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**Toxicology of Smokeless Tobacco Products:  
Bacterial Reverse Mutagenicity**

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***Labstat International ULC  
Test Report***



***Prepared for  
R.J. Reynolds Tobacco Corporation***

**Project Code: M97**

**Original Date: October 9, 2008  
Revision 1 Date: October 17, 2008  
Revision 2 Date: October 26, 2009  
Revision 3 Date: December 15, 2009**

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## 1 Use of Labstat's<sup>1</sup> Analytical Reports<sup>2</sup>

Labstat International ULC is a recognized centre of analytical excellence related to tobacco and tobacco products. Our clients include major international tobacco manufacturers, various Governments and Government agencies such as the Canadian Federal Department of Health and the Massachusetts Department of Public Health, agricultural interests, university researchers and private research interests. Normally our contractual obligations extend **only** to the provision of data and related reports.

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<sup>3</sup> *Unless superseded by a specific contractual obligation or other written agreement.*



## 2 Administrative Information<sup>4</sup>

### 2.1 Quotation Reference

**Quotation Number:** T2645

**Date of Quotation:** August 28, 2008

**Recipient's Name:** Dr. Suzana Theophilus

### 2.2 Client Identification

R.J. Reynolds Tobacco Corporation  
950 Reynolds Boulevard  
Winston-Salem NC 27102-1487  
USA

### 2.3 Date of Sample Receipt

Five samples to be tested for M97 were received on September 16, 2008 via UPS.

### 2.4 Sample Characteristics

The shipment received on September 16, 2008 consisted of one Ziploc bag of one product, one plastic container for each of 2 products, 91 boxes of one product and 20 tins of one product. There was no physical damage to the containers, bag or tins. Individual sticks and strips were normal in appearance.

### 2.5 Test Article Identification

The following sample codes have been used to identify the products associated with the results in each of the tables that are part of this report.

| Sample ID | Sample Description                   |
|-----------|--------------------------------------|
| 084394    | Camel SNUS Frost                     |
| 084395    | 2S3 Research Moist smokeless tobacco |
| 084396    | Kentucky Reference 2R4F              |
| 084454    | Fresh Strips                         |
| 084455    | Mellow Sticks                        |
| 084456    | Copenhagen Long Cut                  |
| 084457    | Ariva Wintergreen                    |
| 084458    | Fresh Orbs                           |

### 2.6 Special Instructions

As requested by the client, "Camel Snus Frost" and "2S3 Research Moist smokeless tobacco" were removed from inventory remaining from projects M78L and M78M. Labstat International ULC supplied "Kentucky Reference 2R4F".

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<sup>4</sup> Provided in accord with International Standard ISO/IEC 17025 "General requirements for the competence of testing and calibration laboratories" Section 5.10

## 2.7 Date of Test Report

Original: October 9, 2008

Revision 1: October 17, 2008

Revision 2: October 26, 2009

Revision 3: December 15, 2009

## 2.8 Revision History

### 2.8.1 Revision 1

This revision was required due to client communication, following the initial submission of the report, requesting further data analysis.

### 2.8.2 Revision 2

This revision was required due to client request for re-analysis and additional information following the submission of the revised report with added data analysis and subsequent conference calls with the client regarding specific data analysis methodologies to be used (client CRO # 2009-004).

### 2.8.3 Revision 3

This revision was required due to a client request for additional analysis following the submission of the revision 2 report (client CRO # 2009-012-M97-Ames).

## 3 Accreditation

### 3.1 Scope (refer to [appendix A](#))

Labstat International ULC has been accredited by the Standards Council of Canada to International Standard ISO/IEC 17025 "General requirements for the competence of testing and calibration laboratories" with a scope that includes all of the mandated tobacco-related Health Canada methods (see Tobacco Reporting Regulations dated 26 June 2000, Canada Gazette Part II, Vol. 134, No. 15 Schedules 1, 2 and 3 pages 1780 – 1785). The testing included in this report is within the scope of this accreditation, unless otherwise noted in Section 4.



Accredited LAB 368  
(SCC Accreditation & Design Mark is an Official Mark of the Standards Council of Canada, used under license)

### 3.2 International Recognition of Tests

Our accrediting organization, Standards Council of Canada, is one of a number of such member bodies participating in a global mutual recognition agreement (MRA), known as the ILAC (International Laboratory Accreditation Cooperation) Arrangement. The arrangement, effective January 31, 2001, requires acceptance of technical test data from accredited laboratories by member bodies in numerous international economies.

## 4 Methods

### 4.1 Total Particulate Matter Collection and Preparation

#### 4.1.1 Collection of Total Particulate Matter (TPM)<sup>5</sup>

(b) (4)



#### 4.1.2 Processing of TPM

(b) (4)



### 4.2 Smokeless Tobacco Sample Preparation

(b) (4)



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<sup>5</sup> See International Standard ISO 4387 Cigarettes – Determination of total and nicotine-free dry particulate matter using a routine analytical smoking machine (Reference number ISO4387:2000)

<sup>6</sup> Health Canada 100% Vent Blocking Method

6(b)(iii) all ventilation holes must be blocked by placing over them a strip of Mylar adhesive tape, Scotch Brand product no. 600 Transparent Tape, and the tape must be cut so that it covers the circumference and is tightly secured from the end of the filter to the tipping overwrap seam, or by another method of equivalent efficiency.

<sup>7</sup> DMSO is the most useful solvent for mutagenicity assays because it dissolves a wide range of chemicals, is relatively non-toxic to the bacteria and to the microsomal S9 enzymes, and is completely miscible with molten top agar.

### 4.3 Mutagenicity Testing (Health Canada Official Method T-501)

#### 4.3.1 Synopsis

(b) (4)

#### 4.3.2 Preparation of Tester Strain

(b) (4)

#### 4.3.3 Treatment of Samples

(b) (4)

#### 4.3.4 Exogenous Metabolic Activation

(b) (4)

### 4.4 Nicotine and Moisture Contents of Smokeless Tobacco Products

Test methods for the analysis of processed tobacco are referenced in the table below and were practiced as written.

#### OFFICIAL METHODS FOR THE COLLECTION OF DATA ON CONSTITUENTS<sup>8</sup>

| Item | Constituent | Official Method   |
|------|-------------|---|
| 1.   | Nicotine    | Official Method T-301, <i>Determination of Alkaloids in Whole Tobacco</i>   |
| 2.   | Moisture    | AOAC Official Method 966.02, <i>Moisture in Tobacco, Gravimetric Method</i> |

### 4.5 Method Deviations

(b) (4)

<sup>8</sup> Canadian Tobacco Reporting Regulations: 2000-01-19 *Canada Gazette Part II, Vol. 134, No. 15* Part 3: Emissions from Designated Tobacco Products. Test method numbers refer to Health Canada methodologies which have been posted by Health Canada on the internet at site [http://www.hc-sc.gc.ca/hl-vs/tobac-tabac/legislation/reg/indust/index\\_e.html](http://www.hc-sc.gc.ca/hl-vs/tobac-tabac/legislation/reg/indust/index_e.html)

## 5 Results

### 5.1 Data Files

Individual results and the corresponding sample statistics may be found on the compact disk (CD) that accompanies this report. The data files have been labeled *M97\_ames\_tpm\_dataCF.xls* (Ames results for TPM of tobacco brand 084396), *M97\_ames\_wt\_dataCF.xls* (Ames results for smokeless tobacco products), *M97\_chem\_wt\_dataCF.xls* (nicotine and moisture analysis results for smokeless tobacco products).

#### 5.1.1 Moisture-Corrected Smokeless Tobacco and Nicotine Dose Basis

(b) (4)

### 5.2 Quality Control

#### 5.2.1 Genotypes of the Tester Strains and Bacterial Growth

##### 5.2.1.1 Requirement

(b) (4)

##### 5.2.1.2 Conclusion

| Strain      | Assay Date | Lot # | Viability<br>(x 10 <sup>9</sup> cells/mL) | Genotype Testing |       |      |                  |        |              |
|-------------|------------|-------|---|------------------|-------|------|------------------|--------|--------------|
|             |            |       |   | R-factor         | rfa   | uvrB | Histidine/Biotin | Biotin | Tetracycline |
| TA98 (+S9)  | 19-Sep-08  | 2276  | 1.30                                      | +                | 16 mm | -    | +                | -      | n/a          |
| TA98 (+S9)  | 24-Sep-08  | 2276  | 1.43                                      | +                | 17 mm | -    | +                | -      | n/a          |
| TA98 (-S9)  | 19-Sep-08  | n/a   | 1.30                                      | +                | 16 mm | -    | +                | -      | n/a          |
| TA98 (-S9)  | 26-Sep-08  | n/a   | 1.19                                      | +                | 17 mm | -    | +                | -      | n/a          |
| TA100 (+S9) | 19-Sep-08  | 2276  | 1.17                                      | +                | 18 mm | -    | +                | -      | n/a          |
| TA100 (+S9) | 26-Sep-08  | 2276  | 1.19                                      | +                | 17 mm | -    | +                | -      | n/a          |
| TA100 (-S9) | 19-Sep-08  | n/a   | 1.17                                      | +                | 18 mm | -    | +                | -      | n/a          |
| TA100 (-S9) | 26-Sep-08  | n/a   | 1.22                                      | +                | 19 mm | -    | +                | -      | n/a          |
| TA102 (+S9) | 19-Sep-08  | 2276  | 1.51                                      | +                | 19 mm | +    | +                | -      | +            |

| Strain       | Assay Date | Lot # | Viability<br>(x 10 <sup>9</sup> cells/mL) | Genotype Testing |       |      |                  |        |              |
|--------------|------------|-------|---|------------------|-------|------|------------------|--------|--------------|
|              |            |       |   | R-factor         | rfa   | uvrB | Histidine/Biotin | Biotin | Tetracycline |
| TA102 (+S9)  | 26-Sep-08  | 2276  | 1.33                                      | +                | 18 mm | +    | +                | -      | +            |
| TA102 (-S9)  | 19-Sep-08  | n/a   | 1.51                                      | +                | 19 mm | +    | +                | -      | +            |
| TA102 (-S9)  | 26-Sep-08  | n/a   | 1.64                                      | +                | 16 mm | +    | +                | -      | +            |
| TA1535 (+S9) | 23-Sep-08  | 2276  | 1.95                                      | -                | 18 mm | -    | +                | -      | n/a          |
| TA1535 (+S9) | 24-Sep-08  | 2276  | 1.56                                      | -                | 14 mm | -    | +                | -      | n/a          |
| TA1535 (-S9) | 23-Sep-08  | n/a   | 1.95                                      | -                | 18 mm | -    | +                | -      | n/a          |
| TA1535 (-S9) | 24-Sep-08  | n/a   | 1.52                                      | -                | 17 mm | -    | +                | -      | n/a          |
| TA1537 (+S9) | 23-Sep-08  | 2291  | 1.35                                      | -                | 19 mm | -    | +                | -      | n/a          |
| TA1537 (+S9) | 23-Sep-08  | 2291  | 1.36                                      | -                | 18 mm | -    | +                | -      | n/a          |
| TA1537 (-S9) | 23-Sep-08  | n/a   | 1.35                                      | -                | 19 mm | -    | +                | -      | n/a          |
| TA1537 (-S9) | 24-Sep-08  | n/a   | 1.40                                      | -                | 19 mm | -    | +                | -      | n/a          |

All of the appropriate genotypic characteristics were present for each strain used in producing the results that are part of this report. All bacterial cultures were found to have densities in excess of the minimum requirement of 1x10<sup>9</sup> cells/mL defined in section 13.6.1 of T-501.

## 5.2.2 Evaluation of Negative Controls

### 5.2.2.1 Acceptance Criteria for Negative Controls

(b) (4)

### 5.2.2.2 Conclusion

All negative control assay results that are part of this report were found to be acceptable in regards to the above requirement. See the "Control Summary" sheet in the *M97\_ames\_Labstat Internal Controls.xls* data file for evaluation results.

## 5.2.3 Evaluation of Positive Controls

### 5.2.3.1 Acceptance Criteria for Positive Controls

(b) (4)

(b) (4)



#### 5.2.3.2 Conclusion

All positive control assay results that are part of this report were found to be acceptable in regards to the above requirements for positive control results. See the "[Control Summary](#)" sheet in the *M97\_ames\_Labstat Internal Controls.xls* data file for evaluation results.

#### 5.2.4 Evaluation of Laboratory Controls (Kentucky Reference 3R4F)

##### 5.2.4.1 Acceptance Criteria for Mutagenicity<sup>9</sup>

(b) (4)



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<sup>9</sup> Acceptance criteria have not been defined in the Official Health Canada Test Method T-501

<sup>10</sup> A minimum of 30 results is normally required for the purpose of this comparison.

#### 5.2.4.2 Conclusion (Mutagenicity)

| Strain       | Assay Date | Target [rev./mg TPM] |         | Observed [rev./mg TPM] | Z Score | P Value |
|--------------|------------|----------------------|---------|------------------------|---------|---------|
|              |            | Average              | Std Dev |                        |         |         |
| TA98 (+S9)   | 19-Sep-08  | 1399                 | 202     | 1228                   | 0.847   | 0.397   |
| TA98 (+S9)   | 24-Sep-08  | 1399                 | 202     | 1457                   | -0.289  | 0.773   |
| TA98 (-S9)   | 19-Sep-08  | 47.3                 | 30.2    | 24                     | 0.783   | 0.434   |
| TA98 (-S9)   | 26-Sep-08  | 47.3                 | 30.2    | 69                     | -0.716  | 0.474   |
| TA100 (+S9)  | 19-Sep-08  | 580                  | 148     | 522                    | 0.395   | 0.693   |
| TA100 (+S9)  | 26-Sep-08  | 580                  | 148     | 367                    | 1.444   | 0.149   |
| TA100 (-S9)  | 19-Sep-08  | 189                  | 76      | 283                    | -1.238  | 0.216   |
| TA100 (-S9)  | 26-Sep-08  | 189                  | 76      | 172                    | 0.221   | 0.825   |
| TA102 (+S9)  | 19-Sep-08  | 444                  | 171     | 366                    | 0.459   | 0.646   |
| TA102 (+S9)  | 26-Sep-08  | 444                  | 171     | 202                    | 1.414   | 0.157   |
| TA102 (-S9)  | 19-Sep-08  | 102                  | 112     | 0                      | 0.912   | 0.362   |
| TA102 (-S9)  | 26-Sep-08  | 102                  | 112     | 0                      | 0.912   | 0.362   |
| TA1535 (+S9) | 23-Sep-08  | 13.5                 | 14.1    | 0                      | 0.955   | 0.339   |
| TA1535 (+S9) | 24-Sep-08  | 13.5                 | 14.1    | 17                     | -0.268  | 0.789   |
| TA1535 (-S9) | 23-Sep-08  | 10.9                 | 13.7    | 0                      | 0.797   | 0.425   |
| TA1535 (-S9) | 24-Sep-08  | 10.9                 | 13.7    | 0                      | 0.797   | 0.425   |
| TA1537 (+S9) | 23-Sep-08  | 225                  | 42      | 217                    | 0.192   | 0.848   |
| TA1537 (+S9) | 23-Sep-08  | 225                  | 42      | 228                    | -0.078  | 0.938   |
| TA1537 (-S9) | 23-Sep-08  | 23.8                 | 14.9    | 0                      | 1.596   | 0.110   |
| TA1537 (-S9) | 24-Sep-08  | 23.8                 | 14.9    | 10                     | 0.911   | 0.362   |

The results of the Kentucky Reference 3R4F assays necessitated by section 13.3.1 of T-501 were acceptable in regards to the criteria defined in section 5.2.4.1 of this report. Thus, it is reasonable to assume that the results reported for the test samples are reflective of the characteristics of the products as received and tested as described in section 4 of this report. See the [“Assay Acceptance Criteria”](#) sheet in the *M97\_ames\_Labstat Internal Controls.xls* data file for evaluation results.

#### 5.2.5 Precipitation/Toxicity

##### 5.2.5.1 Requirement

(b) (4)

##### 5.2.5.2 Conclusion

Precipitation was not evident within the culture media used for this project or on any assay plate reported for this project. There was evidence of toxicity at the highest TPM concentration for each assay with the following exceptions for which all plates were comparable to the negative control:

- Set 2, Run 4 Sample ID 084454 (replicate 1) assay for strain TA1535 (+S9)
- Set 2, Run 5 Sample ID 084455 (replicate 1) assay for strain TA1535 (+S9)



## 6 Mutagenicity Comparisons

### 6.1 Data Files

Data files containing calculated specific activities (slope of the linear portion of the dose-response curve) may be found on the compact disk (CD) that accompanies this report. The data files have been labeled *M97\_ames\_tpm\_stats\_R2.xls* (dose-response curve analysis results for CSC of tobacco brand 084396), *M97\_ames\_wt\_stats\_ST.xls* (dose-response curve analysis results for smokeless tobacco products on a 'mg extracted smokeless tobacco in DMSO' dose basis), *M97\_ames\_wt\_stats\_ST-H2O.xls* (dose-response curve analysis results for smokeless tobacco products on a 'mg extracted moisture-corrected smokeless tobacco in DMSO' dose basis), *M97\_ames\_wt\_stats\_Nicotine.xls* (dose-response curve analysis results for smokeless tobacco products on a 'µg extracted Nicotine in DMSO' dose basis) and *M97\_ames\_tpm+wt\_stats\_Nicotine.xls* (dose-response curve analysis results for smoked and smokeless tobacco products on a Nicotine dose basis).

### 6.2 Methodology

1. (b) (4)

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3.

4.

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7.

8.

### 6.3 Specific Activity Determinations

(b) (4)

## 6.4 Comparisons Among Smokeless Tobacco Products

### 6.4.1 Analysis Files

Tables of results were obtained for the individual replicate slope estimates and the summary statistics over the three replicate slopes for each smokeless tobacco test sample under each tester strain and S9 activation. The tables for each smokeless tobacco dose basis can be found on the 'Statistical Analysis' data sheet in the corresponding dose basis files *M97\_ames\_wt\_stats\_ST.xls* (extracted smokeless tobacco), *M97\_ames\_wt\_stats\_ST-H2O.xls* (extracted moisture-corrected smokeless tobacco), and *M97\_ames\_wt\_stats\_Nicotine.xls* (extracted nicotine).

### 6.4.2 Data Plots

Plots of all replicate smokeless tobacco test samples can be found in the files *M97\_ames\_wt\_stats\_ST.xls*, *M97\_ames\_wt\_stats\_ST-H2O.xls* and *M97\_ames\_wt\_stats\_Nicotine.xls* on the CD that accompanies this report. Box-and-Whisker plots of the calculated specific activities can also be found on the CD that accompanies this report.

### 6.4.3 One-Way ANOVA Results

One-way ANOVA comparisons of mean 'extracted smokeless tobacco', 'extracted moisture-corrected smokeless tobacco' and 'extracted nicotine' slope estimates among test samples yielded the following:

#### 6.4.3.1 Revertants/mg 'Extracted Smokeless Tobacco in DMSO'

| Tester Strain & S9 Activation | Variation Source | Sum of Squares | d.f. | Mean Square | F Ratio | P value |
|-------------------------------|------------------|----------------|------|-------------|---------|---------|
| TA98 (+S9)                    | Among Samples    | 25.343         | 6    | 4.224       | 1.843   | 0.162   |
|                               | Within Samples   | 32.086         | 14   | 2.292       |         |         |
|                               | Total            | 57.430         | 20   |             |         |         |
| TA98 (-S9)                    | Among Samples    | 3.336          | 6    | 0.556       | 1.922   | 0.147   |
|                               | Within Samples   | 4.050          | 14   | 0.289       |         |         |
|                               | Total            | 7.387          | 20   |             |         |         |
| TA100 (+S9)                   | Among Samples    | 246.433        | 6    | 41.072      | 0.574   | 0.745   |
|                               | Within Samples   | 1002.589       | 14   | 71.613      |         |         |
|                               | Total            | 1249.022       | 20   |             |         |         |
| TA100 (-S9)                   | Among Samples    | 463.375        | 6    | 77.229      | 1.496   | 0.250   |
|                               | Within Samples   | 722.733        | 14   | 51.624      |         |         |
|                               | Total            | 1186.108       | 20   |             |         |         |
| TA102 (+S9)                   | Among Samples    | 6329.977       | 6    | 1054.996    | 11.796  | < 0.001 |
|                               | Within Samples   | 1252.092       | 14   | 89.435      |         |         |
|                               | Total            | 7582.069       | 20   |             |         |         |
| TA102 (-S9)                   | Among Samples    | 1218.568       | 6    | 203.095     | 1.207   | 0.359   |

<sup>11</sup> Margolin BH, Kaplan N, Zeiger E. Statistical Analysis of the Ames *Salmonella* microsome test. *Proc Natl Acad Sci USA* 1981;78: 3779-3783.

| Tester Strain & S9 Activation | Variation Source | Sum of Squares | d.f. | Mean Square | F Ratio | P value      |
|-------------------------------|------------------|----------------|------|-------------|---------|--------------|
|                               | Within Samples   | 2355.101       | 14   | 168.222     |         |              |
|                               | Total            | 3573.669       | 20   |             |         |              |
| TA1535 (+S9)                  | Among Samples    | 0.617          | 6    | 0.103       | 0.186   | 0.976        |
|                               | Within Samples   | 7.721          | 14   | 0.552       |         |              |
|                               | Total            | 8.338          | 20   |             |         |              |
| TA1535 (-S9)                  | Among Samples    | 12.845         | 6    | 2.141       | 1.366   | 0.294        |
|                               | Within Samples   | 21.940         | 14   | 1.567       |         |              |
|                               | Total            | 34.785         | 20   |             |         |              |
| TA1537 (+S9)                  | Among Samples    | 29.062         | 6    | 4.844       | 1.882   | 0.154        |
|                               | Within Samples   | 36.025         | 14   | 2.573       |         |              |
|                               | Total            | 65.088         | 20   |             |         |              |
| TA1537 (-S9)                  | Among Samples    | 16.687         | 6    | 2.781       | 4.767   | <b>0.008</b> |
|                               | Within Samples   | 8.167          | 14   | 0.583       |         |              |
|                               | Total            | 24.854         | 20   |             |         |              |

One-way ANOVA analysis indicates significant differences, at  $\alpha = 0.05$ , among mean 'Extracted Smokeless Tobacco in DMSO' slope estimates for test samples assayed with strains TA102 (+S9) and TA1537 (-S9).

#### 6.4.3.2 Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO'

| Tester Strain & S9 Activation | Variation Source | Sum of Squares | d.f. | Mean Square | F Ratio | P value      |
|-------------------------------|------------------|----------------|------|-------------|---------|--------------|
|                               | Among Samples    | 99.097         | 6    | 16.516      | 4.070   | <b>0.014</b> |
|                               | Within Samples   | 56.808         | 14   | 4.058       |         |              |
| TA98 (+S9)                    | Total            | 155.906        | 20   |             |         |              |
|                               | Among Samples    | 4.336          | 6    | 0.723       | 1.240   | 0.344        |
|                               | Within Samples   | 8.159          | 14   | 0.583       |         |              |
| TA98 (-S9)                    | Total            | 12.496         | 20   |             |         |              |
|                               | Among Samples    | 3175.483       | 6    | 529.247     | 3.352   | <b>0.029</b> |
|                               | Within Samples   | 2210.376       | 14   | 157.884     |         |              |
| TA100 (+S9)                   | Total            | 5385.859       | 20   |             |         |              |
|                               | Among Samples    | 1346.051       | 6    | 224.342     | 2.015   | 0.131        |
|                               | Within Samples   | 1558.496       | 14   | 111.321     |         |              |
| TA100 (-S9)                   | Total            | 2904.547       | 20   |             |         |              |
|                               | Among Samples    | 15475.111      | 6    | 2579.185    | 7.046   | <b>0.001</b> |
|                               | Within Samples   | 5124.874       | 14   | 366.062     |         |              |
| TA102 (+S9)                   | Total            | 20599.985      | 20   |             |         |              |
|                               | Among Samples    | 2807.624       | 6    | 467.937     | 1.231   | 0.348        |
|                               | Within Samples   | 5321.469       | 14   | 380.105     |         |              |
| TA102 (-S9)                   | Total            | 8129.093       | 20   |             |         |              |
|                               | Among Samples    | 0.930          | 6    | 0.155       | 0.202   | 0.971        |
|                               | Within Samples   | 10.747         | 14   | 0.768       |         |              |
| TA1535 (+S9)                  | Total            | 11.676         | 20   |             |         |              |
|                               | Among Samples    | 17.736         | 6    | 2.956       | 1.303   | 0.318        |
|                               | Within Samples   | 31.763         | 14   | 2.269       |         |              |
| TA1535 (-S9)                  | Total            | 49.500         | 20   |             |         |              |
|                               | Among Samples    | 134.635        | 6    | 22.439      | 2.000   | 0.134        |
|                               | Within Samples   | 157.035        | 14   | 11.217      |         |              |
| TA1537 (+S9)                  | Total            | 291.669        | 20   |             |         |              |

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| Tester Strain & S9 Activation | Variation Source | Sum of Squares | d.f. | Mean Square | F Ratio | P value      |
|-------------------------------|------------------|----------------|------|-------------|---------|--------------|
| TA1537 (-S9)                  | Among Samples    | 46.256         | 6    | 7.709       | 5.472   | <b>0.004</b> |
|                               | Within Samples   | 19.723         | 14   | 1.409       |         |              |
|                               | Total            | 65.979         | 20   |             |         |              |

One-way ANOVA analysis indicates significant differences, at  $\alpha = 0.05$ , among mean 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' slope estimates for test samples assayed with strains TA98 (+S9), TA100 (+S9), TA102 (+S9) and TA1537 (-S9).

#### 6.4.3.3 Revertants/ $\mu$ g 'Extracted Nicotine in DMSO'

| Tester Strain & S9 Activation | Variation Source | Sum of Squares | d.f. | Mean Square | F Ratio | P value      |
|-------------------------------|------------------|----------------|------|-------------|---------|--------------|
| TA98 (+S9)                    | Among Samples    | 0.792          | 6    | 0.132       | 0.753   | 0.617        |
|                               | Within Samples   | 2.454          | 14   | 0.175       |         |              |
|                               | Total            | 3.246          | 20   |             |         |              |
| TA98 (-S9)                    | Among Samples    | 0.127          | 6    | 0.021       | 2.344   | 0.089        |
|                               | Within Samples   | 0.126          | 14   | 0.009       |         |              |
|                               | Total            | 0.252          | 20   |             |         |              |
| TA100 (+S9)                   | Among Samples    | 19.998         | 6    | 3.333       | 1.294   | 0.322        |
|                               | Within Samples   | 36.059         | 14   | 2.576       |         |              |
|                               | Total            | 56.056         | 20   |             |         |              |
| TA100 (-S9)                   | Among Samples    | 14.802         | 6    | 2.467       | 1.504   | 0.247        |
|                               | Within Samples   | 22.960         | 14   | 1.640       |         |              |
|                               | Total            | 37.762         | 20   |             |         |              |
| TA102 (+S9)                   | Among Samples    | 67.746         | 6    | 11.291      | 7.063   | <b>0.001</b> |
|                               | Within Samples   | 22.380         | 14   | 1.599       |         |              |
|                               | Total            | 90.126         | 20   |             |         |              |
| TA102 (-S9)                   | Among Samples    | 69.157         | 6    | 11.526      | 1.134   | 0.393        |
|                               | Within Samples   | 142.248        | 14   | 10.161      |         |              |
|                               | Total            | 211.405        | 20   |             |         |              |
| TA1535 (+S9)                  | Among Samples    | 0.026          | 6    | 0.004       | 0.214   | 0.966        |
|                               | Within Samples   | 0.283          | 14   | 0.020       |         |              |
|                               | Total            | 0.309          | 20   |             |         |              |
| TA1535 (-S9)                  | Among Samples    | 1.866          | 6    | 0.311       | 2.372   | 0.086        |
|                               | Within Samples   | 1.835          | 14   | 0.131       |         |              |
|                               | Total            | 3.700          | 20   |             |         |              |
| TA1537 (+S9)                  | Among Samples    | 0.174          | 6    | 0.029       | 0.863   | 0.544        |
|                               | Within Samples   | 0.470          | 14   | 0.034       |         |              |
|                               | Total            | 0.644          | 20   |             |         |              |
| TA1537 (-S9)                  | Among Samples    | 0.144          | 6    | 0.024       | 1.534   | 0.238        |
|                               | Within Samples   | 0.220          | 14   | 0.016       |         |              |
|                               | Total            | 0.364          | 20   |             |         |              |

One-way ANOVA analysis indicates significant differences, at  $\alpha = 0.05$ , among mean 'Extracted Nicotine in DMSO' slope estimates for test samples assayed with strain TA102 (+S9).

#### 6.4.4 Contrasts of Interest

Twenty-one contrasts were requested for comparing the means of all possible pairs of the 7 test samples. The client stated the choice of significance level to be  $\alpha = 0.05$  with a Bonferroni adjustment for multiple comparisons (Bonferroni-adjusted p-value =  $\alpha/n = 0.05/21 = 0.0024$ ). The tables below show ANOVA-based comparisons for only those strains where at least one comparison was significant. All other comparison results can be found in the statistical analysis data files on the CD that accompanies this report.

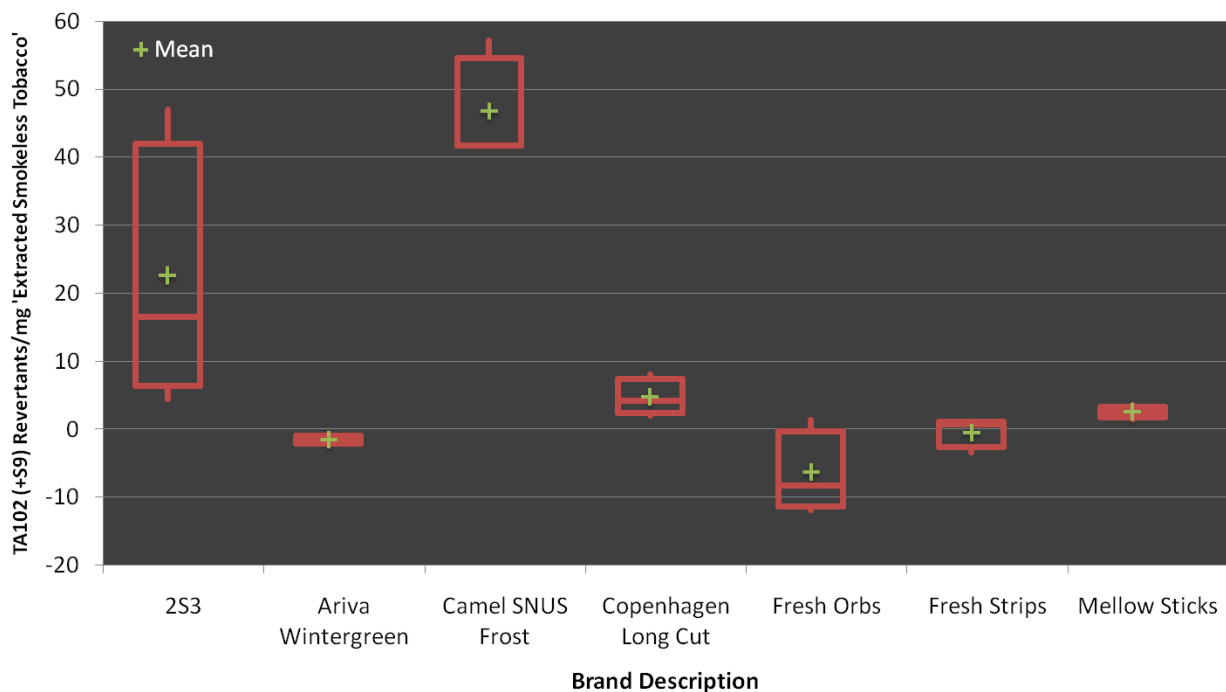
##### 6.4.4.1 Revertants/mg 'Extracted Smokeless Tobacco in DMSO' (Selected Strains)

| Sample Comparison | TA102 (+S9) |         |                                 | TA1537 (-S9) |         |                                 |
|-------------------|-------------|---------|---------------------------------|--------------|---------|---------------------------------|
|                   | f-ratio     | p-value | significance at $\alpha = 0.05$ | f-ratio      | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084395 | 9.8385      | 0.0073  | not significant                 | 2.3399       | 0.1484  | not significant                 |
| 084394 vs. 084454 | 37.627      | 0.0000  | <b>significant</b>              | 13.714       | 0.0024  | <b>significant</b>              |
| 084394 vs. 084455 | 32.883      | 0.0001  | <b>significant</b>              | 16.822       | 0.0011  | <b>significant</b>              |
| 084394 vs. 084456 | 29.727      | 0.0001  | <b>significant</b>              | 14.325       | 0.0020  | <b>significant</b>              |
| 084394 vs. 084457 | 39.333      | 0.0000  | <b>significant</b>              | 15.227       | 0.0016  | <b>significant</b>              |
| 084394 vs. 084458 | 47.373      | 0.0000  | <b>significant</b>              | 10.700       | 0.0056  | not significant                 |
| 084395 vs. 084454 | 8.9845      | 0.0096  | not significant                 | 4.7245       | 0.0474  | not significant                 |
| 084395 vs. 084455 | 6.7481      | 0.0211  | not significant                 | 6.6144       | 0.0222  | not significant                 |
| 084395 vs. 084456 | 5.3622      | 0.0363  | not significant                 | 5.0858       | 0.0407  | not significant                 |
| 084395 vs. 084457 | 9.8282      | 0.0073  | not significant                 | 5.6288       | 0.0325  | not significant                 |
| 084395 vs. 084458 | 14.034      | 0.0022  | <b>significant</b>              | 3.0323       | 0.1035  | not significant                 |
| 084454 vs. 084455 | 0.1598      | 0.6954  | not significant                 | 0.1586       | 0.6965  | not significant                 |
| 084454 vs. 084456 | 0.4648      | 0.5065  | not significant                 | 0.0067       | 0.9361  | not significant                 |
| 084454 vs. 084457 | 0.0189      | 0.8925  | not significant                 | 0.0396       | 0.8452  | not significant                 |
| 084454 vs. 084458 | 0.5606      | 0.4664  | not significant                 | 0.1868       | 0.6721  | not significant                 |
| 084455 vs. 084456 | 0.0796      | 0.7820  | not significant                 | 0.1003       | 0.7562  | not significant                 |
| 084455 vs. 084457 | 0.2887      | 0.5995  | not significant                 | 0.0397       | 0.8449  | not significant                 |
| 084455 vs. 084458 | 1.3189      | 0.2700  | not significant                 | 0.6897       | 0.4202  | not significant                 |
| 084456 vs. 084457 | 0.6713      | 0.4263  | not significant                 | 0.0138       | 0.9083  | not significant                 |
| 084456 vs. 084458 | 2.0463      | 0.1745  | not significant                 | 0.2640       | 0.6154  | not significant                 |
| 084457 vs. 084458 | 0.3735      | 0.5509  | not significant                 | 0.3984       | 0.5381  | not significant                 |

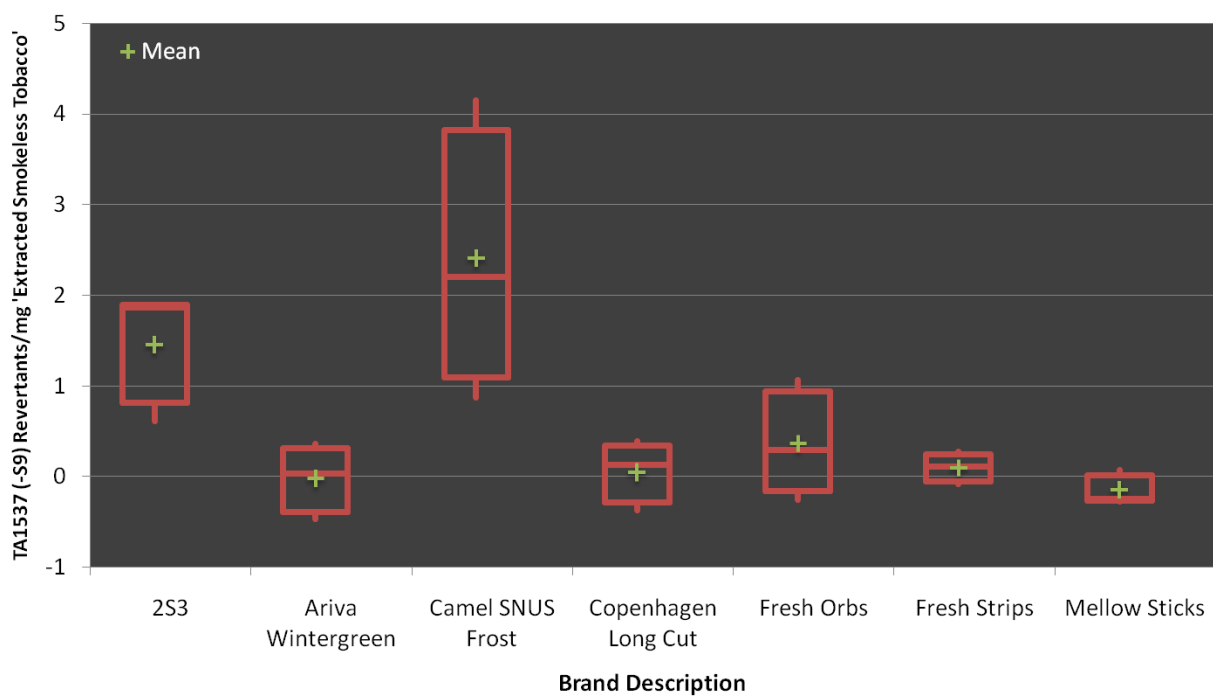
ANOVA-based comparison p-values less than the Bonferroni-adjusted  $\alpha = 0.05$  indicate that significant differences in mean slope, for smokeless tobacco extracts expressed on a mg 'extracted smokeless tobacco in DMSO' basis, were detected in strain TA102 (+S9) between Camel SNUS Frost (084394) and each of {Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456), Ariva Wintergreen (084457), Fresh Orbs (084458)} and between 2S3 Research Moist Snuff (084395) and Fresh Orbs (084458).

Significant differences in mean specific activity slope were also detected in strain TA1537 (-S9) between Camel SNUS Frost (084394) and each of {Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456), Ariva Wintergreen (084457)}

### Box-and-Whisker Plot: TA102 (+S9) Replicate Specific Activity Estimates



### Box-and-Whisker Plot: TA1537 (-S9) Replicate Specific Activity Estimates



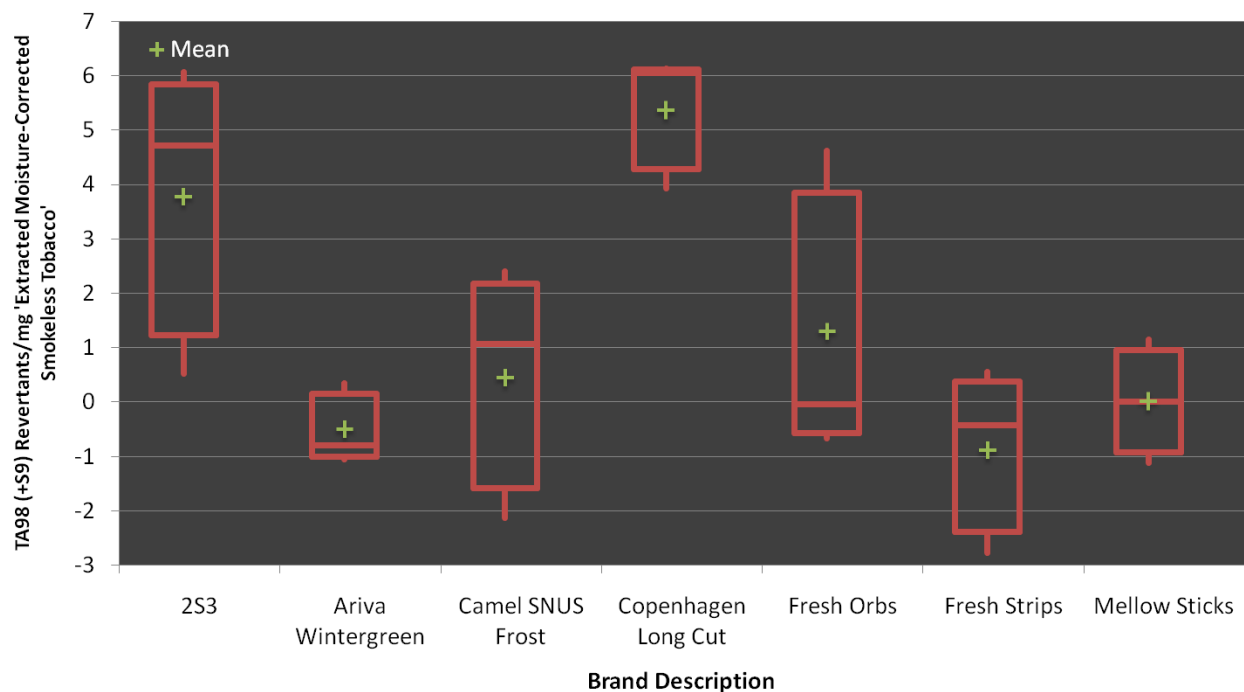
#### 6.4.4.2 Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco' (Selected Strains)

| Sample Comparison | TA98 (+S9) |         |                                 | TA102 (+S9) |         |                                 | TA1537 (-S9) |         |                                 |
|-------------------|------------|---------|---------------------------------|-------------|---------|---------------------------------|--------------|---------|---------------------------------|
|                   | f-ratio    | p-value | significance at $\alpha = 0.05$ | f-ratio     | p-value | significance at $\alpha = 0.05$ | f-ratio      | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084395 | 4.0925     | 0.0626  | not significant                 | 1.5446      | 0.2343  | not significant                 | 0.1419       | 0.7121  | not significant                 |
| 084394 vs. 084454 | 0.6556     | 0.4317  | not significant                 | 19.619      | 0.0006  | <b>significant</b>              | 12.425       | 0.0034  | not significant                 |
| 084394 vs. 084455 | 0.0681     | 0.7980  | not significant                 | 17.783      | 0.0009  | <b>significant</b>              | 14.469       | 0.0019  | <b>significant</b>              |
| 084394 vs. 084456 | 8.9514     | 0.0097  | not significant                 | 13.779      | 0.0023  | <b>significant</b>              | 12.457       | 0.0033  | not significant                 |
| 084394 vs. 084457 | 0.3324     | 0.5734  | not significant                 | 20.223      | 0.0005  | <b>significant</b>              | 13.444       | 0.0025  | not significant                 |
| 084394 vs. 084458 | 0.2737     | 0.6090  | not significant                 | 23.204      | 0.0003  | <b>significant</b>              | 10.490       | 0.0059  | not significant                 |
| 084395 vs. 084454 | 8.0241     | 0.0133  | not significant                 | 10.1537     | 0.0066  | not significant                 | 9.9113       | 0.0071  | not significant                 |
| 084395 vs. 084455 | 5.2162     | 0.0385  | not significant                 | 8.8453      | 0.0101  | not significant                 | 11.7455      | 0.0041  | not significant                 |
| 084395 vs. 084456 | 0.9388     | 0.3490  | not significant                 | 6.0971      | 0.0270  | not significant                 | 9.9402       | 0.0071  | not significant                 |
| 084395 vs. 084457 | 6.7574     | 0.0210  | not significant                 | 10.5895     | 0.0058  | not significant                 | 10.8234      | 0.0054  | not significant                 |
| 084395 vs. 084458 | 2.2495     | 0.1559  | not significant                 | 12.775      | 0.0031  | not significant                 | 8.1919       | 0.0125  | not significant                 |
| 084454 vs. 084455 | 0.3012     | 0.5918  | not significant                 | 0.0451      | 0.8349  | not significant                 | 0.0778       | 0.7844  | not significant                 |
| 084454 vs. 084456 | 14.4520    | 0.0019  | <b>significant</b>              | 0.5145      | 0.4850  | not significant                 | 0.0000       | 0.9964  | not significant                 |
| 084454 vs. 084457 | 0.0544     | 0.8190  | not significant                 | 0.0046      | 0.9470  | not significant                 | 0.0201       | 0.8894  | not significant                 |
| 084454 vs. 084458 | 1.7765     | 0.2039  | not significant                 | 0.1503      | 0.7040  | not significant                 | 0.0818       | 0.7790  | not significant                 |
| 084455 vs. 084456 | 10.5806    | 0.0058  | not significant                 | 0.2549      | 0.6215  | not significant                 | 0.0753       | 0.7878  | not significant                 |
| 084455 vs. 084457 | 0.0996     | 0.7570  | not significant                 | 0.0784      | 0.7835  | not significant                 | 0.0188       | 0.8928  | not significant                 |
| 084455 vs. 084458 | 0.6148     | 0.4461  | not significant                 | 0.3601      | 0.5580  | not significant                 | 0.3192       | 0.5810  | not significant                 |
| 084456 vs. 084457 | 12.7334    | 0.0031  | not significant                 | 0.6161      | 0.4456  | not significant                 | 0.0188       | 0.8929  | not significant                 |
| 084456 vs. 084458 | 6.0946     | 0.0271  | not significant                 | 1.2210      | 0.2878  | not significant                 | 0.0845       | 0.7756  | not significant                 |
| 084457 vs. 084458 | 1.2093     | 0.2900  | not significant                 | 0.1025      | 0.7536  | not significant                 | 0.1830       | 0.6753  | not significant                 |

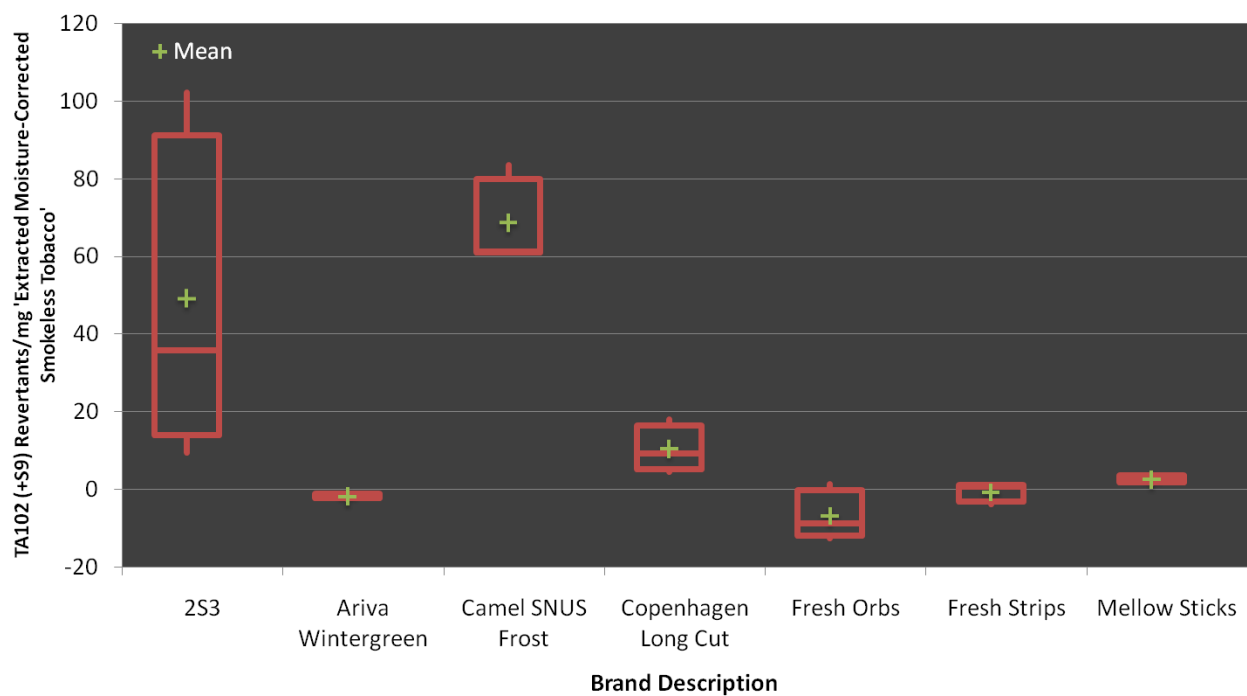
ANOVA-based comparison p-values less than the Bonferroni-adjusted  $\alpha = 0.05$  indicate that significant differences in mean slope, for smokeless tobacco extracts expressed on a mg 'extracted moisture-corrected smokeless tobacco in DMSO' basis, were detected in strain TA102 (+S9) between Camel SNUS Frost (084394) and each of {Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456), Ariva Wintergreen (084457), Fresh Orbs (084458)}

Significant differences in mean specific activity slope were also detected in strain TA98 (+S9) between Fresh Strips (084454) and Copenhagen Long Cut (084456) and in TA1537 (-S9) between Camel SNUS Frost (084394) and Mellow Sticks (084455).

