Standard Deviation Count (N)
Alb/Glo Ratio	Mean Standard Deviation Count (N)

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with Propriet Pr in Sprague Dawley Rats

Key Page**Measurement/Statistics (Continued)**

<u>Measurement</u>	<u>Descriptive</u>
Cholesterol	Mean Standard Deviation Count (N)
Triglyceride	Mean Standard Deviation Count (N)

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Proprie	Dose	Group 4	30 mg/kg	SC

Comment Abbreviations

RC = Result Comment, SC = Sample Comment

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with Propriet Pr in Sprague Dawley Rats

End of Print

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix J

INDIVIDUAL ANIMAL URINALYSIS

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix J-1

INDIVIDUAL URINALYSIS

Page 3124 of 3822 to Page 3220 of 3822

Withheld pursuant to exemption

Proprietary Info

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Key Page**General Footnotes**

Provantis version 10.1.0.1

"." indicates Not Applicable

Statistical significance indicated on a group with an N < 3 is not valid

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
Specific Gravity	Specific Gravity
Urinary Glucose	Urinary Glucose
Urinary Bilirubin	Urinary Bilirubin
Urinary Ketones	Urinary Ketones
Urinary Blood	Urinary Blood
UA pH	UA pH
Urinary Protein	Urinary Protein
UA Urobilinogen	UA Urobilinogen
Urinary Nitrite	Urinary Nitrite
Urinary Leukocytes	Urinary Leukocytes
Urinary WBC	Urinary WBC
Urinary RBC	Urinary RBC
Urinary Epit helial Cells	Urinary Epithelial Cells
Urinary Amorphus Cry	Urinary Amorphus Crystals
Urinary Bacteria	Urinary Bacteria
Urinary Triple Phosp	Urinary Triple Phosphate
Urinary Mucus Thread	Urinary Mucus Thread
Urinary Sperm	Urinary Sperm
Urinary Budding Yeas	Urinary Budding Yeast
Fine Granula	Fine Granular Cast

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with Propriet Pr in Sprague Dawley Rats

Key Page**Unit Descriptions**

<u>Headings Used</u>	<u>Description</u>
EU/dL	EU/dL

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>
Specific Gravity	Mean Standard Deviation Count (N)
Urinary Glucose	Count (N)
Urinary Bilirubin	Count (N)
Urinary Ketones	Count (N)
Urinary Blood	Count (N)
UA pH	Mean Standard Deviation Count (N)
Urinary Protein	Count (N)
UA Urobilinogen	Mean Standard Deviation Count (N)
Urinary Nitrite	Count (N)
Urinary Leukocytes	Count (N)
Urinary WBC	Count (N)
Urinary RBC	Count (N)
Urinary Epit helial Cells	Count (N)
Urinary Amorphus Cry	Count (N)
Urinary Bacteria	Count (N)
Urinary Triple Phosp	Count (N)
Urinary Mucus Thread	Count (N)
Urinary Sperm	Count (N)

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with Propriet Pr in Sprague Dawley Rats

Key Page**Measurement/Statistics (Continued)**

<u>Measurement</u>	<u>Descriptive</u>
Urinary Budding Yeas	Count (N)
Fine Granula	Count (N)

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>
1	Excipient (0)	Control	Group 1 0 mg/kg SC
2	Propriet Pr (1.5)	Dose	Group 2 1.5 mg/kg SC
3	Propriet Pr (15)	Dose	Group 3 15 mg/kg SC
4	Propriet Pr (30)	Dose	Group 4 30 mg/kg SC

Comment Abbreviations

RC = Result Comment

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study with Propriet Pr in Sprague Dawley Rats

End of Print

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix J-2

INDIVIDUAL URINE COLOR, CLARITY AND VOLUME

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with **Proprietary** **Pr** in Sprague Dawley Rats

Sex: Male Day(s) Relative to Start Date

Group 1 0 mg/kg SC						
	Urine Color	Urine Color	Urine Clarity	Urine Clarity	Urine Volume (mL)	Urine Volume (mL)
	28	72	28	72	28	72
001	Yellow	-	Clear	-	15.0	-
002	DarkYellow	-	Clear ¹	-	12.0	-
003	DarkYellow	-	Turbid	-	14.0 ¹	-
004	DarkYellow	-	Turbid	-	10.0 ¹	-
005	DarkYellow	-	Turbid ¹	-	8.5	-
006	Yellow	-	Clear	-	18.0	-
007	Yellow	-	Clear	-	20.0 ¹	-
008	PaleYellow	-	Clear	-	60.0 > ²	-
009	PaleYellow	-	Clear	-	28.0 ²	-
010	PaleYellow	-	Clear	-	48.0 > ²	-
011	-	PaleYellow	-	Clear	-	14.0
012	-	PaleYellow	-	Clear	-	44.0 > ³
013	-	Yellow	-	Clear	-	19.0
014	-	Yellow	-	Clear	-	7.0
015	-	PaleYellow	-	Clear	-	16.0
Mean	-	-	-	-	23.35	20.00
SD	-	-	-	-	17.31	14.12
N	-	-	-	-	10	5

> = Out of range

¹ [RC:unknown particulates in urine]

² [RC:appears rat played with water bottle]

³ [RC:volume verified]

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with **Proprietary** **Pr** in Sprague Dawley Rats

Sex: Male Day(s) Relative to Start Date

Group 2 1.5 mg/kg SC						
	Urine Color	Urine Color	Urine Clarity	Urine Clarity	Urine Volume (mL)	Urine Volume (mL)
	28	72	28	72	28	72
031	Yellow	-	Clear	-	20.0	-
032	Yellow	-	Clear	-	20.0	-
033	PaleYellow	-	Clear	-	48.0 ^{>1}	-
034	Yellow	-	Clear	-	13.5	-
035	Yellow	-	Turbid	-	7.0	-
036	Yellow	-	Clear	-	32.0 ¹	-
037	Yellow	-	Clear	-	32.0 ¹	-
038	PaleYellow	-	Clear	-	36.0 ¹	-
039	DarkYellow	-	Turbid	-	10.5	-
040	PaleYellow	-	Clear	-	36.0 ¹	-
041	-	Yellow	-	Clear	-	11.0
042	-	Yellow	-	Clear	-	6.0
043	-	Yellow	-	Clear	-	6.5
044	-	Yellow	-	Clear	-	13.0
045	-	Yellow	-	Clear	-	12.0
Mean	-	-	-	-	25.50	9.70
SD	-	-	-	-	13.26	3.23
N	-	-	-	-	10	5

> = Out of range

¹ [RC:appears rat played with waterbottle]

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with **Proprietary** **Pr** in Sprague Dawley Rats

Sex: Male Day(s) Relative to Start Date

Group 3 15 mg/kg SC						
	Urine Color	Urine Color	Urine Clarity	Urine Clarity	Urine Volume (mL)	Urine Volume (mL)
	28	72	28	72	28	72
061	Yellow	-	Clear	-	17.0	-
062	Yellow	-	Turbid	-	13.5	-
063	PaleYellow	-	Clear	-	36.0 ¹	-
064	Yellow	-	Turbid	-	6.5	-
065	PaleYellow	-	Clear	-	20.0 ¹	-
066	PaleYellow	-	Clear	-	28.0 ¹	-
068	PaleYellow	-	Clear	-	24.0 ¹	-
069	Yellow	-	Clear	-	17.0	-
070	Yellow	-	Clear	-	18.0	-
071	-	Yellow	-	Clear	-	16.0
072	-	Yellow	-	Clear	-	7.0
073	-	Yellow	-	Clear	-	16.5
074	-	Yellow	-	Clear	-	7.5
075	-	Yellow	-	Clear	-	15.0
Mean	-	-	-	-	20.00	12.40
SD	-	-	-	-	8.53	4.74
N	-	-	-	-	9	5

¹ [RC:appears rat played with waterbottle]

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with **Proprietary** **Pr** in Sprague Dawley Rats

Sex: Male Day(s) Relative to Start Date

Group 4 30 mg/kg SC						
	Urine Color	Urine Color	Urine Clarity	Urine Clarity	Urine Volume (mL)	Urine Volume (mL)
	28	72	28	72	28	72
091	Yellow	-	Clear ¹	-	7.0	-
092	PaleYellow	-	Clear	-	9.5	-
093	PaleYellow	-	Clear	-	32.0 ³	-
094	PaleYellow	-	Clear	-	23.0 ³	-
095	PaleYellow	-	Clear	-	18.0	-
096	Yellow	-	Clear ²	-	11.0	-
097	Yellow	-	Clear	-	14.0	-
098	Yellow	-	Clear ¹	-	13.5	-
099	Yellow	-	Clear	-	7.0	-
100	Yellow	-	Clear ²	-	12.5	-
Pr	-	Yellow	-	Clear	-	10.0
102	-	PaleYellow	-	Clear	-	28.0
103	-	Yellow	-	Clear	-	5.5
104	-	Yellow	-	Clear	-	20.0
105	-	Yellow	-	Clear	-	7.0
Mean	-	-	-	-	14.75	14.10
SD	-	-	-	-	7.78	9.61
N	-	-	-	-	10	5

¹ [RC:urine contained particulates]

² [RC:contains particulates]

³ [RC:appears rat played with waterbottle]

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with **Proprietary** in Sprague Dawley Rats

Sex: Female Day(s) Relative to Start Date

Group 1 0 mg/kg SC						
	Urine Color	Urine Color	Urine Clarity	Urine Clarity	Urine Volume (mL)	Urine Volume (mL)
	28	72	28	72	28	72
016	Yellow	-	Clear	-	4.5	-
017	Yellow	-	Clear	-	7.0	-
018	Yellow	-	Clear	-	6.0	-
019	PaleYellow	-	Clear	-	8.5	-
020	Yellow	-	Clear	-	7.0	-
021	PaleYellow	-	Clear	-	14.5	-
022	DarkYellow	-	Clear	-	2.5	-
023	Yellow	-	Clear	-	10.0	-
024	PaleYellow	-	Clear	-	18.0	-
025	Yellow	-	Clear	-	6.0	-
026	-	Yellow	-	Clear	-	6.0
027	-	Yellow	-	Clear	-	10.0
028	-	Yellow	-	Clear	-	11.0
029	-	Yellow	-	Clear	-	3.0
030	-	Yellow	-	Clear	-	2.0
Mean	-	-	-	-	8.40	6.40
SD	-	-	-	-	4.68	4.04
N	-	-	-	-	10	5

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with **Proprietary** **Pr** in Sprague Dawley Rats

Sex: Female Day(s) Relative to Start Date

Group 2 1.5 mg/kg SC						
	Urine Color	Urine Color	Urine Clarity	Urine Clarity	Urine Volume (mL)	Urine Volume (mL)
	28	72	28	72	28	72
046	Yellow	-	Clear	-	4.5	-
047	DarkYellow	-	Clear	-	3.5	-
048	Yellow	-	Clear	-	6.5	-
049	Yellow	-	Clear	-	3.5	-
050	PaleYellow	-	Clear	-	13.0	-
051	DarkYellow	-	Clear	-	4.0	-
052	DarkYellow	-	Turbid	-	2.5	-
053	PaleYellow	-	Clear	-	25.0	-
054	Yellow	-	Clear	-	7.0	-
055	PaleYellow	-	Clear	-	7.5	-
056	-	Yellow	-	Turbid	-	6.0
057	-	Yellow	-	Turbid	-	7.0
058	-	Yellow	-	Turbid	-	8.0
059	-	Yellow	-	Clear	-	4.0
060	-	Yellow	-	Clear	-	7.0
Mean	-	-	-	-	7.70	6.40
SD	-	-	-	-	6.80	1.52
N	-	-	-	-	10	5

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with **Proprietary** **Pr** in Sprague Dawley Rats

Sex: Female Day(s) Relative to Start Date

Group 3 15 mg/kg SC						
	Urine Color	Urine Color	Urine Clarity	Urine Clarity	Urine Volume (mL)	Urine Volume (mL)
	28	72	28	72	28	72
076	Yellow	-	Clear	-	10.0	-
077	Yellow	-	Clear	-	8.5	-
078	PaleYellow	-	Clear	-	14.0	-
079	PaleYellow	-	Clear	-	13.0	-
080	Yellow	-	Clear	-	7.0	-
081	PaleYellow	-	Clear	-	15.0	-
082	Yellow	-	Clear	-	8.5	-
083	PaleYellow	-	Clear	-	10.0	-
084	PaleYellow	-	Clear	-	28.0	-
085	PaleYellow	-	Clear	-	8.0	-
086	-	PaleYellow	-	Clear	-	40.0 ¹
087	-	Yellow	-	Clear	-	6.0
088	-	Yellow	-	Clear	-	6.0
089	-	Yellow	-	Clear	-	9.0
090	-	Yellow	-	Turbid	-	6.0
Mean	-	-	-	-	12.20	13.40
SD	-	-	-	-	6.17	14.93
N	-	-	-	-	10	5

¹ [RC:Lixit leaked]

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with **Proprietary** in Sprague Dawley Rats

Sex: Female Day(s) Relative to Start Date

Group 4 30 mg/kg SC						
	Urine Color	Urine Color	Urine Clarity	Urine Clarity	Urine Volume (mL)	Urine Volume (mL)
	28	72	28	72	28	72
106	PaleYellow	-	Clear	-	14.0	-
107	Yellow	-	Clear	-	11.5	-
108	PaleYellow	-	Clear	-	30.0	-
109	Yellow	-	Clear	-	7.5	-
110	PaleYellow	-	Clear	-	12.5	-
111	Yellow	-	Clear	-	12.5	-
112	PaleYellow	-	Clear	-	12.5	-
113	PaleYellow	-	Clear	-	12.5	-
114	PaleYellow	-	Clear	-	15.0	-
115	PaleYellow	-	Clear	-	16.0	-
116	-	DarkYellow	-	Turbid	-	6.0
117	-	Yellow	-	Clear	-	10.0
118	-	DarkYellow	-	Turbid	-	4.5
119	-	Yellow	-	Clear	-	14.0
120	-	DarkYellow	-	Clear	-	4.0
Mean	-	-	-	-	14.40	7.70
SD	-	-	-	-	5.93	4.24
N	-	-	-	-	10	5

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary IPr in Sprague Dawley Rats

Comments and Markers

<u>Page</u>	<u>Day</u>	<u>Group</u>	<u>Sex</u>	<u>Subject</u>	<u>Measurement</u>	<u>Type</u>	<u>Marker</u>
1	28	1	Male	002	Urine Clarity	Result	
				<i>Comment: unknown particulates in urine</i>			
1	28	1	Male	003	Urine Volume	Result	
				<i>Comment: unknown particulates in urine</i>			
1	28	1	Male	004	Urine Volume	Result	
				<i>Comment: unknown particulates in urine</i>			
1	28	1	Male	005	Urine Clarity	Result	
				<i>Comment: unknown particulates in urine</i>			
1	28	1	Male	007	Urine Volume	Result	
				<i>Comment: unknown particulates in urine</i>			
1	28	1	Male	008	Urine Volume	Out of Range	>
				<i>Comment: appears rat played with water bottle</i>			
1	28	1	Male	009	Urine Volume	Result	
				<i>Comment: appears rat played with water bottle</i>			
1	28	1	Male	010	Urine Volume	Out of Range	>
				<i>Comment: appears rat played with water bottle</i>			
1	72	1	Male	012	Urine Volume	Out of Range	>
				<i>Comment: volume verified</i>			
2	28	2	Male	033	Urine Volume	Out of Range	>
				<i>Comment: appears rat played with waterbottle</i>			
2	28	2	Male	036	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
2	28	2	Male	037	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
2	28	2	Male	038	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
2	28	2	Male	040	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
3	28	3	Male	063	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary IPr in Sprague Dawley Rats

Comments and Markers

<u>Page</u>	<u>Day</u>	<u>Group</u>	<u>Sex</u>	<u>Subject</u>	<u>Measurement</u>	<u>Type</u>	<u>Marker</u>
3	28	3	Male	065	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
3	28	3	Male	066	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
3	28	3	Male	068	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
4	28	4	Male	091	Urine Clarity	Result	
				<i>Comment: urine contained particulates</i>			
4	28	4	Male	093	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
4	28	4	Male	094	Urine Volume	Result	
				<i>Comment: appears rat played with waterbottle</i>			
4	28	4	Male	096	Urine Clarity	Result	
				<i>Comment: contains particulates</i>			
4	28	4	Male	098	Urine Clarity	Result	
				<i>Comment: urine contained particulates</i>			
4	28	4	Male	100	Urine Clarity	Result	
				<i>Comment: contains particulates</i>			
7	72	3	Female	086	Urine Volume	Result	
				<i>Comment: Lixit leaked</i>			

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Propriet Pr in Sprague Dawley Rats

Key Page

General Footnotes

Provantis version 10.1.0.1

"-" indicates Not Applicable

Measurement Descriptions

<u>Headings Used</u>	<u>Description</u>
Urine Color	Urine Color
Urine Clarity	Urine Clarity
Urine Volume	Urine Volume

Unit Descriptions

<u>Headings Used</u>	<u>Description</u>
mL	mL

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>
Urine Volume	Mean
	Standard Deviation
	Count (N)

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Propriet Pr in Sprague Dawley Rats

Key Page

Comment Abbreviations

RC = Result Comment

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix K

INDIVIDUAL ORGAN WEIGHTS

Page 3239 of 3822 to Page 3417 of 3822

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Proprietary Info

of the Freedom of Information and Privacy Act

Proprietary Info

Key Page**General Footnotes**

Provantis version 10.1.0.1

< or >: Data falls outside of the normal range defined in the software

"- " indicates Not Applicable

Measurement DescriptionsHeadings Used

Adrenal Glands Wt
Brain Weight
Heart Weight
Kidneys Weight
Liver Weight
Ovaries Weight
Spleen Weight
Testes Weight
Thymus Weight
Adrenal/Body weight
Brain/Body weight
Heart/Body weight
Kidney/Body weight
Liver/Body weight
Ovaries/Body weight
Spleen/Body weight
Testes/Body weight
Thymus/Body weight
Adrenal/ Brain
Heart/ Brain
Kidneys/ Brain
Liver/ Brain
Ovaries/ Brain

Description

Adrenal Glands Weight
Brain Weight
Heart Weight
Kidneys Weight
Liver Weight
Ovaries Weight
Spleen Weight
Testes Weight
Thymus Weight
Adrenals/Terminal Bodyweight Ratio
Brain / Terminal Bodyweight Ratio
Heart/ Terminal Bodyweight Ratio
Kidney/Terminal Bodyweight Ratio
Liver/Terminal Bodyweight Ratio
Ovaries/Terminal Bodyweight Ratio
Spleen/Terminal Bodyweight Ratio
Testes/Terminal Bodyweight Ratio
Thymus/Terminal Bodyweight Ratio
Adrenals/Brain Ratio
Heart/Brain Ratio
Kidneys/Brain Ratio
Liver/Brain Ratio
Ovaries/Brain Ratio

Proprietary Info

Key Page**Measurement Descriptions (Continued)**

<u>Headings Used</u>	<u>Description</u>
Spleen/ Brain	Spleen/Brain Ratio
Testes/ Brain	Testes/Brain Ratio
Thymus/ Brain	Thymus/Brain Ratio

Unit Descriptions

<u>Headings Used</u>	<u>Description</u>
%	%
g	g

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>
Adrenal Glands Wt	Mean Standard Deviation Count (N)
Brain Weight	Mean Standard Deviation Count (N)
Heart Weight	Mean Standard Deviation Count (N)
Kidneys Weight	Mean Standard Deviation Count (N)
Liver Weight	Mean Standard Deviation Count (N)

Proprietary Info

Key Page**Measurement/Statistics (Continued)**

<u>Measurement</u>	<u>Descriptive</u>
Ovaries Weight	Mean Standard Deviation Count (N)
Spleen Weight	Mean Standard Deviation Count (N)
Testes Weight	Mean Standard Deviation Count (N)
Thymus Weight	Mean Standard Deviation Count (N)
Adrenal/Body weight	Mean Standard Deviation Count (N)
Brain/Body weight	Mean Standard Deviation Count (N)
Heart/Body weight	Mean Standard Deviation Count (N)
Kidney/Body weight	Mean Standard Deviation Count (N)
Liver/Body weight	Mean Standard Deviation Count (N)

Key Page**Measurement/Statistics (Continued)**

<u>Measurement</u>	<u>Descriptive</u>
Ovaries/Body weight	Mean Standard Deviation Count (N)
Spleen/Body weight	Mean Standard Deviation Count (N)
Testes/Body weight	Mean Standard Deviation Count (N)
Thymus/Body weight	Mean Standard Deviation Count (N)
Adrenal/ Brain	Mean Standard Deviation Count (N)
Heart/ Brain	Mean Standard Deviation Count (N)
Kidneys/ Brain	Mean Standard Deviation Count (N)
Liver/ Brain	Mean Standard Deviation Count (N)
Ovaries/ Brain	Mean Standard Deviation Count (N)

Individual Organ Weights

Proprietary Info

Proprietary Info

Key Page

Measurement/Statistics (Continued)

<u>Measurement</u>	<u>Descriptive</u>
Spleen/ Brain	Mean Standard Deviation Count (N)
Testes/ Brain	Mean Standard Deviation Count (N)
Thymus/ Brain	Mean Standard Deviation Count (N)

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings 1-4</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Comment Abbreviations

RC = Result Comment

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix L

NECROPSY OBSERVATIONS AND HISTOPATHOLOGY

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix L-1

PATHOLOGY NARRATIVE

GLP-Multiple (5 weekly) Repeat Subcutaneous Dose Toxicity Study with
Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18

Pathology Narrative

Methods:

Protocol-listed retained tissues, with the exception of eyes, optic nerves and testes, for Groups 1 and 4, all gross lesions, unscheduled deaths, and identified target tissues for all groups were retained in 10% neutral-buffered formalin, processed routinely, embedded in paraffin, sectioned and stained with hematoxylin and eosin (H&E), and examined microscopically by a veterinary pathologist. Eyes, optic nerves, and testes were placed in Davidson's solution and processed similarly.