### Box-and-Whisker Plot: TA98 (+S9) Replicate Specific Activity Estimates

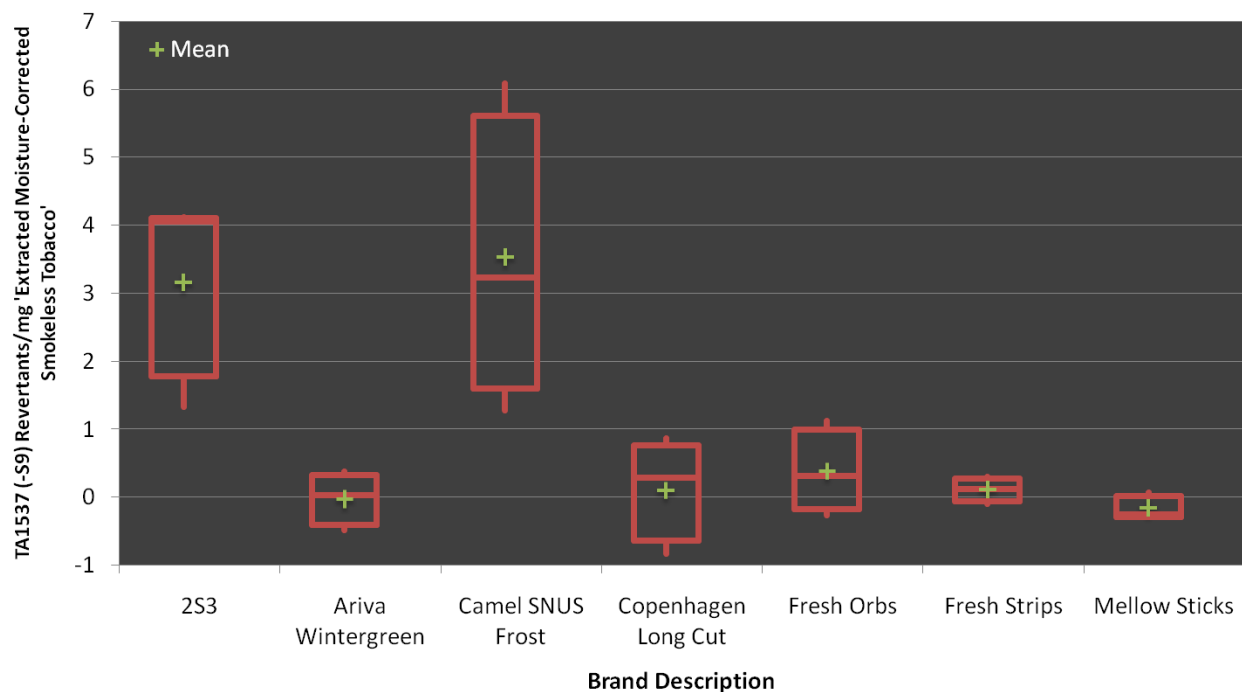


### Box-and-Whisker Plot: TA102 (+S9) Replicate Specific Activity Estimates





### Box-and-Whisker Plot: TA1537 (-S9) Replicate Specific Activity Estimates



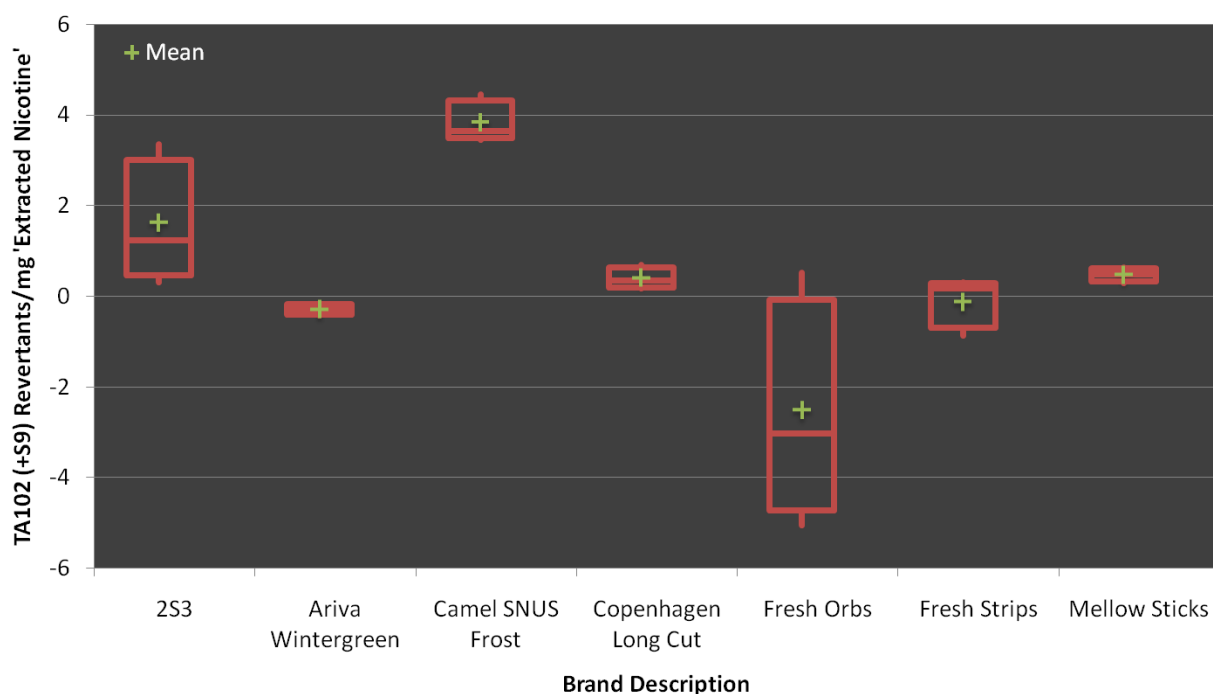
#### 6.4.4.3 Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' (Selected Strains)

| Sample Comparison | TA102 (+S9) |         |                                 |
|-------------------|-------------|---------|---------------------------------|
|                   | f-ratio     | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084395 | 4.5884      | 0.0503  | not significant                 |
| 084394 vs. 084454 | 14.784      | 0.0018  | <b>significant</b>              |
| 084394 vs. 084455 | 10.673      | 0.0056  | not significant                 |
| 084394 vs. 084456 | 11.100      | 0.0049  | not significant                 |
| 084394 vs. 084457 | 16.005      | 0.0013  | <b>significant</b>              |
| 084394 vs. 084458 | 37.961      | 0.0000  | <b>significant</b>              |
| 084395 vs. 084454 | 2.9002      | 0.1107  | not significant                 |
| 084395 vs. 084455 | 1.2655      | 0.2795  | not significant                 |
| 084395 vs. 084456 | 1.4151      | 0.2540  | not significant                 |
| 084395 vs. 084457 | 3.4542      | 0.0842  | not significant                 |
| 084395 vs. 084458 | 16.154      | 0.0013  | <b>significant</b>              |
| 084454 vs. 084455 | 0.3341      | 0.5724  | not significant                 |
| 084454 vs. 084456 | 0.2636      | 0.6157  | not significant                 |
| 084454 vs. 084457 | 0.0242      | 0.8786  | not significant                 |
| 084454 vs. 084458 | 5.3646      | 0.0362  | not significant                 |
| 084455 vs. 084456 | 0.0042      | 0.9494  | not significant                 |
| 084455 vs. 084457 | 0.5382      | 0.4753  | not significant                 |
| 084455 vs. 084458 | 8.3764      | 0.0118  | not significant                 |

| Sample Comparison | TA102 (+S9) |         |                                 |
|-------------------|-------------|---------|---------------------------------|
|                   | f-ratio     | p-value | significance at $\alpha = 0.05$ |
| 084456 vs. 084457 | 0.4475      | 0.5144  | not significant                 |
| 084456 vs. 084458 | 8.0065      | 0.0134  | not significant                 |
| 084457 vs. 084458 | 4.6682      | 0.0485  | not significant                 |

ANOVA-based comparison p-values less than the Bonferroni-adjusted  $\alpha = 0.05$  indicate that significant differences in mean slope, for smokeless tobacco extracts expressed on a  $\mu\text{g}$  'extracted nicotine in DMSO' basis, were detected in strain TA102 (+S9) between Camel SNUS Frost (084394) and each of {Fresh Strips (084454), Ariva Wintergreen (084457), Fresh Orbs (084458)} and between 2S3 Research Moist Snuff (084395) and Fresh Orbs (084458).

### Box-and-Whisker Plot: TA102 (+S9) Replicate Specific Activity Estimates



## 6.5 Comparisons Between Smoked and Smokeless Tobacco Products

### 6.5.1 Methodology

The following request for additional data analysis was received as part of the client inquiry CRO 2009-012-M97-Ames.

- compare the seven smokeless tobacco products to 2R4F on a nicotine dose basis

### 6.5.2 Analysis Files

Tables of results were obtained for the individual replicate slope estimates and the summary statistics over the three replicate slopes for each smoked and smokeless tobacco test sample under each tester strain and S9 activation. The file *M97\_ames\_tpm+wt\_stats\_Nicotine.xls* gives tables of results for all the

smokeless tobacco samples plus the tobacco smoke CSC of the KR 2R4F (084396) samples on an 'extracted nicotine in DMSO' and 'Nicotine in CSC' dose basis, respectively.

### 6.5.3 Data Plots

Plots of all replicate smokeless and smoked tobacco test samples can be found in the file *M97\_ames\_tpm+wt\_stats\_Nicotine.xls* on the CD that accompanies this report. Box-and-Whisker plots of the calculated specific activities can also be found on the CD that accompanies this report.

### 6.5.4 One-Way ANOVA Results

One-way ANOVA comparisons of mean 'extracted nicotine' and 'nicotine in CSC' slope estimates among all 7 smokeless and one smoked test samples yielded the following:

| Tester Strain & S9 Activation | Variation Source | Sum of Squares | d.f. | Mean Square | F Ratio | P value |
|-------------------------------|------------------|----------------|------|-------------|---------|---------|
| TA98 (+S9)                    | Among Samples    | 1782.608       | 7    | 254.658     | 39.5    | < 0.001 |
|                               | Within Samples   | 103.027        | 16   | 6.439       |         |         |
|                               | Total            | 1885.635       | 23   |             |         |         |
| TA98 (-S9)                    | Among Samples    | 2.061          | 7    | 0.294       | 13.6    | < 0.001 |
|                               | Within Samples   | 0.346          | 16   | 0.022       |         |         |
|                               | Total            | 2.407          | 23   |             |         |         |
| TA100 (+S9)                   | Among Samples    | 173.108        | 7    | 24.730      | 9.51    | < 0.001 |
|                               | Within Samples   | 41.623         | 16   | 2.601       |         |         |
|                               | Total            | 214.732        | 23   |             |         |         |
| TA100 (-S9)                   | Among Samples    | 47.826         | 7    | 6.832       | 4.17    | 0.009   |
|                               | Within Samples   | 26.190         | 16   | 1.637       |         |         |
|                               | Total            | 74.017         | 23   |             |         |         |
| TA102 (+S9)                   | Among Samples    | 67.986         | 7    | 9.712       | 6.44    | 0.001   |
|                               | Within Samples   | 24.138         | 16   | 1.509       |         |         |
|                               | Total            | 92.124         | 23   |             |         |         |
| TA102 (-S9)                   | Among Samples    | 69.346         | 7    | 9.907       | 1.07    | 0.425   |
|                               | Within Samples   | 147.952        | 16   | 9.247       |         |         |
|                               | Total            | 217.298        | 23   |             |         |         |
| TA1535 (+S9)                  | Among Samples    | 0.058          | 7    | 0.008       | 0.461   | 0.848   |
|                               | Within Samples   | 0.289          | 16   | 0.018       |         |         |
|                               | Total            | 0.348          | 23   |             |         |         |
| TA1535 (-S9)                  | Among Samples    | 1.937          | 7    | 0.277       | 2.40    | 0.069   |
|                               | Within Samples   | 1.841          | 16   | 0.115       |         |         |
|                               | Total            | 3.778          | 23   |             |         |         |
| TA1537 (+S9)                  | Among Samples    | 45.059         | 7    | 6.437       | 167     | < 0.001 |
|                               | Within Samples   | 0.618          | 16   | 0.039       |         |         |
|                               | Total            | 45.677         | 23   |             |         |         |
| TA1537 (-S9)                  | Among Samples    | 0.310          | 7    | 0.044       | 2.49    | 0.062   |
|                               | Within Samples   | 0.284          | 16   | 0.018       |         |         |
|                               | Total            | 0.595          | 23   |             |         |         |

One-way ANOVA analysis indicates significant differences, at  $\alpha = 0.05$ , among mean 'Nicotine' slope estimates for smoked and smokeless tobacco samples assayed with strains TA98(+S9), TA98(-S9), TA100(+S9), TA100(-S9), TA102(+S9) and TA1537(+S9).

### 6.5.5 Contrasts of Interest

Seven contrasts were requested for comparing the mean specific activity (revertants/ $\mu\text{g}$  'Extracted Nicotine in DMSO') of each of the 7 smokeless tobacco test samples with that of the smoked tobacco test sample, KR 2R4F (revertants/ $\mu\text{g}$  'Nicotine in CSC'). The table below shows ANOVA-based comparisons for only those strains where at least one comparison was significant. All other comparison results can be found in the statistical analysis data file on the CD that accompanies this report.

| Sample Comparison | TA98 (+S9) |         |                                 | TA100 (+S9) |         |                                 | TA102 (+S9) |         |                                 |
|-------------------|------------|---------|---------------------------------|-------------|---------|---------------------------------|-------------|---------|---------------------------------|
|                   | f-ratio    | p-value | significance at $\alpha = 0.05$ | f-ratio     | p-value | significance at $\alpha = 0.05$ | f-ratio     | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084396 | 159        | 1.0E-09 | significant                     | 46.8        | 4.0E-06 | significant                     | 9.26        | 0.008   | not significant                 |
| 084395 vs. 084396 | 157        | 1.1E-09 | significant                     | 43.3        | 6.3E-06 | significant                     | 0.704       | 0.414   | not significant                 |
| 084454 vs. 084396 | 161        | 8.9E-10 | significant                     | 21.7        | 2.6E-04 | significant                     | 0.836       | 0.374   | not significant                 |
| 084455 vs. 084396 | 159        | 1.0E-09 | significant                     | 32.1        | 3.5E-05 | significant                     | 0.102       | 0.754   | not significant                 |
| 084456 vs. 084396 | 157        | 1.1E-09 | significant                     | 39.5        | 1.1E-05 | significant                     | 0.149       | 0.705   | not significant                 |
| 084457 vs. 084396 | 160        | 9.5E-10 | significant                     | 29.4        | 5.6E-05 | significant                     | 1.15        | 0.299   | not significant                 |
| 084458 vs. 084396 | 154        | 1.3E-09 | significant                     | 26.4        | 9.9E-05 | significant                     | 10.9        | 0.005   | significant                     |

| Sample Comparison | TA1537 (+S9) |         |                                 | TA98 (-S9) |         |                                 | TA100 (-S9) |         |                                 |
|-------------------|--------------|---------|---------------------------------|------------|---------|---------------------------------|-------------|---------|---------------------------------|
|                   | f-ratio      | p-value | significance at $\alpha = 0.05$ | f-ratio    | p-value | significance at $\alpha = 0.05$ | f-ratio     | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084396 | 648          | 2.3E-14 | significant                     | 58.4       | 1.0E-06 | significant                     | 8.21        | 0.011   | not significant                 |
| 084395 vs. 084396 | 623          | 3.1E-14 | significant                     | 62.1       | 6.7E-07 | significant                     | 8.42        | 0.010   | not significant                 |
| 084454 vs. 084396 | 703          | 1.2E-14 | significant                     | 42.9       | 6.7E-06 | significant                     | 10.7        | 0.005   | significant                     |
| 084455 vs. 084396 | 689          | 1.4E-14 | significant                     | 35.1       | 2.1E-05 | significant                     | 9.21        | 0.008   | not significant                 |
| 084456 vs. 084396 | 649          | 2.2E-14 | significant                     | 57.8       | 1.1E-06 | significant                     | 6.53        | 0.021   | not significant                 |
| 084457 vs. 084396 | 698          | 1.3E-14 | significant                     | 49.3       | 2.9E-06 | significant                     | 17.1        | 0.001   | significant                     |
| 084458 vs. 084396 | 641          | 2.5E-14 | significant                     | 55.0       | 1.5E-06 | significant                     | 25.1        | 1.3E-04 | significant                     |

| Sample Comparison | TA1537 (-S9) |         |                                 |
|-------------------|--------------|---------|---------------------------------|
|                   | f-ratio      | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084396 | 1.08         | 0.314   | not significant                 |
| 084395 vs. 084396 | 3.85         | 0.067   | not significant                 |
| 084454 vs. 084396 | 7.22         | 0.016   | not significant                 |
| 084455 vs. 084396 | 10.0         | 0.006   | significant                     |
| 084456 vs. 084396 | 8.27         | 0.011   | not significant                 |
| 084457 vs. 084396 | 8.76         | 0.009   | not significant                 |
| 084458 vs. 084396 | 2.15         | 0.161   | not significant                 |

ANOVA-based comparison p-values less than the Bonferroni-adjusted  $\alpha = 0.05$  indicate that significant differences in mean specific activity slope were detected between smokeless tobacco extracts and the cigarette smoke condensate of KR 2R4F (084396) on a 'Nicotine' dose basis in the following instances:

Strains **TA98(+S9)**, **TA98 (-S9)**, **TA100(+S9)**, **TA1537 (+S9)**

- KR 2R4F (084396) specific activity (revertants/ $\mu\text{g}$  'Nicotine in CSC') is significantly different from each of the 7 smokeless tobacco test samples (revertants/ $\mu\text{g}$  'Extracted Nicotine in DMSO')

Strain **TA102(+S9)**

- KR 2R4F (084396) specific activity is significantly different from that of Fresh Orbs (084458)

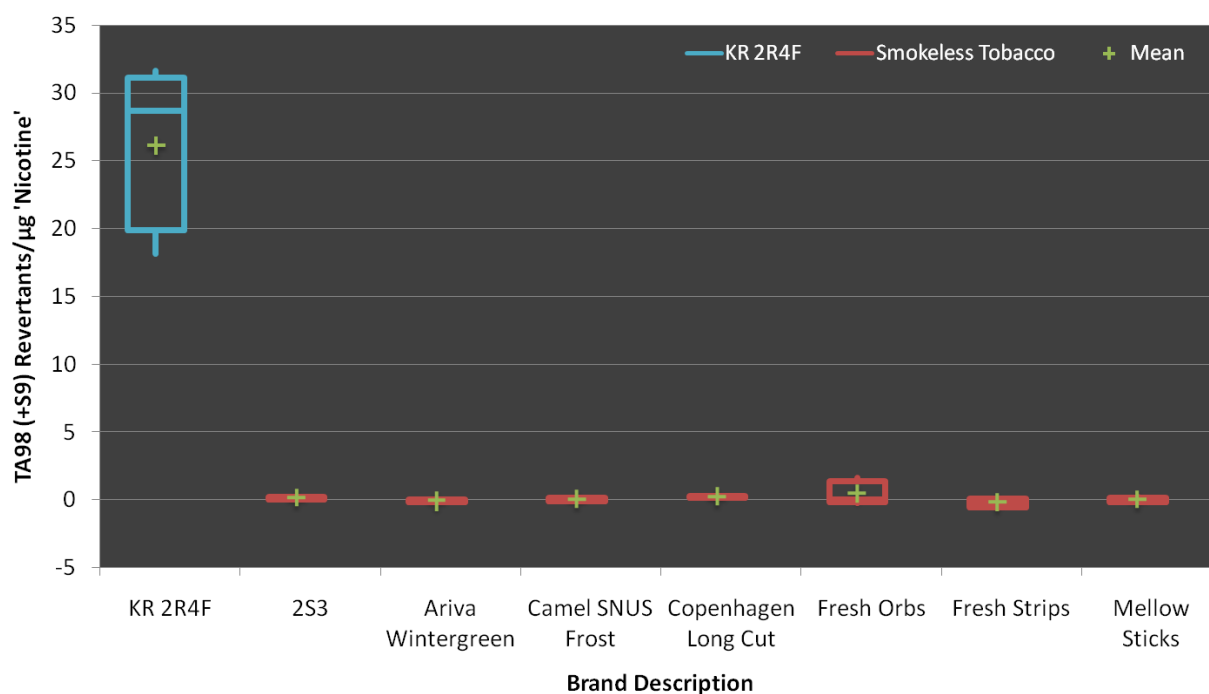
Strain **TA100(-S9)**

- KR 2R4F (084396) specific activity is significantly different from each of {Fresh Strips (084454), Ariva Wintergreen (084457), Fresh Orbs (084458)}

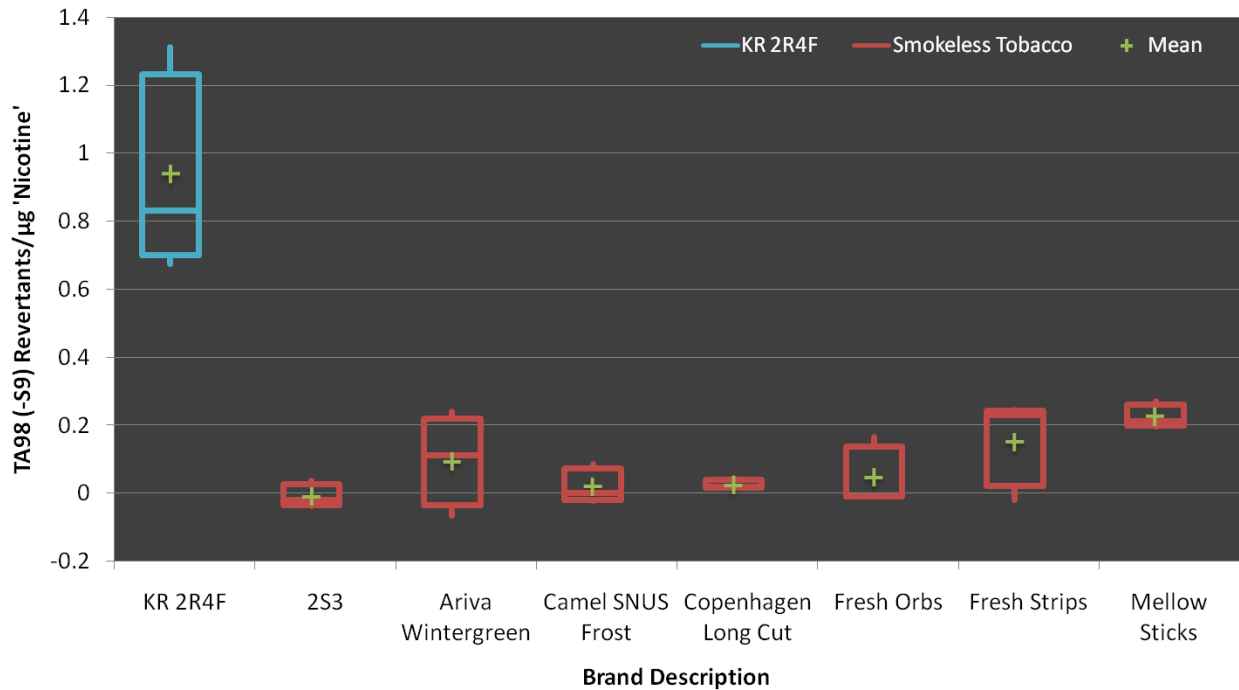
Strain **TA1537(-S9)**

- KR 2R4F (084396) specific activity is significantly different from that of Mellow Sticks (084455)

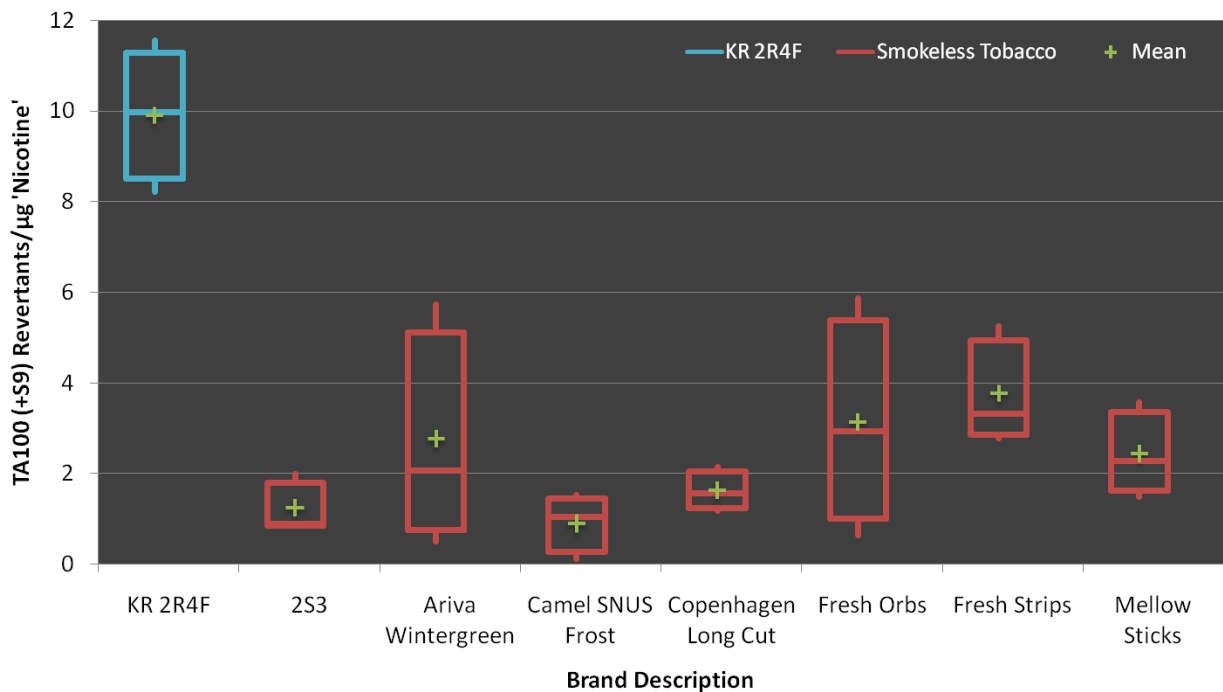
### Box-and-Whisker Plot: TA98 (+S9) Replicate Specific Activity Estimates



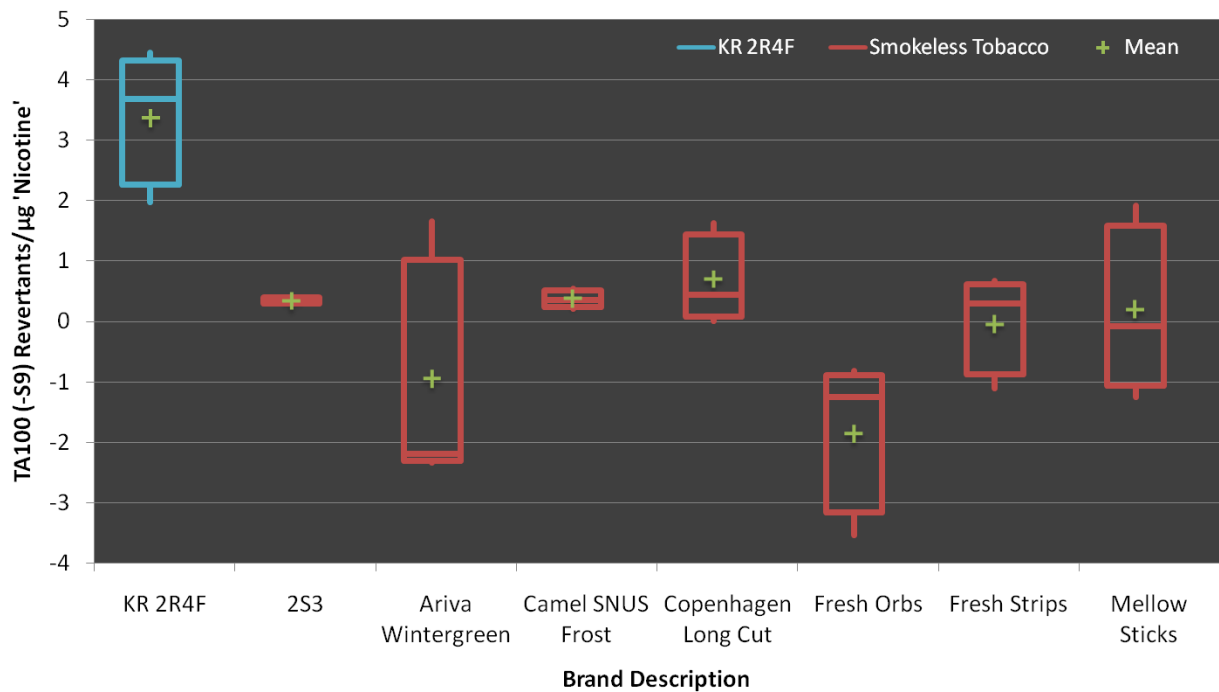
**Box-and-Whisker Plot: TA98 (-S9) Replicate Specific Activity Estimates**



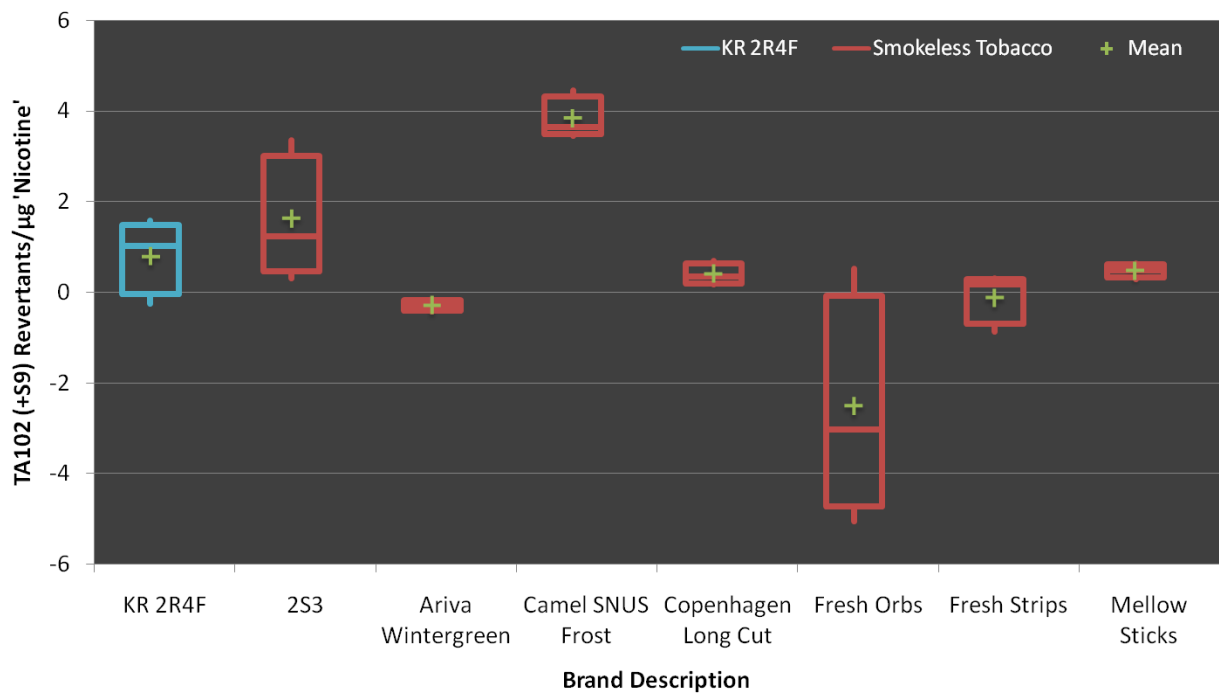
**Box-and-Whisker Plot: TA100 (+S9) Replicate Specific Activity Estimates**



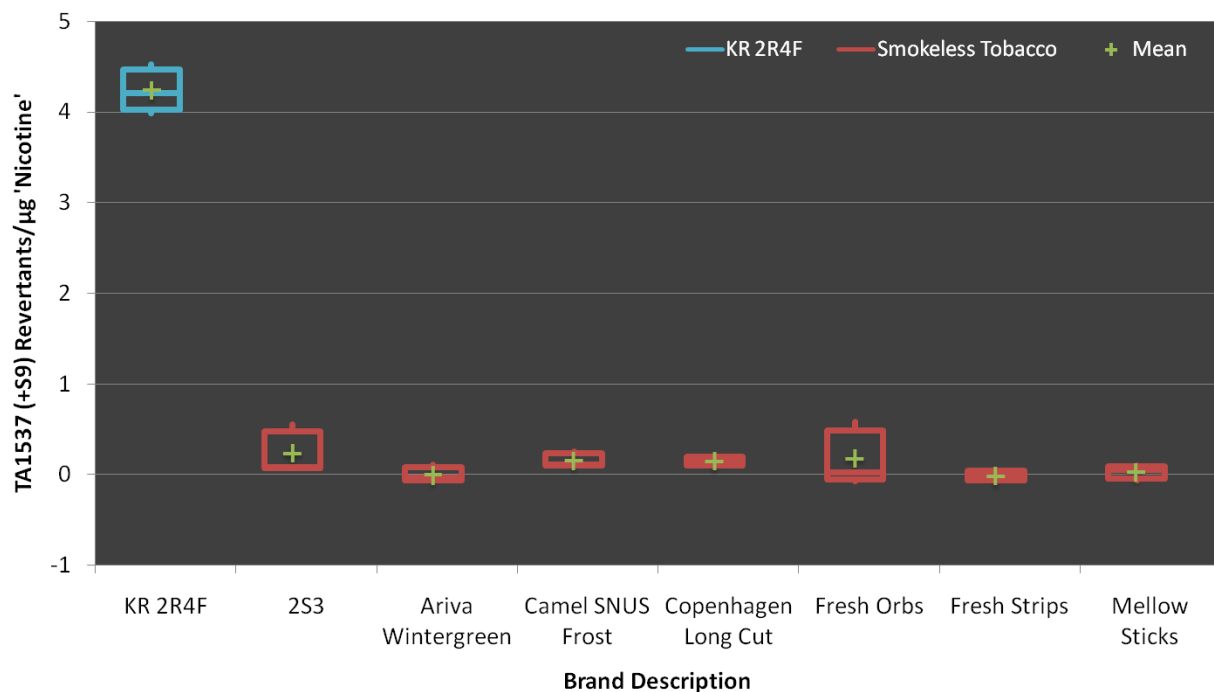
**Box-and-Whisker Plot: TA100 (-S9) Replicate Specific Activity Estimates**



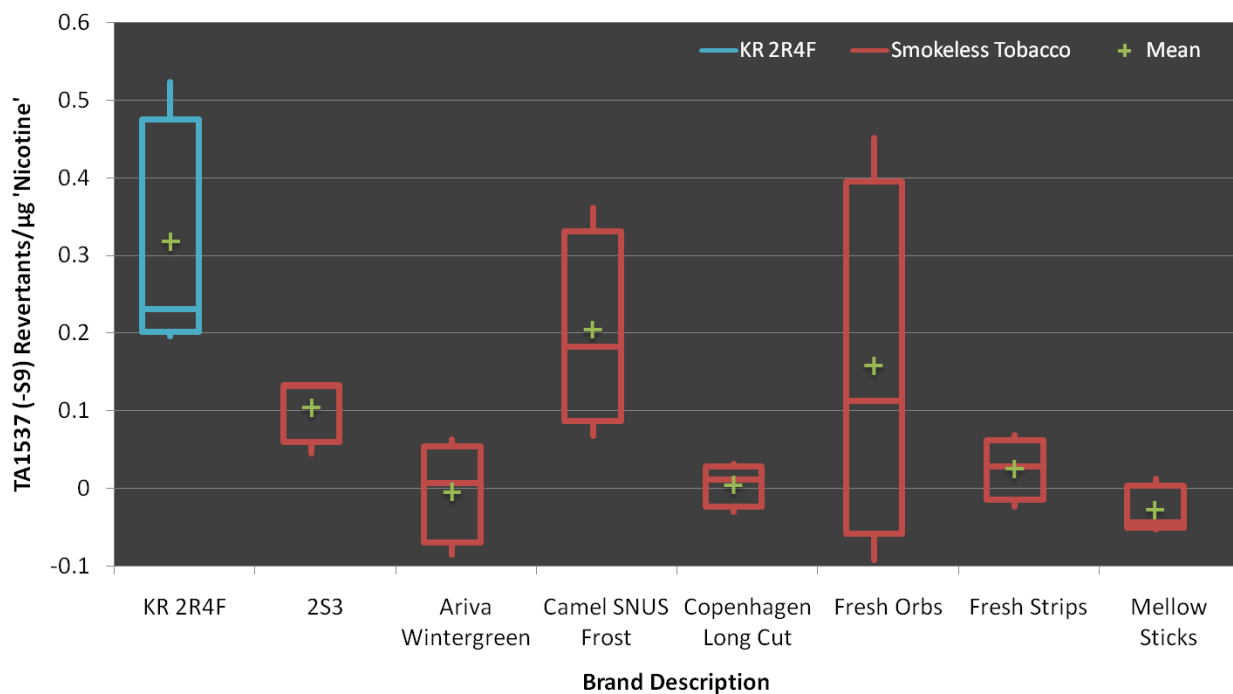
**Box-and-Whisker Plot: TA102 (+S9) Replicate Specific Activity Estimates**



**Box-and-Whisker Plot: TA1537 (+S9) Replicate Specific Activity Estimates**



**Box-and-Whisker Plot: TA1537 (-S9) Replicate Specific Activity Estimates**





## 7 Summary

Based on the results obtained in this study and the corresponding analysis of the toxicological data, the following summarizes the findings in regards to mutagenicity as measured with the *in vitro* Ames Bacterial Reverse Mutation assay.

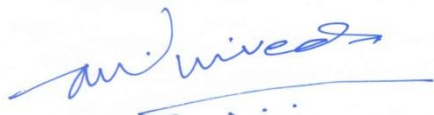
- All 3 dose bases indicated significant differences among smokeless tobacco products in strain TA102 (+S9) for Camel SNUS Frost (084394), indicating that this brand may be more mutagenic than some of the other smokeless tobacco brands tested (with the exception of 2S3 Research Moist Snuff).
- In strains TA98 (+S9), TA98 (-S9), TA100 (+S9) and TA1537 (+S9), the CSC of KR 2R4F test samples on a nicotine dose basis was significantly more mutagenic than the extracts of any of the smokeless tobacco test samples on a nicotine dose basis.
- In general, the responses for all smokeless tobacco test brands were fairly weak, indicating low levels of mutagenic activity for these extracts as compared to the same tests using tobacco smoke condensate.

## 8 Attribution

### 8.1 Original

This report has been reviewed by me and is certified, to the best of my knowledge, to be a true and accurate description of the procedures, protocols and test methods used to arrive at the data and/or findings that accompany this report.

Dated: October 9, 2008

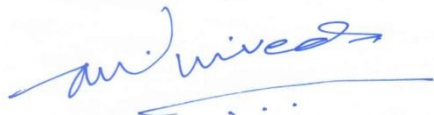


Amit Trivedi, Ph.D.,  
Technical Director (Toxicology)  
Labstat International ULC

### 8.2 Revision 1

This report has been reviewed by me and is certified, to the best of my knowledge, to be a true and accurate description of the procedures, protocols and test methods used to arrive at the data and/or findings that accompany this report.

Dated: October 17, 2008



Amit Trivedi, Ph.D.,  
Technical Director (Toxicology)  
Labstat International ULC

### 8.3 Revision 2

This report has been reviewed by me and is certified, to the best of my knowledge, to be a true and accurate description of the statistical analysis methodologies used to arrive at the findings that accompany this report.

Dated: October 26, 2009



Wendy Wagstaff  
Senior Statistician  
Labstat International ULC

### 8.4 Revision 3

#### 8.4.1 Technical Director (Toxicology)

This report has been reviewed by me and is certified, to the best of my knowledge, to be a true and accurate description of the procedures, protocols and test methods used to arrive at the data and/or findings that accompany this report.

Dated: December 15, 2009



Amit Trivedi, Ph.D.,  
Technical Director (Toxicology)  
Labstat International ULC

#### 8.4.2 Senior Statistician

This report has been reviewed by me and is certified, to the best of my knowledge, to be a true and accurate description of the statistical analysis methodologies used to arrive at the findings that accompany this report.

Dated: December 15, 2009



Wendy Wagstaff  
Senior Statistician  
Labstat International ULC

# **Appendix A**

## **Scope of Accreditation**



Standards Council of Canada  
Conseil canadien des normes

200-270, rue Albert St.  
Ottawa, ON (Canada)  
K1P 6N7

Canada

Tel.: +1 613 238 3222

Fax.: +1 613 569 7808

E-mail/Courriel : [info@scc.ca](mailto:info@scc.ca)

Internet: <http://www.scc.ca>

## SCOPE OF ACCREDITATION

### LABSTAT INTERNATIONAL ULC

262 Manitou Drive, Unit 5

Kitchener, ON

N2C 1L3

Accredited Laboratory No. 368

(Conforms with requirements of CAN-P-4E (ISO/IEC 17025:2005))

CONTACT: Mr. Lucian Hirtie  
TEL: (519) 748-5409  
FAX: (519) 748-1654  
EMAIL: [lhirtie@labstat.com](mailto:lhirtie@labstat.com)

CLIENTS SERVED: All interested parties

FIELDS OF TESTING: Biological, Chemical/Physical

ISSUED ON: 2007-03-08

VALID TO: 2012-01-22

**Remarque:** La présente portée d'accréditation existe également en français, sous la forme d'un document distinct.

**Note:** This scope of accreditation is also available in French as a separately issued document.

### ANIMAL AND PLANTS (AGRICULTURE)

#### Agricultural products: (except food and chemicals)

##### **Tobacco**

|             |  |
|-------------|--|
| AOAC 966.02 | Moisture in Tobacco  |
| ASTM E2187  | Standard Test Method for Measuring the Ignition Strength of Cigarettes |
| ISO 10315   | Cigarettes – Determination of Nicotine in Smoke                        |
|             | Condensates Gas-Chromatographic Method                                 |
| ISO 10362-1 | Cigarettes – Determination of Water in Smoke Condensates –             |

Standards Council of Canada Accredited Laboratory No. 368

|          |   |
|----------|---|
|          | Part 1: Gas-Chromatographic Method  |
| ISO 3308 | Routine Analytical Cigarette-Smoking Machine- Definitions and Standard Conditions   |
| ISO 3402 | Tobacco and Tobacco Products – Atmosphere for Conditioning and Testing  |
| ISO 4387 | Cigarettes – Determination of Total and Nicotine-Free Dry Particulate Matter Using a Routine Analytical Smoking Machine   |
| ISO 6565 | Tobacco and Tobacco Products – Draw Resistance of Cigarettes and Pressure Drop of Filter Rods-Standard Conditions and Measurement   |
| ISO 8454 | Cigarettes – Determination of Carbon Monoxide in the Vapour Phase of Cigarette Smoke – NDIR method  |
| TMS-118  | Determination of Volatile Nitrosamines in Mainstream Tobacco Smoke  |
| TMS-120  | Determination of Selected Polynuclear Aromatic Hydrocarbons (PAHs) in Mainstream Tobacco Smoke  |
| TMS-127  | Determination of Selected Polynuclear Aromatic Hydrocarbons (PAHs) And Aza-Arenes in the Particulate Phase of Mainstream Tobacco Smoke  |
| TMS-128  | Determination of Aromatic Amines in Mainstream Tobacco smoke (Expanded list: Aniline, o-Toluidine, m-Toluidine, p-Toluidine, o-Anisidine, 1- and 2-Aminonaphthalene and 3- and 4-Aminobiphenyl) |
| TMS-132  | Determination of Gas Phase and Particulate Phase Free Radicals in Mainstream Smoke  |
| TMS-133  | Determination of Heterocyclic Aromatic Amines (HAAs) in Mainstream Tobacco Smoke  |
| TMS-135  | Determination of Tobacco Specific Nitrosamines in Mainstream Smoke by High-Performance Liquid Chromatography-ESI-Tandem Mass Spectrometry   |
| TSS-219  | Determination of Selected Polynuclear Aromatic Hydrocarbons (PAHs) in Sidestream Smoke  |
| TWT-303  | Determination of Carbonyls in Whole Tobacco   |
| TWT-315  | Determination of N-Methyl Carbamate Pesticides in Tobacco   |
| TWT-316  | Determination of Organophosphate Pesticides in Tobacco  |
| TWT-317  | Determination of Organochlorine Pesticides in Process Tobacco   |
| TWT-318  | Determination of Ethylene-Bis-Dithiocarbamate (EBDC) in Whole Tobacco   |
| TWT-319  | Determination of Benomyl Carbendazim in Tobacco   |
| TWT-321  | Determination Of Nicotine Alkaloids And Reducing Sugars In Whole Tobacco  |
| TWT-322  | Determination of Chlorophenoxy Acid Herbicides in Process Tobacco   |
| TWT-323  | Determination of Isovaleric Acid and 3-Methylvaleric Acid in Tobacco  |

The approved and most recent version of this document can be viewed on the SCC website at <http://palcan.scc.ca/SpecsSearch/GLSearchForm.do>

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|         |  |
|---------|--|
| TWT-324 | Determination of Nicotine in Whole Tobacco (CDC method)  |
| TWT-325 | Determination of Pectin in Tobacco   |
| TWT-333 | Determination of Tobacco Specific Nitrosamines in Whole Tobacco by High-Performance Liquid Chromatography-ESI-Tandem Mass Spectrometry |

**(Health Canada Tobacco Reporting Regulations Official Methods)**

|        |   |
|--------|---|
| T-101  | Determination of Ammonia in Mainstream Tobacco Smoke  |
| T-102  | Determination of 1- and 2- Aminonaphthalene and 3- and 4- Aminobiphenyl in Mainstream Tobacco Smoke       |
| T-103  | Determination of Benzo[a]pyrene in Mainstream Tobacco Smoke   |
| T-104  | Determination of Selected Carbonyls in Mainstream Tobacco Smoke   |
| T-105  | Determination of Eugenol in Mainstream Tobacco Smoke  |
| T-106  | Determination of Filter Efficiency in Mainstream Tobacco Smoke  |
| T-107  | Determination of Hydrogen Cyanide in Mainstream Tobacco Smoke   |
| T-108  | Determination of Mercury in Mainstream Tobacco Smoke  |
| T-109  | Determination of Ni, Pb, Cd, Cr, As and Se in Mainstream Tobacco Smoke                                    |
| T-110  | Determination of Oxides of Nitrogen in Mainstream Tobacco Smoke   |
| T-111  | Determination of Nitrosamines in Mainstream Tobacco Smoke   |
| T-112  | Determination of Pyridine, Quinoline and Styrene in Mainstream Tobacco Smoke                              |
| T-113  | Determination of Mainstream Tobacco Smoke pH  |
| T-114  | Determination of Phenolic Compounds in Mainstream Tobacco Smoke   |
| T-115  | Determination of Tar, Nicotine and Carbon Monoxide in Mainstream Tobacco Smoke                            |
| T-116  | Determination of 1,3- Butadiene, Isoprene, Acrylonitrile, Benzene and Toluene in Mainstream Tobacco Smoke |
| T-201  | Determination of Ammonia in Sidestream Tobacco Smoke  |
| T-202  | Determination of 1- and 2- Aminonaphthalene and 3- and 4- Aminobiphenyl in Sidestream Tobacco Smoke       |
| T-203  | Determination of Benzo[a]pyrene in Sidestream Tobacco Smoke   |
| T-203A | Determination of Benzo[a]pyrene in Sidestream Tobacco Smoke (GC/MS)                                       |
| T-204  | Determination of Selected Carbonyls in Sidestream Tobacco Smoke   |
| T-205  | Determination of Hydrogen Cyanide in Sidestream Tobacco Smoke   |
| T-206  | Determination of Mercury in Sidestream Tobacco Smoke  |

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Standards Council of Canada Accredited Laboratory No. 368

|       |   |
|-------|---|
| T-207 | Determination of Toxic Trace Metals in Sidestream Smoke   |
| T-208 | Determination of Oxides of Nitrogen in Sidestream Tobacco Smoke   |
| T-209 | Determination of Nitrosamines in Sidestream Tobacco Smoke   |
| T-210 | Determination of Pyridine and Quinoline in Sidestream Tobacco Smoke   |
| T-211 | Determination of Phenolic Compounds in Sidestream Tobacco Smoke   |
| T-212 | Determination of "Tar" and Nicotine in Sidestream Tobacco Smoke   |
| T-213 | Determination of 1,3 Butadiene, Isoprene, Acrylonitrile, Benzene, Toluene and Styrene in Sidestream Tobacco Smoke                           |
| T-214 | Determination of Carbon Monoxide (CO) in Sidestream Tobacco Smoke   |
| T-301 | Determination of Alkaloids in Whole Tobacco   |
| T-302 | Determination of Ammonia in Whole Tobacco   |
| T-304 | Determination of Humectants in Whole Tobacco  |
| T-306 | Determination of Ni, Pb, Cd, Cr, As, Se and Hg in Whole Tobacco   |
| T-307 | Determination of Benzo[a]pyrene in Whole Tobacco  |
| T-308 | Determination of Nitrate in Whole Tobacco   |
| T-309 | Determination of Nitrosamines in Whole Tobacco  |
| T-310 | Determination of Whole Tobacco pH   |
| T-311 | Determination of Triacetin in Whole Tobacco   |
| T-312 | Determination of Sodium Propionate in Whole Tobacco   |
| T-313 | Determination of Sorbic Acid in Whole Tobacco   |
| T-314 | Determination of Eugenol in Whole Tobacco   |
| T-401 | Preparation of Cigarettes from Packaged Leaf Tobacco for Testing  |
| T-402 | Preparation of Cigarettes, Cigarette Tobacco, Cigars, Kreteks, Bidis, Packaged Leaf Tobacco, Pipe Tobacco and Smokeless Tobacco for testing |

**(Microbiology Tests)**

|         |  |
|---------|--|
| T-501   | Bacterial Reverse Mutation Assay for Mainstream Tobacco Smoke                      |
| T-502   | Neutral Red Uptake Assay for Mainstream Tobacco Smoke                              |
| T-503   | In Vitro Micronucleus Assay for Mainstream Tobacco Smoke                           |
| TBA-504 | <i>In vitro</i> Sister Chromatid Exchange (SCE) Assay for Mainstream Tobacco Smoke |

**(Other: Measures of Exposure)**

|         |   |
|---------|---|
| TME-001 | Determination of Nicotine, Cotinine and Caffeine in Human Physiological Fluid Samples |
|---------|---|

The approved and most recent version of this document can be viewed on the SCC website at <http://palcan.scc.ca/SpecsSearch/GLSearchForm.do>

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Standards Council of Canada Accredited Laboratory No. 388

|         |   |
|---------|---|
| TME-002 | Determination of Creatinine in Urine  |
| TME-003 | Determination of 3-Hydroxycotinine in Human Physiological Fluid Samples                                     |
| TME-004 | <i>Salmonella Typhimurium</i> Reverse Mutation Assay: Microsuspension Method For Testing Urine Mutagenicity |
| TME-005 | Determination of Nicotine and Major Metabolites in Human Urine Using LC-MS-MS                               |

**Notes:**

**AOAC:** Association of Official Analytical Chemists

**ASTM:** American Society for Testing and Materials

**CAN-P-4E (ISO/IEC 17025):** General Requirements for the Competence of Testing and Calibration Laboratories (ISO/IEC 17025-2005)

**ISO:** International Organization for Standardization

**T:** Health Canada Tobacco Reporting Regulations Official Methods

**TBA:** Test Method, Biological Activity

**TME:** Test Method, Measures of Exposure

**TMS:** Test method, Mainstream Smoke

**TSS:** Test method, Sidestream Smoke

**TWT:** Test method, Whole Tobacco

---

P. Paladino, P. Eng., Director, Conformity Assessment

Date: 2007-03-08

Number of Scope Listings: 83

SCC 1003-15/420

Partner File #0

Partner: None



# **Appendix B**

## **“Raw” Data and Analysis Results (See Enclosed CD)**

## Use of Labstat's<sup>1</sup> Analytical Reports<sup>2</sup>

Labstat International ULC is a recognized centre of analytical excellence related to tobacco and tobacco products. Our clients include major international tobacco manufacturers, various Governments and Government agencies such as the Canadian Federal Department of Health and the Massachusetts Department of Public Health, agricultural interests, university researchers and private research interests. Normally our contractual obligations extend **only** to the provision of data and related reports.