Microscopic data were recorded in Provantis pathology ver. 10.1.0.1; histopathology data are presented in summary and individual animal tables generated using Provantis software. A four-step grading system (minimal, mild, moderate, and marked) was used to define gradable changes. Terminology for data capture was consistent with International Harmonization of Nomenclature and Diagnostic Criteria (INHAND), as promulgated by the Society of Toxicologic Pathology. Records of necropsy findings and changes found at tissue processing in the histology laboratory were available when evaluating the formalin-fixed, paraffin-embedded, hematoxylin and eosin-stained tissue sections.

Proprietary Info

GLP-Multiple (5 weekly) Repeat Subcutaneous Dose Toxicity Study with
Proprietary Info [Pro] in Sprague Dawley Rats
SRI Study No. M398-18

Group 4 (30 mg/kg Proprietary Info [Pro] males and females. Discolored yellow epididymides

Proprietary Info

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GLP-Multiple (5 weekly) Repeat Subcutaneous Dose Toxicity Study with
Proprietary Pro in Sprague Dawley Rats
SRI Study No. M398-18

Proprietary Info

Redacted by agreement

05/20/2019

Date

References:

McInnes E. (2012). Wistar and Sprague-Dawley Rats. *In: Background Lesions in Laboratory Animals. A Color Atlas.* Saunders Elsevier. 2:17-36.

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix L-2

HISTOPATHOLOGY SUMMARY

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Histopathology Summary

Proprietary Info

Proprietary Info

Key Page

General Footnotes

"." indicates Not Applicable
Provantis version 10.1.0.1

Report Request Items

Proprietary Info

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic /Adjusted</u>	<u>Transformation</u>
Pathology Observation	Count Positives			

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Histopathology Summary

Proprietary Info

Proprietary Info

Key Page

Removal Reason Grouping

Grouping Name

Abbreviation

Removal Reasons

Proprietary Info

Page 3442 of 3822 to Page 3444 of 3822

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Histopathology Summary

Proprietary Info

Proprietary Info

Key Page

General Footnotes

"." indicates Not Applicable
Provantis version 10.1.0.1

Report Request Items

Proprietary Info

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic</u>	<u>Transformation</u>
Pathology Observation	Count Positives		/Adjusted	

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Histopathology Summary

Proprietary Info

Proprietary Info

Key Page

Removal Reason Grouping

<u>Grouping Name</u>	<u>Abbreviation</u>	<u>Removal Reasons</u>
Proprietary Info		

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix L-3

INDIVIDUAL HISTOPATHOLOGY

Page 3448 of 3822 to Page 3568 of 3822

Withheld pursuant to exemption

Proprietary Info

of the Freedom of Information and Privacy Act

Proprietary Info

Key Page**Codes**

(TGL) = Trackable Gross Lesion, (MPF) = Major Pathological Finding, (?) = Questionable, (E) = Excluded,
(C) = Clinical Observation, (M) = Mass, (G) = Gross Pathology, (H) = Histopathology

General Footnotes

Provantis version 10.1.0.1

Report Request Items

Proprietary Info

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>
1	Excipient (0)	Control
2	Propriet Pr (1.5)	Dose
3	Propriet Pr (15)	Dose
4	Propriet Pr (30)	Dose

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Proprietary Info Pro in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix L-4

NECROPSY OBSERVATIONS SUMMARY

Page 3571 of 3822 to Page 3587 of 3822

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Proprietary Info

of the Freedom of Information and Privacy Act

Necropsy Observations Summary

Proprietary Info

Proprietary Info

Key Page**General Footnotes**

"." indicates Not Applicable

Provantis version 10.1.0.1

Report Request Items

Proprietary Info

Measurement/Statistics

<u>Measurement</u>	<u>Descriptive</u>	<u>Comparative</u>	<u>Arithmetic</u> <u>/Adjusted</u>	<u>Transformation</u>
Pathology Observation	Count Positives			

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>	<u>Report Headings</u>		
1	Excipient (0)	Control	Group 1	0 mg/kg	SC
2	Propriet Pr (1.5)	Dose	Group 2	1.5 mg/kg	SC
3	Propriet Pr (15)	Dose	Group 3	15 mg/kg	SC
4	Propriet Pr (30)	Dose	Group 4	30 mg/kg	SC

Removal Reason Grouping

<u>Grouping Name</u>	<u>Abbreviation</u>	<u>Removal Reasons</u>
Interim Sacrifice	Int	Interim Sacrifice
Main Sacrifice	Main	Main Sacrifice
Recovery Sacrifice	Rec	Recovery Sacrifice
Moribund Sacrifice	Mori	Moribund Sacrifice
Found Dead	FD	Found Dead
Unscheduled Sacrifice	UnS	Unscheduled Sacrifice
Terminal Sacrifice	Term	Terminal Sacrifice
Mechanically Killed	Mech	Mechanically Killed
Other, See Text Comments	Oth	Other, See Text Comments
Removed from Study	R	Removed from Study

**GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with [Proprietary Info] [Pro] in Sprague Dawley Rats
SRI Study No. M398-18**

Appendix L-5

INDIVIDUAL NECROPSY OBSERVATIONS

Page 3590 of 3822 to Page 3723 of 3822

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M398-18 - GLP-Multiple (5-Weekly) Repeat Subcutaneous Dose Toxicity Study
with Propriet Pr in Sprague Dawley Rats

Key Page

Codes

(TGL) = Trackable Gross Lesion, (MPF) = Major Pathological Finding, (?) = Questionable, (E) = Excluded,
(C) = Clinical Observation, (M) = Mass, (G) = Gross Pathology, (H) = Histopathology

General Footnotes

Provantis version 10.1.0.1

Report Request Items

Proprietary Info

Group Information

<u>Short Name</u>	<u>Long Name</u>	<u>Type</u>
1	Excipient (0)	Control
2	Propriet Pr (1.5)	Dose
3	Propriet Pr (15)	Dose
4	Propriet Pr (30)	Dose

Final Report • November 27, 2019

SUBTASK 1: TOXICITY STUDY IN DOGS WITH

Proprietary Info

Proprietary Info

Task Order No. HHSN27200008
SRI Project P25035.407 under SRI Master Project P22586

Prepared by:

Redacted by agreement

SRI International
333 Ravenswood Ave.
Menlo Park, CA 94025

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Prepared for:

Redacted by agreement

Drug Development and Clinical Sciences Branch
Therapeutic Research Program, DAIDS
National Institute of Allergy and Infectious Diseases
National Institutes of Health, DHHS
5601 Fishers Lane

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Bethesda, Maryland 20892-9830

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NIAID Contract HHSN272201400006I; Task Order HHSN27200008

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A. Safety Evaluation of [Proprietary Info] after 28 Days of Repeat Dose Administration in Beagle Dogs (SRI Study No. M393-18).....	3

Subtask 1: Toxicity Study in Dogs with [Proprietary Info] [Proprietary]
Task Order No. HHSN27200008

I. INTRODUCTION AND GOALS

The primary objective of Subtask 1 was to conduct a Good Laboratory Practice (GLP) 28-day repeat dose toxicity study in dogs with [Proprietary Info] [Proprietary]

SRI Study No. M393-18 28-day repeat dose toxicity study in dogs was to be conducted in SRI's Menlo Park, CA facility. The study was canceled by the COR on September 10, 2018.

II. COMPLIANCE

The purpose of this study was to provide data that can be used to support research efforts. SRI Study No. M393-18 was to be conducted according to U.S. Food and Drug Administration (FDA) "Good Laboratory Practice for Nonclinical Laboratory Studies" (GLP) regulations, as described in 21 CFR Part 58.

III. PROGRESS

A. Safety Evaluation of [Proprietary Info] **after 28 Days of Repeat Dose Administration in Beagle Dogs (SRI Study No. M393-18)**

SRI Study No. M393-18 draft protocol was submitted on August 10 and comments were requested by August 20, 2018. SRI was notified on September 10, 2018 that the Investigator no longer needed the GLP dog study. The dogs that had already been received for this study were transferred to the Subtask 2 [Proprietary Info] dose range-finding and toxicokinetics study (SRI Study No. M397-18).

Because the protocol was never signed, the study was never formally initiated; therefore, no final report was issued for the study.

Final Report • November 27, 2019

SUBTASK 4: TOXICITY PHARMACOKINETIC STUDY IN MICE WITH Proprietary Info

Task Order No. HHSN27200008
SRI Project P25035.413 under SRI Master Project P22586

Prepared by:Redacted by agreement

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Redacted by agreement**Prepared for:**Redacted by agreement

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NIAID Contract HHSN272201400006I; Task Order HHSN27200008

Subtask 4: Toxicity Pharmacokinetic Study in Mice with Proprietary Info
Task Order No. HHSN27200008

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Subtask 4: Toxicity Pharmacokinetic Study in Mice with [Proprietary Info]

Task Order No. HHSN27200008

I. INTRODUCTION AND GOALS

The primary objective of Subtask 4 was to conduct a non-Good Laboratory Practice (non-GLP) toxicity pharmacokinetic (PK) study in C57BL/6 mice with [Proprietary Info]

SRI Study No. B173-18 PK with [Proprietary Info] was conducted in SRI's Menlo Park, CA facility.

II. COMPLIANCE

The purpose of this study was to provide data that can be used to support research efforts. SRI Study No. B173-18 was exploratory and not within the scope of U.S. Food and Drug Administration (FDA) "Good Laboratory Practice for Nonclinical Laboratory Studies" (GLP) regulations, as described in 21 CFR Part 58. Nevertheless, the study was planned, performed, recorded, and reported in accordance with standard practices to ensure data quality and integrity.

III. PROGRESS

A. Maximum Tolerated Dose and Pharmacokinetic Study of [Proprietary Info] Following a Single Dose Administration to Male and Female C57BL/6 Mice (SRI Study No. B173-18)

SRI Study No. B173-18 was initiated on October 1, 2018. Experimental work began on October 2, 2018 and ended on February 4, 2019. The final report was submitted on May 15, 2019. A summary of the report is included below.

The objective of this study was to determine the tolerability and the plasma pharmacokinetics of [Proprietary Info] following an intravenous (iv), intraperitoneal (ip) or oral gavage (po) administration. Male and female C57BL/6 mice were given a single dose administration of the test article.

This study was conducted in two phases. During Phase A, male and female mice (1/sex/group) were administered [Proprietary Info] as a single dose at 20 mg/kg (iv), 20 mg/kg (ip), or 40 mg/kg (po) and observed immediately postdose, 2-4 hr and 24 hr postdose for signs of toxicity. Based on normal clinical observations noted in each dose group, the dose levels were increased, and new mice were treated at 40 mg/kg (iv), 40 mg/kg (ip) or 100 mg/kg (po). [Proprietary Info]

[Proprietary Info]

The Phase B dose levels selected in consultation with the Sponsor were 20 mg/kg (iv), 40 mg/kg (ip) and 100 mg/kg (po). During Phase B, male and female mice

Subtask 4: Toxicity Pharmacokinetic Study in Mice with Proprietary Info
Task Order No. HHSN27200008

(12/sex/group) were given a single dose administration. Blood was collected for drug plasma levels at 0.083, 0.25, 0.5, 1, 2, 4, 8 and 24 hr postdose (iv, ip) and 0.25, 0.5, 1, 2, 4, 6, 12 and 24 hr postdose (po). Clinical observations were documented immediately postdose and prior to the last blood collection. Proprietary Info

Proprietary Info

Subtask 4: Toxicity Pharmacokinetic Study in Mice with Proprietary Info
Task Order No. HHSN27200008

Proprietary Info

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SUBTASKS 2 & 3: TOXICITY STUDIES IN DOGS AND RATS WITH Proprietary Info

Task Order No. HHSN27200008
SRI Project P25035.411 and P25035.412 under SRI Master Project P22586

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NIAID Contract HHSN272201400006I; Task Order HHSN27200008

Subtask 4: Toxicity Study in Rats and Dogs with Proprietary Info Pro
Task Order No. HHSN27200008

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D. GLP Multiple (5 Weekly) Repeat Subcutaneous Dose Toxicity Study with Proprietary Info Proprietary Info in Sprague Dawley Rats (SRI Study No. M398-18).....	6

Subtask 4: Toxicity Study in Rats and Dogs with [Proprietary Info] [Pro]
Task Order No. HHSN27200008

I. INTRODUCTION AND GOALS

The primary objective of Subtasks 2 and 3 was to conduct a Good Laboratory Practice (GLP) 5-week toxicity and toxicokinetics study in dogs (originally non-GLP; SRI Study No. M397-18) and a 5-week repeat dose toxicity study in rats (SRI Study No. M398-18) with [Proprietary Info] ART [Prop] a fixed-dose combination (FDC) of [Proprietary Info]

II. COMPLIANCE

The purpose of these toxicity studies was to provide data that can be used to support research efforts. SRI Study No. M398-18 was conducted according to U.S. Food and Drug Administration (FDA) “Good Laboratory Practice for Nonclinical Laboratory Studies” (GLP) regulations, as described in 21 CFR Part 58.

III. PROGRESS

A. Method Validation Report for the Quantitative Analysis of [Proprietary Info] [Proprietary] **and** [Proprietary] **in K₂ EDTA Dog Plasma (SRI Study No. B185-18)**

The Validation Plan for SRI Study No. B185-18 was initiated on May 29, 2019. The audited draft report was submitted on September 25 and comments were received on October 21, 2019. The final report was submitted on October 31, 2019. A summary of the report is included below.

A bioanalytical method was validated for the quantitative analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA dog plasma. The validation demonstrated that the method is appropriate for quantitation of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA dog plasma.

This validation was initiated following method development, which included determination of the assay range, selectivity, intra-batch accuracy and precision, sensitivity, recovery, matrix effect on ionization, matrix effects using 6 unique lots of matrix, and stability of the analyte in the matrix. The parameters investigated during this validation were based on the results obtained from these method development experiments. There were no significant changes made to the methodology between method development and validation.

B. GLP-Multiple (5 Weekly) Repeat Subcutaneous Dose Toxicity and Toxicokinetics Study with [Proprietary Info] [Pro] **Male and Female Beagle Dogs (SRI Study No. M397-18)**

SRI Study No. M397-18 was initiated on November 14, 2018. An unaudited draft report was submitted on September 25 and comments were received on October 17, 2019. The audited final report was submitted on October 31, 2019. A summary of the report is included below.

Subtask 4: Toxicity Study in Rats and Dogs with [Proprietary Info] [Pro]
Task Order No. HHSN27200008

The objective of this study was to determine potential toxicity of [Proprietary] [Prop] a new formulation of [Proprietary] [Propriet] 12 mg/ml), [Proprietary] [Propriet] 6.9 mg/ml) and [Proprietary] [Propriet] 3.3 mg/ml), in adult male and female Beagle dogs following a multiple, 5-weekly repeat subcutaneous (sc) administration.

Proprietary Info

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Subtask 4: Toxicity Study in Rats and Dogs with [Proprietary Info] [Pro]
Task Order No. HHSN27200008

Proprietary Info

C. Method Validation Report for the Quantitative Analysis of [Proprietary Info]
[Proprietary] **and** [Proprietary] **in K₂ EDTA Rat Plasma (SRI Study No. B181-18)**

The Partial Validation Plan for SRI Study No. B181-18 was initiated on June 12, 2019. The audited draft report was submitted on October 8 and comments were received on October 21, 2019. The final report was submitted on November 21, 2019. A summary of the report is included below.

A bioanalytical method was validated for the quantitative analysis of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA rat plasma. The validation demonstrated that the method is appropriate for quantitation of [Proprietary] [Proprietary] and [Proprietary] in K₂ EDTA rat plasma.

This validation was initiated following method development, which included determination of the assay range, selectivity, intra-batch accuracy and precision, sensitivity, recovery, matrix effect on ionization, matrix effects using 6 unique lots of matrix, room temperature stability in matrix, and freeze thaw stability in matrix, whole blood processing stability, effect of hemolysis, and effect of concomitant medications. The parameters investigated during this validation were based on the results obtained from these method development experiments. There were no significant changes made to the methodology between method development and validation.

D. GLP Multiple (5 Weekly) Repeat Subcutaneous Dose Toxicity Study with [Proprietary Info] [Pro]
in Sprague Dawley Rats (SRI Study No. M398-18)

SRI Study No. M398-18 was initiated on December 6, 2018. An unaudited draft report was submitted on October 8 and comments were received on October 21, 2019. The audited final report was submitted on November 21, 2019. A summary of the report is included below.

The objective of this study was to determine potential toxicity of [Proprietary] [Proprietary] a new formulation of [Proprietary] [Proprietary] 12 mg/ml), [Proprietary] [Proprietary] 6.9 mg/ml) and [Proprietary] [Proprietary] 3.3 mg/ml), in adult male and female Sprague Dawley rats following a 5-weekly repeat subcutaneous (sc) administration.