It should be noted<sup>3</sup>, in this regard, that

***All analytical data and reports, provided by Labstat International ULC, are for the exclusive use of the person, partnership, or corporation to whom it is addressed, and neither the data, the report nor the name of the laboratory (Labstat International ULC) nor any member of its staff may be used in connection with the advertising or sale of any product or process without written authorization from the CEO of the company or his designate. Labstat International ULC is not responsible for unauthorized use of test reports.***

The following also applies to reported data.

***All Labstat reports on testing relate only to the sample received and tested by it at the time of testing. Labstat warrants that all samples submitted were tested in accordance with its standard test procedures. Except as stated herein, there is no warranty expressed or implied, statutory or otherwise, as to the results of Labstat tests. Labstat does not warrant or guarantee the fitness of the materials from which the samples have been drawn for any particular purpose including without limitation for consumption as cigarettes, cigars, smokeless tobacco or any other form of tobacco or tobacco-related product.***

<sup>1</sup>. Labstat International ULC,  
262 Manitou Drive, Kitchener, ON Canada N2C 1L3  
Phone: (519) 748-5409; Fax: (519) 748-1654; Email: labstat@labstat.com

<sup>2</sup>. This document may not be reproduced, in whole or in part in any form, without the written consent of the author(s) on behalf of Labstat International ULC

<sup>3</sup>. Unless superseded by a specific contractual obligation or other written agreement.

### **Attribution Policy**

Labstat International ULC ("Labstat") is a private independent analytical laboratory whose services are generally limited to the analysis of tobacco and tobacco related products ("product") provided by clients. Neither Labstat, as a company, nor its personnel, as individuals, participate in product development, product preparation or the design of experiments related to product characteristics. It is for this reason that the company does not allow the use of its name (Labstat International ULC), any part of its name, its address (262 Manitou Drive, Kitchener, Ontario Canada), or any part of its address, its logo (as shown below) or the name of any of its employees to be used in either indirect or direct product marketing or advertising including but not limited to press releases, advertisements in the print media, or public statements regarding product attributes based on test results.



| <b>Sample<br/>ID</b> | <b>Sample<br/>Description</b>        |
|----------------------|--------------------------------------|
| 084394               | Camel SNUS Frost                     |
| 084395               | 2S3 Research Moist smokeless tobacco |
| 084454               | Fresh Strips                         |
| 084455               | Mellow Sticks                        |
| 084456               | Copenhagen Long Cut                  |
| 084457               | Ariva Wintergreen                    |
| 084458               | Fresh Orbs                           |



### Limits of Detection (LOD) and Limits of Quantification (LOQ) Determined for Selected Constituents in Processed Tobacco

| Health Canada Method | Analyte   | Units    | Processed Tobacco |      |
|----------------------|-----------|----------|-------------------|------|
|                      |           |          | LOD               | LOQ  |
| T-301                | Alkaloids | Nicotine | µg/g (dry wt)     | 75.0 |
|                      |           |          |                   |      |

Abbreviations: BDL, below detection limit; NQ, below quantitation limit; N/A, not applicable  
Date of last review: March 4, 2008

NOTE: The above limits referred to samples processed as required by the referenced Health Canada Method (ie. either "as received" or "dried"). Corrections for the moisture content, determined independently, must be applied where applicable in order to convert the "as received" limits to limits expressed on a "dry weight" basis.

\*NOTE: The LOD and LOQ are based on the lowest standard used for calibration of the instruments as referenced in the Health Canada Method.

LOD Definition: The limit of detection (LOD) for a particular analyte is a statistically defined decision point that, with a specified probability, measured results falling at or above this point are interpreted to indicate an analyte concentration greater than zero within the sample.

LOQ Definition: The limit of quantification for a particular analyte is another statistically defined decision point that results falling at or above this point can be assigned a statistically significant numerical value with an associated level of precision. Values falling between the LOD and LOQ are interpreted as a positive but not quantifiable result for the analyte in question.

| Matrix Code | Sample ID | Nicotine (µg/g) |        |                |                | Dry Matter (%) |        |                |                | Moisture (%) |        |                |                |
|-------------|-----------|-----------------|--------|----------------|----------------|----------------|--------|----------------|----------------|--------------|--------|----------------|----------------|
|             |           | Average         | St Dev | L. Limit (95%) | U. Limit (95%) | Average        | St Dev | L. Limit (95%) | U. Limit (95%) | Average      | St Dev | L. Limit (95%) | U. Limit (95%) |
| WT          | 084394    | 18575           | 152    | 18197          | 18952          | 68.3           | 0.1    | 67.9           | 68.6           | 31.7         | 0.1    | 31.4           | 32.1           |
| WT          | 084395    | 30659           | 442    | 29561          | 31758          | 46.0           | 0.0    | 45.9           | 46.1           | 54.0         | 0.0    | 53.9           | 54.1           |
| WT          | 084454    | 4314            | 93     | 4084           | 4545           | 88.9           | 0.1    | 88.7           | 89.1           | 11.1         | 0.1    | 10.9           | 11.3           |
| WT          | 084455    | 5110            | 95     | 4873           | 5348           | 93.9           | 0.0    | 93.9           | 94.0           | 6.07         | 0.03   | 6.00           | 6.15           |
| WT          | 084456    | 27568           | 687    | 25861          | 29275          | 44.6           | 0.1    | 44.3           | 45.0           | 55.4         | 0.1    | 55.0           | 55.7           |
| WT          | 084457    | 5203            | 359    | 4311           | 6095           | 96.3           | 0.0    | 96.3           | 96.4           | 3.68         | 0.02   | 3.62           | 3.73           |
| WT          | 084458    | 2784            | 46     | 2670           | 2898           | 94.9           | 0.0    | 94.8           | 94.9           | 5.14         | 0.01   | 5.11           | 5.17           |

**Glossary of Abbreviations**

L. Limit (95%) - lower limit of the 95% confidence interval

U. Limit (95%) - upper limit of the 95% confidence interval

**Table 1: Nicotine and Nicotine Related Contents of Processed Toba  
(‘Dry Weight’ Basis)**

| <b>Sample ID</b>      | <b>Nicotine (µg/g)</b> |
|-----------------------|------------------------|
| 084394                | 18495                  |
| 084394                | 18750                  |
| 084394                | 18479                  |
| <b>Average</b>        | 18575                  |
| <b>Std. Dev.</b>      | 152                    |
| <b>L. Limit (95%)</b> | 18197                  |
| <b>U. Limit (95%)</b> | 18952                  |
| 084395                | 30149                  |
| 084395                | 30910                  |
| 084395                | 30919                  |
| <b>Average</b>        | 30659                  |
| <b>Std. Dev.</b>      | 442                    |
| <b>L. Limit (95%)</b> | 29561                  |
| <b>U. Limit (95%)</b> | 31758                  |
| 084454                | 4325                   |
| 084454                | 4216                   |
| 084454                | 4401                   |
| <b>Average</b>        | 4314                   |
| <b>Std. Dev.</b>      | 93                     |
| <b>L. Limit (95%)</b> | 4084                   |
| <b>U. Limit (95%)</b> | 4545                   |
| 084455                | 5204                   |
| 084455                | 5114                   |
| 084455                | 5013                   |
| <b>Average</b>        | 5110                   |
| <b>Std. Dev.</b>      | 95                     |
| <b>L. Limit (95%)</b> | 4873                   |
| <b>U. Limit (95%)</b> | 5348                   |
| 084456                | 27370                  |
| 084456                | 28332                  |
| 084456                | 27001                  |
| <b>Average</b>        | 27568                  |
| <b>Std. Dev.</b>      | 687                    |
| <b>L. Limit (95%)</b> | 25861                  |
| <b>U. Limit (95%)</b> | 29275                  |

**Table 1: Nicotine and Nicotine Related Contents of Processed Toba  
('Dry Weight' Basis)**

| <b>Sample<br/>ID</b>  | <b>Nicotine<br/>(µg/g)</b> |
|-----------------------|----------------------------|
| 084457                | 5594                       |
| 084457                | 4887                       |
| 084457                | 5130                       |
| <b>Average</b>        | 5203                       |
| <b>Std. Dev.</b>      | 359                        |
| <b>L. Limit (95%)</b> | 4311                       |
| <b>U. Limit (95%)</b> | 6095                       |
| 084458                | 2807                       |
| 084458                | 2814                       |
| 084458                | 2731                       |
| <b>Average</b>        | 2784                       |
| <b>Std. Dev.</b>      | 46                         |
| <b>L. Limit (95%)</b> | 2670                       |
| <b>U. Limit (95%)</b> | 2898                       |



**Table 13: Moisture Content of Processed Tobacco**

| <b>Sample ID</b>      | <b>Dry Matter (%)</b> | <b>Moisture (%)</b> |
|-----------------------|-----------------------|---------------------|
| 084394                | 68.3                  | 31.7                |
| 084394                | 68.4                  | 31.6                |
| 084394                | 68.1                  | 31.9                |
| <b>Average</b>        | 68.3                  | 31.7                |
| <b>Std. Dev.</b>      | 0.1                   | 0.1                 |
| <b>L. Limit (95%)</b> | 67.9                  | 31.4                |
| <b>U. Limit (95%)</b> | 68.6                  | 32.1                |
| 084395                | 45.9                  | 54.1                |
| 084395                | 46.0                  | 54.0                |
| 084395                | 46.0                  | 54.0                |
| <b>Average</b>        | 46.0                  | 54.0                |
| <b>Std. Dev.</b>      | 0.0                   | 0.0                 |
| <b>L. Limit (95%)</b> | 45.9                  | 53.9                |
| <b>U. Limit (95%)</b> | 46.1                  | 54.1                |
| 084454                | 89.0                  | 11.0                |
| 084454                | 88.9                  | 11.1                |
| 084454                | 88.8                  | 11.2                |
| <b>Average</b>        | 88.9                  | 11.1                |
| <b>Std. Dev.</b>      | 0.1                   | 0.1                 |
| <b>L. Limit (95%)</b> | 88.7                  | 10.9                |
| <b>U. Limit (95%)</b> | 89.1                  | 11.3                |
| 084455                | 93.9                  | 6.05                |
| 084455                | 93.9                  | 6.11                |
| 084455                | 93.9                  | 6.06                |
| <b>Average</b>        | 93.9                  | 6.07                |
| <b>Std. Dev.</b>      | 0.0                   | 0.03                |
| <b>L. Limit (95%)</b> | 93.9                  | 6.00                |
| <b>U. Limit (95%)</b> | 94.0                  | 6.15                |
| 084456                | 44.7                  | 55.3                |
| 084456                | 44.5                  | 55.5                |
| 084456                | 44.8                  | 55.2                |
| <b>Average</b>        | 44.6                  | 55.4                |
| <b>Std. Dev.</b>      | 0.1                   | 0.1                 |
| <b>L. Limit (95%)</b> | 44.3                  | 55.0                |
| <b>U. Limit (95%)</b> | 45.0                  | 55.7                |

**Table 13: Moisture Content of Processed Tobacco**

| <b>Sample ID</b>      | <b>Dry Matter (%)</b> | <b>Moisture (%)</b> |
|-----------------------|-----------------------|---------------------|
| 084457                | 96.3                  | 3.65                |
| 084457                | 96.3                  | 3.68                |
| 084457                | 96.3                  | 3.70                |
| <b>Average</b>        | 96.3                  | 3.68                |
| <b>Std. Dev.</b>      | 0.0                   | 0.02                |
| <b>L. Limit (95%)</b> | 96.3                  | 3.62                |
| <b>U. Limit (95%)</b> | 96.4                  | 3.73                |
| 084458                | 94.9                  | 5.13                |
| 084458                | 94.8                  | 5.15                |
| 084458                | 94.9                  | 5.14                |
| <b>Average</b>        | 94.9                  | 5.14                |
| <b>Std. Dev.</b>      | 0.0                   | 0.01                |
| <b>L. Limit (95%)</b> | 94.8                  | 5.11                |
| <b>U. Limit (95%)</b> | 94.9                  | 5.17                |

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Project: M97

Period: September 15, 2008

**Smoking Data<sup>†</sup> for Ames Assay analysis:  
Mutagenesis in *Salmonella typhimurium***

| Set<br>Number | Run<br>Number | Sample<br>ID | Replicate<br>Number | Smoking<br>Date | Cigarettes<br>Smoked | Puff Count<br>(per cig) | Weight of<br>MS TPM<br>(mg)** | Smoking<br>Machine |
|---------------|---------------|--------------|---------------------|-----------------|----------------------|-------------------------|-------------------------------|--------------------|
| 1             | 2             | 084396       | 1                   | 15-Sep-08       | 20                   | 10.1                    | 213                           | Borgwaldt Rotary   |
| 1             | 3             | 084396       | 2                   | 15-Sep-08       | 20                   | 9.2                     | 215                           | Borgwaldt Rotary   |
| 1             | 4             | 084396       | 3                   | 15-Sep-08       | 20                   | 9.1                     | 225                           | Borgwaldt Rotary   |

<sup>†</sup> Samples generated under 'ISO' smoking conditions:

35mL puff volume; 60 second interval; 2 second duration; no vent blocking.

\*\* Samples extracted in DMSO to give a final concentration of 10.0 mg/mL.

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation  
(Revertants per plate)**

| Set<br>Number | Run<br>Number | Sample<br>ID | Replicate<br>Number | TPM Dose<br>(µg/plate) | TPM-H <sub>2</sub> O (DPM)<br>(µg/plate) | Nicotine<br>(µg/plate) | TA98 (+S9) |     |     | TA100 (+S9) |     |     | TA1535 (+S9) |    |    | TA1537 (+S9) |    |    | TA102 (+S9) |     |     |
|---------------|---------------|--------------|---------------------|------------------------|--|------------------------|------------|-----|-----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|               |               |              |                     |                        |  |                        | P1         | P2  | P3  | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 1             | 2             | 084396       | 1                   | 0                      | 0  | 0                      | 46         | 42  | 39  | 158         | 153 | 141 | 14           | 18 | 9  | 7            | 6  | 11 | 321         | 312 | 316 |
| 1             | 2             | 084396       | 1                   | 25                     | 23                                       | 2                      | 90         | 73  | 74  | 158         | 150 | 148 | 10           | 19 | 10 | 15           | 18 | 14 | 320         | 322 | 313 |
| 1             | 2             | 084396       | 1                   | 50                     | 46                                       | 4                      | 124        | 102 | 121 | 180         | 154 | 184 | 7            | 12 | 13 | 27           | 24 | 35 | 346         | 289 | 302 |
| 1             | 2             | 084396       | 1                   | 75                     | 69                                       | 6                      | 166        | 141 | 178 | 197         | 190 | 209 | 16           | 19 | 14 | 32           | 34 | 31 | 287         | 280 | 287 |
| 1             | 2             | 084396       | 1                   | 100                    | 93                                       | 8                      | 191        | 188 | 186 | 213         | 221 | 223 | 13           | 12 | 16 | 34           | 36 | 32 | 283         | 313 | 294 |
| 1             | 2             | 084396       | 1                   | 125                    | 116                                      | 9                      | 206        | 199 | 211 | 230         | 203 | 198 | 9            | 20 | 8  | 52           | 42 | 55 | 295         | 308 | 306 |
| 1             | 2             | 084396       | 1                   | 250                    | 231                                      | 19                     | 369        | 352 | 332 | 296         | 303 | 302 | 23           | 12 | 17 | 88           | 77 | 86 | 318         | 304 | 320 |
| 1             | 2             | 084396       | 1                   | 500                    | 463                                      | 38                     | 483        | 490 | 509 | 351         | 376 | 352 | 16           | 22 | 20 | 100          | 88 | 96 | 305         | 299 | 291 |
|               |               |              |                     |                        |  |                        |            |     |     |             |     |     |              |    |    |              |    |    |             |     |     |
| 1             | 3             | 084396       | 2                   | 0                      | 0  | 0                      | 48         | 48  | 36  | 181         | 161 | 157 | 11           | 17 | 9  | 7            | 6  | 5  | 263         | 294 | 268 |
| 1             | 3             | 084396       | 2                   | 25                     | 23                                       | 2                      | 77         | 83  | 81  | 176         | 171 | 191 | 14           | 11 | 10 | 21           | 17 | 19 | 295         | 317 | 312 |
| 1             | 3             | 084396       | 2                   | 50                     | 46                                       | 4                      | 150        | 139 | 162 | 182         | 186 | 213 | 12           | 9  | 8  | 32           | 35 | 40 | 286         | 326 | 326 |
| 1             | 3             | 084396       | 2                   | 75                     | 69                                       | 6                      | 173        | 154 | 188 | 250         | 232 | 242 | 14           | 13 | 7  | 43           | 37 | 42 | 292         | 322 | 310 |
| 1             | 3             | 084396       | 2                   | 100                    | 93                                       | 8                      | 273        | 293 | 268 | 251         | 242 | 246 | 12           | 20 | 11 | 42           | 47 | 39 | 334         | 302 | 315 |
| 1             | 3             | 084396       | 2                   | 125                    | 116                                      | 9                      | 358        | 324 | 326 | 260         | 251 | 254 | 10           | 14 | 8  | 45           | 50 | 43 | 311         | 332 | 304 |
| 1             | 3             | 084396       | 2                   | 250                    | 231                                      | 19                     | 528        | 499 | 498 | 334         | 357 | 362 | 11           | 16 | 11 | 69           | 67 | 68 | 305         | 290 | 321 |
| 1             | 3             | 084396       | 2                   | 500                    | 463                                      | 38                     | 509        | 533 | 536 | 362         | 347 | 334 | 22           | 12 | 9  | 66           | 74 | 67 | 333         | 313 | 371 |
|               |               |              |                     |                        |  |                        |            |     |     |             |     |     |              |    |    |              |    |    |             |     |     |
| 1             | 4             | 084396       | 3                   | 0                      | 0  | 0                      | 49         | 47  | 33  | 153         | 172 | 168 | 14           | 11 | 12 | 6            | 5  | 7  | 274         | 315 | 294 |
| 1             | 4             | 084396       | 3                   | 25                     | 23                                       | 2                      | 64         | 59  | 89  | 160         | 163 | 181 | 16           | 18 | 16 | 18           | 20 | 19 | 317         | 328 | 349 |
| 1             | 4             | 084396       | 3                   | 50                     | 46                                       | 4                      | 151        | 153 | 173 | 197         | 186 | 166 | 17           | 17 | 11 | 32           | 30 | 42 | 351         | 285 | 336 |
| 1             | 4             | 084396       | 3                   | 75                     | 69                                       | 6                      | 186        | 212 | 202 | 200         | 219 | 236 | 10           | 20 | 17 | 30           | 41 | 42 | 352         | 346 | 355 |
| 1             | 4             | 084396       | 3                   | 100                    | 93                                       | 8                      | 271        | 263 | 269 | 246         | 249 | 268 | 14           | 12 | 12 | 37           | 57 | 32 | 300         | 324 | 320 |
| 1             | 4             | 084396       | 3                   | 125                    | 116                                      | 9                      | 299        | 288 | 291 | 258         | 260 | 286 | 17           | 10 | 12 | 53           | 55 | 45 | 325         | 315 | 318 |
| 1             | 4             | 084396       | 3                   | 250                    | 231                                      | 19                     | 339        | 309 | 331 | 368         | 352 | 382 | 11           | 14 | 16 | 86           | 75 | 64 | 374         | 353 | 330 |
| 1             | 4             | 084396       | 3                   | 500                    | 463                                      | 38                     | 447        | 448 | 482 | NA          | 368 | 397 | 20           | 15 | 22 | 90           | 87 | 78 | 372         | 364 | 380 |

N/A - data not available due to lack of bacterial growth or assay plate contamination

NOTE: TPM, Moisture and Nicotine contents of sample 084396 (Kentucky Reference 2R4F) were estimated based on existing historical data:

TPM = 10 mg/cigarette

Moisture = 0.75 mg/cigarette

Nicotine = 0.75 mg/cigarette

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Revertants per plate)**

| Set<br>Number | Run<br>Number | Sample<br>ID | Replicate<br>Number | TPM Dose<br>(µg/plate) | TPM-H <sub>2</sub> O (DPM)<br>(µg/plate) | Nicotine<br>(µg/plate) | TA98 (-S9) |    |    | TA100 (-S9) |     |     | TA1535 (-S9) |    |    | TA1537 (-S9) |    |    | TA102 (-S9) |     |     |
|---------------|---------------|--------------|---------------------|------------------------|--|------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|               |               |              |                     |                        |  |                        | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 1             | 2             | 084396       | 1                   | 0                      | 0  | 0                      | 34         | 31 | 28 | 136         | 148 | 154 | 18           | 16 | 10 | 5            | 6  | 7  | 278         | 289 | 306 |
| 1             | 2             | 084396       | 1                   | 25                     | 23                                       | 2                      | 30         | 28 | 29 | 161         | 151 | 168 | 11           | 17 | 16 | 8            | 9  | 12 | 273         | 257 | 266 |
| 1             | 2             | 084396       | 1                   | 50                     | 46                                       | 4                      | 31         | 30 | 38 | 173         | 160 | 184 | 19           | 20 | 16 | 9            | 10 | 7  | 293         | 294 | 292 |
| 1             | 2             | 084396       | 1                   | 75                     | 69                                       | 6                      | 28         | 28 | 29 | 185         | 164 | 183 | 10           | 13 | 19 | 11           | 7  | 9  | 306         | 294 | 288 |
| 1             | 2             | 084396       | 1                   | 100                    | 93                                       | 8                      | 47         | 36 | 37 | 186         | 177 | 169 | 18           | 17 | 12 | 11           | 9  | 8  | 280         | 282 | 291 |
| 1             | 2             | 084396       | 1                   | 125                    | 116                                      | 9                      | 26         | 27 | 37 | 186         | 193 | 200 | 20           | 14 | 19 | 7            | 9  | 10 | 296         | 294 | 282 |
| 1             | 2             | 084396       | 1                   | 250                    | 231                                      | 19                     | 36         | 40 | 40 | 210         | 208 | 211 | 14           | 10 | 14 | 9            | 13 | 12 | 266         | 268 | 266 |
| 1             | 2             | 084396       | 1                   | 500                    | 463                                      | 38                     | 66         | 57 | 62 | 232         | 223 | 231 | 23           | 12 | 16 | 7            | 8  | 6  | 264         | 256 | 266 |
|               |               |              |                     |                        |  |                        |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 1             | 3             | 084396       | 2                   | 0                      | 0  | 0                      | 29         | 27 | 20 | 151         | 153 | 153 | 20           | 19 | 16 | 6            | 7  | 5  | 271         | 286 | 270 |
| 1             | 3             | 084396       | 2                   | 25                     | 23                                       | 2                      | 23         | 24 | 25 | 174         | 154 | 160 | 17           | 19 | 19 | 8            | 7  | 6  | 317         | 306 | 301 |
| 1             | 3             | 084396       | 2                   | 50                     | 46                                       | 4                      | 30         | 23 | 26 | 170         | 192 | 179 | 22           | 20 | 14 | 9            | 7  | 6  | 290         | 298 | 301 |
| 1             | 3             | 084396       | 2                   | 75                     | 69                                       | 6                      | 28         | 29 | 27 | 174         | 180 | 170 | 17           | 22 | 18 | 7            | 8  | 9  | 298         | 281 | 286 |
| 1             | 3             | 084396       | 2                   | 100                    | 93                                       | 8                      | 31         | 33 | 30 | 183         | 186 | 196 | 20           | 14 | 14 | 11           | 10 | 7  | 319         | 321 | 308 |
| 1             | 3             | 084396       | 2                   | 125                    | 116                                      | 9                      | 39         | 22 | 29 | 177         | 193 | 189 | 14           | 25 | 17 | 9            | 7  | 8  | 296         | 313 | 311 |
| 1             | 3             | 084396       | 2                   | 250                    | 231                                      | 19                     | 32         | 31 | 24 | 194         | 174 | 201 | 16           | 20 | 13 | 10           | 13 | 9  | 310         | 306 | 298 |
| 1             | 3             | 084396       | 2                   | 500                    | 463                                      | 38                     | 86         | 79 | 66 | 209         | 197 | 211 | 28           | 19 | 24 | 7            | 8  | 6  | 294         | 294 | 283 |
|               |               |              |                     |                        |  |                        |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 1             | 4             | 084396       | 3                   | 0                      | 0  | 0                      | 26         | 27 | 48 | 154         | 153 | 149 | 14           | 18 | 17 | 5            | 6  | 7  | 279         | 285 | 271 |
| 1             | 4             | 084396       | 3                   | 25                     | 23                                       | 2                      | 29         | 21 | 26 | 158         | 148 | 167 | 15           | 18 | 10 | 6            | 8  | 7  | 291         | 277 | 276 |
| 1             | 4             | 084396       | 3                   | 50                     | 46                                       | 4                      | 36         | 27 | 30 | 146         | 157 | 141 | 19           | 17 | 17 | 9            | 12 | 10 | 285         | 288 | 285 |
| 1             | 4             | 084396       | 3                   | 75                     | 69                                       | 6                      | 26         | 23 | 31 | 147         | 173 | 162 | 19           | 16 | 13 | 9            | 10 | 8  | 302         | 303 | 294 |
| 1             | 4             | 084396       | 3                   | 100                    | 93                                       | 8                      | 33         | 33 | 30 | 154         | 144 | 160 | 11           | 14 | 14 | 10           | 9  | 11 | 289         | 274 | 293 |
| 1             | 4             | 084396       | 3                   | 125                    | 116                                      | 9                      | 29         | 34 | 32 | 191         | 184 | 176 | 17           | 13 | 12 | 10           | 11 | 13 | 297         | 294 | 287 |
| 1             | 4             | 084396       | 3                   | 250                    | 231                                      | 19                     | 39         | 32 | 46 | 178         | 187 | 189 | 14           | 14 | 13 | 21           | 19 | 20 | 295         | 278 | 288 |
| 1             | 4             | 084396       | 3                   | 500                    | 463                                      | 38                     | 48         | 62 | 51 | 186         | 190 | 200 | 14           | 18 | 20 | 8            | 9  | 7  | 299         | 304 | 306 |

N/A - data not available due to lack of bacterial growth or assay plate contamination

**NOTE:** TPM, Moisture and Nicotine contents of sample 084396 (Kentucky Reference 2R4F) were estimated based on existing historical data:

TPM = 10 mg/cigarette

Moisture = 0.75 mg/cigarette

Nicotine = 0.75 mg/cigarette

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | TPM Dose (µg/plate) | TPM-H <sub>2</sub> O (DPM) (µg/plate) | Nicotine (µg/plate) | TA98 (+S9) |    | TA100 (+S9) |    | TA1535 (+S9) |    | TA1537 (+S9) |    | TA102 (+S9) |    |
|------------|------------|-----------|------------------|---------------------|---------------------------------------|---------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                     |                                       |                     | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 1          | 2          | 084396    | 1                | 0                   | 0                                     | 0                   | 42         | 4  | 151         | 9  | 14           | 5  | 8            | 3  | 316         | 5  |
| 1          | 2          | 084396    | 1                | 25                  | 23                                    | 2                   | 79         | 10 | 152         | 5  | 13           | 5  | 16           | 2  | 318         | 5  |
| 1          | 2          | 084396    | 1                | 50                  | 46                                    | 4                   | 116        | 12 | 173         | 16 | 11           | 3  | 29           | 6  | 312         | 30 |
| 1          | 2          | 084396    | 1                | 75                  | 69                                    | 6                   | 162        | 19 | 199         | 10 | 16           | 3  | 32           | 2  | 285         | 4  |
| 1          | 2          | 084396    | 1                | 100                 | 93                                    | 8                   | 188        | 3  | 219         | 5  | 14           | 2  | 34           | 2  | 297         | 15 |
| 1          | 2          | 084396    | 1                | 125                 | 116                                   | 9                   | 205        | 6  | 210         | 17 | 12           | 7  | 50           | 7  | 303         | 7  |
| 1          | 2          | 084396    | 1                | 250                 | 231                                   | 19                  | 351        | 19 | 300         | 4  | 17           | 6  | 84           | 6  | 314         | 9  |
| 1          | 2          | 084396    | 1                | 500                 | 463                                   | 38                  | 494        | 13 | 360         | 14 | 19           | 3  | 95           | 6  | 298         | 7  |
|            |            |           |                  |                     |                                       |                     |            |    |             |    |              |    |              |    |             |    |
| 1          | 3          | 084396    | 2                | 0                   | 0                                     | 0                   | 44         | 7  | 166         | 13 | 12           | 4  | 6            | 1  | 275         | 17 |
| 1          | 3          | 084396    | 2                | 25                  | 23                                    | 2                   | 80         | 3  | 179         | 10 | 12           | 2  | 19           | 2  | 308         | 12 |
| 1          | 3          | 084396    | 2                | 50                  | 46                                    | 4                   | 150        | 12 | 194         | 17 | 10           | 2  | 36           | 4  | 313         | 23 |
| 1          | 3          | 084396    | 2                | 75                  | 69                                    | 6                   | 172        | 17 | 241         | 9  | 11           | 4  | 41           | 3  | 308         | 15 |
| 1          | 3          | 084396    | 2                | 100                 | 93                                    | 8                   | 278        | 13 | 246         | 5  | 14           | 5  | 43           | 4  | 317         | 16 |
| 1          | 3          | 084396    | 2                | 125                 | 116                                   | 9                   | 336        | 19 | 255         | 5  | 11           | 3  | 46           | 4  | 316         | 15 |
| 1          | 3          | 084396    | 2                | 250                 | 231                                   | 19                  | 508        | 17 | 351         | 15 | 13           | 3  | 68           | 1  | 305         | 16 |
| 1          | 3          | 084396    | 2                | 500                 | 463                                   | 38                  | 526        | 15 | 348         | 14 | 14           | 7  | 69           | 4  | 339         | 29 |
|            |            |           |                  |                     |                                       |                     |            |    |             |    |              |    |              |    |             |    |
| 1          | 4          | 084396    | 3                | 0                   | 0                                     | 0                   | 43         | 9  | 164         | 10 | 12           | 2  | 6            | 1  | 294         | 21 |
| 1          | 4          | 084396    | 3                | 25                  | 23                                    | 2                   | 71         | 16 | 168         | 11 | 17           | 1  | 19           | 1  | 331         | 16 |
| 1          | 4          | 084396    | 3                | 50                  | 46                                    | 4                   | 159        | 12 | 183         | 16 | 15           | 3  | 35           | 6  | 324         | 35 |
| 1          | 4          | 084396    | 3                | 75                  | 69                                    | 6                   | 200        | 13 | 218         | 18 | 16           | 5  | 38           | 7  | 351         | 5  |
| 1          | 4          | 084396    | 3                | 100                 | 93                                    | 8                   | 268        | 4  | 254         | 12 | 13           | 1  | 42           | 13 | 315         | 13 |
| 1          | 4          | 084396    | 3                | 125                 | 116                                   | 9                   | 293        | 6  | 268         | 16 | 13           | 4  | 51           | 5  | 319         | 5  |
| 1          | 4          | 084396    | 3                | 250                 | 231                                   | 19                  | 326        | 16 | 367         | 15 | 14           | 3  | 75           | 11 | 352         | 22 |
| 1          | 4          | 084396    | 3                | 500                 | 463                                   | 38                  | 459        | 20 | 383         | 21 | 19           | 4  | 85           | 6  | 372         | 8  |

\*Values represent the mean number of revertants (average of three plates)

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | TPM Dose (µg/plate) | TPM-H <sub>2</sub> O (DPM) (µg/plate) | Nicotine (µg/plate) | TA98 (-S9) |    | TA100 (-S9) |    | TA1535 (-S9) |    | TA1537 (-S9) |    | TA102 (-S9) |    |
|------------|------------|-----------|------------------|---------------------|---------------------------------------|---------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                     |                                       |                     | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 1          | 2          | 084396    | 1                | 0                   | 0                                     | 0                   | 31         | 3  | 146         | 9  | 15           | 4  | 6            | 1  | 291         | 14 |
| 1          | 2          | 084396    | 1                | 25                  | 23                                    | 2                   | 29         | 1  | 160         | 9  | 15           | 3  | 10           | 2  | 265         | 8  |
| 1          | 2          | 084396    | 1                | 50                  | 46                                    | 4                   | 33         | 4  | 172         | 12 | 18           | 2  | 9            | 2  | 293         | 1  |
| 1          | 2          | 084396    | 1                | 75                  | 69                                    | 6                   | 28         | 1  | 177         | 12 | 14           | 5  | 9            | 2  | 296         | 9  |
| 1          | 2          | 084396    | 1                | 100                 | 93                                    | 8                   | 40         | 6  | 177         | 9  | 16           | 3  | 9            | 2  | 284         | 6  |
| 1          | 2          | 084396    | 1                | 125                 | 116                                   | 9                   | 30         | 6  | 193         | 7  | 18           | 3  | 9            | 2  | 291         | 8  |
| 1          | 2          | 084396    | 1                | 250                 | 231                                   | 19                  | 39         | 2  | 210         | 2  | 13           | 2  | 11           | 2  | 267         | 1  |
| 1          | 2          | 084396    | 1                | 500                 | 463                                   | 38                  | 62         | 5  | 229         | 5  | 17           | 6  | 7            | 1  | 262         | 5  |
|            |            |           |                  |                     |                                       |                     |            |    |             |    |              |    |              |    |             |    |
| 1          | 3          | 084396    | 2                | 0                   | 0                                     | 0                   | 25         | 5  | 152         | 1  | 18           | 2  | 6            | 1  | 276         | 9  |
| 1          | 3          | 084396    | 2                | 25                  | 23                                    | 2                   | 24         | 1  | 163         | 10 | 18           | 1  | 7            | 1  | 308         | 8  |
| 1          | 3          | 084396    | 2                | 50                  | 46                                    | 4                   | 26         | 4  | 180         | 11 | 19           | 4  | 7            | 2  | 296         | 6  |
| 1          | 3          | 084396    | 2                | 75                  | 69                                    | 6                   | 28         | 1  | 175         | 5  | 19           | 3  | 8            | 1  | 288         | 9  |
| 1          | 3          | 084396    | 2                | 100                 | 93                                    | 8                   | 31         | 2  | 188         | 7  | 16           | 3  | 9            | 2  | 316         | 7  |
| 1          | 3          | 084396    | 2                | 125                 | 116                                   | 9                   | 30         | 9  | 186         | 8  | 19           | 6  | 8            | 1  | 307         | 9  |
| 1          | 3          | 084396    | 2                | 250                 | 231                                   | 19                  | 29         | 4  | 190         | 14 | 16           | 4  | 11           | 2  | 305         | 6  |
| 1          | 3          | 084396    | 2                | 500                 | 463                                   | 38                  | 77         | 10 | 206         | 8  | 24           | 5  | 7            | 1  | 290         | 6  |
|            |            |           |                  |                     |                                       |                     |            |    |             |    |              |    |              |    |             |    |
| 1          | 4          | 084396    | 3                | 0                   | 0                                     | 0                   | 34         | 12 | 152         | 3  | 16           | 2  | 6            | 1  | 278         | 7  |
| 1          | 4          | 084396    | 3                | 25                  | 23                                    | 2                   | 25         | 4  | 158         | 10 | 14           | 4  | 7            | 1  | 281         | 8  |
| 1          | 4          | 084396    | 3                | 50                  | 46                                    | 4                   | 31         | 5  | 148         | 8  | 18           | 1  | 10           | 2  | 286         | 2  |
| 1          | 4          | 084396    | 3                | 75                  | 69                                    | 6                   | 27         | 4  | 161         | 13 | 16           | 3  | 9            | 1  | 300         | 5  |
| 1          | 4          | 084396    | 3                | 100                 | 93                                    | 8                   | 32         | 2  | 153         | 8  | 13           | 2  | 10           | 1  | 285         | 10 |
| 1          | 4          | 084396    | 3                | 125                 | 116                                   | 9                   | 32         | 3  | 184         | 8  | 14           | 3  | 11           | 2  | 293         | 5  |
| 1          | 4          | 084396    | 3                | 250                 | 231                                   | 19                  | 39         | 7  | 185         | 6  | 14           | 1  | 20           | 1  | 287         | 9  |
| 1          | 4          | 084396    | 3                | 500                 | 463                                   | 38                  | 54         | 7  | 192         | 7  | 17           | 3  | 8            | 1  | 303         | 4  |

\*Values represent the mean number of revertants (average of three plates)

**Mutagenesis in *Salmonella typhimurium* with (+) and without (-) S9 Metabolic Activation**  
**(Date of assay)**

| Set<br>Number | Run<br>Number | Sample<br>ID | Replicate<br>Number | TA98      |           | TA100     |           | TA1535    |           | TA1537    |           | TA102     |           |
|---------------|---------------|--------------|---------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|               |               |              |                     | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       |
| 1             | 2             | 084396       | 1                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| 1             | 3             | 084396       | 2                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| 1             | 4             | 084396       | 3                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |



**LABSTAT INTERNATIONAL ULC**

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Project: M97

Period: September 15 - 19, 2008

**Sample Generation and Extraction Data for Ames Assay analysis:**  
**Mutagenesis in *Salmonella typhimurium***

| Set Number | Run Number | Sample ID | Replicate Number | Extraction Date | Tobacco Weight (g) | DMSO Solvent Volume (mL) | mg Tobacco per mL DMSO | Dry Matter (%) | mg (Tobacco-H <sub>2</sub> O) per mL DMSO | mg Nicotine per mL DMSO | Nicotine in WT Equivalent (mg/g) |
|------------|------------|-----------|------------------|-----------------|--------------------|--------------------------|------------------------|----------------|---|-------------------------|----------------------------------|
| 1          | 3          | 084394    | 1                | 15-Sep-08       | 2.5000             | 22.5                     | 111.111                | 68.27          | 75.861                                    | 1.28                    | 11.5                             |
| 1          | 4          | 084394    | 2                | 15-Sep-08       | 2.5009             | 22.5                     | 111.151                |                | 75.888                                    | 1.43                    | 12.9                             |
| 1          | 7          | 084394    | 3                | 15-Sep-08       | 2.5005             | 22.5                     | 111.133                |                | 75.876                                    | 1.34                    | 12.1                             |
| 1          | 2          | 084395    | 1                | 15-Sep-08       | 2.5012             | 22.5                     | 111.164                | 45.98          | 51.116                                    | 1.56                    | 14.0                             |
| 1          | 5          | 084395    | 2                | 15-Sep-08       | 2.5011             | 22.5                     | 111.160                |                | 51.115                                    | 1.59                    | 14.3                             |
| 1          | 6          | 084395    | 3                | 15-Sep-08       | 2.5008             | 22.5                     | 111.147                |                | 51.109                                    | 1.49                    | 13.4                             |
| 2          | 4          | 084454    | 1                | 19-Sep-08       | 2.5010             | 22.5                     | 111.156                | 88.90          | 98.814                                    | 0.400                   | 3.60                             |
| 2          | 6          | 084454    | 2                | 19-Sep-08       | 2.5008             | 22.5                     | 111.147                |                | 98.806                                    | 0.433                   | 3.89                             |
| 2          | 14         | 084454    | 3                | 19-Sep-08       | 2.5010             | 22.5                     | 111.156                |                | 98.814                                    | 0.443                   | 3.98                             |
| 2          | 5          | 084455    | 1                | 19-Sep-08       | 2.5011             | 22.5                     | 111.160                | 93.93          | 104.409                                   | 0.614                   | 5.52                             |
| 2          | 13         | 084455    | 2                | 19-Sep-08       | 2.5017             | 22.5                     | 111.187                |                | 104.434                                   | 0.581                   | 5.23                             |
| 2          | 17         | 084455    | 3                | 19-Sep-08       | 2.5000             | 22.5                     | 111.111                |                | 104.363                                   | 0.618                   | 5.56                             |
| 2          | 3          | 084456    | 1                | 19-Sep-08       | 2.5015             | 22.5                     | 111.178                | 44.63          | 49.622                                    | 1.29                    | 11.6                             |
| 2          | 7          | 084456    | 2                | 19-Sep-08       | 2.5012             | 22.5                     | 111.164                |                | 49.616                                    | 1.33                    | 11.9                             |
| 2          | 9          | 084456    | 3                | 19-Sep-08       | 2.5017             | 22.5                     | 111.187                |                | 49.626                                    | 1.35                    | 12.2                             |
| 2          | 8          | 084457    | 1                | 19-Sep-08       | 2.5004             | 22.5                     | 111.129                | 96.32          | 107.044                                   | 0.589                   | 5.30                             |
| 2          | 12         | 084457    | 2                | 19-Sep-08       | 2.5000             | 22.5                     | 111.111                |                | 107.027                                   | 0.616                   | 5.54                             |
| 2          | 15         | 084457    | 3                | 19-Sep-08       | 2.5004             | 22.5                     | 111.129                |                | 107.044                                   | 0.636                   | 5.72                             |
| 2          | 2          | 084458    | 1                | 19-Sep-08       | 2.5009             | 22.5                     | 111.151                | 94.86          | 105.437                                   | 0.263                   | 2.36                             |
| 2          | 10         | 084458    | 2                | 19-Sep-08       | 2.5006             | 22.5                     | 111.138                |                | 105.425                                   | 0.289                   | 2.60                             |
| 2          | 16         | 084458    | 3                | 19-Sep-08       | 2.5000             | 22.5                     | 111.111                |                | 105.399                                   | 0.306                   | 2.76                             |

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation  
(Revertants per plate)**

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (+S9) |    |    | TA100 (+S9) |     |     | TA1535 (+S9) |    |    | TA1537 (+S9) |    |    | TA102 (+S9) |     |     |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|            |            |           |                  |                    |                                     |                          | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 1          | 3          | 084394    | 1                | 0                  | 0                                   | 0                        | 44         | 32 | 41 | 147         | 142 | 152 | 11           | 18 | 12 | 5            | 6  | 8  | 296         | 311 | 292 |
| 1          | 3          | 084394    | 1                | 278                | 190                                 | 3                        | 44         | 32 | 39 | 163         | 149 | 141 | 10           | 12 | 6  | 8            | 7  | 6  | 328         | 325 | 327 |
| 1          | 3          | 084394    | 1                | 556                | 379                                 | 6                        | 32         | 43 | 38 | 149         | 133 | 167 | 13           | 13 | 8  | 10           | 8  | 11 | 331         | 328 | 327 |
| 1          | 3          | 084394    | 1                | 833                | 569                                 | 10                       | 36         | 39 | 41 | 168         | 159 | 140 | 14           | 9  | 11 | 7            | 8  | 10 | 345         | 341 | 330 |
| 1          | 3          | 084394    | 1                | 1111               | 759                                 | 13                       | 38         | 39 | 37 | 169         | 150 | 156 | 17           | 11 | 13 | 12           | 11 | 9  | 348         | 352 | 355 |
| 1          | 3          | 084394    | 1                | 1389               | 948                                 | 16                       | 34         | 34 | 31 | 130         | 153 | 149 | 11           | 10 | 18 | 10           | 8  | 9  | 354         | 345 | 341 |
| 1          | 3          | 084394    | 1                | 2778               | 1897                                | 32                       | 41         | 30 | 32 | 141         | 144 | 143 | 8            | 16 | 11 | 16           | 17 | 12 | 365         | 373 | 356 |
| 1          | 3          | 084394    | 1                | 5556               | 3793                                | 64                       | 40         | 48 | 43 | 163         | 157 | 148 | 10           | 14 | 13 | 15           | 14 | 10 | 366         | 369 | 364 |
| 1          | 4          | 084394    | 2                | 0                  | 0                                   | 0                        | 43         | 24 | 22 | 163         | 149 | 144 | 13           | 14 | 17 | 7            | 6  | 5  | 220         | 246 | 259 |
| 1          | 4          | 084394    | 2                | 278                | 190                                 | 4                        | 43         | 29 | 20 | 134         | 158 | 137 | 12           | 14 | 12 | 11           | 9  | 8  | 231         | 236 | 255 |
| 1          | 4          | 084394    | 2                | 556                | 379                                 | 7                        | 23         | 18 | 39 | 158         | 139 | 138 | 17           | 10 | 12 | 7            | 6  | 9  | 228         | 244 | 244 |
| 1          | 4          | 084394    | 2                | 834                | 569                                 | 11                       | 41         | 28 | 22 | 144         | 144 | 147 | 13           | 12 | 13 | 11           | 7  | 10 | 253         | 250 | 259 |
| 1          | 4          | 084394    | 2                | 1112               | 759                                 | 14                       | 41         | 30 | 48 | 186         | 172 | 169 | 14           | 12 | 16 | 8            | 9  | 10 | 299         | 302 | 301 |
| 1          | 4          | 084394    | 2                | 1389               | 949                                 | 18                       | 39         | 38 | 30 | 159         | 173 | 144 | 8            | 13 | 13 | 13           | 12 | 7  | 319         | 322 | 300 |
| 1          | 4          | 084394    | 2                | 2779               | 1897                                | 36                       | 41         | 38 | 39 | 137         | 154 | 159 | 12           | 10 | 16 | 14           | 11 | 12 | 316         | 319 | 324 |
| 1          | 4          | 084394    | 2                | 5558               | 3794                                | 71                       | 30         | 44 | 38 | 169         | 148 | 164 | 17           | 19 | 14 | 16           | 11 | 15 | 304         | 291 | 290 |
| 1          | 7          | 084394    | 3                | 0                  | 0                                   | 0                        | 31         | 34 | 31 | 157         | 158 | 148 | 10           | 12 | 11 | 10           | 9  | 8  | 295         | 304 | 303 |
| 1          | 7          | 084394    | 3                | 278                | 190                                 | 3                        | 29         | 27 | 34 | 156         | 143 | 161 | 12           | 19 | 6  | 7            | 13 | 9  | 326         | 330 | 325 |
| 1          | 7          | 084394    | 3                | 556                | 379                                 | 7                        | 29         | 30 | 37 | 162         | 166 | 151 | 16           | 16 | 14 | 10           | 9  | 8  | 330         | 324 | 332 |
| 1          | 7          | 084394    | 3                | 833                | 569                                 | 10                       | 27         | 31 | 34 | 168         | 162 | 156 | 14           | 15 | 10 | 11           | 12 | 8  | 364         | 347 | 336 |
| 1          | 7          | 084394    | 3                | 1111               | 759                                 | 13                       | 46         | 37 | 38 | 194         | 172 | 158 | 12           | 14 | 11 | 11           | 7  | 14 | 360         | 347 | 352 |
| 1          | 7          | 084394    | 3                | 1389               | 948                                 | 17                       | 27         | 33 | 38 | 185         | 179 | 167 | 9            | 8  | 14 | 13           | 12 | 11 | 370         | 364 | 352 |
| 1          | 7          | 084394    | 3                | 2778               | 1897                                | 34                       | 24         | 13 | 29 | 168         | 174 | 178 | 13           | 14 | 12 | 11           | 13 | 14 | 332         | 324 | 327 |
| 1          | 7          | 084394    | 3                | 5557               | 3794                                | 67                       | 26         | 26 | 28 | 171         | 188 | 193 | 6            | 8  | 5  | 19           | 14 | 16 | 345         | 339 | 333 |
| 1          | 2          | 084395    | 1                | 0                  | 0                                   | 0                        | 28         | 29 | 36 | 163         | 157 | 151 | 16           | 9  | 10 | 6            | 7  | 8  | 287         | 306 | 314 |
| 1          | 2          | 084395    | 1                | 278                | 128                                 | 4                        | 43         | 23 | 24 | 158         | 141 | 150 | 8            | 16 | 18 | 9            | 10 | 11 | 344         | 342 | 360 |
| 1          | 2          | 084395    | 1                | 556                | 256                                 | 8                        | 22         | 27 | 31 | 142         | 133 | 159 | 9            | 10 | 17 | 12           | 11 | 13 | 354         | 345 | 355 |
| 1          | 2          | 084395    | 1                | 834                | 383                                 | 12                       | 28         | 27 | 27 | 150         | 166 | 170 | 17           | 13 | 14 | 15           | 13 | 12 | 368         | 354 | 374 |
| 1          | 2          | 084395    | 1                | 1112               | 511                                 | 16                       | 46         | 37 | 27 | 176         | 159 | 169 | 17           | 12 | 9  | 19           | 16 | 18 | 352         | 367 | 359 |
| 1          | 2          | 084395    | 1                | 1390               | 639                                 | 19                       | 47         | 39 | 36 | 139         | 141 | 151 | 6            | 7  | 16 | 16           | 17 | 19 | 351         | 348 | 360 |
| 1          | 2          | 084395    | 1                | 2779               | 1278                                | 39                       | 28         | 46 | 38 | 162         | 160 | 162 | 13           | 11 | 10 | 17           | 18 | 19 | 332         | 346 | 364 |
| 1          | 2          | 084395    | 1                | 5558               | 2556                                | 78                       | 49         | 42 | 42 | 153         | 169 | 178 | 19           | 14 | 13 | 18           | 20 | 18 | 356         | 349 | 339 |
| 1          | 5          | 084395    | 2                | 0                  | 0                                   | 0                        | 46         | 44 | 37 | 167         | 144 | 138 | 17           | 12 | 16 | 9            | 8  | 7  | 294         | 307 | 290 |
| 1          | 5          | 084395    | 2                | 278                | 128                                 | 4                        | 32         | 34 | 28 | 136         | 133 | 142 | 9            | 16 | 8  | 9            | 9  | 8  | 313         | 309 | 315 |
| 1          | 5          | 084395    | 2                | 556                | 256                                 | 8                        | 30         | 31 | 32 | 163         | 138 | 153 | 16           | 12 | 12 | 7            | 8  | 7  | 311         | 305 | 312 |
| 1          | 5          | 084395    | 2                | 834                | 383                                 | 12                       | 29         | 32 | 40 | 169         | 154 | 181 | 11           | 14 | 12 | 11           | 12 | 11 | 319         | 302 | 306 |
| 1          | 5          | 084395    | 2                | 1112               | 511                                 | 16                       | 40         | 38 | 38 | 172         | 180 | 169 | 16           | 7  | 15 | 8            | 11 | 14 | 310         | 324 | 301 |
| 1          | 5          | 084395    | 2                | 1390               | 639                                 | 20                       | 43         | 41 | 38 | 151         | 160 | 168 | 14           | 13 | 9  | 12           | 9  | 10 | 290         | 301 | 303 |
| 1          | 5          | 084395    | 2                | 2779               | 1278                                | 40                       | 39         | 36 | 35 | 176         | 181 | 170 | 10           | 14 | 14 | 11           | 12 | 14 | 304         | 309 | 296 |
| 1          | 5          | 084395    | 2                | 5558               | 2556                                | 80                       | 37         | 32 | 42 | 216         | 219 | 207 | 14           | 12 | 16 | 16           | 12 | 14 | 330         | 343 | 325 |
| 1          | 6          | 084395    | 3                | 0                  | 0                                   | 0                        | 34         | 40 | 30 | 165         | 177 | 152 | 10           | 11 | 8  | 7            | 6  | 5  | 312         | 309 | 313 |
| 1          | 6          | 084395    | 3                | 278                | 128                                 | 4                        | 28         | 20 | 27 | 156         | 186 | 158 | 7            | 16 | 12 | 8            | 6  | 7  | 317         | 316 | 316 |
| 1          | 6          | 084395    | 3                | 556                | 256                                 | 7                        | 30         | 24 | 29 | 166         | 176 | 162 | 14           | 9  | 16 | 8            | 7  | 9  | 317         | 311 | 314 |
| 1          | 6          | 084395    | 3                | 834                | 383                                 | 11                       | 27         | 22 | 32 | 162         | 173 | 186 | 8            | 9  | 13 | 8            | 9  | 10 | 331         | 343 | 332 |
| 1          | 6          | 084395    | 3                | 1111               | 511                                 | 15                       | 47         | 44 | 40 | 193         | 176 | 162 | 8            | 8  | 15 | 10           | 8  | 12 | 324         | 336 | 321 |
| 1          | 6          | 084395    | 3                | 1389               | 639                                 | 19                       | 39         | 34 | 31 | 138         | 143 | 139 | 16           | 11 | 8  | 9            | 7  | 11 | 330         | 339 | 329 |
| 1          | 6          | 084395    | 3                | 2779               | 1278                                | 37                       | 40         | 34 | 34 | 148         | 159 | 153 | 11           | 14 | 8  | 10           | 8  | 13 | 337         | 346 | 330 |
| 1          | 6          | 084395    | 3                | 5557               | 2555                                | 74                       | 40         | 43 | 42 | 177         | 189 | 183 | 10           | 10 | 12 | 14           | 12 | 11 | 329         | 320 | 333 |

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation  
(Revertants per plate)**

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (+S9) |    |    | TA100 (+S9) |     |     | TA1535 (+S9) |    |    | TA1537 (+S9) |    |    | TA102 (+S9) |     |     |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|            |            |           |                  |                    |                                     |                          | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 2          | 4          | 084454    | 1                | 0                  | 0                                   | 0                        | 27         | 27 | 32 | 100         | 96  | 82  | 18           | 18 | 9  | 10           | 14 | 9  | 307         | 302 | 314 |
| 2          | 4          | 084454    | 1                | 278                | 247                                 | 1                        | 31         | 29 | 24 | 101         | 95  | 98  | 10           | 13 | 10 | 7            | 6  | 6  | 304         | 313 | 296 |
| 2          | 4          | 084454    | 1                | 556                | 494                                 | 2                        | 30         | 28 | 20 | 114         | 103 | 96  | 16           | 17 | 10 | 7            | 9  | 7  | 306         | 291 | 271 |
| 2          | 4          | 084454    | 1                | 834                | 741                                 | 3                        | 26         | 29 | 32 | 99          | 114 | 104 | 10           | 11 | 7  | 11           | 7  | 9  | 296         | 294 | 314 |
| 2          | 4          | 084454    | 1                | 1112               | 988                                 | 4                        | 27         | 24 | 22 | 130         | 117 | 106 | 17           | 11 | 11 | 6            | 6  | 7  | 282         | 294 | 311 |
| 2          | 4          | 084454    | 1                | 1389               | 1235                                | 5                        | 26         | 24 | 20 | 126         | 116 | 110 | 14           | 12 | 9  | 8            | 7  | 10 | 320         | 310 | 318 |
| 2          | 4          | 084454    | 1                | 2779               | 2470                                | 10                       | 28         | 31 | 26 | 106         | 115 | 120 | 6            | 18 | 17 | 16           | 12 | 9  | 299         | 301 | 326 |
| 2          | 4          | 084454    | 1                | 5558               | 4941                                | 20                       | 22         | 25 | 28 | 118         | 120 | 125 | 14           | 11 | 19 | 8            | 8  | 9  | 303         | 314 | 301 |
| 2          | 6          | 084454    | 2                | 0                  | 0                                   | 0                        | 23         | 27 | 26 | 96          | 90  | 86  | 11           | 18 | 12 | 9            | 9  | 11 | 298         | 319 | 292 |
| 2          | 6          | 084454    | 2                | 278                | 247                                 | 1                        | 29         | 30 | 21 | 96          | 92  | 88  | 14           | 15 | 19 | 11           | 11 | 8  | 305         | 310 | 307 |
| 2          | 6          | 084454    | 2                | 556                | 494                                 | 2                        | 23         | 21 | 23 | 88          | 99  | 96  | 16           | 18 | 17 | 13           | 9  | 10 | 296         | 294 | 290 |
| 2          | 6          | 084454    | 2                | 834                | 741                                 | 3                        | 19         | 19 | 26 | 90          | 103 | 108 | 11           | 20 | 10 | 7            | 7  | 9  | 293         | 304 | 296 |
| 2          | 6          | 084454    | 2                | 1111               | 988                                 | 4                        | 24         | 25 | 24 | 110         | 100 | 102 | 12           | 10 | 16 | 7            | 14 | 10 | 296         | 307 | 319 |
| 2          | 6          | 084454    | 2                | 1389               | 1235                                | 5                        | 22         | 20 | 24 | 109         | 104 | 109 | 19           | 13 | 20 | 10           | 10 | 12 | 310         | 287 | 277 |
| 2          | 6          | 084454    | 2                | 2779               | 2470                                | 11                       | 27         | 24 | 30 | 120         | 115 | 122 | 13           | 20 | 17 | 11           | 10 | 8  | 276         | 267 | 287 |
| 2          | 6          | 084454    | 2                | 5557               | 4940                                | 22                       | 27         | 27 | 25 | 112         | 113 | 115 | 14           | 18 | 17 | 10           | 12 | 6  | 280         | 298 | 290 |
| 2          | 14         | 084454    | 3                | 0                  | 0                                   | 0                        | 27         | 23 | 37 | 90          | 99  | 96  | 19           | 17 | 20 | 7            | 8  | 8  | 305         | 297 | 308 |
| 2          | 14         | 084454    | 3                | 278                | 247                                 | 1                        | 33         | 24 | 30 | 94          | 100 | 106 | 12           | 16 | 17 | 13           | 14 | 15 | 282         | 273 | 296 |
| 2          | 14         | 084454    | 3                | 556                | 494                                 | 2                        | 21         | 22 | 23 | 96          | 100 | 110 | 13           | 16 | 14 | 6            | 6  | 7  | 272         | 300 | 301 |
| 2          | 14         | 084454    | 3                | 834                | 741                                 | 3                        | 22         | 22 | 22 | 96          | 110 | 104 | 10           | 8  | 18 | 6            | 6  | 7  | 298         | 283 | 293 |
| 2          | 14         | 084454    | 3                | 1112               | 988                                 | 4                        | 26         | 32 | 23 | 107         | 116 | 114 | 11           | 14 | 10 | 6            | 6  | 8  | 285         | 289 | 294 |
| 2          | 14         | 084454    | 3                | 1389               | 1235                                | 6                        | 26         | 21 | 19 | 104         | 114 | 121 | 17           | 11 | 7  | 9            | 7  | 8  | 285         | 290 | 284 |
| 2          | 14         | 084454    | 3                | 2779               | 2470                                | 11                       | 24         | 20 | 20 | 98          | 82  | 95  | 16           | 11 | 9  | 6            | 7  | 9  | 299         | 312 | 292 |
| 2          | 14         | 084454    | 3                | 5558               | 4941                                | 22                       | 21         | 22 | 23 | 103         | 100 | 96  | 17           | 14 | 11 | 8            | 8  | 6  | 281         | 288 | 313 |
| 2          | 5          | 084455    | 1                | 0                  | 0                                   | 0                        | 24         | 30 | 35 | 80          | 82  | 89  | 14           | 13 | 10 | 10           | 6  | 9  | 297         | 300 | 311 |
| 2          | 5          | 084455    | 1                | 278                | 261                                 | 2                        | 24         | 20 | 21 | 84          | 90  | 92  | 11           | 18 | 13 | 15           | 11 | 10 | 299         | 286 | 282 |
| 2          | 5          | 084455    | 1                | 556                | 522                                 | 3                        | 30         | 25 | 36 | 92          | 88  | 93  | 8            | 8  | 10 | 8            | 7  | 11 | 289         | 310 | 292 |
| 2          | 5          | 084455    | 1                | 834                | 783                                 | 5                        | 23         | 24 | 34 | 100         | 88  | 94  | 9            | 9  | 8  | 12           | 9  | 12 | 309         | 310 | 289 |
| 2          | 5          | 084455    | 1                | 1112               | 1044                                | 6                        | 27         | 30 | 27 | 100         | 106 | 113 | 11           | 12 | 13 | 14           | 14 | 11 | 298         | 291 | 323 |
| 2          | 5          | 084455    | 1                | 1390               | 1305                                | 8                        | 23         | 22 | 20 | 98          | 111 | 114 | 12           | 16 | 9  | 9            | 9  | 13 | 296         | 324 | 312 |
| 2          | 5          | 084455    | 1                | 2779               | 2610                                | 15                       | 30         | 22 | 22 | 118         | 110 | 124 | 14           | 7  | 8  | 10           | 7  | 7  | 319         | 304 | 320 |
| 2          | 5          | 084455    | 1                | 5558               | 5220                                | 31                       | 22         | 22 | 21 | 103         | 92  | 106 | 10           | 13 | 12 | 8            | 8  | 10 | 312         | 326 | 304 |
| 2          | 13         | 084455    | 2                | 0                  | 0                                   | 0                        | 28         | 17 | 31 | 86          | 97  | 94  | 17           | 17 | 12 | 6            | 5  | 5  | 294         | 315 | 298 |
| 2          | 13         | 084455    | 2                | 278                | 261                                 | 1                        | 24         | 21 | 21 | 106         | 100 | 95  | 13           | 12 | 14 | 7            | 8  | 5  | 311         | 306 | 311 |
| 2          | 13         | 084455    | 2                | 556                | 522                                 | 3                        | 28         | 18 | 20 | 108         | 101 | 98  | 10           | 17 | 14 | 7            | 9  | 5  | 283         | 290 | 303 |
| 2          | 13         | 084455    | 2                | 834                | 783                                 | 4                        | 23         | 22 | 39 | 111         | 113 | 103 | 13           | 19 | 14 | 6            | 7  | 6  | 297         | 303 | 281 |
| 2          | 13         | 084455    | 2                | 1112               | 1044                                | 6                        | 36         | 28 | 26 | 120         | 130 | 117 | 19           | 16 | 11 | 7            | 10 | 8  | 304         | 292 | 287 |
| 2          | 13         | 084455    | 2                | 1390               | 1305                                | 7                        | 25         | 22 | 28 | 122         | 108 | 112 | 9            | 12 | 17 | 6            | 7  | 6  | 306         | 287 | 304 |
| 2          | 13         | 084455    | 2                | 2780               | 2611                                | 15                       | 26         | 28 | 30 | 127         | 114 | 111 | 17           | 10 | 10 | 5            | 4  | 5  | 308         | 300 | 282 |
| 2          | 13         | 084455    | 2                | 5559               | 5222                                | 29                       | 24         | 26 | 21 | 98          | 111 | 116 | 6            | 11 | 14 | 8            | 7  | 10 | 306         | 308 | 316 |
| 2          | 17         | 084455    | 3                | 0                  | 0                                   | 0                        | 20         | 22 | 21 | 94          | 99  | 90  | 10           | 12 | 14 | 7            | 9  | 8  | 280         | 273 | 282 |
| 2          | 17         | 084455    | 3                | 278                | 261                                 | 2                        | 26         | 22 | 20 | 98          | 106 | 96  | 11           | 10 | 11 | 10           | 10 | 8  | 282         | 286 | 276 |
| 2          | 17         | 084455    | 3                | 556                | 522                                 | 3                        | 31         | 21 | 23 | 98          | 102 | 110 | 12           | 16 | 10 | 7            | 8  | 9  | 291         | 281 | 275 |
| 2          | 17         | 084455    | 3                | 833                | 783                                 | 5                        | 24         | 31 | 22 | 114         | 111 | 119 | 16           | 18 | 12 | 7            | 7  | 6  | 272         | 264 | 256 |
| 2          | 17         | 084455    | 3                | 1111               | 1044                                | 6                        | 20         | 29 | 29 | 104         | 105 | 104 | 13           | 10 | 12 | 7            | 7  | 6  | 283         | 267 | 271 |
| 2          | 17         | 084455    | 3                | 1389               | 1305                                | 8                        | 21         | 24 | 24 | 110         | 108 | 121 | 13           | 12 | 14 | 7            | 6  | 5  | 282         | 300 | 305 |
| 2          | 17         | 084455    | 3                | 2778               | 2609                                | 15                       | 22         | 24 | 30 | 114         | 128 | 116 | 11           | 18 | 19 | 7            | 9  | 7  | 305         | 279 | 286 |
| 2          | 17         | 084455    | 3                | 5556               | 5218                                | 31                       | 29         | 30 | 28 | 115         | 106 | 120 | 11           | 10 | 13 | 12           | 9  | 13 | 279         | 285 | 306 |

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation  
(Revertants per plate)**

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (+S9) |    |    | TA100 (+S9) |     |     | TA1535 (+S9) |    |    | TA1537 (+S9) |    |    | TA102 (+S9) |     |     |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|            |            |           |                  |                    |                                     |                          | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 2          | 3          | 084456    | 1                | 0                  | 0                                   | 0                        | 26         | 33 | 28 | 84          | 87  | 82  | 6            | 13 | 11 | 8            | 8  | 7  | 292         | 279 | 270 |
| 2          | 3          | 084456    | 1                | 278                | 124                                 | 3                        | 26         | 22 | 21 | 87          | 89  | 88  | 11           | 17 | 13 | 10           | 9  | 9  | 280         | 250 | 283 |
| 2          | 3          | 084456    | 1                | 556                | 248                                 | 6                        | 22         | 30 | 22 | 91          | 84  | 82  | 11           | 18 | 12 | 12           | 9  | 12 | 287         | 313 | 314 |
| 2          | 3          | 084456    | 1                | 834                | 372                                 | 10                       | 24         | 28 | 22 | 89          | 102 | 90  | 11           | 12 | 11 | 8            | 6  | 10 | 298         | 297 | 294 |
| 2          | 3          | 084456    | 1                | 1112               | 496                                 | 13                       | 20         | 20 | 24 | 96          | 100 | 111 | 16           | 14 | 10 | 14           | 14 | 12 | 280         | 314 | 313 |
| 2          | 3          | 084456    | 1                | 1390               | 620                                 | 16                       | 27         | 34 | 28 | 122         | 107 | 111 | 9            | 7  | 10 | 11           | 11 | 10 | 303         | 324 | 327 |
| 2          | 3          | 084456    | 1                | 2779               | 1241                                | 32                       | 22         | 27 | 28 | 122         | 120 | 112 | 6            | 12 | 12 | 15           | 16 | 14 | 307         | 319 | 288 |
| 2          | 3          | 084456    | 1                | 5559               | 2481                                | 65                       | 37         | 37 | 50 | 93          | 114 | 98  | 11           | 18 | 12 | 13           | 14 | 12 | 324         | 346 | 320 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 7          | 084456    | 2                | 0                  | 0                                   | 0                        | 31         | 21 | 21 | 92          | 90  | 85  | 20           | 10 | 18 | 6            | 9  | 6  | 300         | 282 | 295 |
| 2          | 7          | 084456    | 2                | 278                | 124                                 | 3                        | 22         | 19 | 24 | 90          | 99  | 96  | 15           | 11 | 13 | 8            | 7  | 8  | 304         | 306 | 297 |
| 2          | 7          | 084456    | 2                | 556                | 248                                 | 7                        | 23         | 23 | 24 | 100         | 97  | 102 | 11           | 13 | 12 | 11           | 9  | 9  | 319         | 307 | 289 |
| 2          | 7          | 084456    | 2                | 834                | 372                                 | 10                       | 24         | 20 | 21 | 94          | 108 | 114 | 20           | 19 | 13 | 10           | 9  | 6  | 288         | 314 | 320 |
| 2          | 7          | 084456    | 2                | 1112               | 496                                 | 13                       | 30         | 33 | 23 | 126         | 137 | 120 | 14           | 11 | 12 | 14           | 14 | 10 | 299         | 305 | 311 |
| 2          | 7          | 084456    | 2                | 1390               | 620                                 | 17                       | 24         | 24 | 23 | 128         | 111 | 115 | 11           | 14 | 17 | 10           | 8  | 11 | 310         | 278 | 295 |
| 2          | 7          | 084456    | 2                | 2779               | 1240                                | 33                       | 21         | 24 | 34 | 112         | 103 | 109 | 20           | 14 | 11 | 13           | 12 | 12 | 285         | 298 | 281 |
| 2          | 7          | 084456    | 2                | 5558               | 2481                                | 66                       | 33         | 42 | 40 | 106         | 118 | 120 | 13           | 15 | 18 | 13           | 12 | 8  | 321         | 313 | 314 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 9          | 084456    | 3                | 0                  | 0                                   | 0                        | 21         | 21 | 22 | 85          | 99  | 90  | 10           | 11 | 19 | 7            | 6  | 5  | 289         | 281 | 304 |
| 2          | 9          | 084456    | 3                | 278                | 124                                 | 3                        | 20         | 23 | 30 | 96          | 98  | 90  | 13           | 11 | 12 | 10           | 8  | 10 | 310         | 296 | 306 |
| 2          | 9          | 084456    | 3                | 556                | 248                                 | 7                        | 20         | 20 | 21 | 103         | 106 | 109 | 12           | 10 | 14 | 8            | 8  | 11 | 290         | 286 | 292 |
| 2          | 9          | 084456    | 3                | 834                | 372                                 | 10                       | 20         | 29 | 22 | 104         | 105 | 113 | 10           | 11 | 23 | 8            | 10 | 10 | 300         | 295 | 284 |
| 2          | 9          | 084456    | 3                | 1112               | 496                                 | 14                       | 36         | 23 | 20 | 119         | 110 | 106 | 12           | 18 | 13 | 10           | 11 | 12 | 272         | 279 | 280 |
| 2          | 9          | 084456    | 3                | 1390               | 620                                 | 17                       | 24         | 20 | 20 | 116         | 118 | 120 | 18           | 10 | 12 | 13           | 13 | 14 | 308         | 317 | 308 |
| 2          | 9          | 084456    | 3                | 2780               | 1241                                | 34                       | 28         | 24 | 21 | 97          | 105 | 98  | 15           | 11 | 13 | 9            | 7  | 8  | 313         | 319 | 286 |
| 2          | 9          | 084456    | 3                | 5559               | 2481                                | 68                       | 37         | 30 | 30 | 84          | 95  | 99  | 10           | 12 | 13 | 13           | 14 | 17 | 319         | 300 | 324 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 8          | 084457    | 1                | 0                  | 0                                   | 0                        | 26         | 21 | 22 | 85          | 92  | 91  | 11           | 10 | 14 | 5            | 7  | 9  | 275         | 288 | 296 |
| 2          | 8          | 084457    | 1                | 278                | 268                                 | 1                        | 21         | 23 | 26 | 99          | 96  | 107 | 11           | 12 | 9  | 7            | 8  | 7  | 293         | 294 | 301 |
| 2          | 8          | 084457    | 1                | 556                | 535                                 | 3                        | 19         | 24 | 18 | 118         | 110 | 114 | 11           | 12 | 13 | 9            | 12 | 8  | 298         | 305 | 311 |
| 2          | 8          | 084457    | 1                | 833                | 803                                 | 4                        | 24         | 26 | 24 | 120         | 116 | 123 | 10           | 17 | 15 | 12           | 14 | 9  | 317         | 308 | 300 |
| 2          | 8          | 084457    | 1                | 1111               | 1070                                | 6                        | 34         | 26 | 24 | 124         | 116 | 126 | 19           | 11 | 10 | 8            | 8  | 8  | 287         | 301 | 282 |
| 2          | 8          | 084457    | 1                | 1389               | 1338                                | 7                        | 20         | 26 | 23 | 102         | 108 | 98  | 11           | 13 | 18 | 11           | 13 | 8  | 312         | 318 | 306 |
| 2          | 8          | 084457    | 1                | 2778               | 2676                                | 15                       | 31         | 20 | 20 | 119         | 121 | 104 | 13           | 16 | 15 | 6            | 5  | 8  | 287         | 289 | 298 |
| 2          | 8          | 084457    | 1                | 5556               | 5352                                | 29                       | 28         | 24 | 23 | 107         | 112 | 107 | 16           | 20 | 19 | 5            | 5  | 11 | 284         | 282 | 289 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 12         | 084457    | 2                | 0                  | 0                                   | 0                        | 29         | 31 | 20 | 95          | 98  | 90  | 13           | 11 | 6  | 5            | 6  | 6  | 278         | 293 | 294 |
| 2          | 12         | 084457    | 2                | 278                | 268                                 | 2                        | 28         | 20 | 26 | 101         | 94  | 92  | 11           | 11 | 16 | 7            | 5  | 7  | 303         | 281 | 296 |
| 2          | 12         | 084457    | 2                | 556                | 535                                 | 3                        | 29         | 20 | 24 | 92          | 103 | 103 | 10           | 17 | 12 | 5            | 5  | 5  | 298         | 294 | 308 |
| 2          | 12         | 084457    | 2                | 833                | 803                                 | 5                        | 20         | 27 | 20 | 108         | 112 | 99  | 17           | 8  | 16 | 6            | 7  | 8  | 299         | 315 | 312 |
| 2          | 12         | 084457    | 2                | 1111               | 1070                                | 6                        | 21         | 20 | 23 | 98          | 106 | 105 | 9            | 13 | 10 | 9            | 10 | 8  | 278         | 293 | 270 |
| 2          | 12         | 084457    | 2                | 1389               | 1338                                | 8                        | 23         | 19 | 20 | 120         | 103 | 105 | 18           | 8  | 11 | 7            | 9  | 8  | 292         | 265 | 287 |
| 2          | 12         | 084457    | 2                | 2778               | 2676                                | 15                       | 20         | 20 | 23 | 114         | 100 | 98  | 8            | 14 | 12 | 7            | 9  | 6  | 303         | 270 | 261 |
| 2          | 12         | 084457    | 2                | 5556               | 5351                                | 31                       | 21         | 19 | 23 | 112         | 113 | 114 | 13           | 20 | 17 | 8            | 9  | 11 | 298         | 294 | 289 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 15         | 084457    | 3                | 0                  | 0                                   | 0                        | 33         | 31 | 28 | 86          | 97  | 95  | 12           | 7  | 12 | 8            | 9  | 9  | 299         | 294 | 310 |
| 2          | 15         | 084457    | 3                | 278                | 268                                 | 2                        | 29         | 24 | 26 | 100         | 92  | 98  | 10           | 16 | 18 | 9            | 6  | NA | 293         | 305 | 298 |
| 2          | 15         | 084457    | 3                | 556                | 535                                 | 3                        | 27         | 35 | 33 | 105         | 100 | 114 | 12           | 12 | 13 | 5            | 5  | 6  | 304         | 296 | 294 |
| 2          | 15         | 084457    | 3                | 833                | 803                                 | 5                        | 26         | 28 | 22 | 102         | 105 | 104 | 14           | 19 | 11 | 12           | 15 | 10 | 301         | 298 | 279 |
| 2          | 15         | 084457    | 3                | 1111               | 1070                                | 6                        | 22         | 30 | 32 | 117         | 100 | 104 | 10           | 9  | 13 | 11           | 10 | 9  | 312         | 322 | 296 |
| 2          | 15         | 084457    | 3                | 1389               | 1338                                | 8                        | 20         | 24 | 25 | 112         | 100 | 118 | 7            | 20 | 13 | 6            | 5  | 6  | 302         | 310 | 280 |
| 2          | 15         | 084457    | 3                | 2778               | 2676                                | 16                       | 29         | 28 | 22 | 101         | 98  | 111 | 8            | 7  | 10 | 6            | 7  | 9  | 285         | 299 | 302 |
| 2          | 15         | 084457    | 3                | 5556               | 5352                                | 32                       | 21         | 26 | 23 | 100         | 95  | 114 | 8            | 7  | 10 | 8            | 8  | 6  | 289         | 279 | 304 |

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation  
(Revertants per plate)**

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (+S9) |    |    | TA100 (+S9) |     |     | TA1535 (+S9) |    |    | TA1537 (+S9) |    |    | TA102 (+S9) |     |     |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|            |            |           |                  |                    |                                     |                          | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 2          | 2          | 084458    | 1                | 0                  | 0                                   | 0                        | 24         | 30 | 20 | 102         | 93  | 86  | 10           | 14 | 10 | 9            | 10 | 10 | 270         | 263 | 255 |
| 2          | 2          | 084458    | 1                | 278                | 264                                 | 1                        | 20         | 29 | 27 | 105         | 94  | 104 | 14           | 11 | 14 | 9            | 8  | 6  | 258         | 268 | 255 |
| 2          | 2          | 084458    | 1                | 556                | 527                                 | 1                        | 26         | 26 | 26 | 107         | 98  | 101 | 11           | 12 | 13 | 8            | 6  | 11 | 320         | 330 | 325 |
| 2          | 2          | 084458    | 1                | 834                | 791                                 | 2                        | 20         | 21 | 28 | 92          | 100 | 95  | 13           | 9  | 11 | 11           | 11 | 10 | 339         | 350 | 320 |
| 2          | 2          | 084458    | 1                | 1112               | 1054                                | 3                        | 37         | 21 | 22 | 96          | 111 | 92  | 9            | 16 | 16 | 6            | 9  | 12 | 250         | 234 | 230 |
| 2          | 2          | 084458    | 1                | 1389               | 1318                                | 3                        | 29         | 26 | 21 | 103         | 100 | 118 | 10           | 13 | 11 | 14           | 9  | 16 | 200         | 204 | 201 |
| 2          | 2          | 084458    | 1                | 2779               | 2636                                | 7                        | 27         | 22 | 28 | 109         | 96  | 94  | 10           | 12 | 12 | 11           | 13 | 8  | 233         | 230 | 214 |
| 2          | 2          | 084458    | 1                | 5558               | 5272                                | 13                       | 23         | 28 | 23 | 99          | 97  | 86  | 14           | 11 | 16 | 19           | 20 | 11 | 230         | 218 | 234 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 10         | 084458    | 2                | 0                  | 0                                   | 0                        | 27         | 24 | 20 | 92          | 94  | 90  | 16           | 13 | NA | 10           | 6  | 6  | 294         | 292 | 280 |
| 2          | 10         | 084458    | 2                | 278                | 264                                 | 1                        | 28         | 26 | 20 | 90          | 97  | 100 | 11           | 11 | 16 | 5            | 8  | 5  | 294         | 281 | 300 |
| 2          | 10         | 084458    | 2                | 556                | 527                                 | 1                        | 20         | 20 | 30 | 97          | 93  | 110 | 9            | 9  | 10 | 5            | 6  | 10 | 304         | 277 | 270 |
| 2          | 10         | 084458    | 2                | 834                | 791                                 | 2                        | 21         | NA | 29 | 102         | 100 | 116 | 12           | 11 | 10 | 6            | 8  | 5  | 307         | 290 | 280 |
| 2          | 10         | 084458    | 2                | 1111               | 1054                                | 3                        | 29         | 21 | 20 | 104         | 104 | 97  | 9            | 9  | 7  | 12           | 7  | 11 | 303         | 286 | 282 |
| 2          | 10         | 084458    | 2                | 1389               | 1318                                | 4                        | 23         | 21 | 26 | 101         | 100 | 105 | 10           | 10 | 8  | 9            | 10 | 8  | 306         | 280 | 313 |
| 2          | 10         | 084458    | 2                | 2778               | 2636                                | 7                        | 22         | 20 | 22 | 96          | 106 | 95  | 9            | 11 | 11 | 8            | 8  | 5  | 309         | 300 | 302 |
| 2          | 10         | 084458    | 2                | 5557               | 5271                                | 14                       | 22         | 21 | 20 | 90          | 106 | 97  | 12           | 10 | 14 | 5            | 6  | 7  | 290         | 302 | 287 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 16         | 084458    | 3                | 0                  | 0                                   | 0                        | 23         | 20 | 20 | 84          | 90  | 96  | 18           | 20 | 14 | 8            | 8  | 7  | 274         | 281 | 301 |
| 2          | 16         | 084458    | 3                | 278                | 263                                 | 1                        | 24         | 21 | 18 | 98          | 94  | 92  | 13           | 14 | 18 | 7            | 8  | 7  | 276         | 285 | 295 |
| 2          | 16         | 084458    | 3                | 556                | 527                                 | 2                        | 21         | 20 | 21 | 94          | 100 | 98  | 17           | 12 | 13 | 6            | 5  | 7  | 254         | 295 | 284 |
| 2          | 16         | 084458    | 3                | 833                | 790                                 | 2                        | 24         | 20 | 22 | 96          | 106 | 110 | 15           | 10 | 14 | 5            | 6  | 5  | 292         | 276 | 286 |
| 2          | 16         | 084458    | 3                | 1111               | 1054                                | 3                        | 24         | 23 | 28 | 117         | 104 | 105 | 11           | 18 | 10 | 8            | 9  | 10 | 254         | 275 | 271 |
| 2          | 16         | 084458    | 3                | 1389               | 1317                                | 4                        | 28         | 24 | 27 | 102         | 118 | 115 | 12           | 16 | 10 | 12           | 10 | 10 | 254         | 268 | 252 |
| 2          | 16         | 084458    | 3                | 2778               | 2635                                | 8                        | 29         | 31 | 36 | 110         | 105 | 110 | 13           | 12 | 11 | 5            | 6  | 6  | 234         | 255 | 261 |
| 2          | 16         | 084458    | 3                | 5556               | 5270                                | 15                       | 31         | 31 | 26 | 99          | 101 | 87  | 10           | 14 | 11 | 7            | 8  | 9  | 250         | 244 | 232 |

N/A - data not available due to lack of bacterial growth or assay plate contamination

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Revertants per plate)**

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (-S9) |    |    | TA100 (-S9) |     |     | TA1535 (-S9) |    |    | TA1537 (-S9) |    |    | TA102 (-S9) |     |     |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|            |            |           |                  |                    |                                     |                          | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 1          | 3          | 084394    | 1                | 0                  | 0                                   | 0                        | 23         | 32 | 23 | 167         | 159 | 154 | 9            | 12 | 10 | 8            | 7  | 9  | 273         | 291 | 287 |
| 1          | 3          | 084394    | 1                | 278                | 190                                 | 3                        | 29         | 28 | 27 | 166         | 174 | 167 | 14           | 12 | 16 | 13           | 9  | 10 | 320         | 325 | 338 |
| 1          | 3          | 084394    | 1                | 556                | 379                                 | 6                        | 38         | 30 | 23 | 148         | 156 | 160 | 13           | 14 | 11 | 12           | 14 | 11 | 292         | 308 | 289 |
| 1          | 3          | 084394    | 1                | 833                | 569                                 | 10                       | 26         | 24 | 28 | 172         | 162 | 159 | 18           | 16 | 16 | 14           | 10 | 12 | 309         | 293 | 294 |
| 1          | 3          | 084394    | 1                | 1111               | 759                                 | 13                       | 30         | 31 | 20 | 179         | 187 | 162 | 14           | 11 | 17 | 14           | 13 | 14 | 304         | 301 | 291 |
| 1          | 3          | 084394    | 1                | 1389               | 948                                 | 16                       | 24         | 24 | 21 | 144         | 152 | 161 | 14           | 17 | 19 | 13           | 16 | 14 | 294         | 300 | 301 |
| 1          | 3          | 084394    | 1                | 2778               | 1897                                | 32                       | 22         | 21 | 23 | 156         | 146 | 157 | 17           | 11 | 13 | 11           | 12 | 18 | 297         | 311 | 304 |
| 1          | 3          | 084394    | 1                | 5556               | 3793                                | 64                       | 29         | 27 | 26 | 178         | 182 | 180 | 18           | 17 | 5  | 16           | 16 | 17 | 285         | 284 | 288 |
| 1          | 4          | 084394    | 2                | 0                  | 0                                   | 0                        | 21         | 20 | 24 | 144         | 149 | 147 | 17           | 11 | 13 | 8            | 6  | 8  | 276         | 287 | 283 |
| 1          | 4          | 084394    | 2                | 278                | 190                                 | 4                        | 30         | 30 | 23 | 147         | 140 | 167 | 14           | 13 | 14 | 11           | 8  | 12 | 286         | 286 | 282 |
| 1          | 4          | 084394    | 2                | 556                | 379                                 | 7                        | 27         | 28 | 20 | 166         | 136 | 157 | 18           | 14 | 11 | 10           | 10 | 12 | 288         | 280 | 278 |
| 1          | 4          | 084394    | 2                | 834                | 569                                 | 11                       | 22         | 32 | 23 | 156         | 144 | 156 | 21           | 12 | 18 | 8            | 12 | 15 | 293         | 306 | 313 |
| 1          | 4          | 084394    | 2                | 1112               | 759                                 | 14                       | 32         | 31 | 26 | 143         | 157 | 159 | 11           | 20 | 18 | 10           | 10 | 14 | 273         | 276 | 272 |
| 1          | 4          | 084394    | 2                | 1389               | 949                                 | 18                       | 33         | 36 | 20 | 151         | 150 | 157 | 10           | 10 | 17 | 9            | 8  | 10 | 300         | 292 | 306 |
| 1          | 4          | 084394    | 2                | 2779               | 1897                                | 36                       | 26         | 26 | 24 | 160         | 154 | 149 | 10           | 16 | 21 | 10           | 14 | 10 | 287         | 302 | 303 |
| 1          | 4          | 084394    | 2                | 5558               | 3794                                | 71                       | 30         | 36 | 29 | 170         | 177 | 181 | 24           | 16 | 19 | 12           | 16 | 15 | 275         | 268 | 272 |
| 1          | 7          | 084394    | 3                | 0                  | 0                                   | 0                        | 28         | 23 | 20 | 128         | 149 | 156 | 15           | 14 | 20 | 6            | 5  | 7  | 275         | 298 | 278 |
| 1          | 7          | 084394    | 3                | 278                | 190                                 | 3                        | 23         | 26 | 26 | 130         | 156 | 143 | 18           | 19 | 20 | 6            | 8  | 6  | 306         | 323 | 308 |
| 1          | 7          | 084394    | 3                | 556                | 379                                 | 7                        | 21         | 28 | 24 | 162         | 166 | 150 | 17           | 21 | 13 | 7            | 9  | 10 | 317         | 327 | 329 |
| 1          | 7          | 084394    | 3                | 833                | 569                                 | 10                       | 28         | 33 | 26 | 152         | 161 | 146 | 17           | 18 | 16 | 9            | 10 | 8  | 335         | 317 | 336 |
| 1          | 7          | 084394    | 3                | 1111               | 759                                 | 13                       | 24         | 26 | 37 | 136         | 158 | 143 | 21           | 15 | 19 | 7            | 9  | 10 | 330         | 296 | 307 |
| 1          | 7          | 084394    | 3                | 1389               | 948                                 | 17                       | 20         | 24 | 29 | 148         | 161 | 156 | 18           | 14 | 17 | 13           | 10 | 12 | 317         | 298 | 297 |
| 1          | 7          | 084394    | 3                | 2778               | 1897                                | 34                       | 22         | 23 | 28 | 177         | 186 | 180 | 12           | 20 | 18 | 14           | 10 | 12 | 324         | 332 | 325 |
| 1          | 7          | 084394    | 3                | 5557               | 3794                                | 67                       | 24         | 28 | 36 | 176         | 169 | 187 | 14           | 16 | 13 | 7            | 8  | 6  | 325         | 276 | 281 |
| 1          | 2          | 084395    | 1                | 0                  | 0                                   | 0                        | 27         | 29 | 20 | 144         | 124 | 150 | 19           | 18 | 14 | 7            | 7  | 9  | 276         | 288 | 272 |
| 1          | 2          | 084395    | 1                | 278                | 128                                 | 4                        | 21         | 20 | 29 | 153         | 161 | 146 | 19           | 13 | 8  | 7            | 8  | 6  | 303         | 298 | 298 |
| 1          | 2          | 084395    | 1                | 556                | 256                                 | 8                        | 21         | 20 | 23 | 134         | 148 | 153 | 21           | 22 | 23 | 10           | 8  | 8  | 286         | 289 | 299 |
| 1          | 2          | 084395    | 1                | 834                | 383                                 | 12                       | 23         | 23 | 22 | 159         | 153 | 164 | 14           | 17 | 12 | 8            | 9  | 7  | 287         | 297 | 286 |
| 1          | 2          | 084395    | 1                | 1112               | 511                                 | 16                       | 28         | 26 | 24 | 144         | 161 | 133 | 14           | 11 | 12 | 8            | 14 | 11 | 268         | 278 | 267 |
| 1          | 2          | 084395    | 1                | 1390               | 639                                 | 19                       | 23         | 24 | 22 | 143         | 162 | 151 | 17           | 16 | 14 | 9            | 12 | 13 | 305         | 294 | 293 |
| 1          | 2          | 084395    | 1                | 2779               | 1278                                | 39                       | 29         | 20 | 24 | 147         | 164 | 158 | 11           | 8  | 10 | 15           | 14 | 12 | 293         | 310 | 299 |
| 1          | 2          | 084395    | 1                | 5558               | 2556                                | 78                       | 26         | 26 | 27 | 136         | 140 | 152 | 13           | 20 | 17 | 16           | 17 | 19 | 294         | 293 | 296 |
| 1          | 5          | 084395    | 2                | 0                  | 0                                   | 0                        | 34         | 28 | 20 | 144         | 149 | 142 | 17           | 18 | 8  | 5            | 6  | 7  | 277         | 274 | 266 |
| 1          | 5          | 084395    | 2                | 278                | 128                                 | 4                        | 27         | 30 | 27 | 147         | 140 | 167 | 18           | 15 | 19 | 8            | 10 | 9  | 299         | 290 | 293 |
| 1          | 5          | 084395    | 2                | 556                | 256                                 | 8                        | 25         | 20 | 25 | 166         | 136 | 157 | 13           | 22 | 12 | 11           | 7  | 14 | 329         | 305 | 334 |
| 1          | 5          | 084395    | 2                | 834                | 383                                 | 12                       | 19         | 22 | 25 | 156         | 144 | 156 | 23           | 11 | 13 | 10           | 9  | 11 | 314         | 309 | 313 |
| 1          | 5          | 084395    | 2                | 1112               | 511                                 | 16                       | 23         | 34 | 22 | 170         | 156 | 151 | 12           | 19 | 17 | 15           | 11 | 12 | 294         | 306 | 294 |
| 1          | 5          | 084395    | 2                | 1390               | 639                                 | 20                       | 20         | 28 | 23 | 158         | 148 | 172 | 13           | 20 | 16 | 9            | 12 | 10 | 300         | 282 | 294 |
| 1          | 5          | 084395    | 2                | 2779               | 1278                                | 40                       | 21         | 20 | 24 | 168         | 175 | 157 | 15           | 16 | 14 | 11           | 9  | 18 | 326         | 324 | 310 |
| 1          | 5          | 084395    | 2                | 5558               | 2556                                | 80                       | 21         | 29 | 21 | 187         | 158 | 168 | 19           | 16 | 18 | 11           | 9  | 13 | 326         | 322 | 312 |
| 1          | 6          | 084395    | 3                | 0                  | 0                                   | 0                        | 30         | 20 | 20 | 158         | 137 | 144 | 9            | 19 | 15 | 5            | 6  | 7  | 290         | 301 | 301 |
| 1          | 6          | 084395    | 3                | 278                | 128                                 | 4                        | 20         | 22 | 21 | 141         | 159 | 138 | 16           | 10 | 20 | 8            | 6  | 9  | 295         | 305 | 302 |
| 1          | 6          | 084395    | 3                | 556                | 256                                 | 7                        | 21         | 20 | 26 | 146         | 152 | 134 | 16           | 20 | 12 | 12           | 8  | 10 | 307         | 318 | 318 |
| 1          | 6          | 084395    | 3                | 834                | 383                                 | 11                       | 23         | 20 | 20 | 152         | 151 | 136 | 19           | 17 | 15 | 7            | 9  | 7  | 326         | 301 | 310 |
| 1          | 6          | 084395    | 3                | 1111               | 511                                 | 15                       | 28         | 21 | 30 | 144         | 152 | 154 | 8            | 20 | 16 | 6            | 9  | 8  | 286         | 271 | 284 |
| 1          | 6          | 084395    | 3                | 1389               | 639                                 | 19                       | 36         | 20 | 22 | 147         | 166 | 153 | 13           | 16 | 12 | 10           | 8  | 10 | 306         | 311 | 306 |
| 1          | 6          | 084395    | 3                | 2779               | 1278                                | 37                       | 20         | 21 | 20 | 153         | 169 | 173 | 21           | 15 | 17 | 10           | 7  | 9  | 306         | 319 | 323 |
| 1          | 6          | 084395    | 3                | 5557               | 2555                                | 74                       | 22         | 22 | 20 | 171         | 164 | 184 | 17           | 23 | 20 | 6            | 5  | 7  | 360         | 381 | 370 |