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SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0001

Invoice Date: 10/2/2018

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 6/15/2018 through 9/8/2018

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 113,274.50

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p>	<p>(c) Invoice/Financing Request No: <u>P25035-0001</u></p> <p>(d) Date Invoice Prepared: <u>10/2/2018</u></p> <p>(e) Contract No. and Order No. <u>HHSN2722014000061 /</u> (if applicable) <u>HHSN27200008</u></p> <p>(f) Contract Title: <u>Pharmacology and Toxicology Studies of</u> <u>Proprietary Info</u> <u>Propriet</u> <u>Proprietary</u> <u>and</u> <u>Proprietary</u> <u>and to Support the Development of</u> <u>Mitochondrial Toxicity Assays</u></p> <p>(g) Current Contract Period of Performance: <u>6/15/2018-6/14/2019</u></p> <p>(h) Total Estimated Cost of Contract/Order: <div style="border: 1px solid black; padding: 2px;">Estimated Costs</div></p> <p>(i) Total Fixed-Fee (if applicable): <div style="border: 1px solid black; padding: 2px;">Fixed Fees</div></p> <p>(j) Two-Way Match: <u>X</u> Three-Way Match:</p> <p>(k) Office of Acquisition: <u>National Institute of Allergy and Infectious Diseases</u></p> <p>(l) Central Point of Distribution: <u>NIAIDOAInvoices@niaid.nih.gov</u></p>
-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Redacted by agreement

DUNS or DUNS+4: 00-923-2752
TIN: 94-1160950

(m) This Invoice/financing request represents reimbursable costs for the period from: 6/15/2018 to 9/8/2018

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor		Labor Hours	Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

SRI INTERNATIONAL

Billing Number: 0001
Control Number: INV-0000344175
Billing Group: B

Invoice Date: 10/02/2018

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN272201400006/HHSN27200008

Cost:

Fee:

Total:

Cumulative Amount Billed:

Funded Value

Estimated Costs

Fixed Fees

\$1,806,515.00

Project Number: P25035
Terms: NET 30

Billing Period From: 06/15/2018

To: 09/08/2018

Tax ID Number: 94-1160950

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Total		

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 9, 2018
NATIONAL INSTITUTES OF HEALTH

Labor	Name	Rate	Hours	Amount
Redacted by agreement		Labor rate;	Labor Hours	Labor Costs
	Total Directors			
	Total Middle Managers			
	Total Entry Level Managers			
	Total Advanced Professionals			
	Total Experienced Professionals			
	Total Intermediate Professionals			
	Total Jr Professional			
	Total Senior Technicians			
	Total Technicians			
	Total Jr Technicians			
	TOTAL SRI LABOR			

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 9, 2018
NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Trans No	Name	Trans Description	Amount
TECH PURCH LBR	40	JE1180907		082518 VILLAVICENCIO CARL 2 5	Itemized Cost
	40	JE1180907		082518 VILLAVICENCIO CARL 2 6	
Total					
Total TECH PURCH LE					
MATERIAL & SERVICES	41	VCHR979035	FISHER SCIENTIFIC CATALOG	SYR 12CC LEUR LOCK NO ND 80PK	
	41	VCHR979035	FISHER SCIENTIFIC CATALOG	MINICOLL COAG 3.2% 1ML C/PK RX	
	41	VCHR978631	VWR INTERNATIONAL CATALOG	FLASK,CANTED NECK 150CM2 CS50	
	41	VCHR978921	AMSBIO LLC	Alvetex Scaffold 24 well plate	
	41	VCHR978921	AMSBIO LLC	Alvetex Scaffold 96 well plate	
	41	VCHR975428	ABCAM INC	Caspase 3 assay kit colorimetr	
	41	JE55180935		08/29/18-O'Leary, Victor	
	41	VCHR975428	ABCAM INC	ATP Synthase (Complex 5) human	
	41	VCHR979465	BURGOON COMPANY CATALOG	NDL CATH IV PLCE 22GX1TW 24G.	
	41	VCHR975428	ABCAM INC	Cytochrome- C reductase (Compl	
	41	VCHR979035	FISHER SCIENTIFIC CATALOG	WYPALL X60 TERI WIPERS 100/PK	
	41	VCHR979464	BURGOON COMPANY CATALOG	ETHANOL 200 PRF 4X1G GLASS	
	41	VCHR978631	VWR INTERNATIONAL CATALOG	FLASK 175CM W VENT CAP CS50	
	41	VCHR978789	BURGOON COMPANY CATALOG	SYRINGE 20ML LUER-LOK PK48.	
	41	VCHR978388	SIGMA ALDRICH CATALOG	Cabotegravir	
	41	VCHR978388	SIGMA ALDRICH CATALOG	Elvitegravir	
	41	VCHR976293	SIGMA ALDRICH CATALOG	NEUTRAL RED SOLUTION	
	41	VCHR978288	SIGMA ALDRICH CATALOG	RALTEGRAVIR POTASSIUM	
	41	VCHR980132	BURGOON COMPANY CATALOG	NEEDLE 21X1 MS PK 100	
	41	VCHR976294	SIGMA ALDRICH CATALOG	IN VITRO TOXICOLOGY ASSAY KIT,	
	41	VCHR976091	FISHER SCIENTIFIC CATALOG	BCA PROTASSAY- REDUCAGENT COM	
	41	VCHR980165	HENRY SCHEIN ANIMAL	Amiglyde-V Intrauterine Soluti	
	41	VCHR978912	BURGOON COMPANY CATALOG	FORMALIN 10% BUF RGT GRD 5GAL	
	41	VCHR979102	BURGOON COMPANY CATALOG	#60 BLADE AUTOPSY PK6.	
	41	VCHR976091	FISHER SCIENTIFIC CATALOG	PIERCE LDH CYTOTOXICITY ASSAY	
	41	VCHR979463	BURGOON COMPANY CATALOG	MODIFIED DAVIDSON'S FIXAT	
	41	VCHR978912	BURGOON COMPANY CATALOG	VWR PIPET PAST 5-3 4IN CS1000	
	41	VCHR978912	BURGOON COMPANY CATALOG	VWR SLIDE MICRO FROSTED 75X25I	
	41	VCHR978912	BURGOON COMPANY CATALOG	PARAFILM RL=2IN X 250FT	
	41	VCHR978921	AMSBIO LLC	Alvetex Scaffold 12 well plate	
	41	VCHR978146	SIGMA ALDRICH CATALOG	2',3'-DIDEOXYCYTIDIN	
	41	VCHR978631	VWR INTERNATIONAL CATALOG	FILTER SYS PES 22UM 250ML CS12	
	41	VCHR978631	VWR INTERNATIONAL CATALOG	FILTER SYSTEM,22UM 1L CS12	
	41	JE55180922		08/20/18-Jambunathan,Kal	
	41	VCHR978388	SIGMA ALDRICH CATALOG	Dolutegravir	
	41	VCHR976091	FISHER SCIENTIFIC CATALOG	PLATE F96WELL TC LID 50/CS	
	41	VCHR979035	FISHER SCIENTIFIC CATALOG	MONJCT LAV EDTA 2ML 100/PK RX	
	41	VCHR979035	FISHER SCIENTIFIC CATALOG	TUBE SST BD PLC 3.5PLBL100PKRX	
Total					
	48	VCHR978912	BURGOON COMPANY CATALOG	Shipping Charges - header leve	
	48	VCHR978912	BURGOON COMPANY CATALOG	Handling Charge - header level	
	48	VCHR979102	BURGOON COMPANY CATALOG	Shipping Charges - header leve	
	48	VCHR979465	BURGOON COMPANY CATALOG	Handling Charge - header level	
	48	VCHR979464	BURGOON COMPANY CATALOG	Shipping Charges - header leve	
	48	VCHR979464	BURGOON COMPANY CATALOG	Handling Charge - header level	
	48	VCHR979463	BURGOON COMPANY CATALOG	Shipping Charges - header leve	
	48	VCHR979102	BURGOON COMPANY CATALOG	Handling Charge - header level	
	48	VCHR980132	BURGOON COMPANY CATALOG	Shipping Charges - header leve	
	48	VCHR980132	BURGOON COMPANY CATALOG	Handling Charge - header level	
	48	VCHR979463	BURGOON COMPANY CATALOG	Handling Charge - header level	
	48	VCHR978388	SIGMA ALDRICH CATALOG	Shipping Charges - header leve	
	48	VCHR978631	VWR INTERNATIONAL CATALOG	Handling Charge - header level	
	48	VCHR975428	ABCAM INC	Shipping Cost	
	48	VCHR978789	BURGOON COMPANY CATALOG	Shipping Charges - header leve	
	48	VCHR978789	BURGOON COMPANY CATALOG	Handling Charge - header level	

**INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 9, 2018
NATIONAL INSTITUTES OF HEALTH**

Description	Obj CD	Trans No	Name	Trans Description	Amount
	48	VCHR979465	BURGOON COMPANY CATALOG	Shipping Charges - header leve	Itemized Cost
				Total 48	
	49	JE41180905		ANIMAL CARE CHARGESP9 WK3 2018	
	49	JE41180905		ANIMAL CARE CHARGESP9 WK3 2018	
	49	JE41180905		ANIMAL CARE CHARGESP9 WK3 2018	
	49	JE41180905		ANIMAL CARE CHARGESP9 WK3 2018	Itemized Cost
				Total 49	
				Total MATERIAL & SERVICES	
				TOTAL COSTS	

**SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH**

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
MATERIALS & SUPPLIES	41	VCHR 979035	FISHER SCIENTIFIC CATALOG	SYR 12CC LEUR LOCK NO NDL 80PK			Itemized Cost
MATERIALS & SUPPLIES	41	VCHR 979035	FISHER SCIENTIFIC CATALOG	MINICOLL COAG 3.2% 1ML C/PK RX			
MATERIALS & SUPPLIES	41	VCHR 978631	VWR INTERNATIONAL CATALOG	FLASK,CANTED NECK 150CM2 CS50			
MATERIALS & SUPPLIES	41	VCHR 978921	AMSBIO LLC	Alvetex Scaffold 24 well plate			
MATERIALS & SUPPLIES	41	VCHR 978921	AMSBIO LLC	Alvetex Scaffold 96 well plate			
MATERIALS & SUPPLIES	41	VCHR 975428	ABCAM INC	Caspase 3 assay kit colorimetr			
				Itemized Cost			
MATERIALS & SUPPLIES	41	JE 55180935	SRI CHEM STORES				
MATERIALS & SUPPLIES	41	VCHR 975428	ABCAM INC	ATP Synthase (Complex 5) human			
MATERIALS & SUPPLIES	41	VCHR 979465	BURGOON COMPANY CATALOG	NDL CATH IV PLCE 22GX1TW 24G.			
MATERIALS & SUPPLIES	41	VCHR 975428	ABCAM INC	Cytochrome- C reductase (Compl			
MATERIALS & SUPPLIES	41	VCHR 979035	FISHER SCIENTIFIC CATALOG	WYPALL X60 TERI WIPERS 100/PK			
MATERIALS & SUPPLIES	41	VCHR 979464	BURGOON COMPANY CATALOG	ETHANOL 200 PRF 4X1G GLASS			
MATERIALS & SUPPLIES	41	VCHR 978631	VWR INTERNATIONAL CATALOG	FLASK 175CM W VENT CAP CS50			
MATERIALS & SUPPLIES	41	VCHR 978789	BURGOON COMPANY CATALOG	SYRINGE 20ML LUER-LOK PK48.			
MATERIALS & SUPPLIES	41	VCHR 978388	SIGMA ALDRICH CATALOG	Cabotegravir			
MATERIALS & SUPPLIES	41	VCHR 978388	SIGMA ALDRICH CATALOG	Elvitegravir			
MATERIALS & SUPPLIES	41	VCHR 976293	SIGMA ALDRICH CATALOG	NEUTRAL RED SOLUTION			
MATERIALS & SUPPLIES	41	VCHR 978288	SIGMA ALDRICH CATALOG	RALTEGRAVIR POTASSIUM			
MATERIALS & SUPPLIES	41	VCHR 980132	BURGOON COMPANY CATALOG	NEEDLE 21X1 MS PK 100			
MATERIALS & SUPPLIES	41	VCHR 976294	SIGMA ALDRICH CATALOG	IN VITRO TOXICOLOGY ASSAY KIT,			
MATERIALS & SUPPLIES	41	VCHR 976091	FISHER SCIENTIFIC CATALOG	BCA PROTASSAY- REDUCAGENT COMP			
MATERIALS & SUPPLIES	41	VCHR 980165	HENRY SCHEIN ANIMAL	Amiglyde-V Intrauterine Solution	7		Itemized Cost
MATERIALS & SUPPLIES	41	VCHR 978912	BURGOON COMPANY CATALOG	FORMALIN 10% BUF RGT GRD 5GAL			
MATERIALS & SUPPLIES	41	VCHR 979102	BURGOON COMPANY CATALOG	#60 BLADE AUTOPSY PK6.			
MATERIALS & SUPPLIES	41	VCHR 976091	FISHER SCIENTIFIC CATALOG	PIERCE LDH CYTOTOXICITY ASSAY			
MATERIALS & SUPPLIES	41	VCHR 979463	BURGOON COMPANY CATALOG	MODIFIED DAVIDSON'S FIXAT			
MATERIALS & SUPPLIES	41	VCHR 978912	BURGOON COMPANY CATALOG	VWR PIPET PAST 5-3 4IN CS1000			
MATERIALS & SUPPLIES	41	VCHR 978912	BURGOON COMPANY CATALOG	VWR SLIDE MICRO FROSTED 75X25I			
MATERIALS & SUPPLIES	41	VCHR 978912	BURGOON COMPANY CATALOG	PARAFILM RL=2IN X 250FT			
MATERIALS & SUPPLIES	41	VCHR 978921	AMSBIO LLC	Alvetex Scaffold 12 well plate			
MATERIALS & SUPPLIES	41	VCHR 978146	SIGMA ALDRICH CATALOG	2',3'-DIDEOXYCYTIDIN			
MATERIALS & SUPPLIES	41	VCHR 978631	VWR INTERNATIONAL CATALOG	FILTER SYS PES 22UM 250ML CS12			
MATERIALS & SUPPLIES	41	VCHR 978631	VWR INTERNATIONAL CATALOG	FILTER SYSTEM,22UM 1L CS12			
				Itemized Cost			
MATERIALS & SUPPLIES	41	JE 55180922	SRI CHEM STORES				
MATERIALS & SUPPLIES	41	VCHR 978388	SIGMA ALDRICH CATALOG	Dolutegravir			
MATERIALS & SUPPLIES	41	VCHR 976091	FISHER SCIENTIFIC CATALOG	PLATE F96WELL TC LID 50/CS			
MATERIALS & SUPPLIES	41	VCHR 979035	FISHER SCIENTIFIC CATALOG	MONJCT LAV EDTA 2ML 100/PK RX			
MATERIALS & SUPPLIES	41	VCHR 979035	FISHER SCIENTIFIC CATALOG	TUBE SST BD PLC 3.5PLBL100PKRX			
				Total 41			
Description	Obj CD	Jnl / Trans No	Name	Trans Description			
SHIPPING & RECEIVING	48	VCHR 978912	BURGOON COMPANY CATALOG	Shipping Charges - header leve			
SHIPPING & RECEIVING	48	VCHR 978912	BURGOON COMPANY CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 979102	BURGOON COMPANY CATALOG	Shipping Charges - header leve			
SHIPPING & RECEIVING	48	VCHR 979465	BURGOON COMPANY CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 979464	BURGOON COMPANY CATALOG	Shipping Charges - header leve			
SHIPPING & RECEIVING	48	VCHR 979464	BURGOON COMPANY CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 979463	BURGOON COMPANY CATALOG	Shipping Charges - header leve			
SHIPPING & RECEIVING	48	VCHR 979102	BURGOON COMPANY CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 980132	BURGOON COMPANY CATALOG	Shipping Charges - header leve			
SHIPPING & RECEIVING	48	VCHR 980132	BURGOON COMPANY CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 979463	BURGOON COMPANY CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 978388	SIGMA ALDRICH CATALOG	Shipping Charges - header leve			
SHIPPING & RECEIVING	48	VCHR 978631	VWR INTERNATIONAL CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 975428	ABCAM INC	Shipping Cost			
SHIPPING & RECEIVING	48	VCHR 978789	BURGOON COMPANY CATALOG	Shipping Charges - header leve			
SHIPPING & RECEIVING	48	VCHR 978789	BURGOON COMPANY CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 979465	BURGOON COMPANY CATALOG	Shipping Charges - header leve			
				Total 48			

P25035-0001

10/1/2018

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
INTERNAL SERVICES	49	JE 41180905	ANIMAL CARE	Room:N/A, Study:N/A, ARR:N/A, P.I.:N/A, Type:Per Dog, Qty:	69	Itemized Cost	Itemized Cost
INTERNAL SERVICES	49	JE 41180905	ANIMAL CARE	Room:KBRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated Set-Up/First Day , Qty: 1. @Rate:Itemized Cost	1		
INTERNAL SERVICES	49	JE 41180905	ANIMAL CARE	Room:N/A, Study:N/A, ARR:N/A, P.I.:N/A, Type:Per Dog, Qty:	69		
INTERNAL SERVICES	49	JE 41180905	ANIMAL CARE	Room:N/A, Study:N/A, ARR:N/A, P.I.:N/A, Type:Set-Up/First Day , Qty: 46.	46		
				Total 49			
				Total MATERIAL & SERVICES			

SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0002

Invoice Date: 10/19/2018

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: Estimated Costs

Total Fixed Fee: Fixed Fees

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 9/9/2018 through 10/6/2018

Forwarded From Attached Continuation Sheet-Total Amount Due Itemized Cost

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

10/19/18

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p>	<p>(c) Invoice/Financing Request No: <u>P25035-0002</u></p> <p>(d) Date Invoice Prepared: <u>10/19/2018</u></p> <p>(e) Contract No. and Order No. <u>HHSN2722014000061 /</u> (if applicable) <u>HHSN27200008</u></p> <p>(f) Contract Title: <u>Pharmacology and Toxicology Studies of</u> <u>Proprietary Info</u> <u>Proprietary</u> <u>Proprietary</u> <u>and</u> <u>Proprietary</u> <u>and to Support the Development of</u> <u>Mitochondrial Toxicity Assays</u></p> <p>(g) Current Contract Period of Performance: <u>6/15/2018-6/14/2019</u></p> <p>(h) Total Estimated Cost of Contract/Order: <div style="border: 1px solid black; padding: 2px;">Estimated Costs</div></p> <p>(i) Total Fixed-Fee (if applicable): <div style="border: 1px solid black; padding: 2px;">Fixed Fees</div></p> <p>(j) Two-Way Match: <u>X</u> Three-Way Match:</p> <p>(k) Office of Acquisition: <u>National Institute of Allergy and Infectious Diseases</u></p> <p>(l) Central Point of Distribution: <u>NIAIDOAInvoices@niaid.nih.gov</u></p>
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DUNS or DUNS+4: 00-923-2752
TIN: 94-1160950

(m) This Invoice/financing request represents reimbursable costs for the period from: 9/9/2018 to 10/6/2018

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor		Labor Hours		Labor Costs			
(2) Fringe Benefits				Itemized Cost			
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

SRI INTERNATIONAL

Billing Number: 0002
Control Number: INV-0000345258
Billing Group: B

Invoice Date: 10/19/2018

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN272201400006/HHSN27200008

Cost:

Fee:

Total:

Cumulative Amount Billed:

Itemized Cost

Funded Value

Estimated Costs

Fixed Fees

\$1,806,515.00

Project Number: P25035
Terms: NET 30

Billing Period From: 09/09/2018

To: 10/06/2018

Tax ID Number: 94-1160950

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Total		

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
STG-ONSITE PURCH LBR	40	JE 1181001	Advantage Technical Resources	Proprietary Info	Itemized Cost
STG-ONSITE PURCH LBR	40	JE 1181001	Advantage Technical Resources		
Total 40					
Total STG-ONSITE PURCH LBR					
MATERIALS & SERVICES					
Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty
MATERIALS & SUPPLIES	41	VCHR 982149	SIGMA ALDRICH CATALOG	TRYPsin-EDTA SOLUTION 0.25%, B	
MATERIALS & SUPPLIES	41	VCHR 980520	MARSHALL BIORESOURCES	Marshall Canine Beagles 23 male / 23 female	46
MATERIALS & SUPPLIES	41	VCHR 980520	MARSHALL BIORESOURCES	Corpectomy	46
MATERIALS & SUPPLIES	41	VCHR 980520	MARSHALL BIORESOURCES	albon (Sulfadimethoxine) Treatment	46
MATERIALS & SUPPLIES	41	VCHR 980520	MARSHALL BIORESOURCES	Metronidazole Treatment	46
MATERIALS & SUPPLIES	41	VCHR 980520	MARSHALL BIORESOURCES	Bordetella, Intranasal Vaccine	
MATERIALS & SUPPLIES	41	VCHR 982894	ATCC	Eagle's Minimum Essential	
MATERIALS & SUPPLIES	41	VCHR 982144	FISHER SCIENTIFIC CATALOG	FORCEP, OFFSET, FLAT TIP	
MATERIALS & SUPPLIES	41	VCHR 982144	FISHER SCIENTIFIC CATALOG	FORCEP, OFFSET, FLAT TIP	
MATERIALS & SUPPLIES	41	VCHR 982475	SIGMA ALDRICH CATALOG	IN VITRO TOXICOLOGY ASSAY KIT,	
MATERIALS & SUPPLIES	41	VCHR 981627	ATCC	Fetal Bovine Serum (FBS)	
MATERIALS & SUPPLIES	41	JE 59181002	ALLIANCE GAS	EI-CD50	
Total 41					
Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty
SHIPPING & RECEIVING	48	VCHR 980520	MARSHALL BIORESOURCES	Freight JKL Secure Freight	46
SHIPPING & RECEIVING	48	JE 144181001	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 159181002	ALLIANCE GAS	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 981627	ATCC	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 982149	SIGMA ALDRICH CATALOG	Shipping Charges - header leve	
SHIPPING & RECEIVING	48	JE 144180902	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144180902	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 982894	ATCC	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144181001	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144181001	FEDEX	Shipping Cost	
Total 48					
Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty
INTERNAL SERVICES	49	JE 41181001	ANIMAL CARE	Room:K BRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	161
INTERNAL SERVICES	49	JE 41181001	ANIMAL CARE	Room:K BRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	161
INTERNAL SERVICES	49	JE 41181002	ANIMAL CARE	Room:K BRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	161
INTERNAL SERVICES	49	JE 41181002	ANIMAL CARE	Room:K BRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	161
INTERNAL SERVICES	49	JE 41181003	ANIMAL CARE	Room:K BRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	69
INTERNAL SERVICES	49	JE 41181003	ANIMAL CARE	Room:K BRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	69
INTERNAL SERVICES	49	JE 41181003	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	92
INTERNAL SERVICES	49	JE 41181003	ANIMAL CARE	Room:K BRUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	48
INTERNAL SERVICES	49	JE 41181003	ANIMAL CARE	Room:K CRUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	44
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:K ARUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	1
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:K BRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	161
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	84
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:K CRUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	77
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:K BRUN, Study:M393-18, ARR:8/30/18, P.I.:NG, Type:Regulated	24
Total 49					
Total MATERIAL & SERVICES					

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 10, 2018
NATIONAL INSTITUTES OF HEALTH

Labor	Name	Rate	Hours	Amount
Redacted by agreement	Total Middle Managers	Labor rate	Labor Hours	Labor Costs
	Total Entry Level Managers			
	Total Advanced Professionals			
	Total Experienced Professionals			
	Total Jr Professional			
	Total Senior Technicians			
	Total Technicians			
	Total Jr Technicians			
	TOTAL SRI LABOR			

Description	Obj CD	Trans No	Name	Trans Description	Amount
TECH PURCH LBR	40	JE1181001		Proprietary info	Itemized Cost
	40	JE1181001			
					Total 40
					Total TECH PURCH LBR
MATERIAL & SERVICES	41	VCHR982149	SIGMA ALDRICH CATALOG	TRYPSIN-EDTA SOLUTION 0.25%, B	
	41	VCHR980520	MARSHALL BIORESOURCES	Corpectomy	
	41	VCHR980520	MARSHALL BIORESOURCES	Bordetella, Intranasal Vaccine	
	41	VCHR980520	MARSHALL BIORESOURCES	Metronidazole Treatment	
	41	VCHR982894	ATCC	Eagle's Minimum Essential	
	41	VCHR982144	FISHER SCIENTIFIC CATALOG	FORCEP,OFFSET,FLAT TIP	
	41	VCHR982144	FISHER SCIENTIFIC CATALOG	FORCEP,OFFSET,FLAT TIP	
	41	VCHR982475	SIGMA ALDRICH CATALOG	IN VITRO TOXICOLOGY ASSAY KIT,	
	41	VCHR980520	MARSHALL BIORESOURCES	Marshall Canine Beagles 23 mal	
	41	VCHR981627	ATCC	Fetal Bovine Serum (FBS)	
	41	JE59181002		EI-CD50	
	41	VCHR980520	MARSHALL BIORESOURCES	albon (Sulfadimethoxine)Treatm	
					Total 41
	48	VCHR980520	MARSHALL BIORESOURCES	Freight JKL Secure Freight	
	48	JE144181001		628841350	
	48	JE159181002		JACK DABBS	
	48	VCHR981627	ATCC	Shipping Cost	
	48	VCHR982149	SIGMA ALDRICH CATALOG	Shipping Charges - header leve	
	48	JE144180902		627320115	
	48	JE144180902		627320115	
	48	VCHR982894	ATCC	Shipping Cost	
	48	JE144181001		628841351	
	48	JE144181001		628841351	
					Total 48
	49	JE41181003		ANIMAL CARE CHARGESP10 WK2 201	
	49	JE41181004		ANIMAL CARE CHARGESP10 WK3 201	
	49	JE41181002		ANIMAL CARE CHARGESP10 WK1 201	
	49	JE41181004		ANIMAL CARE CHARGESP10 WK3 201	
	49	JE41181002		ANIMAL CARE CHARGESP10 WK1 201	
	49	JE41181003		ANIMAL CARE CHARGESP10 WK2 201	
	49	JE41181003		ANIMAL CARE CHARGESP10 WK2 201	
	49	JE41181001		ANIMAL CARE CHARGESP9 WK4 2018	
	49	JE41181004		ANIMAL CARE CHARGESP10 WK3 201	
	49	JE41181004		ANIMAL CARE CHARGESP10 WK3 201	
	49	JE41181004		ANIMAL CARE CHARGESP10 WK3 201	
	49	JE41181003		ANIMAL CARE CHARGESP10 WK2 201	
	49	JE41181003		ANIMAL CARE CHARGESP10 WK2 201	
	49	JE41181001		ANIMAL CARE CHARGESP9 WK4 2018	
					Total 49
					Total MATERIAL & SERVICES
					TOTAL COSTS

SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0003

Invoice Date: 11/06/2018

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: Estimated Costs

Total Fixed Fee: Fixed Fees

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 10/7/2018 through 11/3/2018

Forwarded From Attached Continuation Sheet-Total Amount Due Itemized Cost

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

SRI INTERNATIONAL

Billing Number: 0003
 Control Number: INV-0000348459
 Billing Group: B

Invoice Date: 11/06/2018

Bill To:
 NATIONAL INSTITUTES OF HEALTH
 OFFICE OF FINANCIAL MANAGEMENT
 COMMERCIAL ACCOUNTS
 2115 E. JEFFERSON ST., RM 4B-432 MSC8500
 BETHESDA, MD 20892-8500

Remit To:
 SRI International
 P.O. Box 2767
 Cage Code 03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
 Prime Contract Number: HHSN272201400006I/HHSN27200008

Cost:

Fee:

Total:

Cumulative Amount Billed:

Funded Value

Estimated Costs

Fixed Fees

\$1,806,515.00

Project Number: P25035

Terms: NET 30

Tax ID Number: 94-1160950

Billing Period From: 10/07/2018

To: 11/03/2018

Current
Amount

Cumulative
Amount

TECH-ONSITE SALARIES
 TECH-ONSITE BENEFITS
 TECH PURCH LBR
 TECH-ONSITE RES OVHD
 MATERIAL & SERVICES
 SUPP BURD BEGIN 1/92
 G&A BEGIN 1/92
COST CLAIMED
 FEE EARNED
FEE CLAIMED
Invoice Total

Itemized Cost

MG
11/27/18

SRI International NIH Schedule
INVOICE SUPPORT FOR PROJECT P25035 FOR PERIOD 11, 2018
NATIONAL INSTITUTES OF HEALTH

[illegible]

SRI International NIH Schedule
 INVOICE SUPPORT FOR PROJECT P25035 FOR PERIOD 11, 2018
 NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Jnl / Trans No	Trans Description	Amount	
TECH PURCH LBR	40	JE 1181105	Proprietary Info	\$	Itemized Cost
TECH PURCH LBR	40	JE 1181110		\$	
			Total 40	\$	
			Total TECH PURCH LBR	\$	

SRI International NIH Schedule
INVOICE SUPPORT FOR PROJECT P25035 FOR PERIOD 11, 2018
NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Unl / Trans No	Trans Description	Amount
MATERIAL & SERVICES	41	VCHR 985172	BD 3ML LUER-LOK SYRINGE PK200.	Itemized Cost
MATERIAL & SERVICES	41	VCHR 985172	TUBE MICRO-HEM. W HEP. 200 PK	
MATERIAL & SERVICES	41	VCHR 985340	MODIFIED DAVIDSON's FIXAT	
MATERIAL & SERVICES	41	VCHR 985172	VWR PIPET PAST 5-3 4IN CS1000	
MATERIAL & SERVICES	41	VCHR 984547	MicroClave PVC Connector with	
MATERIAL & SERVICES	41	VCHR 984547	AceproJect (Acepromazine) Inje	
MATERIAL & SERVICES	41	VCHR 984547	MicroClave Multi-Dose Vial Ads	
MATERIAL & SERVICES	41	VCHR 984547	Kendall Standard Porous Tape R	
MATERIAL & SERVICES	41	VCHR 984547	Cardinal Health (2531C)	
MATERIAL & SERVICES	41	VCHR 984547	Injection Plug, Luer Slip	
MATERIAL & SERVICES	41	VCHR 984633	VWR PIPET PAST 5-3 4IN CS1000	
MATERIAL & SERVICES	41	VCHR 985483	FORMALIN 10% BFFRD RGTGRD CS4	
MATERIAL & SERVICES	41	VCHR 985479	0.5ML K2EDTA MINI COL C/PK RX	
MATERIAL & SERVICES	41	VCHR 985479	TUBE SST BD PLC 3.5PLBL100PKRX	
MATERIAL & SERVICES	41	VCHR 985479	SYR 12CC LEUR LOCK NO NDL 80PK	
MATERIAL & SERVICES	41	JE 55181123	10/18/18-Gotuaco, Leslie	
MATERIAL & SERVICES	41	VCHR 985651	ALCOHOL PREP PADS STRL BX200.	
MATERIAL & SERVICES	41	VCHR 985651	CONTAINER HISTOLGY 500ML CS100	
MATERIAL & SERVICES	41	VCHR 985651	HISTOLOGY CONTAINER NS CS100	
MATERIAL & SERVICES	41	VCHR 985346	PARAFILM RL-2IN X 250FT	
MATERIAL & SERVICES	41	VCHR 984595	IV CATH 22GX1IN 50PK	
MATERIAL & SERVICES	41	VCHR 984595	TUBE SST BD PLC 3.5PLBL100PKRX	
MATERIAL & SERVICES	41	VCHR 984595	WYPALL X60 TERI WIPERS 100MPK	
MATERIAL & SERVICES	41	VCHR 985356	Elite Titan Cryogen-X Blade, S	
MATERIAL & SERVICES	41	VCHR 985356	Blade Wash	
MATERIAL & SERVICES	41	VCHR 985356	All-Gauze Cotton Sponges, Non-S	
MATERIAL & SERVICES	41	VCHR 985752	MODIFIED DAVIDSON's FIXAT	
MATERIAL & SERVICES	41	VCHR 984115	K-562 (ATCC CCL-243)	
MATERIAL & SERVICES	41	VCHR 984115	Iscove's Modified Dulbecc	
MATERIAL & SERVICES	41	VCHR 983556	27X1/2 I BEVEL RP 100PK RX	
MATERIAL & SERVICES	41	VCHR 985341	7-ETHYL-10-HYDROXYCAMPTOTHECIN	
MATERIAL & SERVICES	41	VCHR 985172	VWR FREEZER BOX MECHANICL CRYO	
MATERIAL & SERVICES	41	VCHR 985172	TUBE CAPILLARY MICRO-HEMATOCRI	
MATERIAL & SERVICES	41	VCHR 985172	SCALPEL BLADE #22 C-STEEL PK6.	
MATERIAL & SERVICES	41	VCHR 985172	VWR SLIDE MICRO FROSTED 75X25I	
MATERIAL & SERVICES	41	VCHR 985172	CASSETTE MEGA 30X24X11MM CS750	
MATERIAL & SERVICES	41	VCHR 983179	C57BL/6 MOUSE FEMALE 0019-0021	
MATERIAL & SERVICES	41	VCHR 983179	C57BL/6 MOUSE MALE 0023-0025 G	
MATERIAL & SERVICES	41	VCHR 983556	0.5ML K3 EDTA 100PK	
MATERIAL & SERVICES	41	VCHR 983556	CONCL BT CRYOVIAL 1.2ML 500CS	
MATERIAL & SERVICES	41	VCHR 983556	SYR 1ML LR-LK W/O ND 100PK RX	
MATERIAL & SERVICES	41	VCHR 984633	FORMALIN 10% BUF RGT GRD 5GAL	
MATERIAL & SERVICES	41	JE 55181144	10/29/18-Shinn, Walter M.	
MATERIAL & SERVICES	41	VCHR 984476	SomnaSol Euthanasia Solution C	
MATERIAL & SERVICES	41	VCHR 984476	Torbugesic Injection, 10mg/mL	
MATERIAL & SERVICES	41	VCHR 984115	Fetal Bovine Serum (FBS)	
MATERIAL & SERVICES	41	JE 55181123	10/16/18-Jambunathan, Kal	
MATERIAL & SERVICES	41	JE 55181138	10/24/18-Nguyen, Jennifer	
MATERIAL & SERVICES	41	VCHR 985653	VWR PLATE DEEP WELL 2.2ML ST.	
MATERIAL & SERVICES	41	VCHR 984632	BOTTLE VACUUM ASPIRATOR 0.5 GA	
MATERIAL & SERVICES	41	VCHR 984632	FILTER VACUGUARD 16CM2 PK10	
MATERIAL & SERVICES	41	VCHR 985478	VCTNR PLS HMGRD LV 2ML 100PKRX	
Total 41				
MATERIAL & SERVICES	48	VCHR 985752	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 983179	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 985346	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 984632	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 985653	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 985651	Shipping Charges - header leve	
MATERIAL & SERVICES	48	VCHR 985651	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 985483	Shipping Charges - header leve	
MATERIAL & SERVICES	48	VCHR 985483	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 984633	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 983179	Shipping Charges - header leve	
MATERIAL & SERVICES	48	VCHR 985752	Shipping Charges - header leve	
MATERIAL & SERVICES	48	JE 144181102	632393637	
MATERIAL & SERVICES	48	VCHR 984115	Shipping Cost	
MATERIAL & SERVICES	48	VCHR 985340	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 984633	Shipping Charges - header leve	
MATERIAL & SERVICES	48	VCHR 985172	Handling Charge - header level	
MATERIAL & SERVICES	48	VCHR 985172	Shipping Charges - header leve	
MATERIAL & SERVICES	48	VCHR 985346	Shipping Charges - header leve	
Total 48				
MATERIAL & SERVICES	49	JE 41181102	ANIMAL CARE CHARGESP11 WK 1 20	
MATERIAL & SERVICES	49	JE 41181102	ANIMAL CARE CHARGESP11 WK 1 20	
MATERIAL & SERVICES	49	JE 41181102	ANIMAL CARE CHARGESP11 WK 1 20	
MATERIAL & SERVICES	49	JE 41181101	ANIMAL CARE CHARGESP10 WK4 201	
MATERIAL & SERVICES	49	JE 41181101	ANIMAL CARE CHARGESP10 WK4 201	
MATERIAL & SERVICES	49	JE 41181103	ANIMAL CARE CHARGESP11 WK 2 20	
MATERIAL & SERVICES	49	JE 41181103	ANIMAL CARE CHARGESP11 WK 2 20	
MATERIAL & SERVICES	49	JE 41181101	ANIMAL CARE CHARGESP10 WK4 201	
MATERIAL & SERVICES	49	JE 41181102	ANIMAL CARE CHARGESP11 WK 1 20	
MATERIAL & SERVICES	49	JE 41181105	ANIMAL CARE CHARGESP11 WK 3 20	
MATERIAL & SERVICES	49	JE 41181105	ANIMAL CARE CHARGESP11 WK 3 20	
MATERIAL & SERVICES	49	JE 41181101	ANIMAL CARE CHARGESP10 WK4 201	
Total 49				
Total MATERIAL & SERVICES				
TOTAL COSTS				

**SRI INTERNATIONAL
INVOICE/FINANCING REQUEST**

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0004

Invoice Date: 12/13/2018

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: Estimated Costs

Total Fixed Fee: Fixed Fees

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 11/4/2018 through 12/1/2018

Forwarded From Attached Continuation Sheet-Total Amount Due \$ Itemized Cost

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

12/13/18

Obtained via FOIA by White Coat Waste Project

SRI INTERNATIONAL

Billing Number: 0004
Control Number: INV-0000349549
Billing Group: B

Invoice Date: 12/13/2018

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN2722014000061/HHSN27200008

Funded Value
Itemized Cost
\$1,806,515.00

Project Number: P25035
Terms: NET 30

Cost:
Fee:
Total:
Cumulative Amount Billed: Itemized Cost

Tax ID Number: 94-1160950

Billing Period From: 11/04/2018
To: 12/01/2018

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
OVERTIME PREMIUM		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Total		

al
12/13/18

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p> <p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 40px; width: 150px; margin: 10px 0;"></div> <p>Redacted by agreement</p> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	<p>(c) Invoice/Financing Request No: P25035-0004</p> <p>(d) Date Invoice Prepared: 12/12/2018</p> <p>(e) Contract No. and Order No. HHSN2722014000061 / (if applicable) HHSN27200008</p> <p>(f) Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Proprietary and Proprietary and to Support the Development of Mitochondrial Toxicity Assays</p> <p>(g) Current Contract Period of Performance: 6/15/2018-6/14/2019</p> <p>(h) Total Estimated Cost of Contract/Order: \$1,688,333</p> <p>(i) Total Fixed-Fee (if applicable): \$118,182</p> <p>(j) Two-Way Match: X Three-Way Match:</p> <p>(k) Office of Acquisition: National Institute of Allergy and Infectious Diseases</p> <p>(l) Central Point of Distribution: NIAIDOAInvoices@niaid.nih.gov</p>
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(m) This Invoice/financing request represents reimbursable costs for the period from: 11/4/2018 to 12/1/2018