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Revertants per plate)**

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (-S9) |    |    | TA100 (-S9) |     |     | TA1535 (-S9) |    |    | TA1537 (-S9) |    |    | TA102 (-S9) |     |     |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|            |            |           |                  |                    |                                     |                          | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 2          | 4          | 084454    | 1                | 0                  | 0                                   | 0                        | 28         | 26 | 24 | 162         | 178 | 176 | 11           | 7  | 12 | 11           | 11 | 10 | 283         | 281 | 287 |
| 2          | 4          | 084454    | 1                | 278                | 247                                 | 1                        | 28         | 21 | 22 | 207         | 188 | 223 | 15           | 11 | 14 | 13           | 12 | 8  | 286         | 271 | 283 |
| 2          | 4          | 084454    | 1                | 556                | 494                                 | 2                        | 31         | 27 | 25 | 223         | 221 | 163 | 12           | 11 | 10 | 8            | 9  | 5  | 286         | 296 | 303 |
| 2          | 4          | 084454    | 1                | 834                | 741                                 | 3                        | 20         | 27 | 29 | 205         | 187 | 186 | 13           | 15 | 14 | 5            | 5  | 6  | 322         | 296 | 300 |
| 2          | 4          | 084454    | 1                | 1112               | 988                                 | 4                        | 28         | 30 | 31 | 200         | 177 | 174 | 13           | 12 | 11 | 7            | 8  | 7  | 288         | 267 | 274 |
| 2          | 4          | 084454    | 1                | 1389               | 1235                                | 5                        | 20         | 24 | 23 | 143         | 159 | 160 | 12           | 10 | 13 | 11           | 13 | 13 | 270         | 278 | 292 |
| 2          | 4          | 084454    | 1                | 2779               | 2470                                | 10                       | 29         | 34 | 21 | 132         | 173 | 174 | 11           | 14 | 15 | 7            | 12 | 8  | 291         | 286 | 288 |
| 2          | 4          | 084454    | 1                | 5558               | 4941                                | 20                       | 29         | 30 | 32 | 191         | 161 | 174 | 10           | 11 | 12 | 10           | 8  | 8  | 278         | 277 | 292 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 6          | 084454    | 2                | 0                  | 0                                   | 0                        | 31         | 25 | 26 | 198         | 197 | 136 | 6            | 9  | 12 | 7            | 9  | 7  | 264         | 247 | 256 |
| 2          | 6          | 084454    | 2                | 278                | 247                                 | 1                        | 28         | 27 | 31 | 129         | 180 | 177 | 10           | 11 | 14 | 5            | 5  | 5  | 256         | 251 | 263 |
| 2          | 6          | 084454    | 2                | 556                | 494                                 | 2                        | 31         | 28 | 34 | 159         | 188 | 178 | 11           | 10 | 12 | 9            | 8  | 8  | 223         | 217 | 241 |
| 2          | 6          | 084454    | 2                | 834                | 741                                 | 3                        | 23         | 24 | 21 | 167         | 178 | 177 | 12           | 13 | 16 | 5            | 7  | 5  | 263         | 272 | 292 |
| 2          | 6          | 084454    | 2                | 1111               | 988                                 | 4                        | 29         | 36 | 35 | 186         | 149 | 188 | 16           | 10 | 13 | 9            | 10 | 10 | 273         | 279 | 272 |
| 2          | 6          | 084454    | 2                | 1389               | 1235                                | 5                        | 20         | 32 | 27 | 171         | 179 | 181 | 14           | 17 | 10 | 7            | 8  | 8  | 290         | 280 | 288 |
| 2          | 6          | 084454    | 2                | 2779               | 2470                                | 11                       | 24         | 32 | 26 | 181         | 111 | 151 | 18           | 12 | 13 | 10           | 9  | 8  | 282         | 266 | 271 |
| 2          | 6          | 084454    | 2                | 5557               | 4940                                | 22                       | 24         | 31 | 29 | 168         | 194 | 197 | 13           | 14 | 17 | 9            | 7  | 8  | 292         | 291 | 271 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 14         | 084454    | 3                | 0                  | 0                                   | 0                        | 21         | 27 | 22 | 172         | 169 | 169 | 9            | 8  | 13 | 5            | 10 | 6  | 317         | 301 | 324 |
| 2          | 14         | 084454    | 3                | 278                | 247                                 | 1                        | 22         | 21 | 24 | 190         | 150 | 162 | 11           | 14 | 10 | 7            | 5  | 5  | 312         | 309 | 322 |
| 2          | 14         | 084454    | 3                | 556                | 494                                 | 2                        | 21         | 28 | 26 | 177         | 173 | 141 | 12           | 11 | 14 | 11           | 12 | 9  | 313         | 321 | 335 |
| 2          | 14         | 084454    | 3                | 834                | 741                                 | 3                        | 27         | 25 | 37 | 139         | 171 | 143 | 14           | 16 | 14 | 13           | 11 | 11 | 343         | 327 | 359 |
| 2          | 14         | 084454    | 3                | 1112               | 988                                 | 4                        | 30         | 26 | 29 | 178         | 184 | 176 | 14           | 16 | 11 | 9            | 9  | 7  | 341         | 348 | 366 |
| 2          | 14         | 084454    | 3                | 1389               | 1235                                | 6                        | 22         | 26 | 37 | 197         | 173 | 176 | 18           | 12 | 16 | 7            | 6  | 8  | 381         | 371 | 387 |
| 2          | 14         | 084454    | 3                | 2779               | 2470                                | 11                       | 22         | 29 | 26 | 138         | 178 | 194 | 10           | 16 | 14 | 9            | 10 | 10 | 370         | 390 | 390 |
| 2          | 14         | 084454    | 3                | 5558               | 4941                                | 22                       | 29         | 27 | 34 | 148         | 144 | 133 | 12           | 10 | 14 | 7            | 9  | 9  | 381         | 358 | 384 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 5          | 084455    | 1                | 0                  | 0                                   | 0                        | 26         | 20 | 26 | 183         | NA  | 178 | 13           | 12 | 17 | 8            | 5  | 7  | 288         | 279 | 286 |
| 2          | 5          | 084455    | 1                | 278                | 261                                 | 2                        | 21         | 23 | 25 | 154         | 168 | 157 | 10           | 11 | 13 | 5            | 6  | 6  | 297         | 288 | 293 |
| 2          | 5          | 084455    | 1                | 556                | 522                                 | 3                        | 21         | 24 | 20 | 160         | 148 | 150 | 13           | 10 | 6  | 8            | 10 | 11 | 277         | 272 | 282 |
| 2          | 5          | 084455    | 1                | 834                | 783                                 | 5                        | 24         | 26 | 29 | 172         | 190 | 174 | 12           | 11 | 8  | 7            | 7  | 8  | 260         | 261 | 276 |
| 2          | 5          | 084455    | 1                | 1112               | 1044                                | 6                        | 30         | 32 | 28 | 197         | 194 | 194 | 7            | 6  | 8  | 5            | 10 | 8  | 277         | 299 | 288 |
| 2          | 5          | 084455    | 1                | 1390               | 1305                                | 8                        | 37         | 23 | 29 | 201         | 190 | 219 | 8            | 7  | 8  | 7            | 6  | 9  | 319         | 306 | 301 |
| 2          | 5          | 084455    | 1                | 2779               | 2610                                | 15                       | 30         | 21 | 29 | 194         | 181 | 186 | NA           | 7  | 7  | 7            | 8  | 6  | 288         | 294 | 286 |
| 2          | 5          | 084455    | 1                | 5558               | 5220                                | 31                       | 34         | 26 | 37 | 144         | 132 | 162 | 8            | 8  | 7  | 6            | 9  | 8  | 272         | 268 | 277 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 13         | 084455    | 2                | 0                  | 0                                   | 0                        | 37         | 32 | 27 | 168         | 167 | 160 | 9            | 8  | 7  | 6            | 7  | 10 | 323         | 343 | 338 |
| 2          | 13         | 084455    | 2                | 278                | 261                                 | 1                        | 26         | 20 | 24 | 213         | 167 | 158 | 10           | 11 | 12 | 9            | 11 | 14 | 340         | 348 | 372 |
| 2          | 13         | 084455    | 2                | 556                | 522                                 | 3                        | 26         | 32 | 27 | 162         | 163 | 183 | 11           | 12 | 14 | 9            | 11 | 14 | 362         | 372 | 386 |
| 2          | 13         | 084455    | 2                | 834                | 783                                 | 4                        | 26         | 22 | 27 | 191         | 187 | 178 | 12           | 10 | 13 | 11           | 11 | 9  | 348         | 347 | 350 |
| 2          | 13         | 084455    | 2                | 1112               | 1044                                | 6                        | 37         | 29 | 24 | 187         | 226 | 208 | 12           | 16 | 13 | 7            | 7  | 6  | 365         | 357 | 382 |
| 2          | 13         | 084455    | 2                | 1390               | 1305                                | 7                        | 26         | 25 | 31 | 206         | 174 | 177 | 10           | 12 | 11 | 5            | 6  | 5  | 378         | 376 | 363 |
| 2          | 13         | 084455    | 2                | 2780               | 2611                                | 15                       | 26         | 24 | 30 | 134         | 166 | 142 | 13           | 11 | 12 | 8            | 9  | 7  | 380         | 354 | 360 |
| 2          | 13         | 084455    | 2                | 5559               | 5222                                | 29                       | 39         | 32 | 33 | 190         | 203 | 156 | 9            | 12 | 11 | 6            | 10 | 9  | 368         | 351 | 383 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 17         | 084455    | 3                | 0                  | 0                                   | 0                        | 23         | 22 | 20 | 190         | 168 | 167 | 8            | 9  | 11 | 7            | 9  | 10 | 370         | 351 | 348 |
| 2          | 17         | 084455    | 3                | 278                | 261                                 | 2                        | 29         | 24 | 27 | 192         | 154 | 176 | 15           | 12 | 16 | 6            | 5  | 6  | 358         | 352 | 358 |
| 2          | 17         | 084455    | 3                | 556                | 522                                 | 3                        | 29         | 25 | 23 | 209         | 222 | 142 | 14           | 19 | 14 | 5            | 7  | 5  | 356         | 371 | 361 |
| 2          | 17         | 084455    | 3                | 833                | 783                                 | 5                        | 20         | 22 | 30 | 204         | 189 | 167 | 16           | 14 | 12 | 10           | 7  | 7  | 340         | 364 | 366 |
| 2          | 17         | 084455    | 3                | 1111               | 1044                                | 6                        | 29         | 20 | 24 | 181         | 159 | 159 | 13           | 14 | 15 | 8            | 6  | 6  | 373         | 362 | 357 |
| 2          | 17         | 084455    | 3                | 1389               | 1305                                | 8                        | 23         | 25 | 28 | 156         | 177 | 162 | 8            | 17 | 16 | 6            | 5  | 7  | 350         | 351 | 342 |
| 2          | 17         | 084455    | 3                | 2778               | 2609                                | 15                       | 27         | 30 | 23 | 162         | 152 | 159 | 10           | 13 | 9  | 6            | 7  | 7  | 339         | 354 | 373 |
| 2          | 17         | 084455    | 3                | 5556               | 5218                                | 31                       | 28         | 30 | 32 | 141         | 130 | 161 | 16           | 11 | 13 | 7            | 5  | 5  | 370         | 341 | 369 |

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Revertants per plate)**

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (-S9) |    |    | TA100 (-S9) |     |     | TA1535 (-S9) |    |    | TA1537 (-S9) |    |    | TA102 (-S9) |     |     |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|            |            |           |                  |                    |                                     |                          | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 2          | 3          | 084456    | 1                | 0                  | 0                                   | 0                        | 24         | 27 | 20 | 167         | 174 | 122 | 16           | 15 | 12 | 7            | 5  | 8  | 290         | 274 | 269 |
| 2          | 3          | 084456    | 1                | 278                | 124                                 | 3                        | 23         | 27 | 28 | 187         | 146 | 132 | 14           | 17 | 13 | 11           | 14 | 8  | 261         | 287 | 279 |
| 2          | 3          | 084456    | 1                | 556                | 248                                 | 6                        | 32         | 26 | 33 | 159         | 176 | 190 | 18           | 14 | 15 | 10           | 9  | 9  | 278         | 281 | 266 |
| 2          | 3          | 084456    | 1                | 834                | 372                                 | 10                       | 20         | 31 | 39 | 162         | 168 | 176 | 14           | 11 | 14 | 6            | 8  | 7  | 263         | 264 | 279 |
| 2          | 3          | 084456    | 1                | 1112               | 496                                 | 13                       | 28         | 34 | 32 | 180         | 187 | 160 | 13           | 12 | 10 | 12           | 6  | 12 | 290         | 287 | 306 |
| 2          | 3          | 084456    | 1                | 1390               | 620                                 | 16                       | 22         | 28 | 27 | 194         | 184 | 181 | 12           | 15 | 14 | 12           | 9  | 10 | 279         | 280 | 276 |
| 2          | 3          | 084456    | 1                | 2779               | 1241                                | 32                       | 26         | 25 | 28 | 203         | 234 | 182 | 12           | 11 | 15 | 9            | 8  | 7  | 287         | 283 | 281 |
| 2          | 3          | 084456    | 1                | 5559               | 2481                                | 65                       | 26         | 32 | 27 | 204         | 194 | 169 | 19           | 15 | 17 | 5            | 13 | 11 | 260         | 273 | 291 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 7          | 084456    | 2                | 0                  | 0                                   | 0                        | 26         | 23 | 28 | 174         | 164 | 194 | 10           | 8  | 11 | 6            | 5  | 5  | 276         | 286 | 272 |
| 2          | 7          | 084456    | 2                | 278                | 124                                 | 3                        | 27         | 26 | 22 | 153         | 168 | 190 | 13           | 10 | 11 | 10           | 9  | 8  | 277         | 266 | 253 |
| 2          | 7          | 084456    | 2                | 556                | 248                                 | 7                        | 32         | 24 | 31 | 154         | 158 | 189 | 10           | 15 | 12 | 9            | 9  | 11 | 274         | 253 | 251 |
| 2          | 7          | 084456    | 2                | 834                | 372                                 | 10                       | 27         | 24 | 33 | 199         | 159 | 166 | 17           | 10 | 12 | 8            | 8  | 10 | 302         | 292 | 288 |
| 2          | 7          | 084456    | 2                | 1112               | 496                                 | 13                       | 24         | 22 | 24 | 173         | 163 | 193 | 8            | 16 | 9  | 7            | 10 | 9  | 286         | NA  | 268 |
| 2          | 7          | 084456    | 2                | 1390               | 620                                 | 17                       | 24         | 26 | 31 | 204         | 196 | 203 | 10           | 18 | 11 | 7            | 6  | 6  | 278         | 286 | 293 |
| 2          | 7          | 084456    | 2                | 2779               | 1240                                | 33                       | 25         | 27 | 25 | 202         | 164 | 134 | 16           | 15 | 19 | 7            | 8  | 9  | 281         | 273 | 278 |
| 2          | 7          | 084456    | 2                | 5558               | 2481                                | 66                       | 29         | 26 | 28 | 141         | 166 | 150 | 13           | 14 | 18 | 5            | 5  | 7  | 303         | 300 | 300 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 9          | 084456    | 3                | 0                  | 0                                   | 0                        | 26         | 20 | 23 | 138         | 139 | 172 | 10           | 8  | 11 | 7            | 8  | 5  | 294         | 301 | 282 |
| 2          | 9          | 084456    | 3                | 278                | 124                                 | 3                        | 27         | 22 | 25 | 157         | 162 | 200 | 13           | 11 | 13 | 9            | 8  | 6  | 311         | 283 | 278 |
| 2          | 9          | 084456    | 3                | 556                | 248                                 | 7                        | 26         | 33 | 27 | 193         | 178 | 164 | 15           | 13 | 11 | 7            | 8  | 6  | 289         | 256 | 278 |
| 2          | 9          | 084456    | 3                | 834                | 372                                 | 10                       | 28         | 26 | 29 | 155         | 179 | 171 | 11           | 12 | 14 | 8            | 8  | 5  | 286         | 314 | 302 |
| 2          | 9          | 084456    | 3                | 1112               | 496                                 | 14                       | 34         | 30 | 31 | 177         | 174 | 172 | 14           | 13 | 13 | 9            | 5  | 6  | 396         | 362 | 364 |
| 2          | 9          | 084456    | 3                | 1390               | 620                                 | 17                       | 23         | 29 | 28 | 182         | 188 | 176 | 13           | 14 | 10 | 6            | 12 | 6  | 352         | 370 | 331 |
| 2          | 9          | 084456    | 3                | 2780               | 1241                                | 34                       | 27         | 24 | 22 | 189         | 162 | 172 | 16           | 18 | 14 | 6            | 9  | 6  | 357         | 369 | 351 |
| 2          | 9          | 084456    | 3                | 5559               | 2481                                | 68                       | 23         | 34 | 32 | 173         | 150 | 179 | 16           | 17 | 14 | 9            | 9  | 10 | 365         | 388 | 370 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 8          | 084457    | 1                | 0                  | 0                                   | 0                        | 37         | 30 | 38 | 174         | 156 | 147 | 6            | 12 | 10 | 6            | 6  | 5  | 287         | 283 | 267 |
| 2          | 8          | 084457    | 1                | 278                | 268                                 | 1                        | 27         | 21 | 20 | 149         | 163 | 157 | 14           | 11 | 10 | 7            | 5  | 7  | 266         | 243 | 236 |
| 2          | 8          | 084457    | 1                | 556                | 535                                 | 3                        | 31         | 26 | 32 | 117         | 140 | 112 | 9            | 12 | 11 | 5            | 8  | 7  | 263         | 286 | 273 |
| 2          | 8          | 084457    | 1                | 833                | 803                                 | 4                        | 27         | 26 | 23 | 82          | 93  | 98  | 14           | 16 | 12 | 5            | 6  | 11 | 282         | 291 | 271 |
| 2          | 8          | 084457    | 1                | 1111               | 1070                                | 6                        | 23         | 33 | 26 | 174         | 123 | 162 | 17           | 15 | 11 | 5            | 7  | 6  | 274         | 262 | 253 |
| 2          | 8          | 084457    | 1                | 1389               | 1338                                | 7                        | 27         | 32 | 28 | 169         | 172 | 181 | 13           | 18 | 14 | 7            | 5  | 5  | 249         | 234 | 236 |
| 2          | 8          | 084457    | 1                | 2778               | 2676                                | 15                       | 32         | 31 | 26 | 182         | 179 | 189 | 9            | 13 | 15 | 5            | 6  | 6  | 248         | 250 | 242 |
| 2          | 8          | 084457    | 1                | 5556               | 5352                                | 29                       | 28         | 24 | 27 | 177         | 172 | 193 | 8            | 9  | 14 | 5            | 9  | 6  | 257         | 240 | 246 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 12         | 084457    | 2                | 0                  | 0                                   | 0                        | 32         | 31 | 28 | 173         | 163 | 177 | 11           | 13 | 10 | 6            | 5  | 8  | 360         | 347 | 342 |
| 2          | 12         | 084457    | 2                | 278                | 268                                 | 2                        | 29         | 27 | 28 | 182         | 180 | 178 | 10           | 16 | 10 | 7            | 9  | 6  | 381         | 353 | 349 |
| 2          | 12         | 084457    | 2                | 556                | 535                                 | 3                        | 28         | 31 | 24 | 183         | 178 | 176 | 12           | 11 | 15 | 7            | 8  | 6  | 359         | 357 | 372 |
| 2          | 12         | 084457    | 2                | 833                | 803                                 | 5                        | 29         | 30 | 33 | 172         | 169 | 183 | 11           | 14 | 13 | 12           | 9  | 11 | 372         | 368 | 368 |
| 2          | 12         | 084457    | 2                | 1111               | 1070                                | 6                        | 35         | 25 | 29 | 179         | 153 | 202 | 11           | 14 | 10 | 7            | 7  | 10 | 387         | 366 | 384 |
| 2          | 12         | 084457    | 2                | 1389               | 1338                                | 8                        | 29         | 27 | 34 | 193         | 156 | 177 | 17           | 15 | 13 | 7            | 8  | 10 | 367         | 344 | 358 |
| 2          | 12         | 084457    | 2                | 2778               | 2676                                | 15                       | 34         | 28 | 36 | 149         | 143 | 164 | 11           | 14 | 11 | 7            | 5  | 5  | 328         | 324 | 346 |
| 2          | 12         | 084457    | 2                | 5556               | 5351                                | 31                       | 24         | 32 | 24 | 102         | 117 | 119 | 18           | 17 | 15 | 5            | 6  | 5  | 330         | 319 | 322 |
|            |            |           |                  |                    |                                     |                          |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2          | 15         | 084457    | 3                | 0                  | 0                                   | 0                        | 27         | 30 | 31 | 162         | 160 | 148 | 12           | 12 | 14 | 10           | 9  | 9  | 339         | 365 | 348 |
| 2          | 15         | 084457    | 3                | 278                | 268                                 | 2                        | 33         | 31 | 20 | 158         | 197 | 168 | 8            | 16 | 10 | 13           | 10 | 11 | 339         | 338 | 348 |
| 2          | 15         | 084457    | 3                | 556                | 535                                 | 3                        | 20         | 24 | 26 | 160         | 158 | 141 | 15           | 19 | 17 | 11           | 11 | 10 | 346         | 361 | 334 |
| 2          | 15         | 084457    | 3                | 833                | 803                                 | 5                        | 27         | 21 | 22 | 133         | 159 | 128 | 13           | 8  | 9  | 10           | 10 | 11 | 363         | 367 | 358 |
| 2          | 15         | 084457    | 3                | 1111               | 1070                                | 6                        | 24         | 30 | 31 | 148         | 182 | 148 | 8            | 7  | 8  | 5            | 5  | 6  | 342         | 359 | 347 |
| 2          | 15         | 084457    | 3                | 1389               | 1338                                | 8                        | 21         | 28 | 27 | 178         | 151 | 146 | 8            | 8  | 7  | 7            | 6  | 8  | 339         | 358 | 356 |
| 2          | 15         | 084457    | 3                | 2778               | 2676                                | 16                       | 33         | 24 | 28 | 127         | 127 | 124 | 9            | 7  | 8  | 8            | 6  | 8  | 329         | 341 | 344 |
| 2          | 15         | 084457    | 3                | 5556               | 5352                                | 32                       | 38         | 23 | 29 | 82          | 92  | 96  | 21           | 7  | 7  | 12           | 13 | 13 | 342         | 332 | 369 |



**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Revertants per plate)**

| Set<br>Number | Run<br>Number | Sample<br>ID | Replicate<br>Number | ST Dose<br>(µg/plate) | ST-H <sub>2</sub> O Dose<br>(µg/plate) | Nicotine Dose<br>(µg/plate) | TA98 (-S9) |    |    | TA100 (-S9) |     |     | TA1535 (-S9) |    |    | TA1537 (-S9) |    |    | TA102 (-S9) |     |     |
|---------------|---------------|--------------|---------------------|-----------------------|--|-----------------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|               |               |              |                     |                       |  |                             | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| 2             | 2             | 084458       | 1                   | 0                     | 0                                      | 0                           | 29         | 27 | 20 | 177         | 163 | 143 | 9            | 11 | 13 | 6            | 6  | 7  | 293         | 289 | 299 |
| 2             | 2             | 084458       | 1                   | 278                   | 264                                    | 1                           | 33         | 24 | 29 | 174         | 191 | 161 | 11           | 14 | 10 | 5            | 5  | 6  | 284         | 297 | 289 |
| 2             | 2             | 084458       | 1                   | 556                   | 527                                    | 1                           | 20         | 22 | 21 | 147         | 134 | 160 | 13           | 11 | 14 | 7            | 5  | 5  | 292         | 282 | 271 |
| 2             | 2             | 084458       | 1                   | 834                   | 791                                    | 2                           | 22         | 27 | 20 | 187         | 160 | 184 | 14           | 16 | 17 | 8            | 7  | 6  | 279         | 276 | 272 |
| 2             | 2             | 084458       | 1                   | 1112                  | 1054                                   | 3                           | 31         | 28 | 30 | 158         | 154 | 169 | 16           | 17 | 14 | 7            | 12 | 7  | 252         | 260 | 260 |
| 2             | 2             | 084458       | 1                   | 1389                  | 1318                                   | 3                           | 28         | 26 | 27 | 154         | 147 | 168 | 16           | 14 | 18 | 6            | 6  | 12 | 263         | 238 | 264 |
| 2             | 2             | 084458       | 1                   | 2779                  | 2636                                   | 7                           | 28         | 21 | 20 | 152         | 133 | 147 | 16           | 15 | 18 | 6            | 10 | 9  | 218         | 228 | 191 |
| 2             | 2             | 084458       | 1                   | 5558                  | 5272                                   | 13                          | 30         | 23 | 25 | 149         | 143 | 166 | 16           | 17 | 18 | 6            | 5  | 8  | 186         | 200 | 210 |
|               |               |              |                     |                       |  |                             |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2             | 10            | 084458       | 2                   | 0                     | 0                                      | 0                           | 23         | 22 | 30 | 180         | 178 | 184 | 8            | 11 | 7  | 11           | 7  | 7  | 302         | 303 | 335 |
| 2             | 10            | 084458       | 2                   | 278                   | 264                                    | 1                           | 30         | 31 | 22 | 183         | 177 | 188 | 10           | 16 | 11 | 6            | 10 | 8  | 362         | 344 | 356 |
| 2             | 10            | 084458       | 2                   | 556                   | 527                                    | 1                           | 22         | 20 | 24 | 172         | 177 | 173 | 14           | 13 | 11 | 6            | 6  | 9  | 379         | 380 | 366 |
| 2             | 10            | 084458       | 2                   | 834                   | 791                                    | 2                           | 28         | 38 | 25 | 149         | 168 | 199 | 10           | 8  | 13 | 8            | 6  | 8  | 374         | 387 | 372 |
| 2             | 10            | 084458       | 2                   | 1111                  | 1054                                   | 3                           | 24         | 30 | 33 | 149         | 172 | 154 | 17           | 11 | 16 | 7            | 7  | 9  | 363         | 336 | 342 |
| 2             | 10            | 084458       | 2                   | 1389                  | 1318                                   | 4                           | 26         | 27 | 23 | 171         | 164 | 141 | 16           | 13 | 16 | 13           | 10 | 11 | 367         | 337 | 356 |
| 2             | 10            | 084458       | 2                   | 2778                  | 2636                                   | 7                           | 32         | 22 | 28 | 144         | 147 | 152 | 17           | 14 | 16 | 7            | 8  | 8  | 336         | 360 | 346 |
| 2             | 10            | 084458       | 2                   | 5557                  | 5271                                   | 14                          | 30         | 22 | 33 | 141         | 133 | 119 | 16           | 15 | 17 | 10           | 8  | 11 | 351         | 364 | 374 |
|               |               |              |                     |                       |  |                             |            |    |    |             |     |     |              |    |    |              |    |    |             |     |     |
| 2             | 16            | 084458       | 3                   | 0                     | 0                                      | 0                           | 32         | 29 | 39 | 139         | 138 | 171 | 7            | 8  | 10 | 7            | 8  | 8  | 358         | 343 | 343 |
| 2             | 16            | 084458       | 3                   | 278                   | 263                                    | 1                           | 36         | 22 | 21 | 149         | 140 | 138 | 12           | 7  | 11 | 7            | 6  | 7  | 363         | 356 | 361 |
| 2             | 16            | 084458       | 3                   | 556                   | 527                                    | 2                           | 26         | 31 | 29 | 160         | 180 | 166 | 14           | 10 | 15 | 7            | 8  | 7  | 356         | 352 | 348 |
| 2             | 16            | 084458       | 3                   | 833                   | 790                                    | 2                           | 20         | 22 | 27 | 177         | 164 | 87  | 10           | 12 | 10 | 6            | 7  | 6  | 362         | 348 | 367 |
| 2             | 16            | 084458       | 3                   | 1111                  | 1054                                   | 3                           | 28         | 21 | 25 | 179         | 138 | 166 | 12           | 9  | 14 | 14           | 12 | 11 | 357         | 328 | 340 |
| 2             | 16            | 084458       | 3                   | 1389                  | 1317                                   | 4                           | 34         | 22 | 29 | 188         | 132 | 164 | 9            | 12 | 14 | 7            | 5  | 9  | 333         | 330 | 347 |
| 2             | 16            | 084458       | 3                   | 2778                  | 2635                                   | 8                           | 23         | 27 | 30 | 159         | 156 | 161 | 8            | 9  | 12 | 6            | 6  | 8  | 364         | 338 | 342 |
| 2             | 16            | 084458       | 3                   | 5556                  | 5270                                   | 15                          | 29         | 27 | 30 | 134         | 117 | 159 | 9            | 15 | 11 | 5            | 7  | 7  | 372         | 358 | 384 |

N/A - data not available due to lack of bacterial growth or assay plate contamination

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (+S9) |    | TA100 (+S9) |    | TA1535 (+S9) |    | TA1537 (+S9) |    | TA102 (+S9) |    |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                    |                                     |                          | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 1          | 3          | 084394    | 1                | 0                  | 0                                   | 0                        | 39         | 6  | 147         | 5  | 14           | 4  | 6            | 2  | 300         | 10 |
| 1          | 3          | 084394    | 1                | 278                | 190                                 | 3                        | 38         | 6  | 151         | 11 | 9            | 3  | 7            | 1  | 327         | 2  |
| 1          | 3          | 084394    | 1                | 556                | 379                                 | 6                        | 38         | 6  | 150         | 17 | 11           | 3  | 10           | 2  | 329         | 2  |
| 1          | 3          | 084394    | 1                | 833                | 569                                 | 10                       | 39         | 3  | 156         | 14 | 11           | 3  | 8            | 2  | 339         | 8  |
| 1          | 3          | 084394    | 1                | 1111               | 759                                 | 13                       | 38         | 1  | 158         | 10 | 14           | 3  | 11           | 2  | 352         | 4  |
| 1          | 3          | 084394    | 1                | 1389               | 948                                 | 16                       | 33         | 2  | 144         | 12 | 13           | 4  | 9            | 1  | 347         | 7  |
| 1          | 3          | 084394    | 1                | 2778               | 1897                                | 32                       | 34         | 6  | 143         | 2  | 12           | 4  | 15           | 3  | 365         | 9  |
| 1          | 3          | 084394    | 1                | 5556               | 3793                                | 64                       | 44         | 4  | 156         | 8  | 12           | 2  | 13           | 3  | 366         | 3  |
| 1          | 4          | 084394    | 2                | 0                  | 0                                   | 0                        | 30         | 12 | 152         | 10 | 15           | 2  | 6            | 1  | 242         | 20 |
| 1          | 4          | 084394    | 2                | 278                | 190                                 | 4                        | 31         | 12 | 143         | 13 | 13           | 1  | 9            | 2  | 241         | 13 |
| 1          | 4          | 084394    | 2                | 556                | 379                                 | 7                        | 27         | 11 | 145         | 11 | 13           | 4  | 7            | 2  | 239         | 9  |
| 1          | 4          | 084394    | 2                | 834                | 569                                 | 11                       | 30         | 10 | 145         | 2  | 13           | 1  | 9            | 2  | 254         | 5  |
| 1          | 4          | 084394    | 2                | 1112               | 759                                 | 14                       | 40         | 9  | 176         | 9  | 14           | 2  | 9            | 1  | 301         | 2  |
| 1          | 4          | 084394    | 2                | 1389               | 949                                 | 18                       | 36         | 5  | 159         | 15 | 11           | 3  | 11           | 3  | 314         | 12 |
| 1          | 4          | 084394    | 2                | 2779               | 1897                                | 36                       | 39         | 2  | 150         | 12 | 13           | 3  | 12           | 2  | 320         | 4  |
| 1          | 4          | 084394    | 2                | 5558               | 3794                                | 71                       | 37         | 7  | 160         | 11 | 17           | 3  | 14           | 3  | 295         | 8  |
| 1          | 7          | 084394    | 3                | 0                  | 0                                   | 0                        | 32         | 2  | 154         | 6  | 11           | 1  | 9            | 1  | 301         | 5  |
| 1          | 7          | 084394    | 3                | 278                | 190                                 | 3                        | 30         | 4  | 153         | 9  | 12           | 7  | 10           | 3  | 327         | 3  |
| 1          | 7          | 084394    | 3                | 556                | 379                                 | 7                        | 32         | 4  | 160         | 8  | 15           | 1  | 9            | 1  | 329         | 4  |
| 1          | 7          | 084394    | 3                | 833                | 569                                 | 10                       | 31         | 4  | 162         | 6  | 13           | 3  | 10           | 2  | 349         | 14 |
| 1          | 7          | 084394    | 3                | 1111               | 759                                 | 13                       | 40         | 5  | 175         | 18 | 12           | 2  | 11           | 4  | 353         | 7  |
| 1          | 7          | 084394    | 3                | 1389               | 948                                 | 17                       | 33         | 6  | 177         | 9  | 10           | 3  | 12           | 1  | 362         | 9  |
| 1          | 7          | 084394    | 3                | 2778               | 1897                                | 34                       | 22         | 8  | 173         | 5  | 13           | 1  | 13           | 2  | 328         | 4  |
| 1          | 7          | 084394    | 3                | 5557               | 3794                                | 67                       | 27         | 1  | 184         | 12 | 6            | 2  | 16           | 3  | 339         | 6  |
| 1          | 2          | 084395    | 1                | 0                  | 0                                   | 0                        | 31         | 4  | 157         | 6  | 12           | 4  | 7            | 1  | 302         | 14 |
| 1          | 2          | 084395    | 1                | 278                | 128                                 | 4                        | 30         | 11 | 150         | 9  | 14           | 5  | 10           | 1  | 349         | 10 |
| 1          | 2          | 084395    | 1                | 556                | 256                                 | 8                        | 27         | 5  | 145         | 13 | 12           | 4  | 12           | 1  | 351         | 6  |
| 1          | 2          | 084395    | 1                | 834                | 383                                 | 12                       | 27         | 1  | 162         | 11 | 15           | 2  | 13           | 2  | 365         | 10 |
| 1          | 2          | 084395    | 1                | 1112               | 511                                 | 16                       | 37         | 10 | 168         | 9  | 13           | 4  | 18           | 2  | 359         | 8  |
| 1          | 2          | 084395    | 1                | 1390               | 639                                 | 19                       | 41         | 6  | 144         | 6  | 10           | 6  | 17           | 2  | 353         | 6  |
| 1          | 2          | 084395    | 1                | 2779               | 1278                                | 39                       | 37         | 9  | 161         | 1  | 11           | 2  | 18           | 1  | 347         | 16 |
| 1          | 2          | 084395    | 1                | 5558               | 2556                                | 78                       | 44         | 4  | 167         | 13 | 15           | 3  | 19           | 1  | 348         | 9  |
| 1          | 5          | 084395    | 2                | 0                  | 0                                   | 0                        | 42         | 5  | 150         | 15 | 15           | 3  | 8            | 1  | 297         | 9  |
| 1          | 5          | 084395    | 2                | 278                | 128                                 | 4                        | 31         | 3  | 137         | 5  | 11           | 4  | 9            | 1  | 312         | 3  |
| 1          | 5          | 084395    | 2                | 556                | 256                                 | 8                        | 31         | 1  | 151         | 13 | 13           | 2  | 7            | 1  | 309         | 4  |
| 1          | 5          | 084395    | 2                | 834                | 383                                 | 12                       | 34         | 6  | 168         | 14 | 12           | 2  | 11           | 1  | 309         | 9  |
| 1          | 5          | 084395    | 2                | 1112               | 511                                 | 16                       | 39         | 1  | 174         | 6  | 13           | 5  | 11           | 3  | 312         | 12 |
| 1          | 5          | 084395    | 2                | 1390               | 639                                 | 20                       | 41         | 3  | 160         | 9  | 12           | 3  | 10           | 2  | 298         | 7  |
| 1          | 5          | 084395    | 2                | 2779               | 1278                                | 40                       | 37         | 2  | 176         | 6  | 13           | 2  | 12           | 2  | 303         | 7  |
| 1          | 5          | 084395    | 2                | 5558               | 2556                                | 80                       | 37         | 5  | 214         | 6  | 14           | 2  | 14           | 2  | 333         | 9  |
| 1          | 6          | 084395    | 3                | 0                  | 0                                   | 0                        | 35         | 5  | 165         | 13 | 10           | 2  | 6            | 1  | 311         | 2  |
| 1          | 6          | 084395    | 3                | 278                | 128                                 | 4                        | 25         | 4  | 167         | 17 | 12           | 5  | 7            | 1  | 316         | 1  |
| 1          | 6          | 084395    | 3                | 556                | 256                                 | 7                        | 28         | 3  | 168         | 7  | 13           | 4  | 8            | 1  | 314         | 3  |
| 1          | 6          | 084395    | 3                | 834                | 383                                 | 11                       | 27         | 5  | 174         | 12 | 10           | 3  | 9            | 1  | 335         | 7  |
| 1          | 6          | 084395    | 3                | 1111               | 511                                 | 15                       | 44         | 4  | 177         | 16 | 10           | 4  | 10           | 2  | 327         | 8  |
| 1          | 6          | 084395    | 3                | 1389               | 639                                 | 19                       | 35         | 4  | 140         | 3  | 12           | 4  | 9            | 2  | 333         | 6  |
| 1          | 6          | 084395    | 3                | 2779               | 1278                                | 37                       | 36         | 3  | 153         | 6  | 11           | 3  | 10           | 3  | 338         | 8  |
| 1          | 6          | 084395    | 3                | 5557               | 2555                                | 74                       | 42         | 2  | 183         | 6  | 11           | 1  | 12           | 2  | 327         | 7  |

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (+S9) |    | TA100 (+S9) |    | TA1535 (+S9) |    | TA1537 (+S9) |    | TA102 (+S9) |    |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                    |                                     |                          | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 2          | 4          | 084454    | 1                | 0                  | 0                                   | 0                        | 29         | 3  | 93          | 9  | 15           | 5  | 11           | 3  | 308         | 6  |
| 2          | 4          | 084454    | 1                | 278                | 247                                 | 1                        | 28         | 4  | 98          | 3  | 11           | 2  | 6            | 1  | 304         | 9  |
| 2          | 4          | 084454    | 1                | 556                | 494                                 | 2                        | 26         | 5  | 104         | 9  | 14           | 4  | 8            | 1  | 289         | 18 |
| 2          | 4          | 084454    | 1                | 834                | 741                                 | 3                        | 29         | 3  | 106         | 8  | 9            | 2  | 9            | 2  | 301         | 11 |
| 2          | 4          | 084454    | 1                | 1112               | 988                                 | 4                        | 24         | 3  | 118         | 12 | 13           | 3  | 6            | 1  | 296         | 15 |
| 2          | 4          | 084454    | 1                | 1389               | 1235                                | 5                        | 23         | 3  | 117         | 8  | 12           | 3  | 8            | 2  | 316         | 5  |
| 2          | 4          | 084454    | 1                | 2779               | 2470                                | 10                       | 28         | 3  | 114         | 7  | 14           | 7  | 12           | 4  | 309         | 15 |
| 2          | 4          | 084454    | 1                | 5558               | 4941                                | 20                       | 25         | 3  | 121         | 4  | 15           | 4  | 8            | 1  | 306         | 7  |
| 2          | 6          | 084454    | 2                | 0                  | 0                                   | 0                        | 25         | 2  | 91          | 5  | 14           | 4  | 10           | 1  | 303         | 14 |
| 2          | 6          | 084454    | 2                | 278                | 247                                 | 1                        | 27         | 5  | 92          | 4  | 16           | 3  | 10           | 2  | 307         | 3  |
| 2          | 6          | 084454    | 2                | 556                | 494                                 | 2                        | 22         | 1  | 94          | 6  | 17           | 1  | 11           | 2  | 293         | 3  |
| 2          | 6          | 084454    | 2                | 834                | 741                                 | 3                        | 21         | 4  | 100         | 9  | 14           | 6  | 8            | 1  | 298         | 6  |
| 2          | 6          | 084454    | 2                | 1111               | 988                                 | 4                        | 24         | 1  | 104         | 5  | 13           | 3  | 10           | 4  | 307         | 12 |
| 2          | 6          | 084454    | 2                | 1389               | 1235                                | 5                        | 22         | 2  | 107         | 3  | 17           | 4  | 11           | 1  | 291         | 17 |
| 2          | 6          | 084454    | 2                | 2779               | 2470                                | 11                       | 27         | 3  | 119         | 4  | 17           | 4  | 10           | 2  | 277         | 10 |
| 2          | 6          | 084454    | 2                | 5557               | 4940                                | 22                       | 26         | 1  | 113         | 2  | 16           | 2  | 9            | 3  | 289         | 9  |
| 2          | 14         | 084454    | 3                | 0                  | 0                                   | 0                        | 29         | 7  | 95          | 5  | 19           | 2  | 8            | 1  | 303         | 6  |
| 2          | 14         | 084454    | 3                | 278                | 247                                 | 1                        | 29         | 5  | 100         | 6  | 15           | 3  | 14           | 1  | 284         | 12 |
| 2          | 14         | 084454    | 3                | 556                | 494                                 | 2                        | 22         | 1  | 102         | 7  | 14           | 2  | 6            | 1  | 291         | 16 |
| 2          | 14         | 084454    | 3                | 834                | 741                                 | 3                        | 22         | 0  | 103         | 7  | 12           | 5  | 6            | 1  | 291         | 8  |
| 2          | 14         | 084454    | 3                | 1112               | 988                                 | 4                        | 27         | 5  | 112         | 5  | 12           | 2  | 7            | 1  | 289         | 5  |
| 2          | 14         | 084454    | 3                | 1389               | 1235                                | 6                        | 22         | 4  | 113         | 9  | 12           | 5  | 8            | 1  | 286         | 3  |
| 2          | 14         | 084454    | 3                | 2779               | 2470                                | 11                       | 21         | 2  | 92          | 9  | 12           | 4  | 7            | 2  | 301         | 10 |
| 2          | 14         | 084454    | 3                | 5558               | 4941                                | 22                       | 22         | 1  | 100         | 4  | 14           | 3  | 7            | 1  | 294         | 17 |
| 2          | 5          | 084455    | 1                | 0                  | 0                                   | 0                        | 30         | 6  | 84          | 5  | 12           | 2  | 8            | 2  | 303         | 7  |
| 2          | 5          | 084455    | 1                | 278                | 261                                 | 2                        | 22         | 2  | 89          | 4  | 14           | 4  | 12           | 3  | 289         | 9  |
| 2          | 5          | 084455    | 1                | 556                | 522                                 | 3                        | 30         | 6  | 91          | 3  | 9            | 1  | 9            | 2  | 297         | 11 |
| 2          | 5          | 084455    | 1                | 834                | 783                                 | 5                        | 27         | 6  | 94          | 6  | 9            | 1  | 11           | 2  | 303         | 12 |
| 2          | 5          | 084455    | 1                | 1112               | 1044                                | 6                        | 28         | 2  | 106         | 7  | 12           | 1  | 13           | 2  | 304         | 17 |
| 2          | 5          | 084455    | 1                | 1390               | 1305                                | 8                        | 22         | 2  | 108         | 9  | 12           | 4  | 10           | 2  | 311         | 14 |
| 2          | 5          | 084455    | 1                | 2779               | 2610                                | 15                       | 25         | 5  | 117         | 7  | 10           | 4  | 8            | 2  | 314         | 9  |
| 2          | 5          | 084455    | 1                | 5558               | 5220                                | 31                       | 22         | 1  | 100         | 7  | 12           | 2  | 9            | 1  | 314         | 11 |
| 2          | 13         | 084455    | 2                | 0                  | 0                                   | 0                        | 25         | 7  | 92          | 6  | 15           | 3  | 5            | 1  | 302         | 11 |
| 2          | 13         | 084455    | 2                | 278                | 261                                 | 1                        | 22         | 2  | 100         | 6  | 13           | 1  | 7            | 2  | 309         | 3  |
| 2          | 13         | 084455    | 2                | 556                | 522                                 | 3                        | 22         | 5  | 102         | 5  | 14           | 4  | 7            | 2  | 292         | 10 |
| 2          | 13         | 084455    | 2                | 834                | 783                                 | 4                        | 28         | 10 | 109         | 5  | 15           | 3  | 6            | 1  | 294         | 11 |
| 2          | 13         | 084455    | 2                | 1112               | 1044                                | 6                        | 30         | 5  | 122         | 7  | 15           | 4  | 8            | 2  | 294         | 9  |
| 2          | 13         | 084455    | 2                | 1390               | 1305                                | 7                        | 25         | 3  | 114         | 7  | 13           | 4  | 6            | 1  | 299         | 10 |
| 2          | 13         | 084455    | 2                | 2780               | 2611                                | 15                       | 28         | 2  | 117         | 9  | 12           | 4  | 5            | 1  | 297         | 13 |
| 2          | 13         | 084455    | 2                | 5559               | 5222                                | 29                       | 24         | 3  | 108         | 9  | 10           | 4  | 8            | 2  | 310         | 5  |
| 2          | 17         | 084455    | 3                | 0                  | 0                                   | 0                        | 21         | 1  | 94          | 5  | 12           | 2  | 8            | 1  | 278         | 5  |
| 2          | 17         | 084455    | 3                | 278                | 261                                 | 2                        | 23         | 3  | 100         | 5  | 11           | 1  | 9            | 1  | 281         | 5  |
| 2          | 17         | 084455    | 3                | 556                | 522                                 | 3                        | 25         | 5  | 103         | 6  | 13           | 3  | 8            | 1  | 282         | 8  |
| 2          | 17         | 084455    | 3                | 833                | 783                                 | 5                        | 26         | 5  | 115         | 4  | 15           | 3  | 7            | 1  | 264         | 8  |
| 2          | 17         | 084455    | 3                | 1111               | 1044                                | 6                        | 26         | 5  | 104         | 1  | 12           | 2  | 7            | 1  | 274         | 8  |
| 2          | 17         | 084455    | 3                | 1389               | 1305                                | 8                        | 23         | 2  | 113         | 7  | 13           | 1  | 6            | 1  | 296         | 12 |
| 2          | 17         | 084455    | 3                | 2778               | 2609                                | 15                       | 25         | 4  | 119         | 8  | 16           | 4  | 8            | 1  | 290         | 13 |
| 2          | 17         | 084455    | 3                | 5556               | 5218                                | 31                       | 29         | 1  | 114         | 7  | 11           | 2  | 11           | 2  | 290         | 14 |