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor	Labor Hours		Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

P25035-0004

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

12/12/2018

Description	Obj CD	Inl / Trans No	Name	Trans Description	Amount
Labor Hours					\$42.60
					\$113.60
					\$156.20
Total STG-ONSITE PURCH LBR					\$156.20

Description	Obj CD	Inl / Trans No	Name	Trans Description	Amount
OVERTIME PREMIUM	Labor Hours		Overtime Premi	Redacted by agreement	Labor Costs
OVERTIME PREMIUM			Overtime Premi	LD Posting	
OVERTIME PREMIUM			Overtime Premi	LD Posting	
OVERTIME PREMIUM			Overtime Premi	LD Posting	
OVERTIME PREMIUM			Overtime Premi	LD Posting	
OVERTIME PREMIUM			Overtime Premi	LD Posting	
Total OVERTIME PREMIUM					

MATERIALS & SERVICES

Description	Obj CD	Inl / Trans No	Name	Trans Description	Qty	Rate	Amount
MATERIALS & SUPPLIES	41	VCHR 988288	SIGMA ALDRICH CATALOG	Proprietary			Itemized Cost
MATERIALS & SUPPLIES	41	VCHR 987266	CONTAINER & PACKAGING	1 gallon clear PET square grip			
MATERIALS & SUPPLIES	41	VCHR 986187	VWR INTERNATIONAL CATALOG	FILTER SYS PES 22UM 500ML CS12			
MATERIALS & SUPPLIES	41	VCHR 987262	CONTAINER & PACKAGING	White PP 110-400 ribbed skirt			
MATERIALS & SUPPLIES	41	VCHR 987132	VWR INTERNATIONAL CATALOG	VWR TIP 300UL STER RK96 PK980.			
				50ML DISPO;Qty 1;\$21;Doc#379153			
				15ML DISPO;Qty 1;\$21;Doc#379153			
				BOTTLE POL;Qty 2;\$12;Doc#379153			
				GLOVES NIT;Qty 2;\$42;Doc#379280			
				50ML DISPO;Qty 1;\$21;Doc#379280			
MATERIALS & SUPPLIES	41	JE 55181220	SRI CHEM STORES	BOTTLE FLI;Qty 1;\$3;Doc#379259			
MATERIALS & SUPPLIES	41	JE 55181249	SRI CHEM STORES				
MATERIALS & SUPPLIES	41	JE 55181249	SRI CHEM STORES				
MATERIALS & SUPPLIES	41	VCHR 988288	SIGMA ALDRICH CATALOG	Proprietary			
MATERIALS & SUPPLIES	41	VCHR 986187	VWR INTERNATIONAL CATALOG	SYRINGE 30ML LUERLOK 2PRT PK50			
MATERIALS & SUPPLIES	41	VCHR 986187	VWR INTERNATIONAL CATALOG	VWR PIPETTE SERO 5ML PR CS200			
MATERIALS & SUPPLIES	41	VCHR 986187	VWR INTERNATIONAL CATALOG	VWR PIPETTE SERO 10ML PR CS200			
MATERIALS & SUPPLIES	41	VCHR 986187	VWR INTERNATIONAL CATALOG	VWR PIPETTE SERO 25ML PR CS200			
MATERIALS & SUPPLIES	41	VCHR 987126	BURGOON COMPANY CATALOG	FORMALIN 10% BFFRD RGTGRD CS4			
				9 x 12 POL;Qty 25;\$5;Doc#379184			
				12 x 15 PO;Qty 25;\$11;Doc#379184			
MATERIALS & SUPPLIES	41	JE 55181220	SRI CHEM STORES				
MATERIALS & SUPPLIES	41	VCHR 988288	SIGMA ALDRICH CATALOG	Proprietary			
Total 41							

Description	Obj CD	Inl / Trans No	Name	Trans Description
SHIPPING & RECEIVING	48	VCHR 987266	CONTAINER & PACKAGING	Shipping Cost
SHIPPING & RECEIVING	48	VCHR 986187	VWR INTERNATIONAL CATALOG	FREIGHT
SHIPPING & RECEIVING	48	JE 144181203	FEDEX	SHIPPING
SHIPPING & RECEIVING	48	VCHR 987132	VWR INTERNATIONAL CATALOG	SHIPPING
SHIPPING & RECEIVING	48	JE 144181203	FEDEX	SHIPPING
SHIPPING & RECEIVING	48	JE 144181104	FEDEX	SHIPPING
SHIPPING & RECEIVING	48	JE 144181104	FEDEX	SHIPPING
SHIPPING & RECEIVING	48	JE 144181202	FEDEX	SHIPPING
SHIPPING & RECEIVING	48	VCHR 987126	BURGOON COMPANY CATALOG	Shipping Charges - header leve
SHIPPING & RECEIVING	48	VCHR 987126	BURGOON COMPANY CATALOG	Handling Charge - header level
Total 48				

Description	Obj CD	Inl / Trans No	Name	Trans Description	Qty	Rate
INTERNAL SERVICES	49	JE 41181201	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	154	Itemized Cost
INTERNAL SERVICES	49	JE 41181201	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	161	
INTERNAL SERVICES	49	JE 41181203	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	138	
INTERNAL SERVICES	49	JE 41181204	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	140	
INTERNAL SERVICES	49	JE 41181205	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	140	
INTERNAL SERVICES	49	JE 41181203	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	140	
INTERNAL SERVICES	49	JE 41181205	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	140	
INTERNAL SERVICES	49	JE 41181204	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	140	
INTERNAL SERVICES	49	JE 41181202	ANIMAL CARE	2018 RATE ADJ (NonGLP Tox PK Mouse)	8.50%	
INTERNAL SERVICES	49	JE 41181202	ANIMAL CARE	2018 RATE ADJ (Amikacin)	8.50%	
INTERNAL SERVICES	49	JE 41181202	ANIMAL CARE	2018 RATE ADJ (Propriet NonGLP RDTox Dog)	8.50%	
Total 49						

Total MATERIAL & SERVICES

**SRI INTERNATIONAL
INVOICE/FINANCING REQUEST**

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasurvops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0005

Invoice Date: 1/24/2019

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

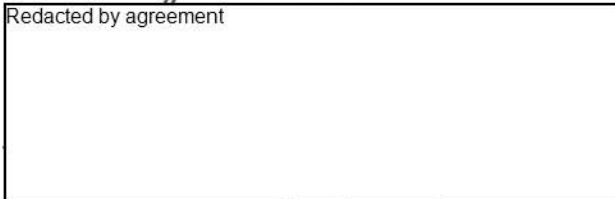
Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 12/2/2018 through 12/29/2018

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 275,908.97

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement



1/24/19

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p> <p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 50px; width: 150px; margin: 10px 0;">Redacted by agreement</div> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	(c) Invoice/Financing Request No:	P25035-0005
	(d) Date Invoice Prepared:	1/24/2019
	(e) Contract No. and Order No. (if applicable)	HHSN2722014000061 / HHSN27200008
	(f) Contract Title:	Pharmacology and Toxicology Studies of Proprietary Info and Proprietary and to Support the Development of Mitochondrial Toxicity Assays
	(g) Current Contract Period of Performance:	6/15/2018-6/14/2019
	(h) Total Estimated Cost of Contract/Order:	\$1,688,333
	(i) Total Fixed-Fee (if applicable):	\$118,182
	(j) Two-Way Match: Three-Way Match:	X
	(k) Office of Acquisition:	National Institute of Allergy and Infectious Diseases
	(l) Central Point of Distribution:	NIAIDOAInvoices@niaid.nih.gov

(m) This Invoice/financing request represents reimbursable costs for the period from: 12/2/2018 to 12/29/2018

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor	Labor Hours		Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

SRI INTERNATIONAL

Billing Number: 0005
Control Number: INV-0000351415
Billing Group: B

Invoice Date: 01/24/2019

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Tel: 650-859-2992 Fax: 650-859-3008

Customer Number: 14094
Prime Contract Number: HHSN272201400006/HHSN27200008

Cost:
Fee:
Total:
Funded Value
Itemized Cost
\$1,806,515.00

Project Number: P25035
Terms: NET 30

Cumulative Amount Billed: Itemized Cost

Tax ID Number: 94-1160950

Billing Period From: 12/02/2018
To: 12/29/2018

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES		Itemized Cost
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
OVERTIME PREMIUM		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Total		

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 13, 2018
NATIONAL INSTITUTES OF HEALTH

Labor	Name	Rate	Hours	Amount
Redacted by agreement	Total Middle Managers	Labor rate	Labor Hours	Labor Costs
	Total Entry Level Managers			
	Total Advanced Professionals			
	Total Experienced Professionals			
	Total Intermediate Professionals			
	Total Jr Professional			
	Total Senior Technicians			
	Total Technicians			
	Total Jr Technicians			
	TOTAL SRI LABOR			

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
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Description	SS, SS, and Transits	Name	Item Description	Itemized Cost
Proprietary Info				

[illegible]

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

MATERIALS & SERVICES

Description	Obj	CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
MATERIALS & SUPPLIES	41	VCHR	989101	CHARLES RIVER	PO31859 INV#93078291: CD RAT MALE 0251-0275 GRAMS (Invoice included)	Itemized Cost		
MATERIALS & SUPPLIES	41	VCHR	989101	CHARLES RIVER	PO31859 INV#93078291: CD RAT FEMALE 0201-0225 GRAMS (Invoice included)			
MATERIALS & SUPPLIES	41	JE	42181301	SRI CAL	Standard Coagulation Panel			
MATERIALS & SUPPLIES	41	JE	42181301	SRI CAL	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	JE	42181301	SRI CAL	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	JE	42181301	SRI CAL	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	JE	42181301	SRI CAL	Standard Coagulation Panel			
MATERIALS & SUPPLIES	41	VCHR	990086	SIGMA ALDRICH CATALOG	Proprietary UNITED STATES PHARM PO32382 INV#546486124			
MATERIALS & SUPPLIES	41	VCHR	990086	SIGMA ALDRICH CATALOG	Proprietary UNITED STATES PHARM (Invoice included)			
MATERIALS & SUPPLIES	41	JE	55181337	SRI CHEM STORES	SHARPS CON;Qty 1;\$68;Doc#379453			
MATERIALS & SUPPLIES	41	JE	59181309	ALLIANCE GAS	EI-CD50			
MATERIALS & SUPPLIES	41	JE	59181309	ALLIANCE GAS	AI-CD50DT			
MATERIALS & SUPPLIES	41	VCHR	988968	SIGMA ALDRICH CATALOG	IN VITRO TOXICOLOGY ASSAY KIT,			
MATERIALS & SUPPLIES	41	VCHR	990223	FISHER SCIENTIFIC CATALOG	ACRODISC SYRINGE FILTERS 0.2UM			
MATERIALS & SUPPLIES	41	VCHR	989461	HENRY SCHEIN ANIMAL	Tropicamide Ophthalmic 1% Solu			
MATERIALS & SUPPLIES	41	VCHR	990603	MEDICAL ISOTOPES INC	d6 Proprietary 1mg			
MATERIALS & SUPPLIES	41	VCHR	990603	MEDICAL ISOTOPES INC	d8 Proprietary 1mg			
MATERIALS & SUPPLIES	41	VCHR	990603	MEDICAL ISOTOPES INC	Proprietary 1mg			
MATERIALS & SUPPLIES	41	JE	42181301	SRI CAL	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	VCHR	989064	FISHER SCIENTIFIC CATALOG	NEEDLES 20GX1 IN 100/PK RX			
MATERIALS & SUPPLIES	41	VCHR	989064	FISHER SCIENTIFIC CATALOG	NEEDLES 20GX1 IN 100/PK RX			
MATERIALS & SUPPLIES	41	VCHR	989064	FISHER SCIENTIFIC CATALOG	CONCL BT CRYOVIAL 1.2ML 500/CS			
MATERIALS & SUPPLIES	41	VCHR	989064	FISHER SCIENTIFIC CATALOG	MONJCT LAV EDTA 2ML 100/PK RX			
MATERIALS & SUPPLIES	41	VCHR	989064	FISHER SCIENTIFIC CATALOG	WYPALL X60 TERI WIPERS 100/PK			
MATERIALS & SUPPLIES	41	JE	55181337	SRI CHEM STORES	BAG BIOHAY;Qty 5;\$10;Doc#379441			
MATERIALS & SUPPLIES	41	JE	59181309	ALLIANCE GAS	OPTIMA PAP;Qty 1;\$2;Doc#379441			
MATERIALS & SUPPLIES	41	JE	59181309	ALLIANCE GAS	EI-CD50			
MATERIALS & SUPPLIES	41	VCHR	989898	CHARLES RIVER	PO31541 INV#93073780 C57BL/6 MOUSE FEMALE 0019-0021 (Invoice included)			
MATERIALS & SUPPLIES	41	VCHR	989898	CHARLES RIVER	PO31541 INV#93073780 C57BL/6 MOUSE MALE 0023-0025 G (Invoice included)			
MATERIALS & SUPPLIES	41	JE	55181324	SRI CHEM STORES	SHARPS CON;Qty 2;\$135;Doc#379361			
MATERIALS & SUPPLIES	41	JE	999181302	UNLEASHED	Canned puppy food for Study Use (M397-18)			
					Total 41			
Description	Obj	CD	Jnl / Trans No	Name	Trans Description			
SHIPPING & RECEIVING	48	JE	159181304	ALLIANCE GAS	Shipping Cost			
SHIPPING & RECEIVING	48	JE	159181304	ALLIANCE GAS	Shipping Cost			
SHIPPING & RECEIVING	48	JE	144181305	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	JE	144181305	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	VCHR	989898	CHARLES RIVER	Handling Charge - line level			
SHIPPING & RECEIVING	48	VCHR	989898	CHARLES RIVER	Shipping Charges - line level			
SHIPPING & RECEIVING	48	VCHR	989101	CHARLES RIVER	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR	989898	CHARLES RIVER	Handling Charge - line level			
SHIPPING & RECEIVING	48	VCHR	989898	CHARLES RIVER	Shipping Charges - line level			
SHIPPING & RECEIVING	48	VCHR	989101	CHARLES RIVER	Shipping Charges - header leve			
SHIPPING & RECEIVING	48	JE	144181301	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	JE	159181304	ALLIANCE GAS	Shipping Cost			
SHIPPING & RECEIVING	48	JE	144181301	FEDEX	Shipping Cost			
					Total 48			

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
INTERNAL SERVICES	49	JE 41181201	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated	Itemized Cost		
INTERNAL SERVICES	49	JE 41181201	ANIMAL CARE	Room:TM170, Study:B173-18p, ARR:11/26/18, P.I.:IL/KGO, Type:Mouse (Small Cage)			
INTERNAL SERVICES	49	JE 41181203	ANIMAL CARE	Room:SERVICE, Study:METAB CAGES, ARR:N/A, P.I.:12/6/18 AND 12/7/18, Type:Per Dog			
INTERNAL SERVICES	49	JE 41181204	ANIMAL CARE	Room:TM170, Study:B173-18p, ARR:11/26/18, P.I.:IL/KGO, Type:Mouse (Small Cage)			
INTERNAL SERVICES	49	JE 41181205	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41181203	ANIMAL CARE	Room:TM170, Study:B173-18p, ARR:11/26/18, P.I.:IL/KGO, Type:Set-Up/First Day			
INTERNAL SERVICES	49	JE 41181205	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41181204	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41181101	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:TM163, Study:M398-18, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:TM170, Study:B173-18p, ARR:11/26/18, P.I.:IL/KGO, Type:Set-Up/First Day			
INTERNAL SERVICES	49	JE 41181004	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
				Total 49			
				Total MATERIAL & SERVICES			

**INV93078291-83382**

Issued on Wednesday, December 5, 2018 PST

Created on Wednesday, December 5, 2018 PST by aribasystem on behalf of Gloria Hom

Header Level Information

ID : INV93078291-83382
Supplier Invoice # : 93078291
Invoice Date : Wednesday, December 5, 2018 PST
Order : PO31859
Supplier Tax ID : 760509980
Remit To ID : 05395-B
Payment Terms : NET 30
Sold To : Email: AP@sri.com
Purchasing Unit : 001 - SRI International
Remit To Address : GPO 27812
Invoice Submission Method : Online
Invoice Origin : Supplier
Invoice Source Document : Purchase Order

Invoice Summary

Base Amount	Itemized Cost
Discount	
Charges	
Taxes	
Gross Amount	

Treasury Special Instructions:

Buyer:

ID: Redacted by

User:**Supplier:**

CHARLES RIVER
GPO 27812
NEW YORK, NY 10087-7812
United States
Contact: NO CONTACT NAME

Ship To:

SRI International, Email: AP@sri.com
333 Ravenswood Ave
Menlo Park, CA 94025-3493
United States

Bill To:

SRI International, Email: AP@sri.com
Send invoices to the following Email: AP@sri.com
Menlo Park, CA 94026-2203
United States

Deliver To:

Redacted by

Project/WorkOrder:

Name: P25035.412 - Propriet GLP RD Tox Rat

HEADER ITEM DETAILS

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
0	Handling Charge - header level		each	1	NoValue	Line Item Costs		Special Handling

Full Description: Handling Charge - header level

Commodity Code:

Partitioned Commodity Code:

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
0	Shipping Charges - header level		each	1	NoValue	Line Item Costs		Shipping

Full Description: Shipping Charges - header level

Commodity Code:

Partitioned Commodity Code:

LINE ITEM DETAILS

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
1	CD RAT MALE 0251-0275 GRAMS 057-059 DAYS	24100536	each	93	NoValue	Line Item Costs		Item 1

Full Description: CD RAT MALE 0251-0275 GRAMS 057-059 DAYS

Commodity Code: LABORATORY, Bio Live Lab Specimens
Partitioned Commodity Code: 41 - Materials & Supplies, Books

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
2	CD RAT FEMALE 0201-0225 GRAMS 057-070 DAYS	24100510	each	93	NoValue	Line Item Costs		Item 2

Full Description: CD RAT FEMALE 0201-0225 GRAMS 057-070 DAYS

Commodity Code: LABORATORY, Bio Live Lab Specimens
Partitioned Commodity Code: 41 - Materials & Supplies, Books**Invoice Comments**

- Redacted by agreement

**INV0546486124-83880**

Issued on Monday, December 10, 2018 PST
Created on Monday, December 10, 2018 PST by aribasystem on behalf of Claire McFarlane

Header Level Information

ID : INV0546486124-83880
Supplier Invoice # : 0546486124
Invoice Date : Sunday, December 9,
2018 PST
Order : PO32382
Remit To ID : 0035077-B
Payment Terms : NET 30
Sold To : SRI INTERNATIONAL
Purchasing Unit : 001 - SRI
International
Remit To Address : Sigma-Aldrich.
Invoice Source Document : Purchase
Order

Invoice Summary

	Itemized Cost
Base Amount	
Discount	
Charges	
Taxes	
Gross Amount	

Treasury Special Instructions:
Buyer:

Supplier:

SIGMA ALDRICH CATALOG
Sigma-Aldrich. P.O. BOX 535182
ATLANTA, GA 30353-5182
United States
Contact: NO CONTACT NAME

Ship To:

SRI International, Email: AP@sri.com
333 Ravenswood Ave
Menlo Park, CA 94025-3493
United States

Bill To:

SRI International, Email: AP@sri.com
Send invoices to the following Email: AP@sri.com
Menlo Park, CA 94026-2203
United States

Project/WorkOrder:

Name: P25035.412 - **Proprietary** GLP RD Tox Rat

HEADER ITEM DETAILS

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
	Total Item Tax				NoValue		Line Item Costs	Sales tax

Full Description: Total Item Tax

Commodity Code:

Partitioned Commodity Code:

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
0	Shipping Charges - header level		each	1	NoValue		Line Item Costs	Shipping

Full Description: Shipping Charges - header level

Commodity Code:

Partitioned Commodity Code:

LINE ITEM DETAILS

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
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Proprietary Info

Obtained via FOIA by White Coat Waste Project

Full Description: **Proprietary** UNITED STATES PHARMACOPEIA (U

Commodity Code: LABORATORY. Observation, Test and Measurement Equipment and Supplies
Partitioned Commodity Code: 41 - Materials & Supplies, Books

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
Proprietary Info								

Full Description: **Proprietary** UNITED STATES PHARMACOPEIA (U

Commodity Code: LABORATORY. Observation, Test and Measurement Equipment and Supplies
Partitioned Commodity Code: 41 - Materials & Supplies, Books

**INV93073780-84297**

Issued on Thursday, December 13, 2018 PST
 Created on Thursday, December 13, 2018 PST by aribasystem on behalf of Gloria Hom

Header Level Information

ID : INV93073780-84297
 Supplier Invoice # : 93073780
 Invoice Date : Thursday, December 13, 2018 PST
 Order : PO31541
 Supplier Tax ID : 760509980
 Remit To ID : 05395-B
 Payment Terms : NET 30
 Sold To : Email: AP@sri.com
 Purchasing Unit : 001 - SRI International
 Remit To Address : GPO 27812
 Invoice Submission Method : Online
 Invoice Origin : Supplier
 Invoice Source Document : Purchase Order

Invoice Summary

Base Amount	Itemized Cost
Discount	
Charges	
Taxes	
Gross Amount	

Treasury Special Instructions:
 Buyer:

Supplier:

CHARLES RIVER
 GPO 27812
 NEW YORK, NY 10087-7812
 United States
 Contact: NO CONTACT NAME

Bill To:

SRI International, Email: AP@sri.com
 Send invoices to the following Email: AP@sri.com
 Menlo Park, CA 94026-2203
 United States

Project/WorkOrder:

Name: P25035.413 - NonGLP Tox PK Mouse

Commodity Code: LABORATORY. Bio Live Lab Specimens
 Partitioned Commodity Code: 41 - Materials & Supplies, Books

LINE ITEM DETAILS

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
1	C57BL/6 MOUSE FEMALE 0019-0021 GRAMS 050-056 DAYS	24109293	each	44	NoValue	Line Item Costs		Item 1

Full Description: C57BL/6 MOUSE FEMALE 0019-0021 GRAMS 050-056 DAYS

Ship To:

SRI International, Email: AP@sri.com
 333 Ravenswood Ave
 Menlo Park, CA 94025-3493
 United States

Deliver To:

Gloria Hom

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
1	Handling Charge - line level		each	1	NoValue	Line Item Costs		Item 1, Special Handling

Full Description: Handling Charge - line level

Obtained via FOIA by White Coat Waste Project

Ship To:

SRI International, Email: AP@sri.com
333 Ravenswood Ave
Menlo Park, CA 94025-3493
United States

Deliver To:

Ariba System

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
1	Shipping Charges - line level		each	1	NoValue	Line Item Costs		Item 1, Shipping

Full Description: Shipping Charges - line level

Ship To:

SRI International, Email: AP@sri.com
333 Ravenswood Ave
Menlo Park, CA 94025-3493
United States

Deliver To:

Ariba System

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
2	C57BL/6 MOUSE MALE 0023-0025 GRAMS 050-056 DAYS	24109319	each	44	NoValue	Line Item Costs		Item 2

Full Description: C57BL/6 MOUSE MALE 0023-0025 GRAMS 050-056 DAYS

Ship To:

SRI International, Email: AP@sri.com
333 Ravenswood Ave
Menlo Park, CA 94025-3493
United States

Deliver To:

Redacted by agreement

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
2	Handling Charge - line level		each	1	NoValue	Line Item Costs		Item 2, Special Handling

Full Description: Handling Charge - line level

Ship To:

SRI International, Email: AP@sri.com
333 Ravenswood Ave
Menlo Park, CA 94025-3493
United States

Deliver To:

Ariba System

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
2	Shipping Charges - line level		each	1	NoValue	Line Item Costs		Item 2, Shipping

Full Description: Shipping Charges - line level

Ship To:

SRI International, Email: AP@sri.com
333 Ravenswood Ave
Menlo Park, CA 94025-3493
United States

Deliver To:

Ariba System

Obtained via FOIA by White Coat Waste Project

Invoice Comments

Redacted by agreement

**SRI INTERNATIONAL
INVOICE/FINANCING REQUEST**

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0006

Invoice Date: 2/13/2019

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 12/30/2018 through 1/26/2019

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 243,735.31

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p> <p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 50px; width: 100%; margin-top: 10px;"></div> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	<p>(c) Invoice/Financing Request No: P25035-0006</p> <p>(d) Date Invoice Prepared: 2/13/2019</p> <p>(e) Contract No. and Order No. HHSN2722014000061 / (if applicable) HHSN27200008</p> <p>(f) Contract Title: <u>Pharmacology and Toxicology Studies of</u> <u>Proprietary Info</u> <u>Proprietary</u> <u>Proprietary</u> <u>and</u> <u>Proprietary</u> <u>and to Support the Development of</u> <u>Mitochondrial Toxicity Assays</u></p> <p>(g) Current Contract Period of Performance: 6/15/2018-6/14/2019</p> <p>(h) Total Estimated Cost of Contract/Order: \$1,688,333</p> <p>(i) Total Fixed-Fee (if applicable): \$118,182</p> <p>(j) Two-Way Match: X Three-Way Match:</p> <p>(k) Office of Acquisition: National Institute of Allergy and Infectious Diseases</p> <p>(l) Central Point of Distribution: NIAIDOAInvoices@niaid.nih.gov</p>
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(m) This Invoice/financing request represents reimbursable costs for the period from: 12/30/2018 to 1/26/2019

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor		Labor Hours	Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

SRI INTERNATIONAL

Billing Number: 0006
Control Number: INV-0000351616
Billing Group: B

Invoice Date: 02/13/2019

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN272201400006I/HHSN27200008

Cost:

Funded Value

Itemized Cost

Fee:

Total:

\$1,806,515.00

Project Number: P25035
Terms: NET 30

Cumulative Amount Billed:

Itemized Cost

Tax ID Number: 94-1160950

Billing Period From: 12/30/2018
To: 01/26/2019

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
OVERTIME PREMIUM		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Total		

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 1, 2019
NATIONAL INSTITUTES OF HEALTH

Labor	Name	Rate	Hours	Amount
Redacted by agreement		Labor rate	Labor Hours	Labor Costs
	Total Middle Managers			
	Total Entry Level Managers			
	Total Advanced Professionals			
	Total Experienced Professionals			
	Total Intermediate Professionals			
	Total Jr Professional			
	Total Senior Technicians			
	Total Technicians			
	Total Jr Technicians			
	TOTAL SRI LABOR			

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
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Description
Proprietary Info

MATERIALS & SERVICES

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
MATERIALS & SUPPLIES	41	JE 55190136	SRI CHEM STORES	Itemized Cost			Itemized Cost
MATERIALS & SUPPLIES	41	JE 999190101	AMAZON	M03IP6KF0:Canned dog food for Study M397			
MATERIALS & SUPPLIES	41	JE 999190101	AMAZON	M22OP64V0:canned dog food for Study M397 PO#32382 INV#0546582.393:			
MATERIALS & SUPPLIES	41	VCHR 990962	SIGMA ALDRICH CATALOG	Proprietary UNITED STATES PHARMACOPEIA (Invoice included)			
MATERIALS & SUPPLIES	41	VCHR 992814	HENRY SCHEIN ANIMAL	Wright's Dip Stat Stain,			
MATERIALS & SUPPLIES	41	JE 55190110	SRI CHEM STORES	Itemized Cost			
MATERIALS & SUPPLIES	41	JE 55190136	SRI CHEM STORES	Itemized Cost			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Coagulation Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Urinalysis Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Urinalysis Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Coagulation Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Coagulation Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Urinalysis Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Coagulation Panel			
MATERIALS & SUPPLIES	41	JE 42190101	SRI CAL	Standard Urinalysis Panel			
				Total 41			

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
Proprietary Info					

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
SHIPPING & RECEIVING	48	JE 144190104	FEDEX	Shipping Cost	Itemized Cost
SHIPPING & RECEIVING	48	JE 144190104	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190101	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190102	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190105	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190104	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190104	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190104	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190104	FEDEX	Shipping Cost	
Total 48					

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
INTERNAL SERVICES	49	JE 41190101	ANIMAL CARE	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage	Itemized Cost		
INTERNAL SERVICES	49	JE 41190101	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41190101	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41190101	ANIMAL CARE	Room:SERVICE, Study:Dog METAB CAGES, ARR:12/18-12/20, P.I.:N/A, Type:Per Dog			
INTERNAL SERVICES	49	JE 41190102	ANIMAL CARE	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	JE 41190102	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41190103	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41190103	ANIMAL CARE	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	JE 41190103	ANIMAL CARE	Room:SERVICE, Study:METAB CAGES, ARR:1/4/19, P.I.:N/A, Type:Metabolism			
INTERNAL SERVICES	49	JE 41190104	ANIMAL CARE	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	JE 41190104	ANIMAL CARE	Room:SERVICE, Study:METAB CAGES, ARR:1/8/19, P.I.:N/A, Type:Metabolism			
INTERNAL SERVICES	49	JE 41190104	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	JE 41190105	ANIMAL CARE	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	JE 41190105	ANIMAL CARE	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
Total 49							
Total MATERIAL & SERVICES							

**INV0546582393-85314**

Issued on Friday, December 21, 2018 PST

Created on Friday, December 21, 2018 PST by aribasystem on behalf of Claire McFarlane

Header Level Information

ID : INV0546582393-85314
Supplier Invoice # : 0546582393
Invoice Date : Thursday, December 20, 2018 PST
Order : PO32382
Remit To ID : 0035077-B
Payment Terms : NET 30
Sold To : SRI INTERNATIONAL
Purchasing Unit : 001 - SRI International
Remit To Address : Sigma-Aldrich.
Invoice Source Document : Purchase Order

Invoice Summary

Base Amount	Itemized Cost
Discount	
Charges	
Taxes	
Gross Amount	

Treasury Special Instructions:

Buyer:

Supplier:

SIGMA ALDRICH CATALOG
Sigma-Aldrich, P.O. BOX 535182
ATLANTA, GA 30353-5182
United States
Contact: NO CONTACT NAME

Ship To:

SRI International, Email: AP@sri.com
333 Ravenswood Ave
Menlo Park, CA 94025-3493
United States

Bill To:

SRI International, Email: AP@sri.com
Send invoices to the following Email: AP@sri.com
Menlo Park, CA 94026-2203
United States

Project/WorkOrder:

Name: P25035.412 - Proprietary GLP RD Tox Rat**HEADER ITEM DETAILS**

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
	Total Item Tax				NoValue		Line Item Costs	Sales tax

Full Description: Total Item Tax

Commodity Code:

Partitioned Commodity Code:

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
0	Shipping Charges - header level		each	1	NoValue		Line Item Costs	Shipping

Full Description: Shipping Charges - header level

Commodity Code:

Partitioned Commodity Code:

LINE ITEM DETAILS

No.	Description	Part Number	Unit	Qty	Need-By Date	Unit Price	Amount	Matched To
	Proprietary Info							

Full Description: Proprietary UNITED STATES PHARMACOPEIA (U

Commodity Code: LABORATORY, Observation, Test and Measurement Equipment and Supplies

Partitioned Commodity Code: 41 - Materials & Supplies, Books

Redacted by agreement

Redacted by agreement

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

SRI BILL

DATE	STUDY #	Description	Time	Hours	Total
Dec 10, 2018	M 398-18	134 rats	8:00-12:00	3 hr	Itemized Cost
.TOTAL					

Please remit

Proprietary Info

OK TO PAY

CHARGE TO

P25035.412 -

Itemized Cost

PO # 98-000258

Redacted by agreement

SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0007

Invoice Date: 3/12/2019

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 1/27/2019 through 2/23/2019

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 192,789.78

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

Obtained via FOIA by White Coat Waste Project



CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p> <p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 50px; width: 150px; margin: 10px 0;">Redacted by agreement</div> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	(c) Invoice/Financing Request No:	P25035-0007
	(d) Date Invoice Prepared:	3/12/2019
	(e) Contract No. and Order No. (if applicable)	HHSN2722014000061 / HHSN27200008
	(f) Contract Title:	Pharmacology and Toxicology Studies of Proprietary Info and Proprietary and to Support the Development of Mitochondrial Toxicity Assays
	(g) Current Contract Period of Performance:	6/15/2018-6/14/2019
	(h) Total Estimated Cost of Contract/Order:	\$1,688,333
	(i) Total Fixed-Fee (if applicable):	\$118,182
	(j) Two-Way Match: Three-Way Match:	X
	(k) Office of Acquisition:	National Institute of Allergy and Infectious Diseases
	(l) Central Point of Distribution:	NIAIDOAInvoices@niaid.nih.gov

(m) This Invoice/financing request represents reimbursable costs for the period from: 1/27/2019 to 2/23/2019

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor	Labor Hours		Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

SRI INTERNATIONAL

Billing Number: 0007
Control Number: INV-0000353825
Billing Group: B

Invoice Date: 03/12/2019

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN272201400006I/HHSN27200008

Cost:

Fee:

Total:

Cumulative Amount Billed:

Funded Value

Itemized Cost

\$1,806,515.00

Project Number: P25035
Terms: NET 30

Itemized Cost

Billing Period From: 01/27/2019

To: 02/23/2019

Tax ID Number: 94-1160950

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
OVERTIME PREMIUM		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Total		

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 2, 2019
NATIONAL INSTITUTES OF HEALTH

Labor	Name	Rate	Hours	Amount
		Labor rate	Labor Hours	Labor Costs
Redacted by agreement	Total Middle Managers			
	Total Entry Level Managers			
	Total Advanced Professionals			
	Total Experienced Professionals			
	Total Intermediate Professionals			
	Total Jr Professional			
	Total Senior Technicians			
	Total Technicians			
	Total Jr Technicians			
	TOTAL SRI LABOR			

Description	Obi CD / Inl / Trans No	Name	Trans Description	Amount
Proprietary Info				

Description	Proprietary Info
<p>1. Project Overview:</p> <ul style="list-style-type: none"> Project Name: [Redacted] Client: [Redacted] Start Date: [Redacted] End Date: [Redacted] 	<p>1. Project Overview:</p> <ul style="list-style-type: none"> Project Name: [Redacted] Client: [Redacted] Start Date: [Redacted] End Date: [Redacted]

MATERIALS & SERVICES							
Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
MATERIALS & SUPPLIES	41	55190215	SRI CHEM STORES	12 x 15 PO;Qty 25;\$11;Doc#379673			Itemized Cost
MATERIALS & SUPPLIES	41	55190215	SRI CHEM STORES	BAG BIO SM;Qty 20;\$21;Doc#379673			
				BAG BIOHAY;Qty 15;\$30;Doc#379675			
MATERIALS & SUPPLIES	41	55190215	SRI CHEM STORES	ALCOHOL ET;Qty 1;\$12;Doc#379682 50ML DISPO;Qty 2;\$41;Doc#379684 15ML DISPO;Qty 1;\$21;Doc#379684 680052 MIC;Qty 1;\$72;Doc#379684 OPTIMA PAP;Qty 2;\$5;Doc#379684 GLOVES NIT;Qty 2;\$32;Doc#379684 BAG BIOHAY;Qty 5;\$10;Doc#379811 680052 MIC;Qty 1;\$72;Doc#379811 15ML DISPO;Qty 1;\$22;Doc#379811 			
MATERIALS & SUPPLIES	41	55190232	SRI CHEM STORES				
MATERIALS & SUPPLIES	41	42190201	CAL SRI-19-004	Standard Urinalysis Panel			
MATERIALS & SUPPLIES	41	42190201	CAL SRI-19-005	Standard Urinalysis Panel			
MATERIALS & SUPPLIES	41	42190201	CAL SRI-19-008	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	42190201	CAL SRI-19-008	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	42190201	CAL SRI-19-009	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	42190201	CAL SRI-19-009	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	42190202	CAL SRI-19-024	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	42190202	CAL SRI-19-024	Standard Coagulation Panel			
MATERIALS & SUPPLIES	41	42190202	CAL SRI-19-024	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	42190202	CAL SRI-19-025	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	42190202	CAL SRI-19-025	Standard Urinalysis Panel			
MATERIALS & SUPPLIES	41	42190202	CAL SRI-19-025	Standard Coagulation Panel			
MATERIALS & SUPPLIES	41	42190202	CAL SRI-19-025	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	59190201	ALLIANCE GAS	CD 50			
MATERIALS & SUPPLIES	41	59190201	ALLIANCE GAS	CD EX50			
MATERIALS & SUPPLIES	41	59190201	ALLIANCE GAS	CD OX40K			
MATERIALS & SUPPLIES	41	59190201	ALLIANCE GAS	CD OX40K			
MATERIALS & SUPPLIES	41	59190201	ALLIANCE GAS	CD OX40K			
MATERIALS & SUPPLIES	41	59190201	ALLIANCE GAS	CD OX40K			
MATERIALS & SUPPLIES	41	59190201	ALLIANCE GAS	CD OX40K			
MATERIALS & SUPPLIES	41	159190203	ALLIANCE GAS	GAS			
MATERIALS & SUPPLIES	41	159190203	ALLIANCE GAS	GAS			
MATERIALS & SUPPLIES	41	999190201	AMAZON	Eukanuba puppy canned diet			
MATERIALS & SUPPLIES	41	994266	AMSBIO LLC	2X Well Insert holder in a dee			
MATERIALS & SUPPLIES	41	994266	AMSBIO LLC	6X Alvetek Scaffold 6-well ins			
MATERIALS & SUPPLIES	41	994266	AMSBIO LLC	Alvetek Scaffold -well insert			
MATERIALS & SUPPLIES	41	993981	ATCC	Eagle's minimum essential			
MATERIALS & SUPPLIES	41	993981	ATCC	Fetal Bovine Serum (FBS)			
MATERIALS & SUPPLIES	41	993981	ATCC	RPMI-1640 Medium			
MATERIALS & SUPPLIES	41	994415	ATCC	Trypsin-EDTA solution 1X			
MATERIALS & SUPPLIES	41	993980	ATCC	Fetal bovine serum (FBS)			
MATERIALS & SUPPLIES	41	993980	ATCC	Iscove's modified dulbecc			
MATERIALS & SUPPLIES	41	993459	FISHER SCIENTIFIC CATALOG	PENICILLIN STREPTOMYCIN SOL			
MATERIALS & SUPPLIES	41	993721	FISHER SCIENTIFIC CATALOG	CELLTRACKER(TM) CM-DII S			
MATERIALS & SUPPLIES	41	993822	FISHER SCIENTIFIC CATALOG	HOECHST 33342 TRIHYDROCH			
MATERIALS & SUPPLIES	41	994458	SIGMA ALDRICH CATALOG	N,N-DIMETHYLFORMAMIDE, MOLECUL			

**SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH**

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
MATERIALS & SUPPLIES	41	994345	ULINE	4 - 1 Gallon Industrial Shippe	Itemized Cost
MATERIALS & SUPPLIES	41	993511	VWR INTERNATIONAL CATALOG	CENTRIFUGE TUBE PP 250ML CS102	
MATERIALS & SUPPLIES	41	993511	VWR INTERNATIONAL CATALOG	FILTER SYSTEM22UM 1L CS12	
MATERIALS & SUPPLIES	41	993511	VWR INTERNATIONAL CATALOG	FLASK,CANTED NECK 150CM2 CS50	
MATERIALS & SUPPLIES	41	993511	VWR INTERNATIONAL CATALOG	RACK, CENT BTL, POXGR,LG,250ML	
MATERIALS & SUPPLIES	41	993511	VWR INTERNATIONAL CATALOG	TUBE CENTRIFG POLYP 50ML CS500	
MATERIALS & SUPPLIES	41	993948	VWR INTERNATIONAL CATALOG	CELLSCRAPER 40CM HANDLE CS100	
MATERIALS & SUPPLIES	41	993664	VWR INTERNATIONAL CATALOG	VWR PIPET ASPIRATING 2ML CS200	
MATERIALS & SUPPLIES	41	993664	VWR INTERNATIONAL CATALOG	VWR PIPETTE SERO 10ML PR CS200	
MATERIALS & SUPPLIES	41	993664	VWR INTERNATIONAL CATALOG	VWR PIPETTE SERO 25ML PL CS200	
MATERIALS & SUPPLIES	41	993664	VWR INTERNATIONAL CATALOG	VWR PIPETTE SERO 5ML PR CS200	
Total 41					

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
SHIPPING & RECEIVING	48	144190201	FEDEX	Shipping Cost	Itemized Cost
SHIPPING & RECEIVING	48	144190201	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190201	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190201	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190201	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	144190204	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	993981	ATCC	Shipping Cost	
SHIPPING & RECEIVING	48	994415	ATCC	Shipping Cost	
SHIPPING & RECEIVING	48	993980	ATCC	Shipping Cost	
SHIPPING & RECEIVING	48	994345	ULINE	Shipping Cost	
SHIPPING & RECEIVING	48	993511	VWR INTERNATIONAL CATALOG	Shipping Cost	
SHIPPING & RECEIVING	48	993948	VWR INTERNATIONAL CATALOG	Shipping Cost	
SHIPPING & RECEIVING	48	993664	VWR INTERNATIONAL CATALOG	Shipping Cost	
Total 48					

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
INTERNAL SERVICES	49	41190201	ANIMAL CARE CHARGESP1 WK4 2019	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			Itemized Cost
INTERNAL SERVICES	49	41190201	ANIMAL CARE CHARGESP1 WK4 2019	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	41190202	ANIMAL CARE CHARGESP2 WK1 2019	Room:K ARUN, Study:M397-18, ARR:8/30/18, P.I.:NG, Type:Regulated			
INTERNAL SERVICES	49	41190202	ANIMAL CARE CHARGESP2 WK1 2019	Room:SERVICE, Study:M397-18, ARR:N/A, P.I.:1/30 & 1/31, Type:Per Dog			
INTERNAL SERVICES	49	41190202	ANIMAL CARE CHARGESP2 WK1 2019	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	41190203	ANIMAL CARE CHARGESP2 WK2 2019	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
INTERNAL SERVICES	49	41190204	ANIMAL CARE CHARGESP2 WK3 2019	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
Total 49							
Total MATERIAL & SERVICES							

SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0008

Invoice Date: 4/8/2019

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 2/24/2019 through 3/23/2019

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 78,095.01

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

4/8/19

[Handwritten signature]
4/8/19

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p> <p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 40px; width: 150px; margin: 10px 0;">Redacted by agreement</div> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	(c) Invoice/Financing Request No:	P25035-0008
	(d) Date Invoice Prepared:	4/8/2019
	(e) Contract No. and Order No. (if applicable)	HHSN2722014000061 / HHSN27200008
	(f) Contract Title:	Pharmacology and Toxicology Studies of Proprietary Info and Proprietary and to Support the Development of Mitochondrial Toxicity Assays
	(g) Current Contract Period of Performance:	6/15/2018-6/14/2019
	(h) Total Estimated Cost of Contract/Order:	\$1,688,333
	(i) Total Fixed-Fee (if applicable):	\$118,182
	(j) Two-Way Match: Three-Way Match:	X
	(k) Office of Acquisition:	National Institute of Allergy and Infectious Diseases
	(l) Central Point of Distribution:	NIAIDOAInvoices@niaid.nih.gov

(m) This Invoice/financing request represents reimbursable costs for the period from: 2/24/2019 to 3/23/2019

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor		Labor Hours	Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

SRI INTERNATIONAL

Billing Number: 0008
Control Number: INV-0000355042
Billing Group: B

Invoice Date: 04/08/2019

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN272201400006I/HHSN27200008

Funded Value
Itemized Cost
\$1,806,515.00

Project Number: P25035
Terms: NET 30

Cumulative Amount Billed: Itemized Cost

Tax ID Number: 94-1160950

Billing Period From: 02/24/2019
To: 03/23/2019

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
OVERTIME PREMIUM		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Total		

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 3, 2019
NATIONAL INSTITUTES OF HEALTH

Labor	Name	Rate	Hours	Amount
Redacted by agreement		Labor rate	Labor Hours	Labor Costs
	Total Directors			
	Total Middle Managers			
	Total Entry Level Managers			
	Total Advanced Professionals			
	Total Experienced Professionals			
	Total Intermediate Professionals			
	Total Jr Professional			
	Total Senior Technicians			
	Total Technicians			
	Total Jr Technicians			
	TOTAL SRI LABOR			

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
OVERTIME PREMIUM	Labor		Redacted by	LD Posting	Labor
OVERTIME PREMIUM	Hours		agreement	LD Posting	Costs
OVERTIME PREMIUM				LD Posting	
				Labor Hours	
				Total OVERTIME PREMIUM	

MATERIALS & SERVICES

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
MATERIALS & SUPPLIES	41	JE 42190302	SRI CAL	Standard Chemistry Panel	Itemized Cost		
MATERIALS & SUPPLIES	41	JE 42190302	SRI CAL	Standard Urinalysis Panel			
MATERIALS & SUPPLIES	41	JE 42190302	SRI CAL	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	JE 42190302	SRI CAL	Standard Hematology Panel			
MATERIALS & SUPPLIES	41	JE 42190302	SRI CAL	Standard Chemistry Panel			
MATERIALS & SUPPLIES	41	VCHR 995985	ABCAM INC	Caspase 3 Assay Kit (Colorimet...)			
MATERIALS & SUPPLIES	41	JE 42190302	SRI CAL	Invoice 1727272SRI001 attached			
MATERIALS & SUPPLIES	41	JE 42190302	SRI CAL	Standard Urinalysis Panel			
MATERIALS & SUPPLIES	41	VCHR 995985	ABCAM INC	ATP Assay Kit			
MATERIALS & SUPPLIES	41	VCHR 995985	ABCAM INC	Invoice 1727272SRI001 attached			
MATERIALS & SUPPLIES	41	VCHR 995985	ABCAM INC	Human ATP Synthase ELISA Kit (
MATERIALS & SUPPLIES	41	VCHR 995985	ABCAM INC	Human Complex IV ELISA Kit			
MATERIALS & SUPPLIES	41	VCHR 995985	ABCAM INC	Human Cyt C Reductase ELISA Ki			
MATERIALS & SUPPLIES	41	VCHR 995985	ABCAM INC	Human NADH dehydrogenase ELISA			
MATERIALS & SUPPLIES	41	VCHR 997382	VWR INTERNATIONAL CATALOG	Invoice 1727272SRI001 attached			
MATERIALS & SUPPLIES	41	VCHR 997382	VWR INTERNATIONAL CATALOG	FLASK 175CM W VENT CAP CS50			
MATERIALS & SUPPLIES	41	VCHR 997382	VWR INTERNATIONAL CATALOG	FLASK,CANTED NECK 150CM2 CS50			
				Total 41			
Description	Obj CD	Jnl / Trans No	Name	Trans Description			
SHIPPING & RECEIVING	48	JE 144190302	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	VCHR 997382	VWR INTERNATIONAL CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	JE 144190303	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	JE 144190303	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	JE 144190303	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	VCHR 995985	ABCAM INC	Shipping Cost			
				Total 48			
Description	Obj CD	Jnl / Trans No	Name	Trans Description			
INTERNAL SERVICES	49	41190301	ANIMAL CARE CHARGESP2 WK4 2019	Room:SERVICE, Study:M398-18 GLP, ARR:2/20&2/21, P.I.:METAB CAGES, Type:Metabolism			
INTERNAL SERVICES	49	41190301	ANIMAL CARE CHARGESP2 WK4 2019	Room:TM163, Study:M398-18 GLP, ARR:12/3/18, P.I.:IL/KGO, Type:Rat cage			
				Total 49			
				Total MATERIAL & SERVICES			



Sales invoice (page 1 of 1)

AP AP SRI INTERNATIONAL PO Box 2203 MENLO PARK CA 94026 United States	Invoice Number	1727272-SRI001	Date: 27 Feb, 2019
	Customer	Redacted by agreement	Redacted by agreement
	Billing Contact	AP	
	Purchase Order Number	PO34657	
	Order Reference Number	3294947	

Quantity	Product	Lot No.	Description	Unit Price	Unit Dis.	Total
4 x 100tests	ab39401	GR3233216	Caspase-3 Assay Kit (Colorimetri...	Itemized Cost		
4 x 100tests	ab83355	GR3254917	ATP Assay Kit (Colorimetric/Fluo...			
1 x 1x 96 tests	ab124537	GR3228553	Human Cyt C Reductase ELISA Kit ...			
2 x 1x 96 tests	ab124539	GR3226748	Human ATP Synthase ELISA Kit (Co...			
4 x 1x 96 tests	ab178011	GR3228475	Human NADH dehydrogenase ELISA K...			
1 x 1x 96 tests	ab179880	GR3223530	Human Complex IV ELISA Kit			

**Products to be used for in vitro scientific research use only. For laboratory use only.
Not for diagnostic or therapeutic purposes or for use on humans or live animals.**

Payment Terms:

Payment is due 30 days from invoice date and should be made via check or bank transfer quoting all invoices to be paid.

If making payment by transfer please note that the customer is responsible for paying ALL bank charges

Please email your payment details to [us.wirepayments@abcam.com](mailto:wirepayments@abcam.com) once payment has been made.

Please mail checks to:

Abcam Inc
PO Box 3460
Boston, MA 02241-3460

Direct bank payments:

A/C No: 9421204512
Bank of America
International Corporate Business
3rd Floor
1185 Avenue of the Americas
New York, NY10036
Swift code BOFAUS3N
Wire Transfer: ABA number 021200339
ACH: ABA no. 021 000 322

Total Goods:	US\$	Itemized Cost
Total Discount:	US\$	
Freight and/or Packing:	US\$	
Total Payable:	US\$	

Abcam Inc. 1 Kendall Square, Suite B2304 Cambridge, MA 02139-1517 USA Toll Free Tel: (888) 77-ABCAM (22226) Fax: (877) 774-8286
International Tel: (617) 225-2272 Fax: (617) 577-4201 www.abcam.com

SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0009

Invoice Date: 5/10/2019

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 3/24/2019 through 4/20/2019

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 85,966.65

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

5/10/19

Obtained via FOIA by White Coat Waste Project

mg
5/10/19

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p>	<p>(c) Invoice/Financing Request No: <u>P25035-0009</u></p> <p>(d) Date Invoice Prepared: <u>5/10/2019</u></p> <p>(e) Contract No. and Order No. <u>HHSN2722014000061 /</u> (if applicable) <u>HHSN27200008</u></p> <p>(f) Contract Title: <u>Pharmacology and Toxicology Studies of</u> <u>Proprietary Info</u> <u>Propriet</u> <u>Proprietary</u> <u>and</u> <u>Proprietary</u> <u>and to Support the Development of</u> <u>Mitochondrial Toxicity Assays</u></p> <p>(g) Current Contract Period of Performance: <u>6/15/2018-6/14/2019</u></p> <p>(h) Total Estimated Cost of Contract/Order: <u>\$1,688,333</u></p> <p>(i) Total Fixed-Fee (if applicable): <u>\$118,182</u></p> <p>(j) Two-Way Match: <u>X</u> Three-Way Match:</p> <p>(k) Office of Acquisition: <u>National Institute of Allergy and Infectious Diseases</u></p> <p>(l) Central Point of Distribution: <u>NIAIDOInvoices@niaid.nih.gov</u></p>
<p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 40px; width: 100%; margin-top: 10px;"></div> <p>Redacted by agreement</p> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	

(m) This Invoice/financing request represents reimbursable costs for the period from: 3/24/2019 to 4/20/2019

Expenditure Category*	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion	Contract Amount	Variance**
	Negotiated	Actual	(n) Current	(o) Cumulative			
A	B	C	D	E	F	G	H
(p) Direct Costs:							
(1) Direct Labor	Labor Hours		Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

SRI INTERNATIONAL

Billing Number: 0009
Control Number: INV-0000356814
Billing Group: B

Invoice Date: 05/10/2019

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN272201400006I/HHSN27200008

Cost:

Fee:

Total:

Cumulative Amount Billed:

Funded Value

Itemized Cost

\$1,806,515.00

Project Number: P25035
Terms: NET 30

Billing Period From: 03/24/2019

To: 04/20/2019

Tax ID Number: 94-1160950

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
OVERTIME PREMIUM		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Total		

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 4, 2019
NATIONAL INSTITUTES OF HEALTH

Labor	Name	Rate	Hours	Amount
Redacted by agreement		Labor rate	Labor Hours	Labor Costs
	Total Middle Managers			
	Total Entry Level Managers			
	Total Advanced Professionals			
	Total Experienced Professionals			
	Total Intermediate Professionals			
	Total Jr Professional			
	Total Senior Technicians			
	Total Jr Technicians			
	TOTAL SRI LABOR			

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

MATERIALS & SERVICES

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
MATERIALS & SUPPLIES	41	VCHR 998469	SIGMA ALDRICH CATALOG	IN VITRO TOXICOLOGY ASSAY KIT,	Itemized Cost		
MATERIALS & SUPPLIES	41	VCHR 999622	ABCAM INC	Human Cyt C Reductase ELISA Ki			
MATERIALS & SUPPLIES	41	VCHR 999622	ABCAM INC	Human Complex IV ELISA Kit			
MATERIALS & SUPPLIES	41	VCHR 999622	ABCAM INC	Human ATP Synthase ELISA Kit			
MATERIALS & SUPPLIES	41	JE 55190446	SRI CHEM STORES	15ML DISPO;Qty 2;\$47;Doc#380307 GLOVES NIT;Qty 1;\$26;Doc#380307			
MATERIALS & SUPPLIES	41	VCHR 999234	SIGMA ALDRICH CATALOG	HS F5 3UM 5CMX4.0MM DISCOVERY HPLC			
MATERIALS & SUPPLIES	41	VCHR 998676	FISHER SCIENTIFIC CATALOG	OPTIMA LCMS ACETIC ACID			
MATERIALS & SUPPLIES	41	VCHR 999312	BIOIVT	3 unique female lots beagle pl			
MATERIALS & SUPPLIES	41	VCHR 999312	BIOIVT	3 lots male beagle plasma 3 x			
MATERIALS & SUPPLIES	41	VCHR 999310	AGILENT TECHNOLOGIES INC	Agilent Polaris 3 C18-Ether 50			
MATERIALS & SUPPLIES	41	VCHR 999312	BIOIVT	Beagle plasma, pooled K2 EDTA			
Total 41							
Description	Obj CD	Jnl / Trans No	Name	Trans Description			
SHIPPING & RECEIVING	48	VCHR 999310	AGILENT TECHNOLOGIES INC	Shipping Cost			
SHIPPING & RECEIVING	48	VCHR 999312	BIOIVT	Shipping Cost			
SHIPPING & RECEIVING	48	JE 144190404	FEDEX	Shipping Cost			
Total 48							
Total MATERIAL & SERVICES							

SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0010

Invoice Date: 6/13/2019

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 4/21/2019 through 5/18/2019

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 219,144.08

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in
SECTION I of the referenced contract.

Redacted by agreement

6/13/19

SRI INTERNATIONAL

Billing Number: 0010
Control Number: INV-0000358197
Billing Group: B

Invoice Date: 06/13/2019

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN272201400006I/HHSN27200008

Cost: Funded Value
Fee: Itemized Cost
Total: \$1,806,515.00

Project Number: P25035
Terms: NET 30

Cumulative Amount Billed: Itemized Cost

Tax ID Number: 94-1160950

Billing Period From: 04/21/2019
To: 05/18/2019

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
OVERTIME PREMIUM		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Subtotal		
Less Cost Over Ceiling		
Less Fee Over Ceiling		
Invoice Total		

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p> <p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 50px; width: 150px; margin: 10px 0;">Redacted by agreement</div> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	<p>(c) Invoice/Financing Request No: P25035-0010</p> <p>(d) Date Invoice Prepared: 6/13/2019</p> <p>(e) Contract No. and Order No. HHSN2722014000061 / (if applicable) HHSN27200008</p> <p>(f) Contract Title: <u>Pharmacology and Toxicology Studies of</u> <u>Proprietary Info</u> <u>Propriet</u> <u>Proprietary</u> and <u>Proprietary</u> and to Support the Development of <u>Mitochondrial Toxicity Assays</u></p> <p>(g) Current Contract Period of Performance: 6/15/2018-6/14/2019</p> <p>(h) Total Estimated Cost of Contract/Order: \$1,688,333</p> <p>(i) Total Fixed-Fee (if applicable): \$118,182</p> <p>(j) Two-Way Match: X Three-Way Match:</p> <p>(k) Office of Acquisition: National Institute of Allergy and Infectious Diseases</p> <p>(l) Central Point of Distribution: NIAIDOAInvoices@niaid.nih.gov</p>
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(m) This Invoice/financing request represents reimbursable costs for the period from: 4/21/2019 to 5/18/2019

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor	Labor Hours		Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
Less Cost Over Ceiling							
Less Fee Over Ceiling							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

**Line (o)9 Purchased Labor: SRI uses budgeted project labor to buy purchased labor when we do not have the staff available to perform necessary work. Purchased Labor is temporary staff.