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (+S9) |    | TA100 (+S9) |    | TA1535 (+S9) |    | TA1537 (+S9) |    | TA102 (+S9) |    |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                    |                                     |                          | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 2          | 3          | 084456    | 1                | 0                  | 0                                   | 0                        | 29         | 4  | 84          | 3  | 10           | 4  | 8            | 1  | 280         | 11 |
| 2          | 3          | 084456    | 1                | 278                | 124                                 | 3                        | 23         | 3  | 88          | 1  | 14           | 3  | 9            | 1  | 271         | 18 |
| 2          | 3          | 084456    | 1                | 556                | 248                                 | 6                        | 25         | 5  | 86          | 5  | 14           | 4  | 11           | 2  | 305         | 15 |
| 2          | 3          | 084456    | 1                | 834                | 372                                 | 10                       | 25         | 3  | 94          | 7  | 11           | 1  | 8            | 2  | 296         | 2  |
| 2          | 3          | 084456    | 1                | 1112               | 496                                 | 13                       | 21         | 2  | 102         | 8  | 13           | 3  | 13           | 1  | 302         | 19 |
| 2          | 3          | 084456    | 1                | 1390               | 620                                 | 16                       | 30         | 4  | 113         | 8  | 9            | 2  | 11           | 1  | 318         | 13 |
| 2          | 3          | 084456    | 1                | 2779               | 1241                                | 32                       | 26         | 3  | 118         | 5  | 10           | 3  | 15           | 1  | 305         | 16 |
| 2          | 3          | 084456    | 1                | 5559               | 2481                                | 65                       | 41         | 8  | 102         | 11 | 14           | 4  | 13           | 1  | 330         | 14 |
| 2          | 7          | 084456    | 2                | 0                  | 0                                   | 0                        | 24         | 6  | 89          | 4  | 16           | 5  | 7            | 2  | 292         | 9  |
| 2          | 7          | 084456    | 2                | 278                | 124                                 | 3                        | 22         | 3  | 95          | 5  | 13           | 2  | 8            | 1  | 302         | 5  |
| 2          | 7          | 084456    | 2                | 556                | 248                                 | 7                        | 23         | 1  | 100         | 3  | 12           | 1  | 10           | 1  | 305         | 15 |
| 2          | 7          | 084456    | 2                | 834                | 372                                 | 10                       | 22         | 2  | 105         | 10 | 17           | 4  | 8            | 2  | 307         | 17 |
| 2          | 7          | 084456    | 2                | 1112               | 496                                 | 13                       | 29         | 5  | 128         | 9  | 12           | 2  | 13           | 2  | 305         | 6  |
| 2          | 7          | 084456    | 2                | 1390               | 620                                 | 17                       | 24         | 1  | 118         | 9  | 14           | 3  | 10           | 2  | 294         | 16 |
| 2          | 7          | 084456    | 2                | 2779               | 1240                                | 33                       | 26         | 7  | 108         | 5  | 15           | 5  | 12           | 1  | 288         | 9  |
| 2          | 7          | 084456    | 2                | 5558               | 2481                                | 66                       | 38         | 5  | 115         | 8  | 15           | 3  | 11           | 3  | 316         | 4  |
| 2          | 9          | 084456    | 3                | 0                  | 0                                   | 0                        | 21         | 1  | 91          | 7  | 13           | 5  | 6            | 1  | 291         | 12 |
| 2          | 9          | 084456    | 3                | 278                | 124                                 | 3                        | 24         | 5  | 95          | 4  | 12           | 1  | 9            | 1  | 304         | 7  |
| 2          | 9          | 084456    | 3                | 556                | 248                                 | 7                        | 20         | 1  | 106         | 3  | 12           | 2  | 9            | 2  | 289         | 3  |
| 2          | 9          | 084456    | 3                | 834                | 372                                 | 10                       | 24         | 5  | 107         | 5  | 15           | 7  | 9            | 1  | 293         | 8  |
| 2          | 9          | 084456    | 3                | 1112               | 496                                 | 14                       | 26         | 9  | 112         | 7  | 14           | 3  | 11           | 1  | 277         | 4  |
| 2          | 9          | 084456    | 3                | 1390               | 620                                 | 17                       | 21         | 2  | 118         | 2  | 13           | 4  | 13           | 1  | 311         | 5  |
| 2          | 9          | 084456    | 3                | 2780               | 1241                                | 34                       | 24         | 4  | 100         | 4  | 13           | 2  | 8            | 1  | 306         | 18 |
| 2          | 9          | 084456    | 3                | 5559               | 2481                                | 68                       | 32         | 4  | 93          | 8  | 12           | 2  | 15           | 2  | 314         | 13 |
| 2          | 8          | 084457    | 1                | 0                  | 0                                   | 0                        | 23         | 3  | 89          | 4  | 12           | 2  | 7            | 2  | 286         | 11 |
| 2          | 8          | 084457    | 1                | 278                | 268                                 | 1                        | 23         | 3  | 101         | 6  | 11           | 2  | 7            | 1  | 296         | 4  |
| 2          | 8          | 084457    | 1                | 556                | 535                                 | 3                        | 20         | 3  | 114         | 4  | 12           | 1  | 10           | 2  | 305         | 7  |
| 2          | 8          | 084457    | 1                | 833                | 803                                 | 4                        | 25         | 1  | 120         | 4  | 14           | 4  | 12           | 3  | 308         | 9  |
| 2          | 8          | 084457    | 1                | 1111               | 1070                                | 6                        | 28         | 5  | 122         | 5  | 13           | 5  | 8            | 0  | 290         | 10 |
| 2          | 8          | 084457    | 1                | 1389               | 1338                                | 7                        | 23         | 3  | 103         | 5  | 14           | 4  | 11           | 3  | 312         | 6  |
| 2          | 8          | 084457    | 1                | 2778               | 2676                                | 15                       | 24         | 6  | 115         | 9  | 15           | 2  | 6            | 2  | 291         | 6  |
| 2          | 8          | 084457    | 1                | 5556               | 5352                                | 29                       | 25         | 3  | 109         | 3  | 18           | 2  | 7            | 3  | 285         | 4  |
| 2          | 12         | 084457    | 2                | 0                  | 0                                   | 0                        | 27         | 6  | 94          | 4  | 10           | 4  | 6            | 1  | 288         | 9  |
| 2          | 12         | 084457    | 2                | 278                | 268                                 | 2                        | 25         | 4  | 96          | 5  | 13           | 3  | 6            | 1  | 293         | 11 |
| 2          | 12         | 084457    | 2                | 556                | 535                                 | 3                        | 24         | 5  | 99          | 6  | 13           | 4  | 5            | 0  | 300         | 7  |
| 2          | 12         | 084457    | 2                | 833                | 803                                 | 5                        | 22         | 4  | 106         | 7  | 14           | 5  | 7            | 1  | 309         | 9  |
| 2          | 12         | 084457    | 2                | 1111               | 1070                                | 6                        | 21         | 2  | 103         | 4  | 11           | 2  | 9            | 1  | 280         | 12 |
| 2          | 12         | 084457    | 2                | 1389               | 1338                                | 8                        | 21         | 2  | 109         | 9  | 12           | 5  | 8            | 1  | 281         | 14 |
| 2          | 12         | 084457    | 2                | 2778               | 2676                                | 15                       | 21         | 2  | 104         | 9  | 11           | 3  | 7            | 2  | 278         | 22 |
| 2          | 12         | 084457    | 2                | 5556               | 5351                                | 31                       | 21         | 2  | 113         | 1  | 17           | 4  | 9            | 2  | 294         | 5  |
| 2          | 15         | 084457    | 3                | 0                  | 0                                   | 0                        | 31         | 3  | 93          | 6  | 10           | 3  | 9            | 1  | 301         | 8  |
| 2          | 15         | 084457    | 3                | 278                | 268                                 | 2                        | 26         | 3  | 97          | 4  | 15           | 4  | 8            | 2  | 299         | 6  |
| 2          | 15         | 084457    | 3                | 556                | 535                                 | 3                        | 32         | 4  | 106         | 7  | 12           | 1  | 5            | 1  | 298         | 5  |
| 2          | 15         | 084457    | 3                | 833                | 803                                 | 5                        | 25         | 3  | 104         | 2  | 15           | 4  | 12           | 3  | 293         | 12 |
| 2          | 15         | 084457    | 3                | 1111               | 1070                                | 6                        | 28         | 5  | 107         | 9  | 11           | 2  | 10           | 1  | 310         | 13 |
| 2          | 15         | 084457    | 3                | 1389               | 1338                                | 8                        | 23         | 3  | 110         | 9  | 13           | 7  | 6            | 1  | 297         | 16 |
| 2          | 15         | 084457    | 3                | 2778               | 2676                                | 16                       | 26         | 4  | 103         | 7  | 8            | 2  | 7            | 2  | 295         | 9  |
| 2          | 15         | 084457    | 3                | 5556               | 5352                                | 32                       | 23         | 3  | 103         | 10 | 8            | 2  | 7            | 1  | 291         | 13 |

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (+S9) |    | TA100 (+S9) |    | TA1535 (+S9) |    | TA1537 (+S9) |    | TA102 (+S9) |    |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                    |                                     |                          | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 2          | 2          | 084458    | 1                | 0                  | 0                                   | 0                        | 25         | 5  | 94          | 8  | 11           | 2  | 10           | 1  | 263         | 8  |
| 2          | 2          | 084458    | 1                | 278                | 264                                 | 1                        | 25         | 5  | 101         | 6  | 13           | 2  | 8            | 2  | 260         | 7  |
| 2          | 2          | 084458    | 1                | 556                | 527                                 | 1                        | 26         | 0  | 102         | 5  | 12           | 1  | 8            | 3  | 325         | 5  |
| 2          | 2          | 084458    | 1                | 834                | 791                                 | 2                        | 23         | 4  | 96          | 4  | 11           | 2  | 11           | 1  | 336         | 15 |
| 2          | 2          | 084458    | 1                | 1112               | 1054                                | 3                        | 27         | 9  | 100         | 10 | 14           | 4  | 9            | 3  | 238         | 11 |
| 2          | 2          | 084458    | 1                | 1389               | 1318                                | 3                        | 25         | 4  | 107         | 10 | 11           | 2  | 13           | 4  | 202         | 2  |
| 2          | 2          | 084458    | 1                | 2779               | 2636                                | 7                        | 26         | 3  | 100         | 8  | 11           | 1  | 11           | 3  | 226         | 10 |
| 2          | 2          | 084458    | 1                | 5558               | 5272                                | 13                       | 25         | 3  | 94          | 7  | 14           | 3  | 17           | 5  | 227         | 8  |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 10         | 084458    | 2                | 0                  | 0                                   | 0                        | 24         | 4  | 92          | 2  | 15           | 2  | 7            | 2  | 289         | 8  |
| 2          | 10         | 084458    | 2                | 278                | 264                                 | 1                        | 25         | 4  | 96          | 5  | 13           | 3  | 6            | 2  | 292         | 10 |
| 2          | 10         | 084458    | 2                | 556                | 527                                 | 1                        | 23         | 6  | 100         | 9  | 9            | 1  | 7            | 3  | 284         | 18 |
| 2          | 10         | 084458    | 2                | 834                | 791                                 | 2                        | 25         | 6  | 106         | 9  | 11           | 1  | 6            | 2  | 292         | 14 |
| 2          | 10         | 084458    | 2                | 1111               | 1054                                | 3                        | 23         | 5  | 102         | 4  | 8            | 1  | 10           | 3  | 290         | 11 |
| 2          | 10         | 084458    | 2                | 1389               | 1318                                | 4                        | 23         | 3  | 102         | 3  | 9            | 1  | 9            | 1  | 300         | 17 |
| 2          | 10         | 084458    | 2                | 2778               | 2636                                | 7                        | 21         | 1  | 99          | 6  | 10           | 1  | 7            | 2  | 304         | 5  |
| 2          | 10         | 084458    | 2                | 5557               | 5271                                | 14                       | 21         | 1  | 98          | 8  | 12           | 2  | 6            | 1  | 293         | 8  |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 16         | 084458    | 3                | 0                  | 0                                   | 0                        | 21         | 2  | 90          | 6  | 17           | 3  | 8            | 1  | 285         | 14 |
| 2          | 16         | 084458    | 3                | 278                | 263                                 | 1                        | 21         | 3  | 95          | 3  | 15           | 3  | 7            | 1  | 285         | 10 |
| 2          | 16         | 084458    | 3                | 556                | 527                                 | 2                        | 21         | 1  | 97          | 3  | 14           | 3  | 6            | 1  | 278         | 21 |
| 2          | 16         | 084458    | 3                | 833                | 790                                 | 2                        | 22         | 2  | 104         | 7  | 13           | 3  | 5            | 1  | 285         | 8  |
| 2          | 16         | 084458    | 3                | 1111               | 1054                                | 3                        | 25         | 3  | 109         | 7  | 13           | 4  | 9            | 1  | 267         | 11 |
| 2          | 16         | 084458    | 3                | 1389               | 1317                                | 4                        | 26         | 2  | 112         | 9  | 13           | 3  | 11           | 1  | 258         | 9  |
| 2          | 16         | 084458    | 3                | 2778               | 2635                                | 8                        | 32         | 4  | 108         | 3  | 12           | 1  | 6            | 1  | 250         | 14 |
| 2          | 16         | 084458    | 3                | 5556               | 5270                                | 15                       | 29         | 3  | 96          | 8  | 12           | 2  | 8            | 1  | 242         | 9  |

\*Values represent the mean number of revertants (average of three plates)

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (-S9) |    | TA100 (-S9) |    | TA1535 (-S9) |    | TA1537 (-S9) |    | TA102 (-S9) |    |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                    |                                     |                          | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 1          | 3          | 084394    | 1                | 0                  | 0                                   | 0                        | 26         | 5  | 160         | 7  | 10           | 2  | 8            | 1  | 284         | 9  |
| 1          | 3          | 084394    | 1                | 278                | 190                                 | 3                        | 28         | 1  | 169         | 4  | 14           | 2  | 11           | 2  | 328         | 9  |
| 1          | 3          | 084394    | 1                | 556                | 379                                 | 6                        | 30         | 8  | 155         | 6  | 13           | 2  | 12           | 2  | 296         | 10 |
| 1          | 3          | 084394    | 1                | 833                | 569                                 | 10                       | 26         | 2  | 164         | 7  | 17           | 1  | 12           | 2  | 299         | 9  |
| 1          | 3          | 084394    | 1                | 1111               | 759                                 | 13                       | 27         | 6  | 176         | 13 | 14           | 3  | 14           | 1  | 299         | 7  |
| 1          | 3          | 084394    | 1                | 1389               | 948                                 | 16                       | 23         | 2  | 152         | 9  | 17           | 3  | 14           | 2  | 298         | 4  |
| 1          | 3          | 084394    | 1                | 2778               | 1897                                | 32                       | 22         | 1  | 153         | 6  | 14           | 3  | 14           | 4  | 304         | 7  |
| 1          | 3          | 084394    | 1                | 5556               | 3793                                | 64                       | 27         | 2  | 180         | 2  | 13           | 7  | 16           | 1  | 286         | 2  |
| 1          | 4          | 084394    | 2                | 0                  | 0                                   | 0                        | 22         | 2  | 147         | 3  | 14           | 3  | 7            | 1  | 282         | 6  |
| 1          | 4          | 084394    | 2                | 278                | 190                                 | 4                        | 28         | 4  | 151         | 14 | 14           | 1  | 10           | 2  | 285         | 2  |
| 1          | 4          | 084394    | 2                | 556                | 379                                 | 7                        | 25         | 4  | 153         | 15 | 14           | 4  | 11           | 1  | 282         | 5  |
| 1          | 4          | 084394    | 2                | 834                | 569                                 | 11                       | 26         | 6  | 152         | 7  | 17           | 5  | 12           | 4  | 304         | 10 |
| 1          | 4          | 084394    | 2                | 1112               | 759                                 | 14                       | 30         | 3  | 153         | 9  | 16           | 5  | 11           | 2  | 274         | 2  |
| 1          | 4          | 084394    | 2                | 1389               | 949                                 | 18                       | 30         | 9  | 153         | 4  | 12           | 4  | 9            | 1  | 299         | 7  |
| 1          | 4          | 084394    | 2                | 2779               | 1897                                | 36                       | 25         | 1  | 154         | 6  | 16           | 6  | 11           | 2  | 297         | 9  |
| 1          | 4          | 084394    | 2                | 5558               | 3794                                | 71                       | 32         | 4  | 176         | 6  | 20           | 4  | 14           | 2  | 272         | 4  |
| 1          | 7          | 084394    | 3                | 0                  | 0                                   | 0                        | 24         | 4  | 144         | 15 | 16           | 3  | 6            | 1  | 284         | 13 |
| 1          | 7          | 084394    | 3                | 278                | 190                                 | 3                        | 25         | 2  | 143         | 13 | 19           | 1  | 7            | 1  | 312         | 9  |
| 1          | 7          | 084394    | 3                | 556                | 379                                 | 7                        | 24         | 4  | 159         | 8  | 17           | 4  | 9            | 2  | 324         | 6  |
| 1          | 7          | 084394    | 3                | 833                | 569                                 | 10                       | 29         | 4  | 153         | 8  | 17           | 1  | 9            | 1  | 329         | 11 |
| 1          | 7          | 084394    | 3                | 1111               | 759                                 | 13                       | 29         | 7  | 146         | 11 | 18           | 3  | 9            | 2  | 311         | 17 |
| 1          | 7          | 084394    | 3                | 1389               | 948                                 | 17                       | 24         | 5  | 155         | 7  | 16           | 2  | 12           | 2  | 304         | 11 |
| 1          | 7          | 084394    | 3                | 2778               | 1897                                | 34                       | 24         | 3  | 181         | 5  | 17           | 4  | 12           | 2  | 327         | 4  |
| 1          | 7          | 084394    | 3                | 5557               | 3794                                | 67                       | 29         | 6  | 177         | 9  | 14           | 2  | 7            | 1  | 294         | 27 |
| 1          | 2          | 084395    | 1                | 0                  | 0                                   | 0                        | 25         | 5  | 139         | 14 | 17           | 3  | 8            | 1  | 279         | 8  |
| 1          | 2          | 084395    | 1                | 278                | 128                                 | 4                        | 23         | 5  | 153         | 8  | 13           | 6  | 7            | 1  | 300         | 3  |
| 1          | 2          | 084395    | 1                | 556                | 256                                 | 8                        | 21         | 2  | 145         | 10 | 22           | 1  | 9            | 1  | 291         | 7  |
| 1          | 2          | 084395    | 1                | 834                | 383                                 | 12                       | 23         | 1  | 159         | 6  | 14           | 3  | 8            | 1  | 290         | 6  |
| 1          | 2          | 084395    | 1                | 1112               | 511                                 | 16                       | 26         | 2  | 146         | 14 | 12           | 2  | 11           | 3  | 271         | 6  |
| 1          | 2          | 084395    | 1                | 1390               | 639                                 | 19                       | 23         | 1  | 152         | 10 | 16           | 2  | 11           | 2  | 297         | 7  |
| 1          | 2          | 084395    | 1                | 2779               | 1278                                | 39                       | 24         | 5  | 156         | 9  | 10           | 2  | 14           | 2  | 301         | 9  |
| 1          | 2          | 084395    | 1                | 5558               | 2556                                | 78                       | 26         | 1  | 143         | 8  | 17           | 4  | 17           | 2  | 294         | 2  |
| 1          | 5          | 084395    | 2                | 0                  | 0                                   | 0                        | 27         | 7  | 145         | 4  | 14           | 6  | 6            | 1  | 272         | 6  |
| 1          | 5          | 084395    | 2                | 278                | 128                                 | 4                        | 28         | 2  | 151         | 14 | 17           | 2  | 9            | 1  | 294         | 5  |
| 1          | 5          | 084395    | 2                | 556                | 256                                 | 8                        | 23         | 3  | 153         | 15 | 16           | 6  | 11           | 4  | 323         | 16 |
| 1          | 5          | 084395    | 2                | 834                | 383                                 | 12                       | 22         | 3  | 152         | 7  | 16           | 6  | 10           | 1  | 312         | 3  |
| 1          | 5          | 084395    | 2                | 1112               | 511                                 | 16                       | 26         | 7  | 159         | 10 | 16           | 4  | 13           | 2  | 298         | 7  |
| 1          | 5          | 084395    | 2                | 1390               | 639                                 | 20                       | 24         | 4  | 159         | 12 | 16           | 4  | 10           | 2  | 292         | 9  |
| 1          | 5          | 084395    | 2                | 2779               | 1278                                | 40                       | 22         | 2  | 167         | 9  | 15           | 1  | 13           | 5  | 320         | 9  |
| 1          | 5          | 084395    | 2                | 5558               | 2556                                | 80                       | 24         | 5  | 171         | 15 | 18           | 2  | 11           | 2  | 320         | 7  |
| 1          | 6          | 084395    | 3                | 0                  | 0                                   | 0                        | 23         | 6  | 146         | 11 | 14           | 5  | 6            | 1  | 297         | 6  |
| 1          | 6          | 084395    | 3                | 278                | 128                                 | 4                        | 21         | 1  | 146         | 11 | 15           | 5  | 8            | 2  | 301         | 5  |
| 1          | 6          | 084395    | 3                | 556                | 256                                 | 7                        | 22         | 3  | 144         | 9  | 16           | 4  | 10           | 2  | 314         | 6  |
| 1          | 6          | 084395    | 3                | 834                | 383                                 | 11                       | 21         | 2  | 146         | 9  | 17           | 2  | 8            | 1  | 312         | 13 |
| 1          | 6          | 084395    | 3                | 1111               | 511                                 | 15                       | 26         | 5  | 150         | 5  | 15           | 6  | 8            | 2  | 280         | 8  |
| 1          | 6          | 084395    | 3                | 1389               | 639                                 | 19                       | 26         | 9  | 155         | 10 | 14           | 2  | 9            | 1  | 308         | 3  |
| 1          | 6          | 084395    | 3                | 2779               | 1278                                | 37                       | 20         | 1  | 165         | 11 | 18           | 3  | 9            | 2  | 316         | 9  |
| 1          | 6          | 084395    | 3                | 5557               | 2555                                | 74                       | 21         | 1  | 173         | 10 | 20           | 3  | 6            | 1  | 370         | 11 |

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (-S9) |    | TA100 (-S9) |    | TA1535 (-S9) |    | TA1537 (-S9) |    | TA102 (-S9) |    |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                    |                                     |                          | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 2          | 4          | 084454    | 1                | 0                  | 0                                   | 0                        | 26         | 2  | 172         | 9  | 10           | 3  | 11           | 1  | 284         | 3  |
| 2          | 4          | 084454    | 1                | 278                | 247                                 | 1                        | 24         | 4  | 206         | 18 | 13           | 2  | 11           | 3  | 280         | 8  |
| 2          | 4          | 084454    | 1                | 556                | 494                                 | 2                        | 28         | 3  | 202         | 34 | 11           | 1  | 7            | 2  | 295         | 9  |
| 2          | 4          | 084454    | 1                | 834                | 741                                 | 3                        | 25         | 5  | 193         | 11 | 14           | 1  | 5            | 1  | 306         | 14 |
| 2          | 4          | 084454    | 1                | 1112               | 988                                 | 4                        | 30         | 2  | 184         | 14 | 12           | 1  | 7            | 1  | 276         | 11 |
| 2          | 4          | 084454    | 1                | 1389               | 1235                                | 5                        | 22         | 2  | 154         | 10 | 12           | 2  | 12           | 1  | 280         | 11 |
| 2          | 4          | 084454    | 1                | 2779               | 2470                                | 10                       | 28         | 7  | 160         | 24 | 13           | 2  | 9            | 3  | 288         | 3  |
| 2          | 4          | 084454    | 1                | 5558               | 4941                                | 20                       | 30         | 2  | 175         | 15 | 11           | 1  | 9            | 1  | 282         | 8  |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 6          | 084454    | 2                | 0                  | 0                                   | 0                        | 27         | 3  | 177         | 36 | 9            | 3  | 8            | 1  | 256         | 9  |
| 2          | 6          | 084454    | 2                | 278                | 247                                 | 1                        | 29         | 2  | 162         | 29 | 12           | 2  | 5            | 0  | 257         | 6  |
| 2          | 6          | 084454    | 2                | 556                | 494                                 | 2                        | 31         | 3  | 175         | 15 | 11           | 1  | 8            | 1  | 227         | 12 |
| 2          | 6          | 084454    | 2                | 834                | 741                                 | 3                        | 23         | 2  | 174         | 6  | 14           | 2  | 6            | 1  | 276         | 15 |
| 2          | 6          | 084454    | 2                | 1111               | 988                                 | 4                        | 33         | 4  | 174         | 22 | 13           | 3  | 10           | 1  | 275         | 4  |
| 2          | 6          | 084454    | 2                | 1389               | 1235                                | 5                        | 26         | 6  | 177         | 5  | 14           | 4  | 8            | 1  | 286         | 5  |
| 2          | 6          | 084454    | 2                | 2779               | 2470                                | 11                       | 27         | 4  | 148         | 35 | 14           | 3  | 9            | 1  | 273         | 8  |
| 2          | 6          | 084454    | 2                | 5557               | 4940                                | 22                       | 28         | 4  | 186         | 16 | 15           | 2  | 8            | 1  | 285         | 12 |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 14         | 084454    | 3                | 0                  | 0                                   | 0                        | 23         | 3  | 170         | 2  | 10           | 3  | 7            | 3  | 314         | 12 |
| 2          | 14         | 084454    | 3                | 278                | 247                                 | 1                        | 22         | 2  | 167         | 21 | 12           | 2  | 6            | 1  | 314         | 7  |
| 2          | 14         | 084454    | 3                | 556                | 494                                 | 2                        | 25         | 4  | 164         | 20 | 12           | 2  | 11           | 2  | 323         | 11 |
| 2          | 14         | 084454    | 3                | 834                | 741                                 | 3                        | 30         | 6  | 151         | 17 | 15           | 1  | 12           | 1  | 343         | 16 |
| 2          | 14         | 084454    | 3                | 1112               | 988                                 | 4                        | 28         | 2  | 179         | 4  | 14           | 3  | 8            | 1  | 352         | 13 |
| 2          | 14         | 084454    | 3                | 1389               | 1235                                | 6                        | 28         | 8  | 182         | 13 | 15           | 3  | 7            | 1  | 380         | 8  |
| 2          | 14         | 084454    | 3                | 2779               | 2470                                | 11                       | 26         | 4  | 170         | 29 | 13           | 3  | 10           | 1  | 383         | 12 |
| 2          | 14         | 084454    | 3                | 5558               | 4941                                | 22                       | 30         | 4  | 142         | 8  | 12           | 2  | 8            | 1  | 374         | 14 |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 5          | 084455    | 1                | 0                  | 0                                   | 0                        | 24         | 3  | 181         | 4  | 14           | 3  | 7            | 2  | 284         | 5  |
| 2          | 5          | 084455    | 1                | 278                | 261                                 | 2                        | 23         | 2  | 160         | 7  | 11           | 2  | 6            | 1  | 293         | 5  |
| 2          | 5          | 084455    | 1                | 556                | 522                                 | 3                        | 22         | 2  | 153         | 6  | 10           | 4  | 10           | 2  | 277         | 5  |
| 2          | 5          | 084455    | 1                | 834                | 783                                 | 5                        | 26         | 3  | 179         | 10 | 10           | 2  | 7            | 1  | 266         | 9  |
| 2          | 5          | 084455    | 1                | 1112               | 1044                                | 6                        | 30         | 2  | 195         | 2  | 7            | 1  | 8            | 3  | 288         | 11 |
| 2          | 5          | 084455    | 1                | 1390               | 1305                                | 8                        | 30         | 7  | 203         | 15 | 8            | 1  | 7            | 2  | 309         | 9  |
| 2          | 5          | 084455    | 1                | 2779               | 2610                                | 15                       | 27         | 5  | 187         | 7  | 7            | 0  | 7            | 1  | 289         | 4  |
| 2          | 5          | 084455    | 1                | 5558               | 5220                                | 31                       | 32         | 6  | 146         | 15 | 8            | 1  | 8            | 2  | 272         | 5  |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 13         | 084455    | 2                | 0                  | 0                                   | 0                        | 32         | 5  | 165         | 4  | 8            | 1  | 8            | 2  | 335         | 10 |
| 2          | 13         | 084455    | 2                | 278                | 261                                 | 1                        | 23         | 3  | 179         | 30 | 11           | 1  | 11           | 3  | 353         | 17 |
| 2          | 13         | 084455    | 2                | 556                | 522                                 | 3                        | 28         | 3  | 169         | 12 | 12           | 2  | 11           | 3  | 373         | 12 |
| 2          | 13         | 084455    | 2                | 834                | 783                                 | 4                        | 25         | 3  | 185         | 7  | 12           | 2  | 10           | 1  | 348         | 2  |
| 2          | 13         | 084455    | 2                | 1112               | 1044                                | 6                        | 30         | 7  | 207         | 20 | 14           | 2  | 7            | 1  | 368         | 13 |
| 2          | 13         | 084455    | 2                | 1390               | 1305                                | 7                        | 27         | 3  | 186         | 18 | 11           | 1  | 5            | 1  | 372         | 8  |
| 2          | 13         | 084455    | 2                | 2780               | 2611                                | 15                       | 27         | 3  | 147         | 17 | 12           | 1  | 8            | 1  | 365         | 14 |
| 2          | 13         | 084455    | 2                | 5559               | 5222                                | 29                       | 35         | 4  | 183         | 24 | 11           | 2  | 8            | 2  | 367         | 16 |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 17         | 084455    | 3                | 0                  | 0                                   | 0                        | 22         | 2  | 175         | 13 | 9            | 2  | 9            | 2  | 356         | 12 |
| 2          | 17         | 084455    | 3                | 278                | 261                                 | 2                        | 27         | 3  | 174         | 19 | 14           | 2  | 6            | 1  | 356         | 3  |
| 2          | 17         | 084455    | 3                | 556                | 522                                 | 3                        | 26         | 3  | 191         | 43 | 16           | 3  | 6            | 1  | 363         | 8  |
| 2          | 17         | 084455    | 3                | 833                | 783                                 | 5                        | 24         | 5  | 187         | 19 | 14           | 2  | 8            | 2  | 357         | 14 |
| 2          | 17         | 084455    | 3                | 1111               | 1044                                | 6                        | 24         | 5  | 166         | 13 | 14           | 1  | 7            | 1  | 364         | 8  |
| 2          | 17         | 084455    | 3                | 1389               | 1305                                | 8                        | 25         | 3  | 165         | 11 | 14           | 5  | 6            | 1  | 348         | 5  |
| 2          | 17         | 084455    | 3                | 2778               | 2609                                | 15                       | 27         | 4  | 158         | 5  | 11           | 2  | 7            | 1  | 355         | 17 |
| 2          | 17         | 084455    | 3                | 5556               | 5218                                | 31                       | 30         | 2  | 144         | 16 | 13           | 3  | 6            | 1  | 360         | 16 |

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (-S9) |    | TA100 (-S9) |    | TA1535 (-S9) |    | TA1537 (-S9) |    | TA102 (-S9) |    |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                    |                                     |                          | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 2          | 3          | 084456    | 1                | 0                  | 0                                   | 0                        | 24         | 4  | 154         | 28 | 14           | 2  | 7            | 2  | 278         | 11 |
| 2          | 3          | 084456    | 1                | 278                | 124                                 | 3                        | 26         | 3  | 155         | 29 | 15           | 2  | 11           | 3  | 276         | 13 |
| 2          | 3          | 084456    | 1                | 556                | 248                                 | 6                        | 30         | 4  | 175         | 16 | 16           | 2  | 9            | 1  | 275         | 8  |
| 2          | 3          | 084456    | 1                | 834                | 372                                 | 10                       | 30         | 10 | 169         | 7  | 13           | 2  | 7            | 1  | 269         | 9  |
| 2          | 3          | 084456    | 1                | 1112               | 496                                 | 13                       | 31         | 3  | 176         | 14 | 12           | 2  | 10           | 3  | 294         | 10 |
| 2          | 3          | 084456    | 1                | 1390               | 620                                 | 16                       | 26         | 3  | 186         | 7  | 14           | 2  | 10           | 2  | 278         | 2  |
| 2          | 3          | 084456    | 1                | 2779               | 1241                                | 32                       | 26         | 2  | 206         | 26 | 13           | 2  | 8            | 1  | 284         | 3  |
| 2          | 3          | 084456    | 1                | 5559               | 2481                                | 65                       | 28         | 3  | 189         | 18 | 17           | 2  | 10           | 4  | 275         | 16 |
| 2          | 7          | 084456    | 2                | 0                  | 0                                   | 0                        | 26         | 3  | 177         | 15 | 10           | 2  | 5            | 1  | 278         | 7  |
| 2          | 7          | 084456    | 2                | 278                | 124                                 | 3                        | 25         | 3  | 170         | 19 | 11           | 2  | 9            | 1  | 265         | 12 |
| 2          | 7          | 084456    | 2                | 556                | 248                                 | 7                        | 29         | 4  | 167         | 19 | 12           | 3  | 10           | 1  | 259         | 13 |
| 2          | 7          | 084456    | 2                | 834                | 372                                 | 10                       | 28         | 5  | 175         | 21 | 13           | 4  | 9            | 1  | 294         | 7  |
| 2          | 7          | 084456    | 2                | 1112               | 496                                 | 13                       | 23         | 1  | 176         | 15 | 11           | 4  | 9            | 2  | 277         | 13 |
| 2          | 7          | 084456    | 2                | 1390               | 620                                 | 17                       | 27         | 4  | 201         | 4  | 13           | 4  | 6            | 1  | 286         | 8  |
| 2          | 7          | 084456    | 2                | 2779               | 1240                                | 33                       | 26         | 1  | 167         | 34 | 17           | 2  | 8            | 1  | 277         | 4  |
| 2          | 7          | 084456    | 2                | 5558               | 2481                                | 66                       | 28         | 2  | 152         | 13 | 15           | 3  | 6            | 1  | 301         | 2  |
| 2          | 9          | 084456    | 3                | 0                  | 0                                   | 0                        | 23         | 3  | 150         | 19 | 10           | 2  | 7            | 2  | 292         | 10 |
| 2          | 9          | 084456    | 3                | 278                | 124                                 | 3                        | 25         | 3  | 173         | 24 | 12           | 1  | 8            | 2  | 291         | 18 |
| 2          | 9          | 084456    | 3                | 556                | 248                                 | 7                        | 29         | 4  | 178         | 15 | 13           | 2  | 7            | 1  | 274         | 17 |
| 2          | 9          | 084456    | 3                | 834                | 372                                 | 10                       | 28         | 2  | 168         | 12 | 12           | 2  | 7            | 2  | 301         | 14 |
| 2          | 9          | 084456    | 3                | 1112               | 496                                 | 14                       | 32         | 2  | 174         | 3  | 13           | 1  | 7            | 2  | 374         | 19 |
| 2          | 9          | 084456    | 3                | 1390               | 620                                 | 17                       | 27         | 3  | 182         | 6  | 12           | 2  | 8            | 3  | 351         | 20 |
| 2          | 9          | 084456    | 3                | 2780               | 1241                                | 34                       | 24         | 3  | 174         | 14 | 16           | 2  | 7            | 2  | 359         | 9  |
| 2          | 9          | 084456    | 3                | 5559               | 2481                                | 68                       | 30         | 6  | 167         | 15 | 16           | 2  | 9            | 1  | 374         | 12 |
| 2          | 8          | 084457    | 1                | 0                  | 0                                   | 0                        | 35         | 4  | 159         | 14 | 9            | 3  | 6            | 1  | 279         | 11 |
| 2          | 8          | 084457    | 1                | 278                | 268                                 | 1                        | 23         | 4  | 156         | 7  | 12           | 2  | 6            | 1  | 248         | 16 |
| 2          | 8          | 084457    | 1                | 556                | 535                                 | 3                        | 30         | 3  | 123         | 15 | 11           | 2  | 7            | 2  | 274         | 12 |
| 2          | 8          | 084457    | 1                | 833                | 803                                 | 4                        | 25         | 2  | 91          | 8  | 14           | 2  | 7            | 3  | 281         | 10 |
| 2          | 8          | 084457    | 1                | 1111               | 1070                                | 6                        | 27         | 5  | 153         | 27 | 14           | 3  | 6            | 1  | 263         | 11 |
| 2          | 8          | 084457    | 1                | 1389               | 1338                                | 7                        | 29         | 3  | 174         | 6  | 15           | 3  | 6            | 1  | 240         | 8  |
| 2          | 8          | 084457    | 1                | 2778               | 2676                                | 15                       | 30         | 3  | 183         | 5  | 12           | 3  | 6            | 1  | 247         | 4  |
| 2          | 8          | 084457    | 1                | 5556               | 5352                                | 29                       | 26         | 2  | 181         | 11 | 10           | 3  | 7            | 2  | 248         | 9  |
| 2          | 12         | 084457    | 2                | 0                  | 0                                   | 0                        | 30         | 2  | 171         | 7  | 11           | 2  | 6            | 2  | 350         | 9  |
| 2          | 12         | 084457    | 2                | 278                | 268                                 | 2                        | 28         | 1  | 180         | 2  | 12           | 3  | 7            | 2  | 361         | 17 |
| 2          | 12         | 084457    | 2                | 556                | 535                                 | 3                        | 28         | 4  | 179         | 4  | 13           | 2  | 7            | 1  | 363         | 8  |
| 2          | 12         | 084457    | 2                | 833                | 803                                 | 5                        | 31         | 2  | 175         | 7  | 13           | 2  | 11           | 2  | 369         | 2  |
| 2          | 12         | 084457    | 2                | 1111               | 1070                                | 6                        | 30         | 5  | 178         | 25 | 12           | 2  | 8            | 2  | 379         | 11 |
| 2          | 12         | 084457    | 2                | 1389               | 1338                                | 8                        | 30         | 4  | 175         | 19 | 15           | 2  | 8            | 2  | 356         | 12 |
| 2          | 12         | 084457    | 2                | 2778               | 2676                                | 15                       | 33         | 4  | 152         | 11 | 12           | 2  | 6            | 1  | 333         | 12 |
| 2          | 12         | 084457    | 2                | 5556               | 5351                                | 31                       | 27         | 5  | 113         | 9  | 17           | 2  | 5            | 1  | 324         | 6  |
| 2          | 15         | 084457    | 3                | 0                  | 0                                   | 0                        | 29         | 2  | 157         | 8  | 13           | 1  | 9            | 1  | 351         | 13 |
| 2          | 15         | 084457    | 3                | 278                | 268                                 | 2                        | 28         | 7  | 174         | 20 | 11           | 4  | 11           | 2  | 342         | 6  |
| 2          | 15         | 084457    | 3                | 556                | 535                                 | 3                        | 23         | 3  | 153         | 10 | 17           | 2  | 11           | 1  | 347         | 14 |
| 2          | 15         | 084457    | 3                | 833                | 803                                 | 5                        | 23         | 3  | 140         | 17 | 10           | 3  | 10           | 1  | 363         | 5  |
| 2          | 15         | 084457    | 3                | 1111               | 1070                                | 6                        | 28         | 4  | 159         | 20 | 8            | 1  | 5            | 1  | 349         | 9  |
| 2          | 15         | 084457    | 3                | 1389               | 1338                                | 8                        | 25         | 4  | 158         | 17 | 8            | 1  | 7            | 1  | 351         | 10 |
| 2          | 15         | 084457    | 3                | 2778               | 2676                                | 16                       | 28         | 5  | 126         | 2  | 8            | 1  | 7            | 1  | 338         | 8  |
| 2          | 15         | 084457    | 3                | 5556               | 5352                                | 32                       | 30         | 8  | 90          | 7  | 12           | 8  | 13           | 1  | 348         | 19 |



**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Average No. of Revertants per plate)\***

| Set Number | Run Number | Sample ID | Replicate Number | ST Dose (µg/plate) | ST-H <sub>2</sub> O Dose (µg/plate) | Nicotine Dose (µg/plate) | TA98 (-S9) |    | TA100 (-S9) |    | TA1535 (-S9) |    | TA1537 (-S9) |    | TA102 (-S9) |    |
|------------|------------|-----------|------------------|--------------------|-------------------------------------|--------------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|            |            |           |                  |                    |                                     |                          | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| 2          | 2          | 084458    | 1                | 0                  | 0                                   | 0                        | 25         | 5  | 161         | 17 | 11           | 2  | 6            | 1  | 294         | 5  |
| 2          | 2          | 084458    | 1                | 278                | 264                                 | 1                        | 29         | 5  | 175         | 15 | 12           | 2  | 5            | 1  | 290         | 7  |
| 2          | 2          | 084458    | 1                | 556                | 527                                 | 1                        | 21         | 1  | 147         | 13 | 13           | 2  | 6            | 1  | 282         | 11 |
| 2          | 2          | 084458    | 1                | 834                | 791                                 | 2                        | 23         | 4  | 177         | 15 | 16           | 2  | 7            | 1  | 276         | 4  |
| 2          | 2          | 084458    | 1                | 1112               | 1054                                | 3                        | 30         | 2  | 160         | 8  | 16           | 2  | 9            | 3  | 257         | 5  |
| 2          | 2          | 084458    | 1                | 1389               | 1318                                | 3                        | 27         | 1  | 156         | 11 | 16           | 2  | 8            | 3  | 255         | 15 |
| 2          | 2          | 084458    | 1                | 2779               | 2636                                | 7                        | 23         | 4  | 144         | 10 | 16           | 2  | 8            | 2  | 212         | 19 |
| 2          | 2          | 084458    | 1                | 5558               | 5272                                | 13                       | 26         | 4  | 153         | 12 | 17           | 1  | 6            | 2  | 199         | 12 |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 10         | 084458    | 2                | 0                  | 0                                   | 0                        | 25         | 4  | 181         | 3  | 9            | 2  | 8            | 2  | 313         | 19 |
| 2          | 10         | 084458    | 2                | 278                | 264                                 | 1                        | 28         | 5  | 183         | 6  | 12           | 3  | 8            | 2  | 354         | 9  |
| 2          | 10         | 084458    | 2                | 556                | 527                                 | 1                        | 22         | 2  | 174         | 3  | 13           | 2  | 7            | 2  | 375         | 8  |
| 2          | 10         | 084458    | 2                | 834                | 791                                 | 2                        | 30         | 7  | 172         | 25 | 10           | 3  | 7            | 1  | 378         | 8  |
| 2          | 10         | 084458    | 2                | 1111               | 1054                                | 3                        | 29         | 5  | 158         | 12 | 15           | 3  | 8            | 1  | 347         | 14 |
| 2          | 10         | 084458    | 2                | 1389               | 1318                                | 4                        | 25         | 2  | 159         | 16 | 15           | 2  | 11           | 2  | 353         | 15 |
| 2          | 10         | 084458    | 2                | 2778               | 2636                                | 7                        | 27         | 5  | 148         | 4  | 16           | 2  | 8            | 1  | 347         | 12 |
| 2          | 10         | 084458    | 2                | 5557               | 5271                                | 14                       | 28         | 6  | 131         | 11 | 16           | 1  | 10           | 2  | 363         | 12 |
|            |            |           |                  |                    |                                     |                          |            |    |             |    |              |    |              |    |             |    |
| 2          | 16         | 084458    | 3                | 0                  | 0                                   | 0                        | 33         | 5  | 149         | 19 | 8            | 2  | 8            | 1  | 348         | 9  |
| 2          | 16         | 084458    | 3                | 278                | 263                                 | 1                        | 26         | 8  | 142         | 6  | 10           | 3  | 7            | 1  | 360         | 4  |
| 2          | 16         | 084458    | 3                | 556                | 527                                 | 2                        | 29         | 3  | 169         | 10 | 13           | 3  | 7            | 1  | 352         | 4  |
| 2          | 16         | 084458    | 3                | 833                | 790                                 | 2                        | 23         | 4  | 143         | 49 | 11           | 1  | 6            | 1  | 359         | 10 |
| 2          | 16         | 084458    | 3                | 1111               | 1054                                | 3                        | 25         | 4  | 161         | 21 | 12           | 3  | 12           | 2  | 342         | 15 |
| 2          | 16         | 084458    | 3                | 1389               | 1317                                | 4                        | 28         | 6  | 161         | 28 | 12           | 3  | 7            | 2  | 337         | 9  |
| 2          | 16         | 084458    | 3                | 2778               | 2635                                | 8                        | 27         | 4  | 159         | 3  | 10           | 2  | 7            | 1  | 348         | 14 |
| 2          | 16         | 084458    | 3                | 5556               | 5270                                | 15                       | 29         | 2  | 137         | 21 | 12           | 3  | 6            | 1  | 371         | 13 |

\*Values represent the mean number of revertants (average of three plates)

**Mutagenesis in *Salmonella typhimurium* with (+) and without (-) S9 Metabolic Activation  
(Date of assay)**

| Set<br>Number | Run<br>Number | Sample<br>ID | Replicate<br>Number | TA98      |           | TA100     |           | TA1535    |           | TA1537    |           | TA102     |           |
|---------------|---------------|--------------|---------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|               |               |              |                     | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       |
| 1             | 3             | 084394       | 1                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| 1             | 4             | 084394       | 2                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| 1             | 7             | 084394       | 3                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| 1             | 2             | 084395       | 1                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| 1             | 5             | 084395       | 2                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| 1             | 6             | 084395       | 3                   | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| 2             | 4             | 084454       | 1                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 6             | 084454       | 2                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 14            | 084454       | 3                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 5             | 084455       | 1                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 13            | 084455       | 2                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 17            | 084455       | 3                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 3             | 084456       | 1                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 7             | 084456       | 2                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 9             | 084456       | 3                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 8             | 084457       | 1                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 12            | 084457       | 2                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 15            | 084457       | 3                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 2             | 084458       | 1                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 10            | 084458       | 2                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |
| 2             | 16            | 084458       | 3                   | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |

| <b>Sample<br/>ID</b> | <b>Sample<br/>Description</b> |
|----------------------|-------------------------------|
| control              | Kentucky Reference 3R4F       |

**LABSTAT INTERNATIONAL ULC**

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Project: M97

Period: September 19 - 26, 2008

**Positive and Negative Control Colony Counts for Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation  
(Revertants per plate)**

| Control Substance    | Assay Date | Concentration (µg/plate) | TA98 (+S9) |      |      | TA100 (+S9) |      |      | TA1535 (+S9) |     |     | TA1537 (+S9) |     |     | TA102 (+S9) |      |      |
|----------------------|------------|--------------------------|------------|------|------|-------------|------|------|--------------|-----|-----|--------------|-----|-----|-------------|------|------|
|                      |            |                          | P1         | P2   | P3   | P1          | P2   | P3   | P1           | P2  | P3  | P1           | P2  | P3  | P1          | P2   | P3   |
| Negative Control (-) | 19-Sep-08  |                          | 34         | 30   | 30   | 151         | 140  | 141  |              |     |     |              |     |     | 290         | 274  | 297  |
|                      | 23-Sep-08  |                          |            |      |      |             |      |      | 13           | 13  | 16  | 12           | 13  | 12  |             |      |      |
|                      | 23-Sep-08  |                          |            |      |      |             |      |      |              |     |     | 5            | 7   | 9   |             |      |      |
|                      | 24-Sep-08  |                          | 20         | 23   | 21   |             |      |      | 8            | 10  | 12  |              |     |     |             |      |      |
|                      | 26-Sep-08  |                          |            |      |      | 86          | 76   | 103  |              |     |     |              |     |     | 235         | 236  | 244  |
| Positive Control (+) |            |                          |            |      |      |             |      |      |              |     |     |              |     |     |             |      |      |
| 2-aminoanthracene    | 19-Sep-08  | 2                        | 1630       | 1680 | 1610 | 1630        | 1610 | 1610 |              |     |     |              |     |     |             |      |      |
|                      | 24-Sep-08  | 2                        | 1290       | 1250 | 1200 |             |      |      |              |     |     |              |     |     |             |      |      |
|                      | 26-Sep-08  | 2                        |            |      |      | 1408        | 1655 | 1558 |              |     |     |              |     |     |             |      |      |
| 2-aminoanthracene    | 23-Sep-08  | 4                        |            |      |      |             |      |      | 312          | 304 | 312 | 406          | 415 | 369 |             |      |      |
|                      | 23-Sep-08  | 4                        |            |      |      |             |      |      |              |     |     | 301          | 302 | 367 |             |      |      |
|                      | 24-Sep-08  | 4                        |            |      |      |             |      |      | 292          | 312 | 303 |              |     |     |             |      |      |
| 2-aminoanthracene    | 19-Sep-08  | 7.5                      |            |      |      |             |      |      |              |     |     |              |     |     | 1550        | 1638 | 1496 |
|                      | 26-Sep-08  | 7.5                      |            |      |      |             |      |      |              |     |     |              |     |     | 1642        | 1674 | 1550 |

+S9 Controls

Revision: 0

SST-284-07

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Project: M97

Period: September 19 - 26, 2008

**Positive and Negative Control Colony Counts for Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Revertants per plate)**

| Control Substance    | Assay Date | Concentration (µg/plate) | TA98 (-S9) |     |      | TA100 (-S9) |     |     | TA1535 (-S9) |     |     | TA1537 (-S9) |     |     | TA102 (-S9) |      |      |
|----------------------|------------|--------------------------|------------|-----|------|-------------|-----|-----|--------------|-----|-----|--------------|-----|-----|-------------|------|------|
|                      |            |                          | P1         | P2  | P3   | P1          | P2  | P3  | P1           | P2  | P3  | P1           | P2  | P3  | P1          | P2   | P3   |
| Negative Control (-) | 19-Sep-08  |                          | 29         | 29  | 21   | 160         | 164 | 148 |              |     |     |              |     |     | 287         | 274  | 307  |
|                      | 23-Sep-08  |                          |            |     |      |             |     |     | 18           | 16  | 11  | 8            | 9   | 11  |             |      |      |
|                      | 24-Sep-08  |                          |            |     |      |             |     |     | 14           | 12  | 16  | 7            | 7   | 5   |             |      |      |
|                      | 26-Sep-08  |                          | 21         | 28  | 26   | 141         | 129 | 182 |              |     |     |              |     |     | 249         | 240  | 254  |
| Positive Control (+) |            |                          |            |     |      |             |     |     |              |     |     |              |     |     |             |      |      |
| Sodium Azide         | 19-Sep-08  | 1                        |            |     |      | 781         | 760 | 778 |              |     |     |              |     |     |             |      |      |
|                      | 23-Sep-08  | 1                        |            |     |      |             |     |     | 624          | 630 | 658 |              |     |     |             |      |      |
|                      | 24-Sep-08  | 1                        |            |     |      |             |     |     | 515          | 645 | 617 |              |     |     |             |      |      |
|                      | 26-Sep-08  | 1                        |            |     |      | 474         | 491 | 476 |              |     |     |              |     |     |             |      |      |
| 9-aminoacridine      | 23-Sep-08  | 100                      |            |     |      |             |     |     |              |     |     | 569          | 532 | 524 |             |      |      |
|                      | 24-Sep-08  | 100                      |            |     |      |             |     |     |              |     |     | 653          | 533 | 644 |             |      |      |
| 2-nitrofluorene      | 19-Sep-08  | 4                        | 1190       | 936 | 1000 |             |     |     |              |     |     |              |     |     |             |      |      |
|                      | 26-Sep-08  | 4                        | 908        | 899 | 917  |             |     |     |              |     |     |              |     |     |             |      |      |
| Mitomycin C          | 19-Sep-08  | 0.5                      |            |     |      |             |     |     |              |     |     |              |     |     | 1334        | 1307 | 1388 |
|                      | 26-Sep-08  | 0.5                      |            |     |      |             |     |     |              |     |     |              |     |     | 1210        | 1240 | 1390 |

-S9 Controls

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Project: M97

Period: September 19 - 26, 2008

**Positive and Negative Control Colony Counts for Mutagenesis in *Salmonella typhimurium***  
**(Average Number of Revertants per plate)**

| Strain                     | Assay Date | S9 Metabolic Activation | Control Substance | Dose (µg/plate) | Average Revertants | Acceptance Criteria |
|----------------------------|------------|-------------------------|-------------------|-----------------|--------------------|---------------------|
| <b>Positive Control *</b>  |            |                         |                   |                 |                    |                     |
| TA98                       | 19-Sep-08  | +S9                     | 2-aminoanthracene | 2               | 1640               | PASS                |
| TA98                       | 24-Sep-08  | +S9                     | 2-aminoanthracene | 2               | 1247               | PASS                |
| TA98                       | 19-Sep-08  | -S9                     | 2-nitrofluorene   | 4               | 1042               | PASS                |
| TA98                       | 26-Sep-08  | -S9                     | 2-nitrofluorene   | 4               | 908                | PASS                |
| TA100                      | 19-Sep-08  | +S9                     | 2-aminoanthracene | 2               | 1617               | PASS                |
| TA100                      | 26-Sep-08  | +S9                     | 2-aminoanthracene | 2               | 1540               | PASS                |
| TA100                      | 19-Sep-08  | -S9                     | sodium azide      | 1               | 773                | PASS                |
| TA100                      | 26-Sep-08  | -S9                     | sodium azide      | 1               | 480                | PASS                |
| TA1535                     | 23-Sep-08  | +S9                     | 2-aminoanthracene | 4               | 309                | PASS                |
| TA1535                     | 24-Sep-08  | +S9                     | 2-aminoanthracene | 4               | 302                | PASS                |
| TA1535                     | 23-Sep-08  | -S9                     | Sodium Azide      | 1               | 637                | PASS                |
| TA1535                     | 24-Sep-08  | -S9                     | Sodium Azide      | 1               | 592                | PASS                |
| TA1537                     | 23-Sep-08  | +S9                     | 2-aminoanthracene | 4               | 397                | PASS                |
| TA1537                     | 23-Sep-08  | +S9                     | 2-aminoanthracene | 4               | 323                | PASS                |
| TA1537                     | 23-Sep-08  | -S9                     | 9-aminoacridine   | 100             | 542                | PASS                |
| TA1537                     | 24-Sep-08  | -S9                     | 9-aminoacridine   | 100             | 610                | PASS                |
| TA102                      | 19-Sep-08  | +S9                     | 2-aminoanthracene | 7.5             | 1561               | PASS                |
| TA102                      | 26-Sep-08  | +S9                     | 2-aminoanthracene | 7.5             | 1622               | PASS                |
| TA102                      | 19-Sep-08  | -S9                     | Mitomycin C       | 0.5             | 1343               | PASS                |
| TA102                      | 26-Sep-08  | -S9                     | Mitomycin C       | 0.5             | 1280               | PASS                |
| <b>Negative Control **</b> |            |                         |                   |                 |                    |                     |
| TA98                       | 19-Sep-08  | +S9                     | none              | N/A             | 31                 | PASS                |
| TA98                       | 24-Sep-08  | +S9                     | none              | N/A             | 21                 | PASS                |
| TA98                       | 19-Sep-08  | -S9                     | none              | N/A             | 26                 | PASS                |
| TA98                       | 26-Sep-08  | -S9                     | none              | N/A             | 25                 | PASS                |
| TA100                      | 19-Sep-08  | +S9                     | none              | N/A             | 144                | PASS                |
| TA100                      | 26-Sep-08  | +S9                     | none              | N/A             | 88                 | PASS                |
| TA100                      | 19-Sep-08  | -S9                     | none              | N/A             | 157                | PASS                |
| TA100                      | 26-Sep-08  | -S9                     | none              | N/A             | 151                | PASS                |
| TA1535                     | 23-Sep-08  | +S9                     | none              | N/A             | 14                 | PASS                |
| TA1535                     | 24-Sep-08  | +S9                     | none              | N/A             | 10                 | PASS                |
| TA1535                     | 23-Sep-08  | -S9                     | none              | N/A             | 15                 | PASS                |
| TA1535                     | 24-Sep-08  | -S9                     | none              | N/A             | 14                 | PASS                |
| TA1537                     | 23-Sep-08  | +S9                     | none              | N/A             | 12                 | PASS                |
| TA1537                     | 23-Sep-08  | +S9                     | none              | N/A             | 7                  | PASS                |
| TA1537                     | 23-Sep-08  | -S9                     | none              | N/A             | 9                  | PASS                |
| TA1537                     | 24-Sep-08  | -S9                     | none              | N/A             | 6                  | PASS                |
| TA102                      | 19-Sep-08  | +S9                     | none              | N/A             | 287                | PASS                |
| TA102                      | 26-Sep-08  | +S9                     | none              | N/A             | 238                | PASS                |
| TA102                      | 19-Sep-08  | -S9                     | none              | N/A             | 289                | PASS                |
| TA102                      | 26-Sep-08  | -S9                     | none              | N/A             | 248                | PASS                |

\* **Positive Controls:** Each mean positive control value must exhibit at least a three-fold increase over the respective mean negative control value for each tester strain.

\*\* **Negative Controls:** mean reverents per plate must be within the listed ranges.

**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation  
(Revertants per plate)**

| Sample ID | Replicate Number | TPM Dose (µg/plate) | TA98 (+S9) |     |     | TA100 (+S9) |     |     | TA1535 (+S9) |    |    | TA1537 (+S9) |     |    | TA102 (+S9) |     |     |
|-----------|------------------|---------------------|------------|-----|-----|-------------|-----|-----|--------------|----|----|--------------|-----|----|-------------|-----|-----|
|           |                  |                     | P1         | P2  | P3  | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2  | P3 | P1          | P2  | P3  |
| control   | 1                | 0                   | 42         | 22  | 40  | 125         | 131 | 151 | 8            | 13 | 12 | 7            | 6   | 9  | 283         | 302 | 318 |
| control   | 1                | 25                  | 53         | 70  | 62  | 137         | 131 | 134 | 12           | 9  | 8  | 11           | 14  | 16 | 306         | 316 | 352 |
| control   | 1                | 50                  | 97         | 110 | 107 | 167         | 151 | 138 | 10           | 10 | 11 | 22           | 23  | 20 | 350         | 349 | 318 |
| control   | 1                | 75                  | 161        | 143 | 154 | 167         | 158 | 182 | 10           | 6  | 11 | 22           | 28  | 23 | 337         | 349 | 340 |
| control   | 1                | 100                 | 170        | 164 | 164 | 180         | 200 | 168 | 12           | 7  | 7  | 31           | 27  | 35 | 358         | 340 | NA  |
| control   | 1                | 125                 | 182        | 178 | 172 | 196         | 190 | 197 | 6            | 8  | 8  | 33           | 37  | 33 | NA          | 353 | 340 |
| control   | 1                | 250                 | 260        | 239 | 238 | 220         | 189 | 220 | 8            | 10 | 13 | 52           | 62  | 46 | 357         | 373 | 353 |
| control   | 1                | 500                 | 445        | 447 | 481 | 309         | 342 | 316 | 15           | 8  | 10 | 84           | 101 | 94 | 385         | 369 | 373 |
| control   | 2                | 0                   | 33         | 20  | 20  | 83          | 95  | 81  | 11           | 9  | 16 | 9            | 8   | 6  | 295         | 313 | 302 |
| control   | 2                | 25                  | 40         | 46  | 33  | 95          | 106 | 81  | 18           | 13 | 14 | 14           | 12  | 12 | 311         | 321 | 320 |
| control   | 2                | 50                  | 83         | 72  | 94  | 117         | 110 | 96  | 12           | 17 | 10 | 18           | 19  | 21 | 318         | 330 | 315 |
| control   | 2                | 75                  | 108        | 83  | 101 | 114         | 130 | 107 | 10           | 13 | 9  | 21           | 27  | 21 | 318         | 314 | 333 |
| control   | 2                | 100                 | 144        | 138 | 151 | 138         | 126 | 116 | 17           | 13 | 9  | 30           | 33  | 31 | 344         | 315 | 326 |
| control   | 2                | 125                 | 208        | 206 | 227 | NA          | 124 | 130 | 16           | 11 | 9  | 36           | 37  | 34 | 324         | 342 | 330 |
| control   | 2                | 250                 | 357        | 362 | 359 | 141         | 152 | 139 | 23           | 13 | 17 | 61           | 64  | 65 | 304         | 339 | 332 |
| control   | 2                | 500                 | 521        | 517 | 541 | 142         | 155 | 164 | 28           | 12 | 13 | 88           | 85  | 90 | 348         | 358 | 356 |

**N/A** - data not available due to lack of bacterial growth or assay plate contamination

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation  
(Revertants per plate)**

| Sample ID | Replicate Number | TPM Dose (µg/plate) | TA98 (-S9) |    |    | TA100 (-S9) |     |     | TA1535 (-S9) |    |    | TA1537 (-S9) |    |    | TA102 (-S9) |     |     |
|-----------|------------------|---------------------|------------|----|----|-------------|-----|-----|--------------|----|----|--------------|----|----|-------------|-----|-----|
|           |                  |                     | P1         | P2 | P3 | P1          | P2  | P3  | P1           | P2 | P3 | P1           | P2 | P3 | P1          | P2  | P3  |
| control   | 1                | 0                   | 23         | 29 | 23 | 156         | 129 | 139 | 16           | 20 | 17 | 8            | 6  | 8  | 298         | 296 | 291 |
| control   | 1                | 25                  | 22         | 26 | 24 | 156         | 141 | 157 | 13           | 18 | 12 | 9            | 10 | 13 | 299         | 310 | 300 |
| control   | 1                | 50                  | 38         | 34 | 33 | 166         | 162 | 148 | 11           | 11 | 8  | 11           | 14 | 12 | 279         | 289 | 296 |
| control   | 1                | 75                  | 37         | 27 | 31 | 163         | 158 | 179 | 16           | 11 | 16 | 11           | 9  | 12 | 298         | 314 | 296 |
| control   | 1                | 100                 | 30         | 28 | 21 | 182         | 177 | 170 | 14           | 13 | 18 | 9            | 11 | 12 | 310         | 294 | 285 |
| control   | 1                | 125                 | 20         | 27 | 27 | 193         | 160 | 170 | 12           | 12 | 16 | 9            | 18 | 13 | 293         | 291 | 303 |
| control   | 1                | 250                 | 37         | 33 | 31 | 184         | 178 | 151 | 14           | 19 | 15 | 10           | 11 | 10 | 268         | 286 | 262 |
| control   | 1                | 500                 | 62         | 50 | 59 | 164         | 159 | 177 | 24           | 26 | 19 | 13           | 16 | 15 | 266         | 268 | 239 |
| control   | 2                | 0                   | 24         | 23 | 25 | 187         | 171 | 161 | 9            | 12 | 13 | 7            | 7  | 8  | 264         | 272 | 264 |
| control   | 2                | 25                  | 23         | 28 | 29 | 153         | 154 | 152 | 15           | 9  | 11 | 12           | 8  | 7  | 279         | 279 | 267 |
| control   | 2                | 50                  | 31         | 39 | 36 | 179         | 160 | 163 | 8            | 14 | 9  | 9            | 6  | 6  | 271         | 284 | 273 |
| control   | 2                | 75                  | 31         | 35 | 23 | 196         | 159 | 188 | 9            | 14 | 12 | 10           | 9  | 9  | 256         | 264 | 257 |
| control   | 2                | 100                 | 38         | 33 | 37 | 196         | 172 | 216 | 14           | 11 | 14 | 11           | 8  | 5  | 278         | 298 | 290 |
| control   | 2                | 125                 | 28         | 35 | 29 | 180         | 174 | 172 | 12           | 13 | 11 | 6            | 8  | 8  | 264         | 262 | 257 |
| control   | 2                | 250                 | 48         | 40 | 43 | 167         | 171 | 180 | 12           | 11 | 13 | 9            | 12 | 11 | 251         | 231 | 233 |
| control   | 2                | 500                 | 58         | 62 | 63 | 104         | 116 | 133 | 13           | 17 | 18 | 7            | 6  | 5  | 249         | 252 | 277 |



**Mutagenesis in *Salmonella typhimurium* with (+) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Sample ID | Replicate Number | TPM Dose (µg/plate) | TA98 (+S9) |    | TA100 (+S9) |    | TA1535 (+S9) |    | TA1537 (+S9) |    | TA102 (+S9) |    |
|-----------|------------------|---------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|           |                  |                     | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| control   | 1                | 0                   | 35         | 11 | 136         | 14 | 11           | 3  | 7            | 2  | 301         | 18 |
| control   | 1                | 25                  | 62         | 9  | 134         | 3  | 10           | 2  | 14           | 3  | 325         | 24 |
| control   | 1                | 50                  | 105        | 7  | 152         | 15 | 10           | 1  | 22           | 2  | 339         | 18 |
| control   | 1                | 75                  | 153        | 9  | 169         | 12 | 9            | 3  | 24           | 3  | 342         | 6  |
| control   | 1                | 100                 | 166        | 3  | 183         | 16 | 9            | 3  | 31           | 4  | 349         | 13 |
| control   | 1                | 125                 | 177        | 5  | 194         | 4  | 7            | 1  | 34           | 2  | 347         | 9  |
| control   | 1                | 250                 | 246        | 12 | 210         | 18 | 10           | 3  | 53           | 8  | 361         | 11 |
| control   | 1                | 500                 | 458        | 20 | 322         | 17 | 11           | 4  | 93           | 9  | 376         | 8  |
|           |                  |                     |            |    |             |    |              |    |              |    |             |    |
| control   | 2                | 0                   | 24         | 8  | 86          | 8  | 12           | 4  | 8            | 2  | 303         | 9  |
| control   | 2                | 25                  | 40         | 7  | 94          | 13 | 15           | 3  | 13           | 1  | 317         | 6  |
| control   | 2                | 50                  | 83         | 11 | 108         | 11 | 13           | 4  | 19           | 2  | 321         | 8  |
| control   | 2                | 75                  | 97         | 13 | 117         | 12 | 11           | 2  | 23           | 3  | 322         | 10 |
| control   | 2                | 100                 | 144        | 7  | 127         | 11 | 13           | 4  | 31           | 2  | 328         | 15 |
| control   | 2                | 125                 | 214        | 12 | 127         | 4  | 12           | 4  | 36           | 2  | 332         | 9  |
| control   | 2                | 250                 | 359        | 3  | 144         | 7  | 18           | 5  | 63           | 2  | 325         | 19 |
| control   | 2                | 500                 | 526        | 13 | 154         | 11 | 18           | 9  | 88           | 3  | 354         | 5  |

\*Values represent the mean number of revertants (average of three plates)

**Mutagenesis in *Salmonella typhimurium* without (-) S9 Metabolic Activation**  
**(Average No. of Revertants per plate)\***

| Sample ID | Replicate Number | TPM Dose (µg/plate) | TA98 (-S9) |    | TA100 (-S9) |    | TA1535 (-S9) |    | TA1537 (-S9) |    | TA102 (-S9) |    |
|-----------|------------------|---------------------|------------|----|-------------|----|--------------|----|--------------|----|-------------|----|
|           |                  |                     | Mean       | SD | Mean        | SD | Mean         | SD | Mean         | SD | Mean        | SD |
| control   | 1                | 0                   | 25         | 3  | 141         | 14 | 18           | 2  | 7            | 1  | 295         | 4  |
| control   | 1                | 25                  | 24         | 2  | 151         | 9  | 14           | 3  | 11           | 2  | 303         | 6  |
| control   | 1                | 50                  | 35         | 3  | 159         | 9  | 10           | 2  | 12           | 2  | 288         | 9  |
| control   | 1                | 75                  | 32         | 5  | 167         | 11 | 14           | 3  | 11           | 2  | 303         | 10 |
| control   | 1                | 100                 | 26         | 5  | 176         | 6  | 15           | 3  | 11           | 2  | 296         | 13 |
| control   | 1                | 125                 | 25         | 4  | 174         | 17 | 13           | 2  | 13           | 5  | 296         | 6  |
| control   | 1                | 250                 | 34         | 3  | 171         | 18 | 16           | 3  | 10           | 1  | 272         | 12 |
| control   | 1                | 500                 | 57         | 6  | 167         | 9  | 23           | 4  | 15           | 2  | 258         | 16 |
|           |                  |                     |            |    |             |    |              |    |              |    |             |    |
| control   | 2                | 0                   | 24         | 1  | 173         | 13 | 11           | 2  | 7            | 1  | 267         | 5  |
| control   | 2                | 25                  | 27         | 3  | 153         | 1  | 12           | 3  | 9            | 3  | 275         | 7  |
| control   | 2                | 50                  | 35         | 4  | 167         | 10 | 10           | 3  | 7            | 2  | 276         | 7  |
| control   | 2                | 75                  | 30         | 6  | 181         | 19 | 12           | 3  | 9            | 1  | 259         | 4  |
| control   | 2                | 100                 | 36         | 3  | 195         | 22 | 13           | 2  | 8            | 3  | 289         | 10 |
| control   | 2                | 125                 | 31         | 4  | 175         | 4  | 12           | 1  | 7            | 1  | 261         | 4  |
| control   | 2                | 250                 | 44         | 4  | 173         | 7  | 12           | 1  | 11           | 2  | 238         | 11 |
| control   | 2                | 500                 | 61         | 3  | 118         | 15 | 16           | 3  | 6            | 1  | 259         | 15 |

\*Values represent the mean number of revertants (average of three plates)

**Mutagenesis in *Salmonella typhimurium* with (+) and without (-) S9 Metabolic Activation**  
**(Date of assay)**

| Sample ID | Replicate Number | TA98      |           | TA100     |           | TA1535    |           | TA1537    |           | TA102     |           |
|-----------|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|           |                  | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       | +S9       | -S9       |
| control   | 1                | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 19-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 23-Sep-08 | 19-Sep-08 | 19-Sep-08 |
| control   | 2                | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 | 26-Sep-08 | 24-Sep-08 | 24-Sep-08 | 23-Sep-08 | 24-Sep-08 | 26-Sep-08 | 26-Sep-08 |

## LABSTAT INTERNATIONAL ULC

262 Manitou Drive, Kitchener, Ontario, Canada N2C 1L3

Phone (519) 748-5409 FAX (519) 748-1654

Project: M97

Period: September 19 - 26, 2008

Control: Kentucky Reference 3R4F

### Comparison of Internal KR 3R4F Control Slopes with Expected (Historical) Slopes (Mainstream Tobacco Smoke 'Intense' Conditions \*)

| Strain       | Assay Date | Target Slope |         | Unit          | This Study Slope | Z Score | P Value |
|--------------|------------|--------------|---------|---------------|------------------|---------|---------|
|              |            | Average      | Std Dev |               |                  |         |         |
| TA98 (+S9)   | 19-Sep-08  | 1399         | 202     | (rev./mg TPM) | 1228             | 0.847   | 0.397   |
| TA98 (+S9)   | 24-Sep-08  | 1399         | 202     | (rev./mg TPM) | 1457             | -0.289  | 0.773   |
| TA98 (-S9)   | 19-Sep-08  | 47.3         | 30.2    | (rev./mg TPM) | 24               | 0.783   | 0.434   |
| TA98 (-S9)   | 26-Sep-08  | 47.3         | 30.2    | (rev./mg TPM) | 69               | -0.716  | 0.474   |
| TA100 (+S9)  | 19-Sep-08  | 580          | 148     | (rev./mg TPM) | 522              | 0.395   | 0.693   |
| TA100 (+S9)  | 26-Sep-08  | 580          | 148     | (rev./mg TPM) | 367              | 1.444   | 0.149   |
| TA100 (-S9)  | 19-Sep-08  | 189          | 76      | (rev./mg TPM) | 283              | -1.238  | 0.216   |
| TA100 (-S9)  | 26-Sep-08  | 189          | 76      | (rev./mg TPM) | 172              | 0.221   | 0.825   |
| TA102 (+S9)  | 19-Sep-08  | 444          | 171     | (rev./mg TPM) | 366              | 0.459   | 0.646   |
| TA102 (+S9)  | 26-Sep-08  | 444          | 171     | (rev./mg TPM) | 202              | 1.414   | 0.157   |
| TA102 (-S9)  | 19-Sep-08  | 102          | 112     | (rev./mg TPM) | 0                | 0.912   | 0.362   |
| TA102 (-S9)  | 26-Sep-08  | 102          | 112     | (rev./mg TPM) | 0                | 0.912   | 0.362   |
| TA1535 (+S9) | 23-Sep-08  | 13.5         | 14.1    | (rev./mg TPM) | 0                | 0.955   | 0.339   |
| TA1535 (+S9) | 24-Sep-08  | 13.5         | 14.1    | (rev./mg TPM) | 17               | -0.268  | 0.789   |
| TA1535 (-S9) | 23-Sep-08  | 10.9         | 13.7    | (rev./mg TPM) | 0                | 0.797   | 0.425   |
| TA1535 (-S9) | 24-Sep-08  | 10.9         | 13.7    | (rev./mg TPM) | 0                | 0.797   | 0.425   |
| TA1537 (+S9) | 23-Sep-08  | 225          | 42      | (rev./mg TPM) | 217              | 0.192   | 0.848   |
| TA1537 (+S9) | 23-Sep-08  | 225          | 42      | (rev./mg TPM) | 228              | -0.078  | 0.938   |
| TA1537 (-S9) | 23-Sep-08  | 23.8         | 14.9    | (rev./mg TPM) | 0                | 1.596   | 0.110   |
| TA1537 (-S9) | 24-Sep-08  | 23.8         | 14.9    | (rev./mg TPM) | 10               | 0.911   | 0.362   |

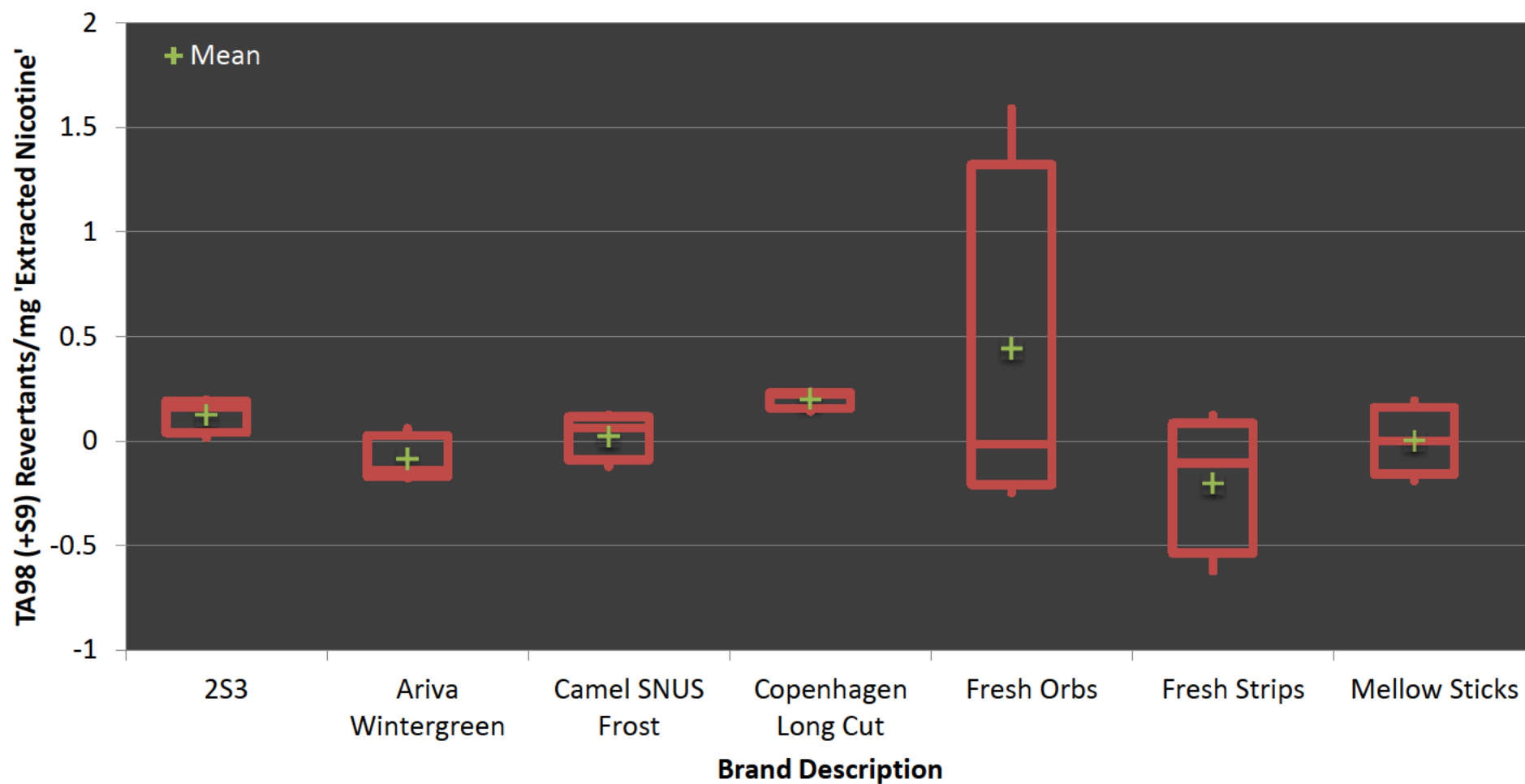
\* internal control samples generated under 'Intense' smoking conditions:

55mL puff volume; 30 second interval; 2 second duration; 100% vent blocking.