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 5, 2019
NATIONAL INSTITUTES OF HEALTH

Labor

Name

Rate

Hours

Amount

Redacted by agreement

Total Directors

Total Entry Level Managers

Total Advanced Professionals

Total Experienced Professionals

Total Intermediate Professionals

Total Jr Professional

Total Senior Technicians

Total Jr Technicians

TOTAL SRI LABOR

Labor rate

Labor Hours

Labor Costs

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

MATERIALS & SERVICES

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Qty	Rate	Amount
MATERIALS & SUPPLIES	41	VCHR 1000757	SIGMA ALDRICH CATALOG	Proprietary			Itemized Cost
MATERIALS & SUPPLIES	41	VCHR 1001496	VWR INTERNATIONAL CATALOG	COMBITIP 10ML ORANGE CS100			
MATERIALS & SUPPLIES	41	VCHR 1000540	PHENOMENEX INC	Synergi polar RP 100 x 2.0, 4u			
MATERIALS & SUPPLIES	41	VCHR 1001496	VWR INTERNATIONAL CATALOG	COMBITIP 0.5ML PURPLE CS100			
MATERIALS & SUPPLIES	41	JE 55190522	SRI CHEM STORES	Itemized Cost			
MATERIALS & SUPPLIES	41	JE 55190522	SRI CHEM STORES				
MATERIALS & SUPPLIES	41	VCHR 1000489	CHARLES RIVER	CD RAT MALE 0251-0275 GRAMS			
MATERIALS & SUPPLIES	41	VCHR 1001496	VWR INTERNATIONAL CATALOG	COMBITIP 2.5ML GREEN CS100			
MATERIALS & SUPPLIES	41	VCHR 1000552	ABCAM INC	Human Complex IV ELISA Kit			
MATERIALS & SUPPLIES	41	VCHR 1000537	PHENOMENEX INC	Synergi polar RP 100 x 2.0, 4u			
MATERIALS & SUPPLIES	41	VCHR 1001496	VWR INTERNATIONAL CATALOG	COMBITIP 1ML YELLOW CS100			
MATERIALS & SUPPLIES	41	JE 55190518	SRI CHEM STORES	Itemized Cost			
				Total 41			
Description	Obj CD	Jnl / Trans No	Name	Trans Description			
OUTSIDE SERVICES	42	PO98-000258	Proprietary Info	OPHTHALMOLOGIC EXAMS (Vendor invoice attached)			
OUTSIDE SERVICES	42	PO29164		EPL Histology and Pathology Services (Vendor invoice attached)			
OUTSIDE SERVICES	42	PO29164		EPL Histology and Pathology Services (Vendor invoice attached)			
				Total 42			
Description	Obj CD	Jnl / Trans No	Name	Trans Description			
SHIPPING & RECEIVING	48	VCHR 1002092	UPS	DOMESTIC FREIGHT			
SHIPPING & RECEIVING	48	VCHR 1000656	UPS	DOMESTIC FREIGHT			
SHIPPING & RECEIVING	48	VCHR 1001496	VWR INTERNATIONAL CATALOG	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 1000537	PHENOMENEX INC	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 1000540	PHENOMENEX INC	Handling Charge - header level			
SHIPPING & RECEIVING	48	VCHR 1000822	Proprietary Info	Shipping Cost			
SHIPPING & RECEIVING	48	JE 144190502	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	JE 144190503	FEDEX	Shipping Cost			
SHIPPING & RECEIVING	48	VCHR 1001489	Proprietary Info	Shipping Cost			
SHIPPING & RECEIVING	48	VCHR 1002092	UPS	DOMESTIC FREIGHT			
SHIPPING & RECEIVING	48	JE 144190501	FEDEX	Shipping Cost			
				Total 48			
				Total MATERIAL & SERVICES			

Invoice Date: April 19, 2019

Received on: April 22, 2019

To: Accounting, AG022

From: Redacted by agreement

Subject: Proprietary Info Invoice Number: 30887

Please charge the following projects the value under the 'Amount' column.
In addition, please send me an **email** (minh.bui@sri.com) when the check is mailed out.
Please include invoice, check # and amount.

<u>Study Number</u>	<u>Project Number</u>	<u>PA</u>	<u>Study Director</u>	<u>Invoice #</u>	<u>Amount</u>
M398-18	P25035.412	Redacted by agreement		Itemized Cost	

Invoice Total	Itemized Cost
----------------------	----------------------------

Funds remaining in Blanket Order: **PO29164**

Itemized Cost

APPROVED FOR PAYMENT

Charge Pay as per above

Project Leader Approval: _____

Proprietary Info

SRI International
Accounts Payable (email ap@sri.com)
Bldg. PN 197
333 Ravenswood Ave.
Menlo Park CA 94025-3493

INVOICE NO.: 30887
INVOICE DATE: April 19, 2019

CONTRACT/P.O.: 29164
REFERENCE: M398-18
EPL PROJECT: 748-120

DESCRIPTION	TOTAL
-------------	-------

Histology/Pathology Services:

	Quantity	Unit Price	Current Amount
Histology	Itemized Cost		
Pathology			
Histology, Target Tissues			
Pathology, Target Tissues			
Total Amount Now Due:			Itemized Cost

ACCOUNT INFORMATION HAS CHANGED:

Domestic Wire Transfers:

Bank Name: United Bank
Bank Address: 14048 Parkeast Circle
Suite 100
Chantilly, VA 20151

Bank Telephone: Proprietary Info
ABA Routing No: Proprietary Info
Account#: Proprietary Info
Account Name: Proprietary Info

Proprietary Info

SRI International
Accounts Payable (email ap@sri.com)
Bldg. PN 197
333 Ravenswood Ave.
Menlo Park CA 94025-3493

INVOICE NO.: 30853
INVOICE DATE: March 31, 2019

CONTRACT/P.O.: 29164
REFERENCE: M397-18
EPL PROJECT: 748-118

DESCRIPTION

TOTAL

Histology/Pathology Services:

	Quantity	Unit Price	Current Amount
Histology (Includes 3% Discount)	Itemized Cost		
Pathology			
Histology, Target tissues (Includes 3% Discount)			
Pathology, Target tissues			
Total Amount Now Due:			Itemized Cost

ACCOUNT INFORMATION HAS CHANGED:

Domestic Wire Transfers:

Bank Name: United Bank
Bank Address: 14048 Parkeast Circle
Suite 100
Chantilly, VA 20151

Bank Telephone: 800-615-0112
ABA Routing No: Proprietary Info
Account#:
Account Name:

Invoice Date: March 31, 2019

Received on: April 3, 2019

To: Accounting, AG022

From: Minh Bui, ext 3289

Subject: EPL Pathology Service Invoice Number: 30853

Please charge the following projects the value under the 'Amount' column.
In addition, please send me an **email** (minh.bui@sri.com) when the check is mailed out.
Please include invoice, check # and amount.

<u>Study Number</u>	<u>Project Number</u>	<u>PA</u>	<u>Study Director</u>	<u>Invoice #</u>	<u>Amount</u>
M397-18	P25035.411	Redacted by agreement		Itemized Cost	

Invoice Total

Itemized Cost

Funds remaining in Blanket Order: **PO29164**

Itemized Cost

APPROVED FOR PAYMENT

Charge Pay as per above

Redacted by agreement

Project Leader Approval:

Redacted by
agreement

From: Account Payable
Sent: Wednesday, May 01, 2019 5:30 AM
To: Redacted by
Subject: FW: Proprietary Info Invoice 30853 (4-30-19), ready for payment
Attachments: Proprietary Info Invoice 30853 (M397).pdf

From: Redacted by agreement
Sent: Tuesday, April 30, 2019 5:11 PM
To: Account Payable <account.payable@sri.com>
Subject: Proprietary Info Invoice 30853 (4-30-19), ready for payment

Hello AP,

The attached invoice has been reviewed and approved, please process it for payment via EASY BUY. Thank you.

Regards

Redacted by

Project Manager, Biosciences
SRI International, PS311
333 Ravenswood Avenue
Menlo Park, CA 94025

Redacted by agreement

www.sri.com/biosciences

SRI Biosciences

A DIVISION OF SRI INTERNATIONAL

This email and its attachments are confidential.

If you receive this email in error, please delete it and notify the sender. Thank you.

Redacted by agreement

Redacted by agreement

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

SRI BILL

DATE	STUDY #	Description	Time	Hours	Total Itemized Cost
Jan 7, 2019	M 398-18	129 rats	8:00-11:00	3 hr	
TOTAL					

Please remit

Redacted by agreement

OK TO PAY

CHARGE TO P25035.4/2

PO# 98-000258

Redacted by agreement

1/22/19

SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0011

Invoice Date: 7/11/2019

Contract No: HHSN272201400006I / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 5/19/2019 through 6/15/2019

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 87,977.03

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in SECTION I of the referenced contract.

Redacted by agreement

7/11/19

Obtained via FOIA by White Coat Waste Project

SRI INTERNATIONAL

Billing Number: 0011
Control Number: INV-0000359505
Billing Group: B

Invoice Date: 07/11/2019

Bill To:
NATIONAL INSTITUTES OF HEALTH
OFFICE OF FINANCIAL MANAGEMENT
COMMERCIAL ACCOUNTS
2115 E. JEFFERSON ST., RM 4B-432 MSC8500
BETHESDA, MD 20892-8500

Remit To:
SRI International
P.O. Box 2767
Cage Code
03652

Menlo Park, CA 94025-2767

Inquiries: Redacted by agreement

Customer Number: 14094
Prime Contract Number: HHSN272201400006I/HHSN27200008

Cost: Funded Value
Itemized Cost

Fee: Total: \$1,926,553.00
Itemized Cost

Project Number: P25035
Terms: NET 30

Cumulative Amount Billed:

Tax ID Number: 94-1160950

Billing Period From: 05/19/2019
To: 06/15/2019

	Current Amount	Cumulative Amount
TECH-ONSITE SALARIES	Itemized Cost	
TECH-ONSITE BENEFITS		
TECH PURCH LBR		
TECH-ONSITE RES OVHD		
OVERTIME PREMIUM		
MATERIAL & SERVICES		
SUPP BURD BEGIN 1/92		
G&A BEGIN 1/92		
COST CLAIMED		
FEE EARNED		
FEE CLAIMED		
Invoice Subtotal		
Less Cost Over Ceiling		
Less Fee Over Ceiling		
Invoice Total		

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p> <p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 40px; width: 150px; margin: 10px 0;">Redacted by agreement</div> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	(c) Invoice/Financing Request No:	P25035-0011
	(d) Date Invoice Prepared:	7/11/2019
	(e) Contract No. and Order No. (if applicable)	HHSN2722014000061 / HHSN27200008
	(f) Contract Title:	Pharmacology and Toxicology Studies of Proprietary Info Proprietary Info to Support the Development of Mitochondrial Toxicity Assays
	(g) Current Contract Period of Performance:	6/15/2018-11/30/2019
	(h) Total Estimated Cost of Contract/Order:	\$1,808,371
	(i) Total Fixed-Fee (if applicable):	\$118,182
	(j) Two-Way Match: Three-Way Match:	X
	(k) Office of Acquisition:	National Institute of Allergy and Infectious Diseases
	(l) Central Point of Distribution:	NIAIDOAInvoices@niaid.nih.gov

(m) This Invoice/financing request represents reimbursable costs for the period from: 5/19/2019 to 6/15/2019

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor	Labor Hours		Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
Less Cost Over Ceiling							
Less Fee Over Ceiling							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 6, 2019
NATIONAL INSTITUTES OF HEALTH

Labor	Name	Rate	Hours	Amount
Redacted by agreement		Labor rate	Labor Hour	Labor Costs
	Total Directors			
	Total Entry Level Managers			
	Total Advanced Professionals			
	Total Experienced Professionals			
	Total Intermediate Professionals			
	Total Jr Professional			

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
Proprietary Info					Itemized Cost
MATERIALS & SERVICES					
Description	Obj CD	Jnl / Trans No	Name	Trans Description	
MATERIALS & SUPPLIES	41	VCHR 1002628	BIOIVT	Sprague Dawley Rat Plasma K2ED	
MATERIALS & SUPPLIES	41	VCHR 1003531	ABCAM INC	Human NADH dehydrogenase ELISA	
MATERIALS & SUPPLIES	41	VCHR 1002635	BIOIVT	Sprague Dawley Rat Plasma, poo	
MATERIALS & SUPPLIES	41	JE 55190613	SRI CHEM STORES	Itemized Cost	
MATERIALS & SUPPLIES	41	JE 55190638	SRI CHEM STORES		
MATERIALS & SUPPLIES	41	VCHR 1003531	ABCAM INC	Human Complex IV ELISA Kit (ab	
MATERIALS & SUPPLIES	41	JE 999190601	CELL BIOLABS INC	OXISELECT KITS	
MATERIALS & SUPPLIES	41	VCHR 1003640	US PHARMACOEPIA	Proprieta 15 mg	
MATERIALS & SUPPLIES	41	VCHR 1004714	BIOIVT	K2 EDTA Dog Whole Blood, poole	
MATERIALS & SUPPLIES	41	VCHR 1003531	ABCAM INC	Human Cyt C Reductase ELISA Ki	
MATERIALS & SUPPLIES	41	VCHR 1003442	BIOIVT	Rat Whole Blood, K2 EDTA, pool	
MATERIALS & SUPPLIES	41	VCHR 1003556	FISHER SCIENTIFIC CATALOG	OPTIMA LCMS ACETIC ACID	
MATERIALS & SUPPLIES	41	VCHR 1004712	BIOIVT	K2 EDTA Dog Plasma, pooled, 10	
MATERIALS & SUPPLIES	41	JE 55190613	SRI CHEM STORES	Itemized Cost	
MATERIALS & SUPPLIES	41	JE 55190626	SRI CHEM STORES		
MATERIALS & SUPPLIES	41	VCHR 1002628	BIOIVT	Sprague Dawley Rat Plasma K2ED	
Total 41					
Description	Obj CD	Jnl / Trans No	Name	Trans Description	
SHIPPING & RECEIVING	48	VCHR 1002635	BIOIVT	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190602	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190603	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 1004714	BIOIVT	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 1004712	BIOIVT	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 1004726	UPS	DOMESTIC FREIGHT	
SHIPPING & RECEIVING	48	JE 144190605	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 1003531	ABCAM INC	Shipping Cost	
SHIPPING & RECEIVING	48	JE 999190601	CELL BIOLABS INC	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190605	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190605	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190605	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 1003442	BIOIVT	Shipping Cost	
Total 48					
Total MATERIAL & SERVICES					

SRI INTERNATIONAL
INVOICE/FINANCING REQUEST

National Institutes of Health
Office of Financial Management
Commercial Accounts
2115 East Jefferson Street, Room 4B-432, MSC 8500
Bethesda, MD 20892-8500

SRI International
333 Ravenswood Avenue
Menlo Park, CA 94025

Treasury Department
650-859-4756
treasuryops@sri.com

TIN: 94-1160950
DUNS: 00-923-2752

Invoice No: P25035-0012

Invoice Date: 7/31/2019

Contract No: HHSN2722014000061 / HHSN27200008

Contract Title: Pharmacology and Toxicology Studies of Proprietary Info Support the
Development of Mitochondrial Toxicity Assays

Effective Date: 6/15/2018 - 6/14/2019

Total Estimated Cost: \$1,688,333.00

Total Fixed Fee: \$118,182.00

Two Way Match: X

Office of Acquisitions: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Central Point of Distribution: NIAIDOA Invoices

This invoice/financing request represents reimbursable costs from 6/16/2019 through 7/13/2019

Forwarded From Attached Continuation Sheet-Total Amount Due \$ 32,060.97

I hereby certify that the salaries charged in this invoice are in compliance with HHSAR Clause 352.231-70, Salary Rate Limitation in SECTION I of the referenced contract.

Redacted by agreement

7/31/19

Obtained via FOIA by White Coat Waste Project

WCC
7/31/19

CONTRACT FINANCIAL REPORT

<p>(a) Designated Billing Office Name and Address: National Institutes of Health Office of Financial Management Commercial Accounts 2115 East Jefferson Street Room 4B-432, MSC 8500 Bethesda, MD 20892-8500</p> <p>(b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: SRI International 333 Ravenswood Ave Menlo Park, CA 94025</p> <div style="border: 1px solid black; height: 40px; margin: 10px 0;">Redacted by agreement</div> <p>DUNS or DUNS+4: 00-923-2752 TIN: 94-1160950</p>	<p>(c) Invoice/Financing Request No: P25035-0012</p> <p>(d) Date Invoice Prepared: 7/31/2019</p> <p>(e) Contract No. and Order No. HHSN2722014000061 / (if applicable) HHSN27200008</p> <p>(f) Contract Title: <u>Pharmacology and Toxicology Studies of</u> <u>Proprietary Info</u> <u>Propriet</u> <u>Proprietary</u> and <u>Proprietary</u> and to Support the Development of <u>Mitochondrial Toxicity Assays</u></p> <p>(g) Current Contract Period of Performance: 6/15/2018-11/30/2019</p> <p>(h) Total Estimated Cost of Contract/Order: \$1,808,371</p> <p>(i) Total Fixed-Fee (if applicable): \$118,182</p> <p>(j) Two-Way Match: X Three-Way Match:</p> <p>(k) Office of Acquisition: National Institute of Allergy and Infectious Diseases</p> <p>(l) Central Point of Distribution: NIAIDOAInvoices@niaid.nih.gov</p>
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(m) This Invoice/financing request represents reimbursable costs for the period from: 6/16/2019 to 7/13/2019

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance** H
	Negotiated B	Actual C	(n) Current D	(o) Cumulative E			
(p) Direct Costs:							
(1) Direct Labor		Labor Hours	Labor Costs				
(2) Fringe Benefits			Itemized Cost				
(3) Accountable Property							
(4) Materials & Services							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Purchased Labor							
Total Direct Costs							
(q) Cost of Money							
(r) Overhead							
G&A							
Support Cost Burden							
(s) Fixed Fee							
(t) Total Amount Claimed							
(u) Adjustments							
Less Cost Over Ceiling							
Less Fee Over Ceiling							
(v) Grand Totals		Labor Hours					

"Pursuant to authority vested in me, I certify that this voucher is correct and proper for payment."

(Signature on Form 1034)

(Name of Official)

(Title)

* Attach details as specified in the contract

SRI International
INVOICE SUPPORT FOR PROJECT P25035
FOR PERIOD 7, 2019
NATIONAL INSTITUTES OF HEALTH

Labor		Name	Rate	Hours	Amount
Redacted by agreement			Labor rate	Labor Hours	Labor Costs
		Total Middle Managers			
		Total Entry Level Managers			
		Total Advanced Professionals			
		Total Experienced Professionals			
		Total Intermediate Professionals			
		Total Jr Professional			
		Total Senior Technicians			
		Total Jr Technicians			
		TOTAL SRI LABOR			

P25035-0012

7/31/2019

SRI International
INVOICE SUPPORT
NATIONAL INSTITUTES OF HEALTH

MATERIALS & SERVICES

Description	Obj CD	Jnl / Trans No	Name	Trans Description	Amount
MATERIALS & SUPPLIES	41	VCHR 1005319	BIOIVT	Rat Whole Blood, K2 EDTA, pool	Itemized Cost
				DEACTIVATE;Qty 6;\$457;Doc#380834	
MATERIALS & SUPPLIES	41	JE 55190721	SRI CHEM STORES	15ML DISPO;Qty 1;\$22;Doc#380834	
				695080 MIC;Qty 1;\$39;Doc#380834	
MATERIALS & SUPPLIES	41	VCHR 1004806	BIOIVT	Rat Plasma K2 EDTA, pooled, 15	
MATERIALS & SUPPLIES	41	JE 59190704	ALLIANCE GAS	CD EX50	
MATERIALS & SUPPLIES	41	VCHR 1005018	ABCAM INC	Human Cyt C Reductase ELISA Ki	
Total 41					
Description	Obj CD	Jnl / Trans No	Name	Trans Description	
SHIPPING & RECEIVING	48	JE 144190704	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 1004806	BIOIVT	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190703	FEDEX	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 1005018	ABCAM INC	Shipping Cost	
SHIPPING & RECEIVING	48	VCHR 1005319	BIOIVT	Shipping Cost	
SHIPPING & RECEIVING	48	JE 144190703	FEDEX	Shipping Cost	
Total 48					
Total MATERIAL & SERVICES					