Test Describe - Comparative

Performed by TA98 (+S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

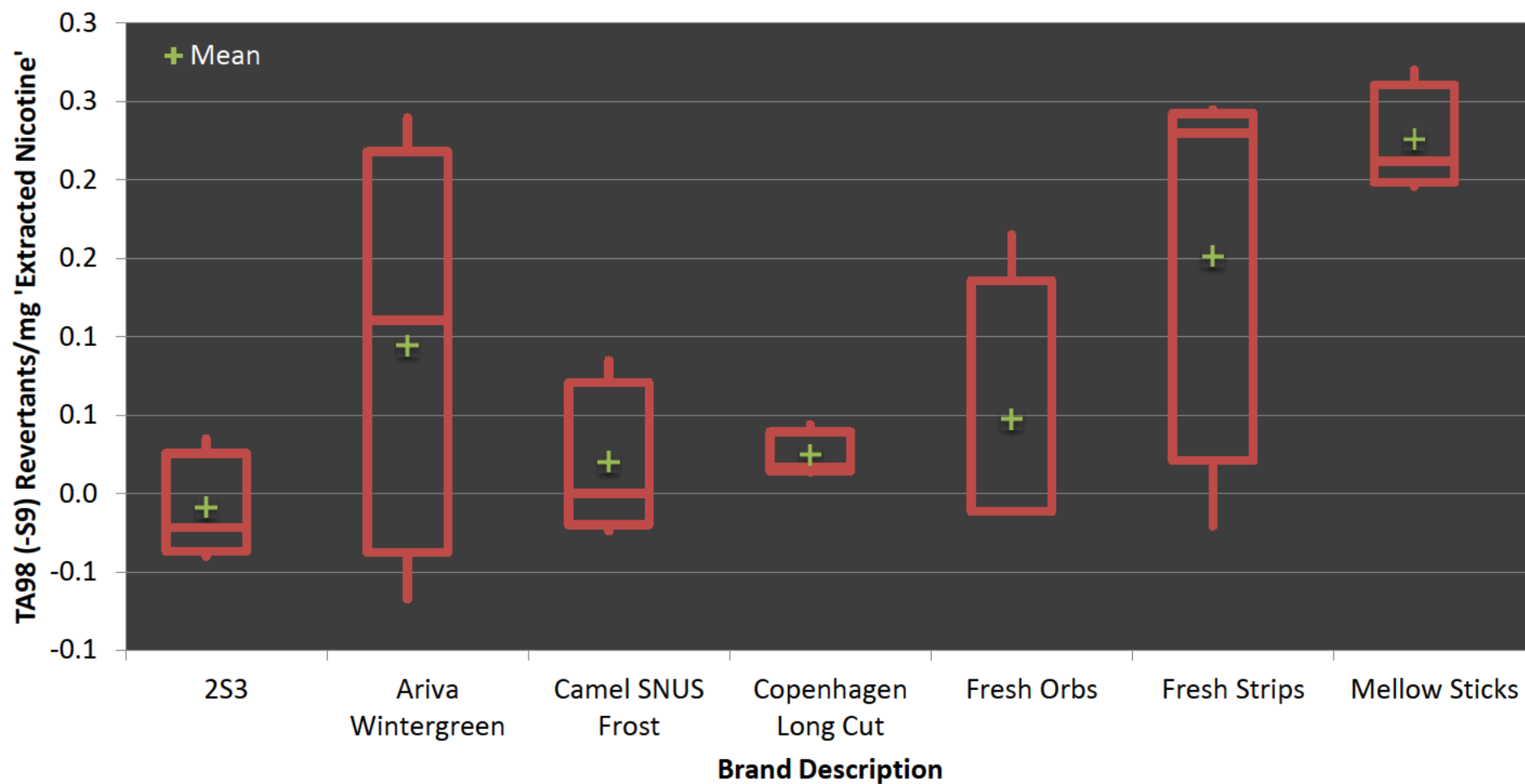
Date 26 October 2009



Test Describe - Comparative

Performed by TA98 (-S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

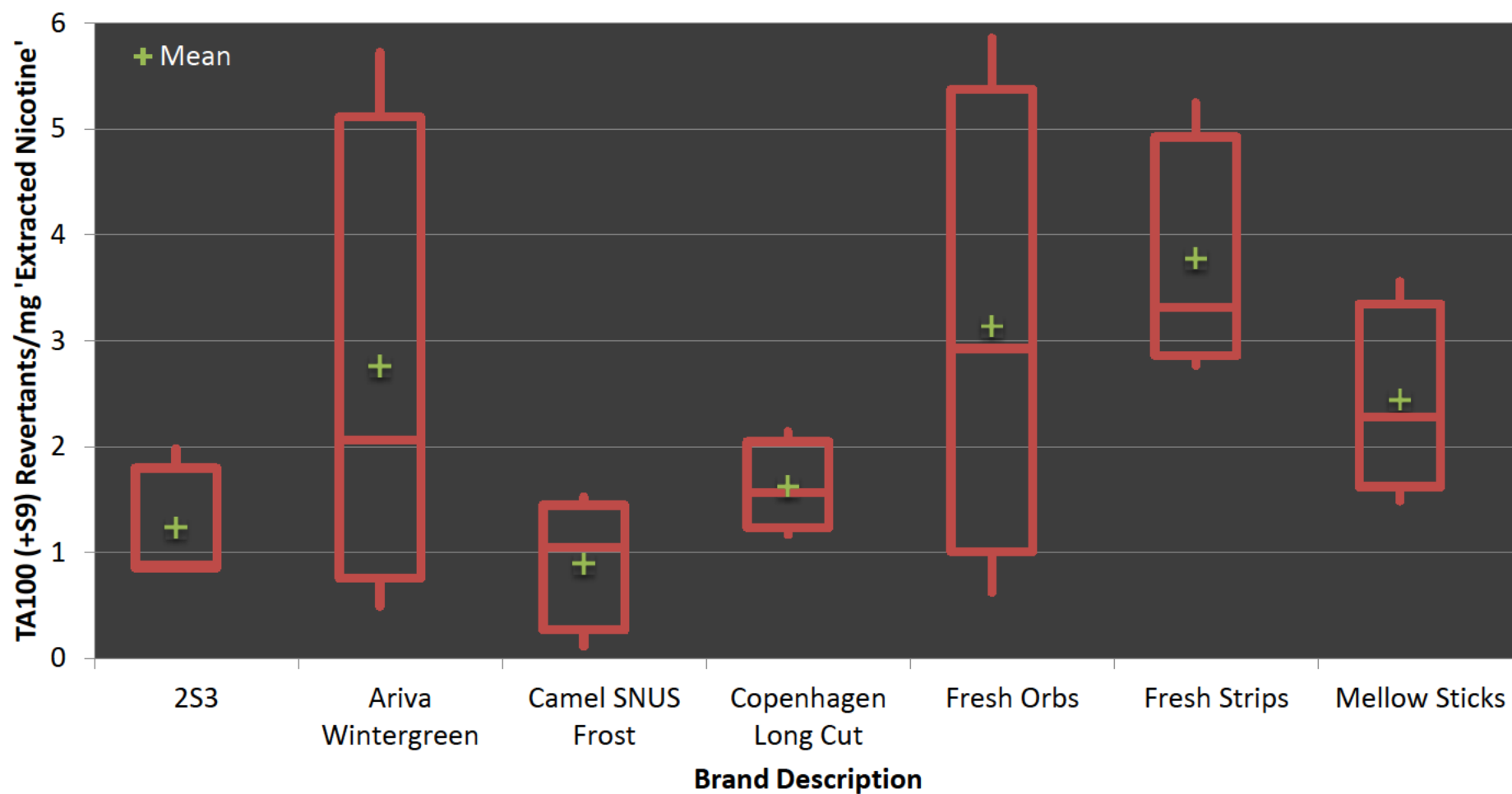
Date 26 October 2009



Test Describe - Comparative

Performed by TA100 (+S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

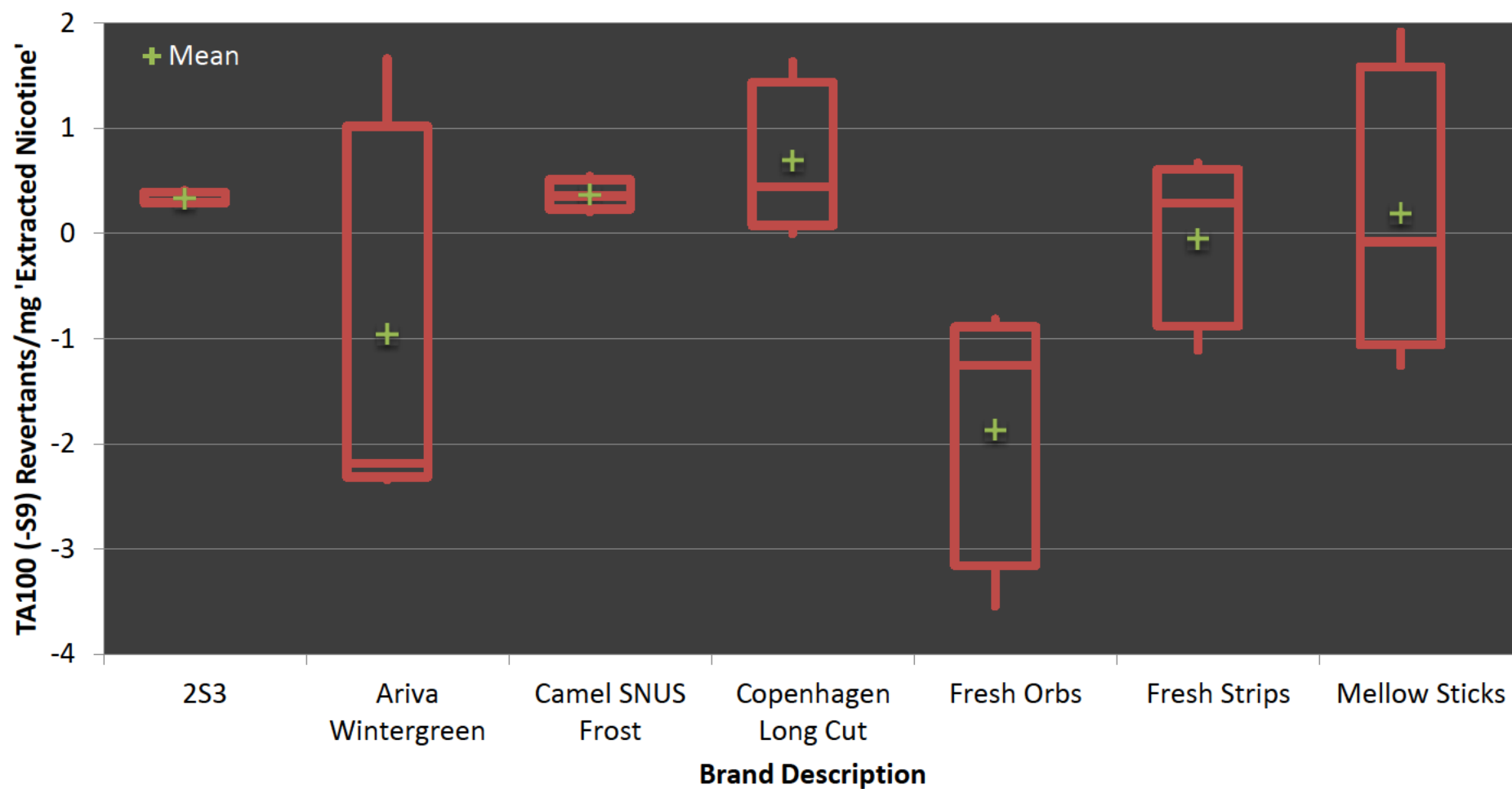
Date 26 October 2009



Test Describe - Comparative

Performed by TA100 (-S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009

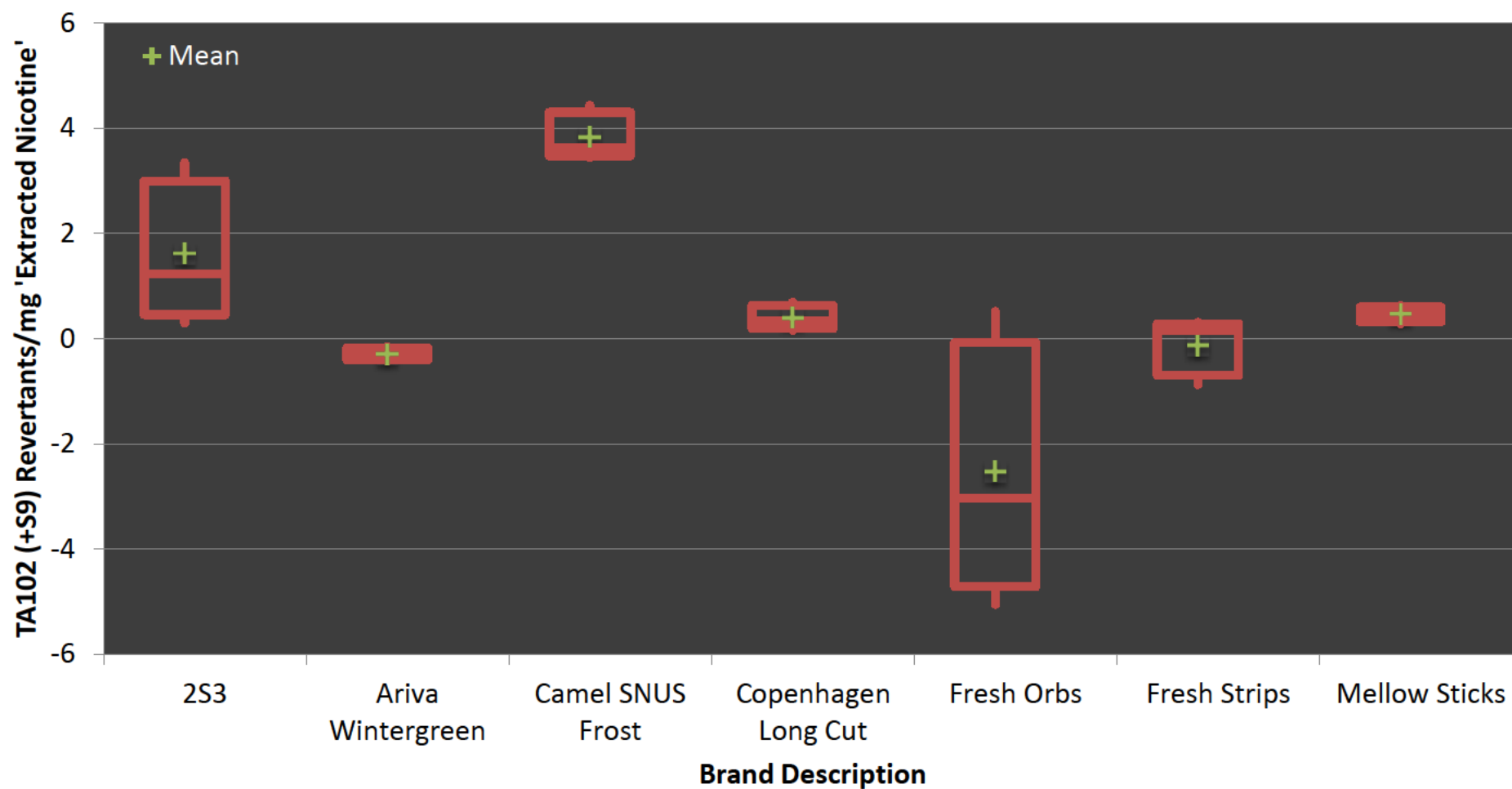




Test Describe - Comparative

Performed by TA102 (+S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

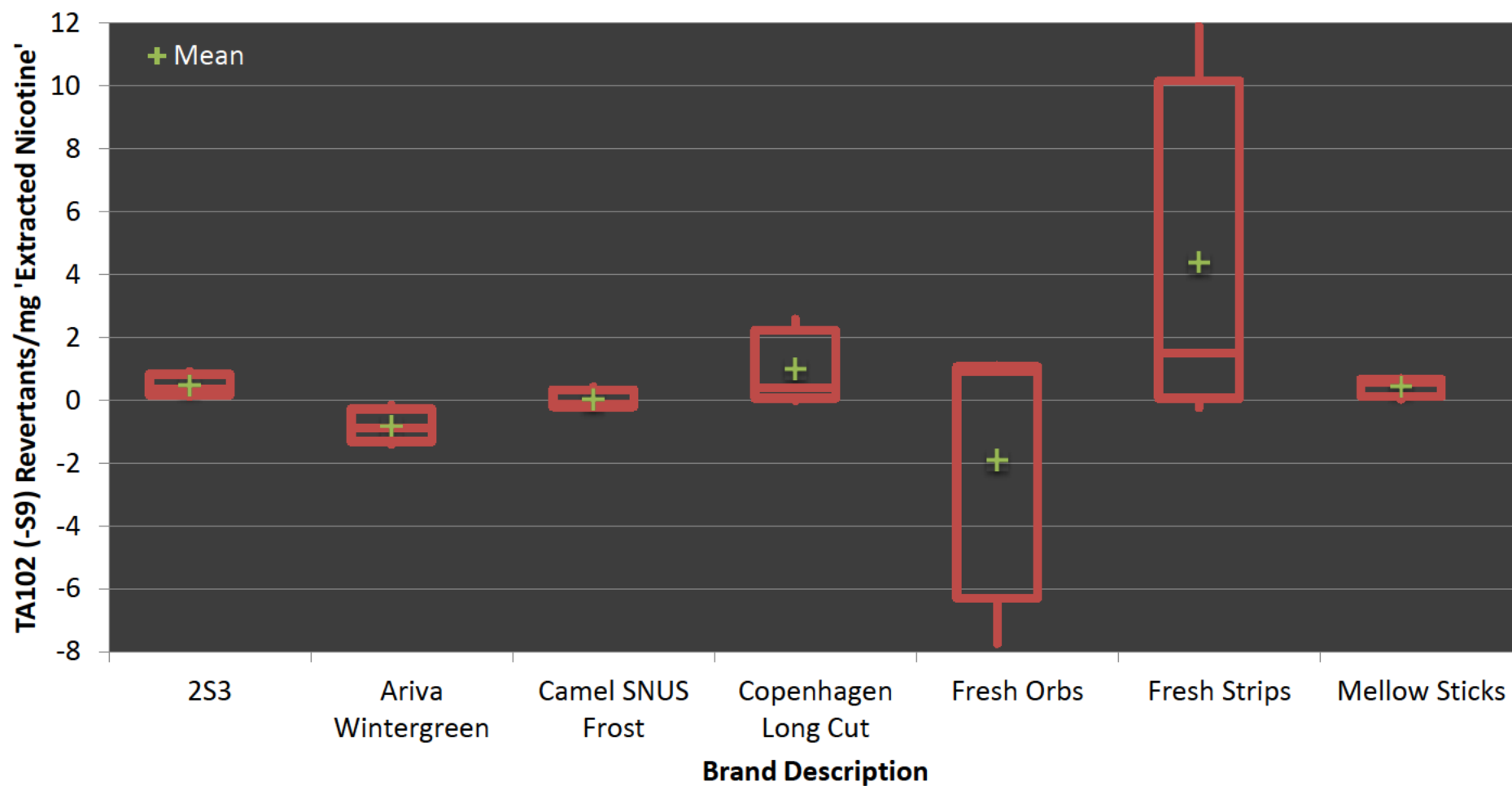
Date 26 October 2009



Test Describe - Comparative

Performed by TA102 (-S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

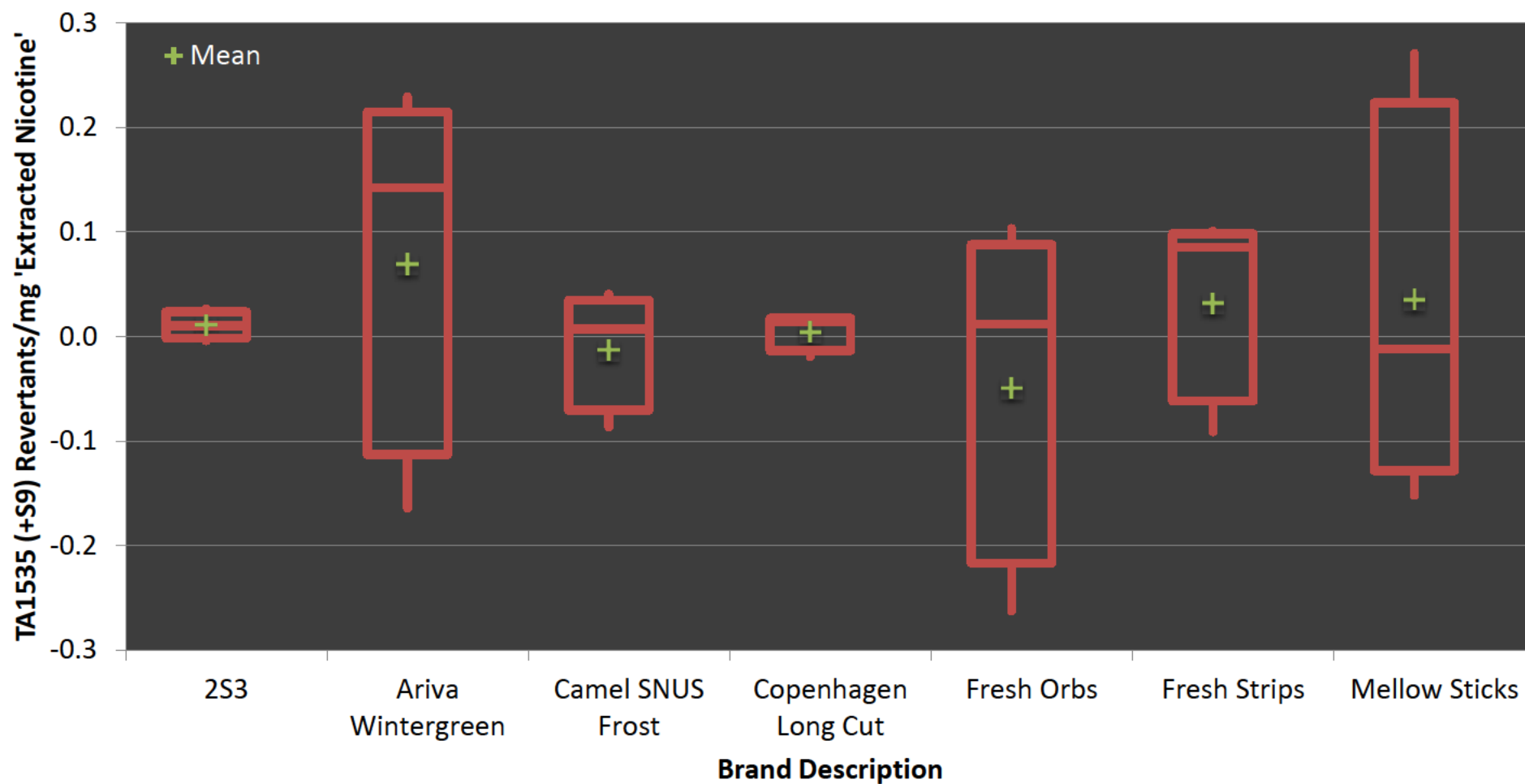
Date 26 October 2009



Test Describe - Comparative

Performed by TA1535 (+S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

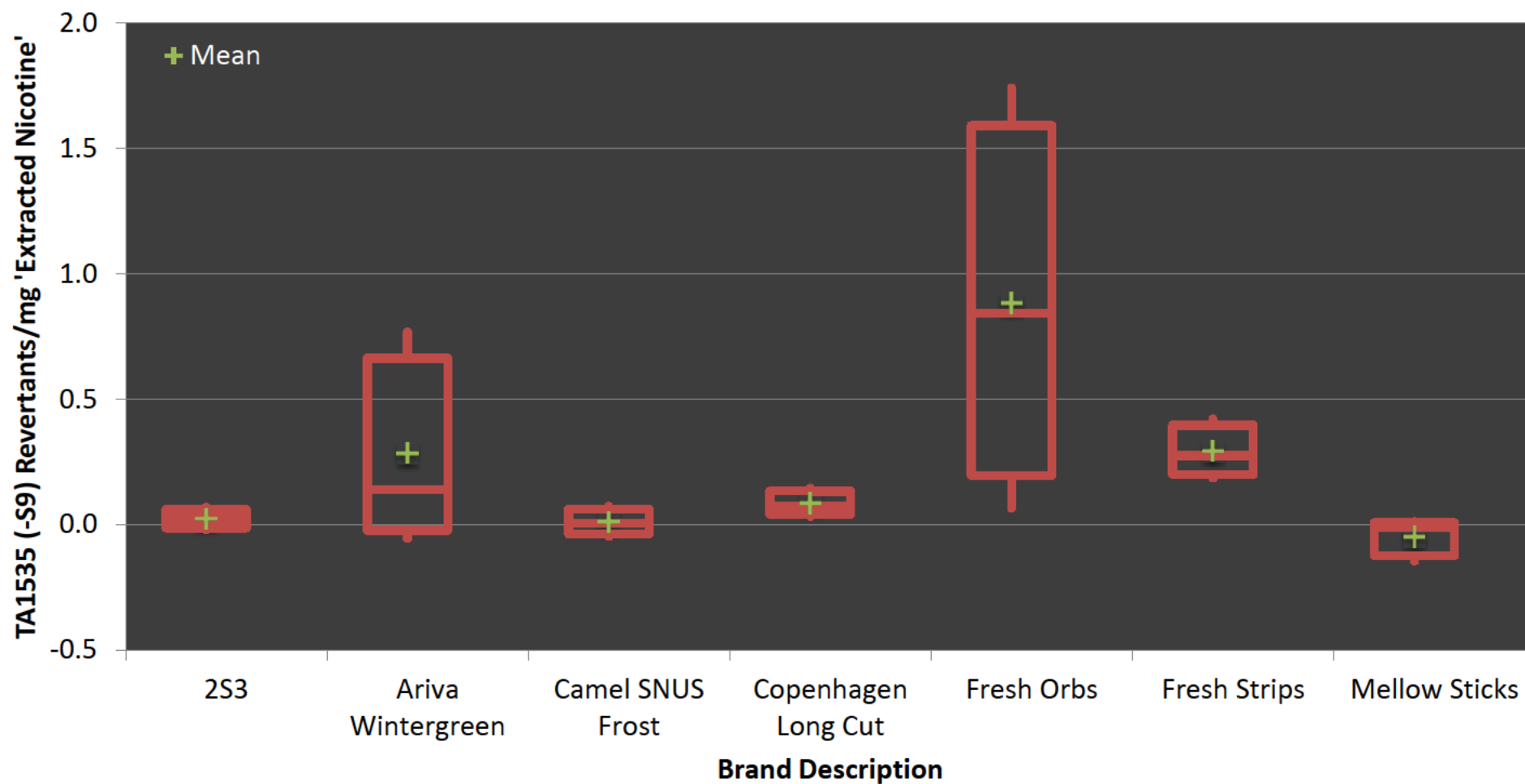
Date 26 October 2009



Test Describe - Comparative

Performed by TA1535 (-S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

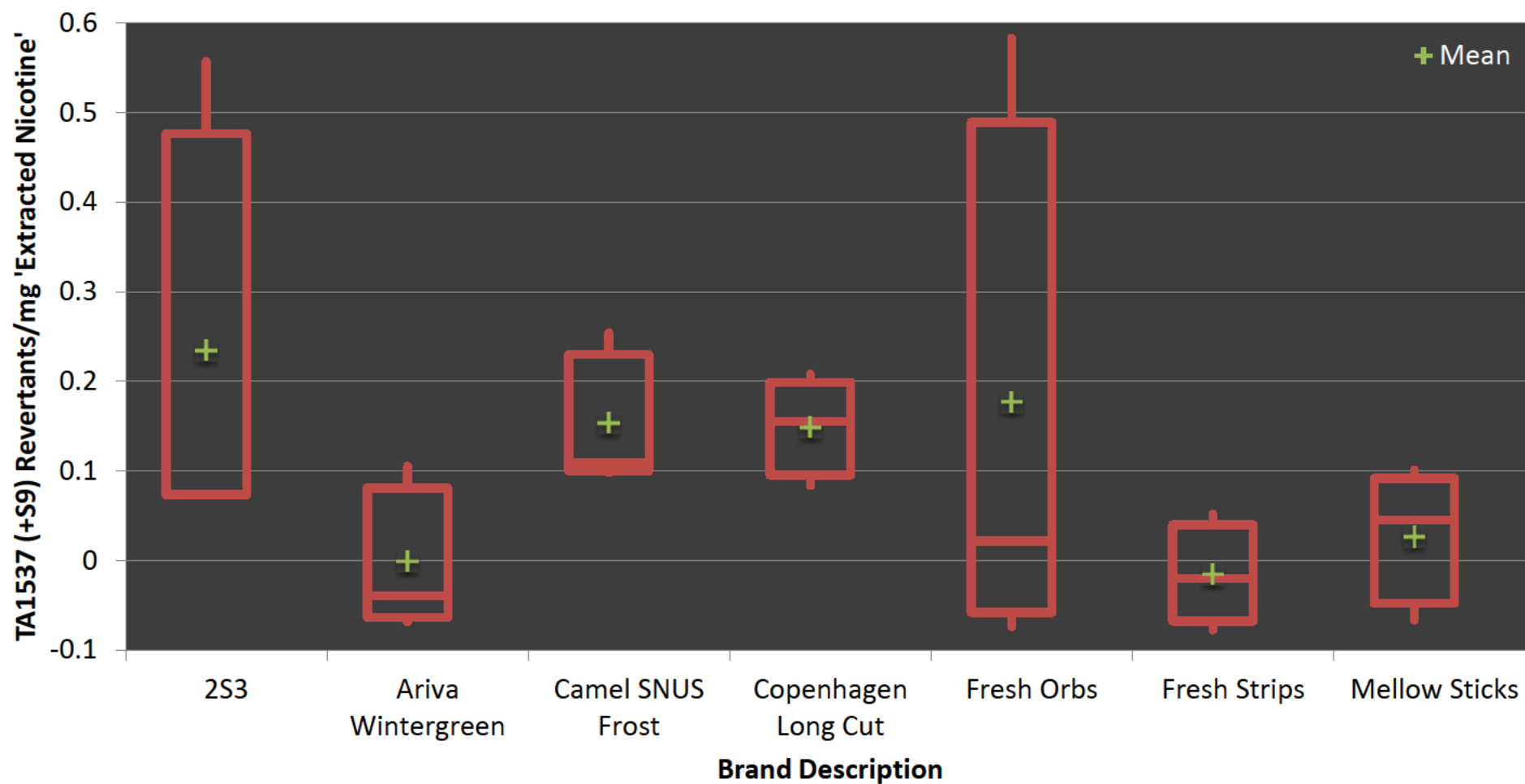
Date 26 October 2009



Test Describe - Comparative

Performed by TA1537 (+S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

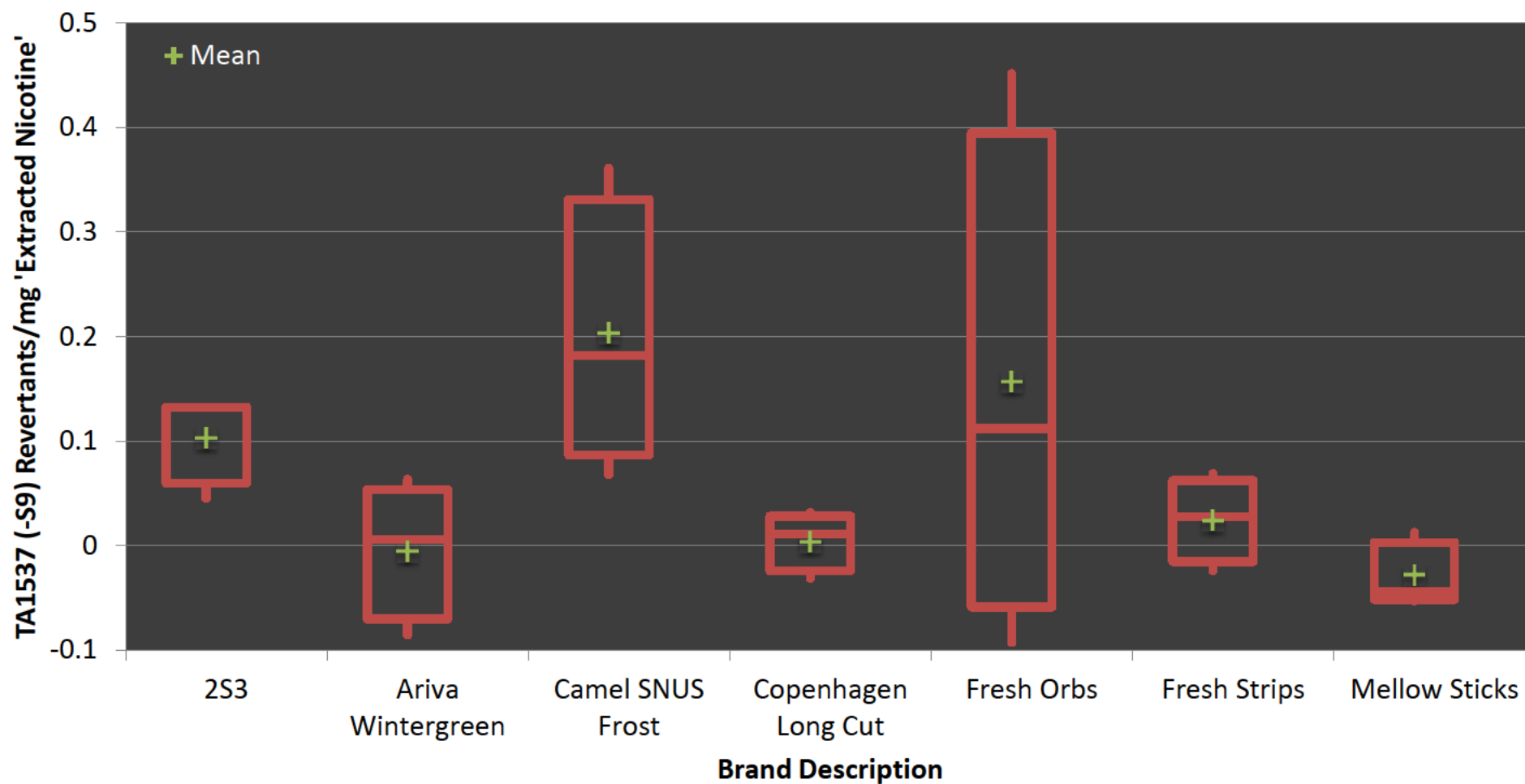
Date 26 October 2009



Test Describe - Comparative

Performed by TA1537 (-S9): Revertants/mg 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009



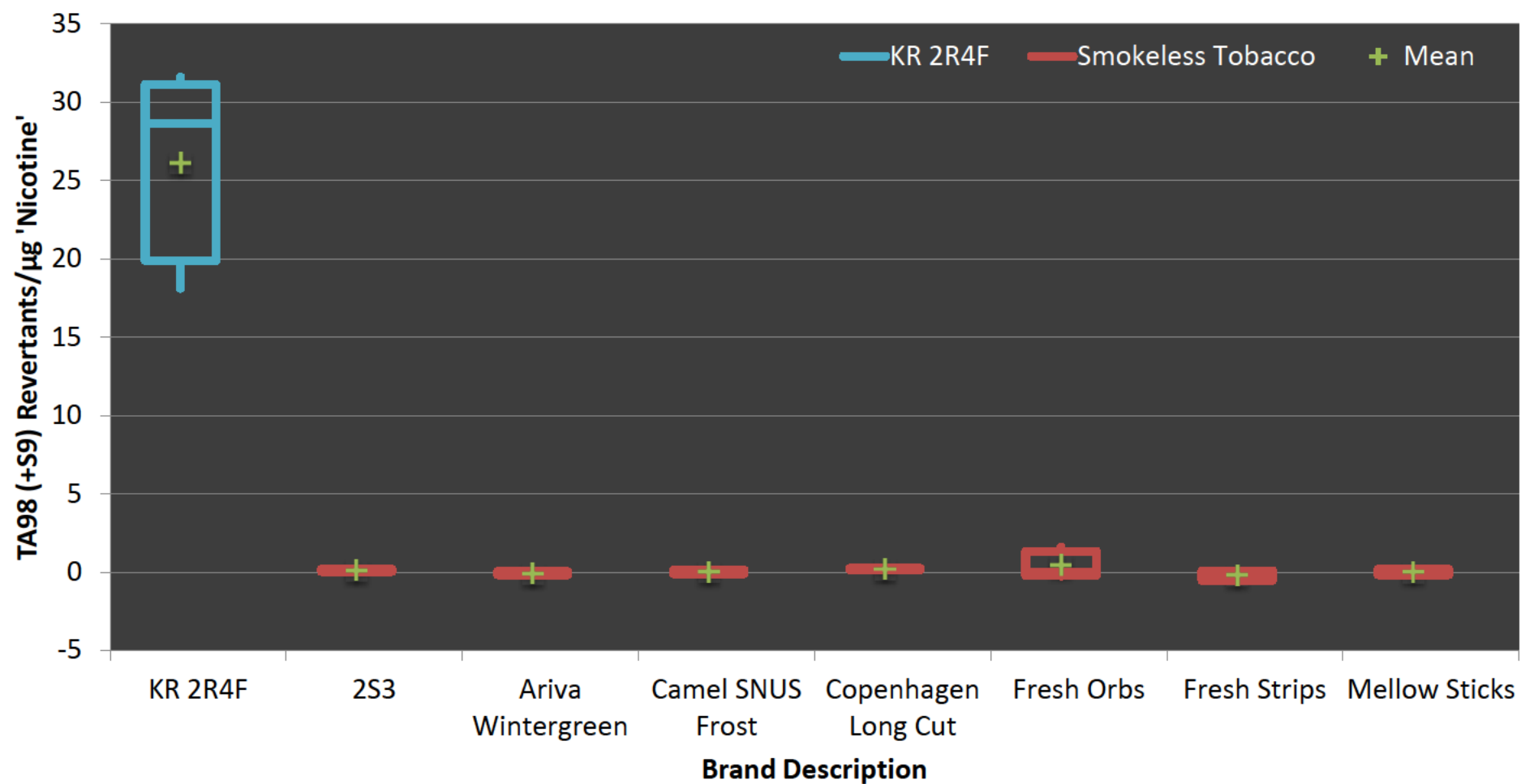
Test Describe - Comparative

Performed by

TA98 (+S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

Date

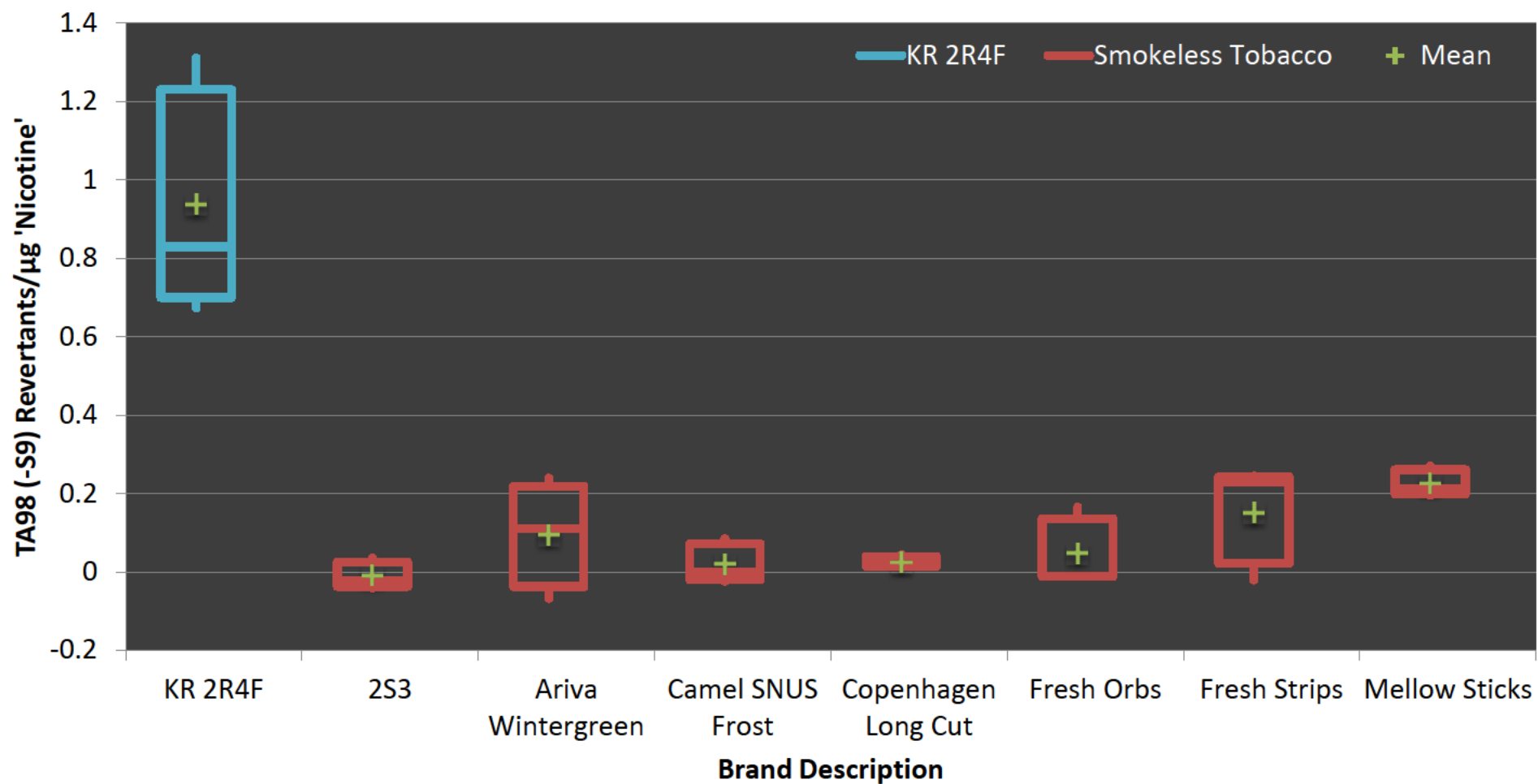
11 December 2009



Test Describe - Comparative

Performed by TA98 (-S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

Date 11 December 2009





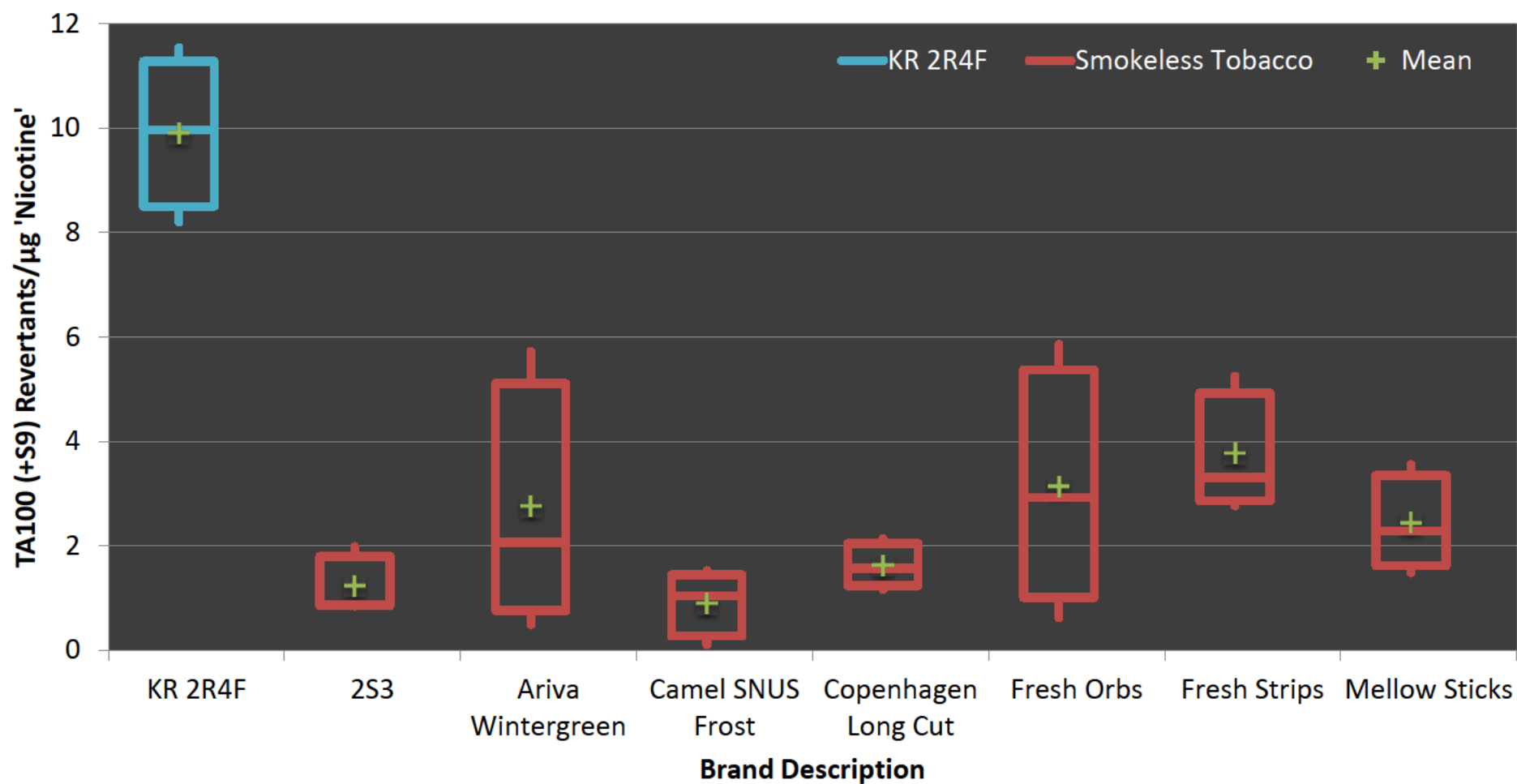
Test Describe - Comparative

Performed by

TA100 (+S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

Date

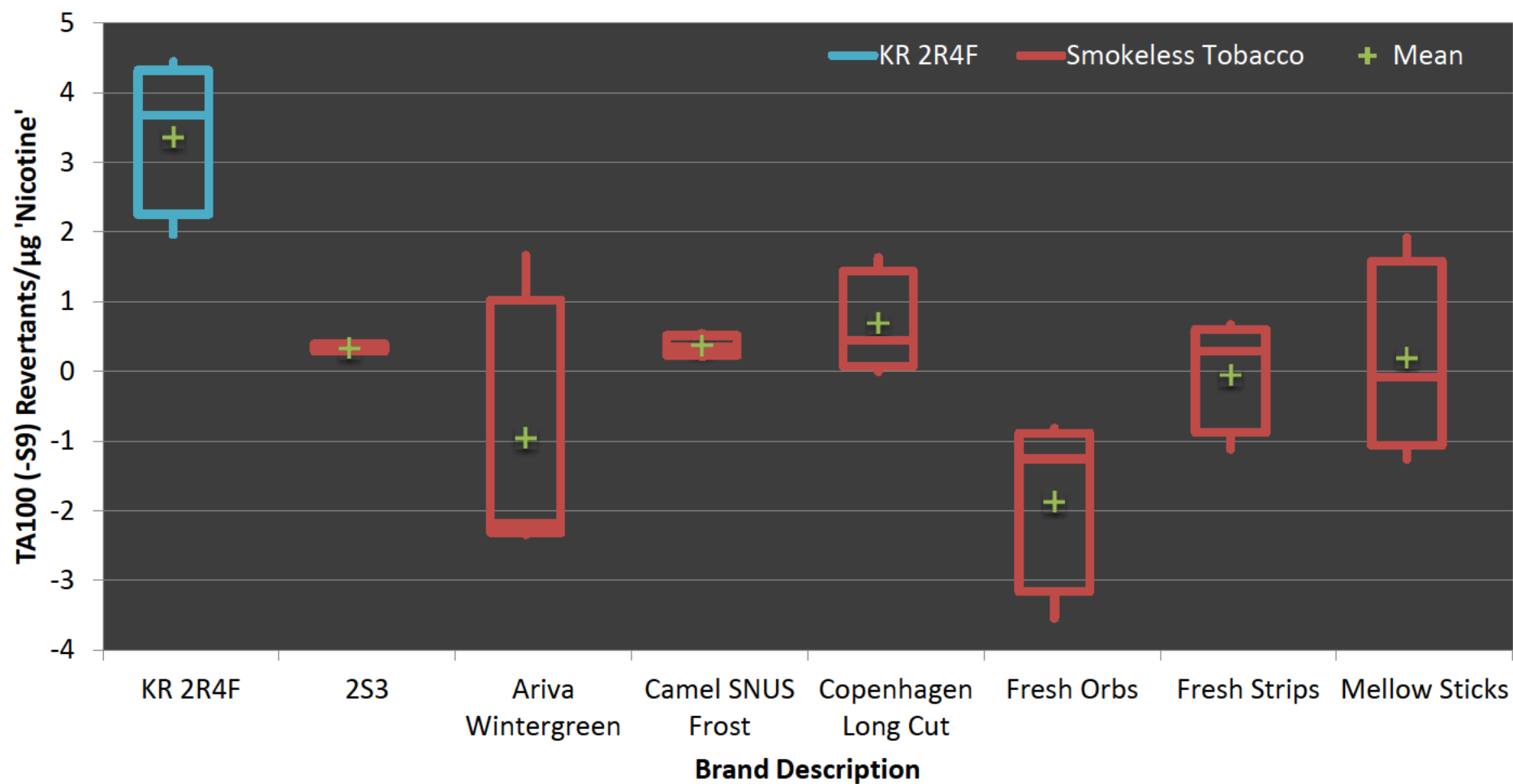
11 December 2009



Test Describe - Comparative

Performed by TA100 (-S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

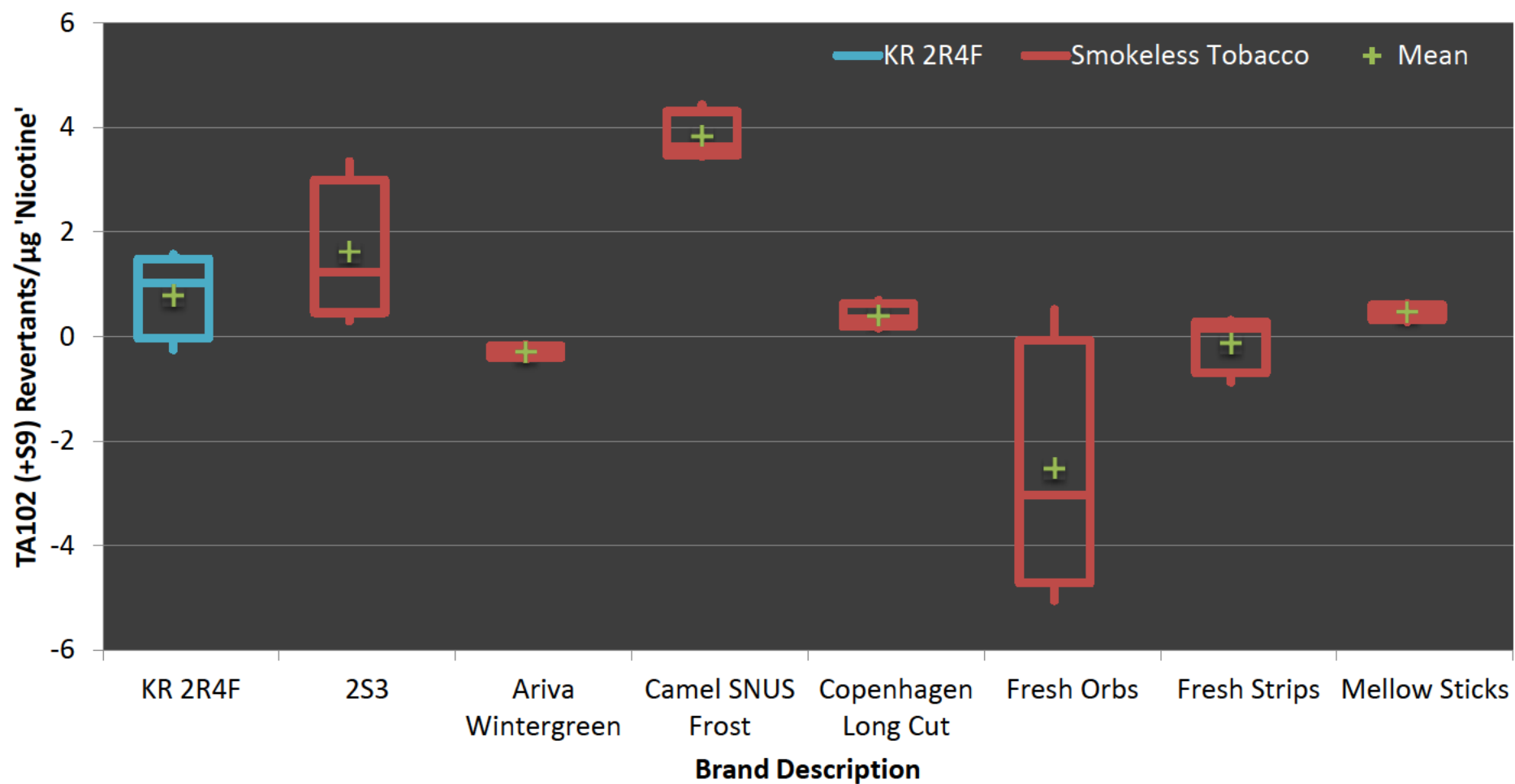
Date 11 December 2009



Test Describe - Comparative

Performed by TA102 (+S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

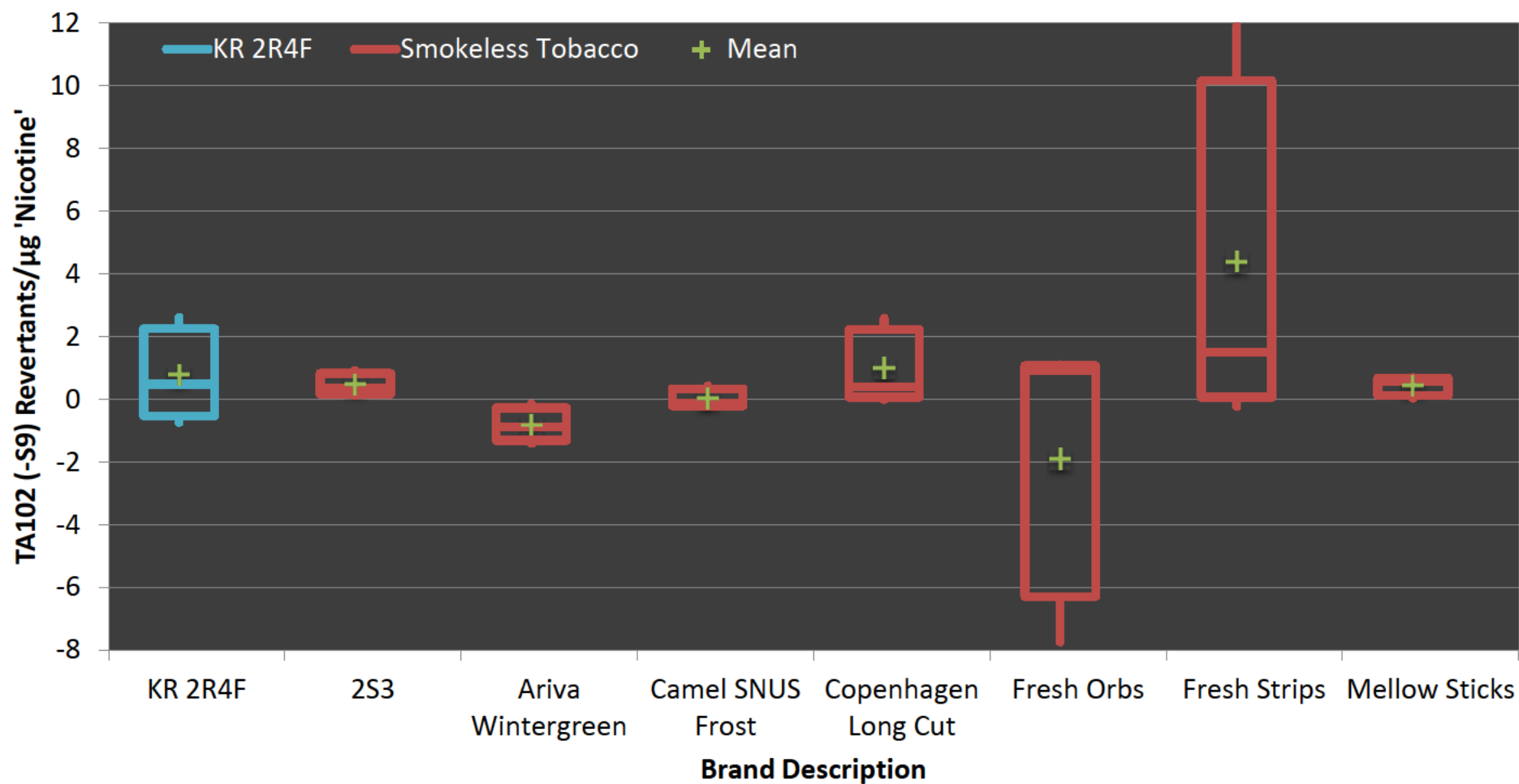
Date 11 December 2009



Test Describe - Comparative

Performed by TA102 (-S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

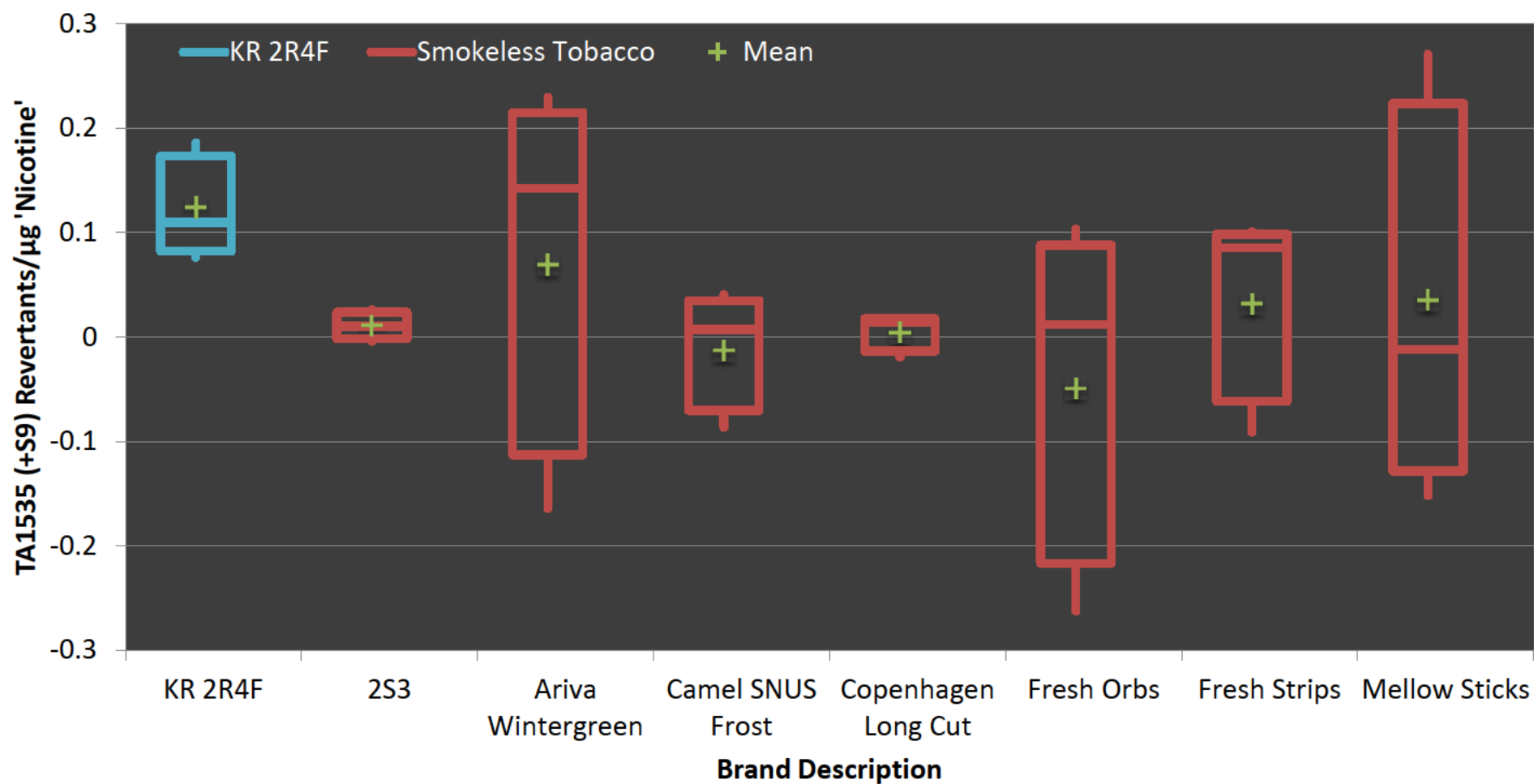
Date 11 December 2009



Test Describe - Comparative

Performed by TA1535 (+S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

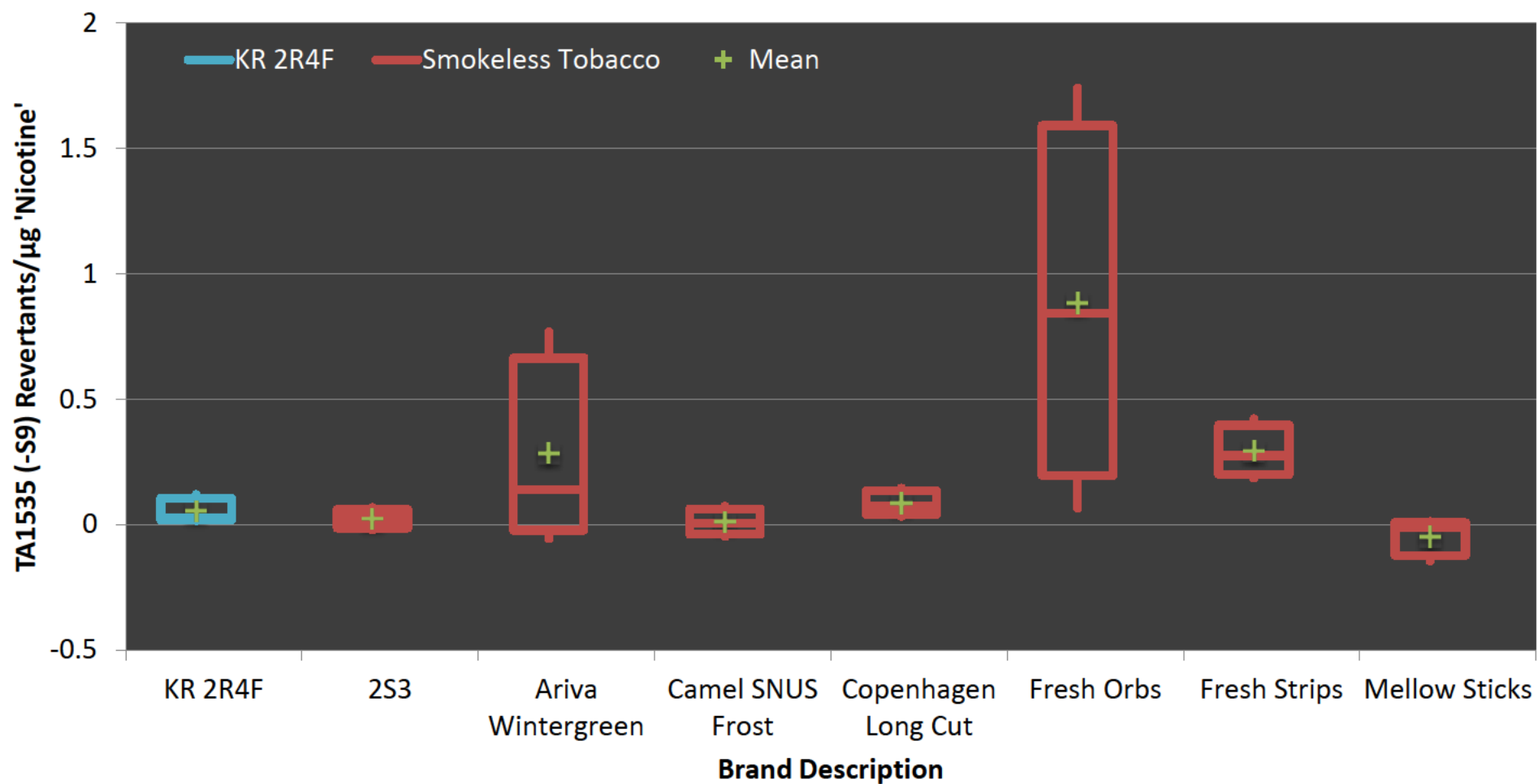
Date 11 December 2009



Test Describe - Comparative

Performed by TA1535 (-S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

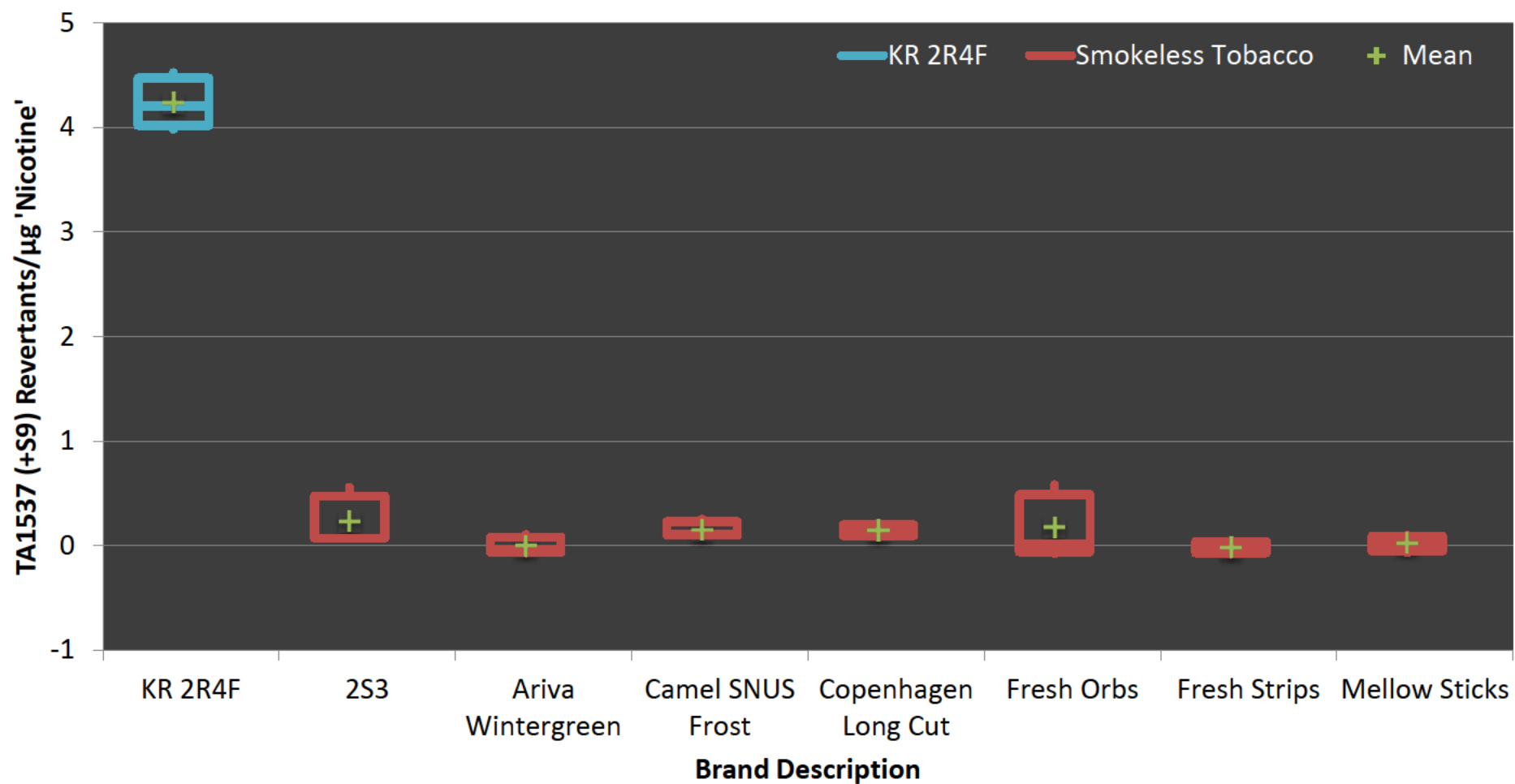
Date 11 December 2009



Test Describe - Comparative

Performed by TA1537 (+S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand  
Wendy Wagstaff

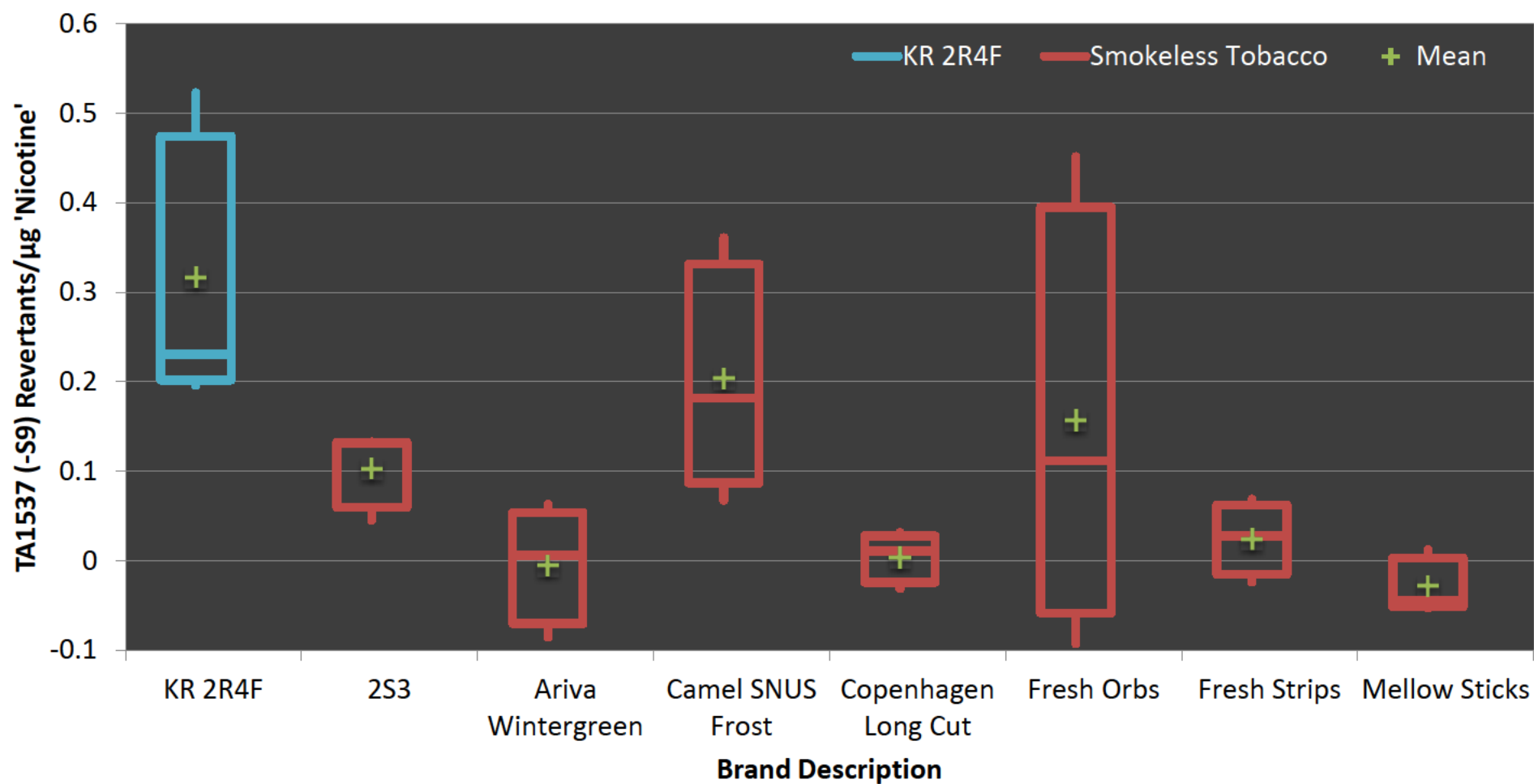
Date 11 December 2009



Test Describe - Comparative

Performed by TA1537 (-S9): Revertants/ $\mu$ g 'Nicotine in CSC' and Revertants/ $\mu$ g 'Extracted Nicotine in DMSO' Slope by Brand Wendy Wagstaff

Date 11 December 2009

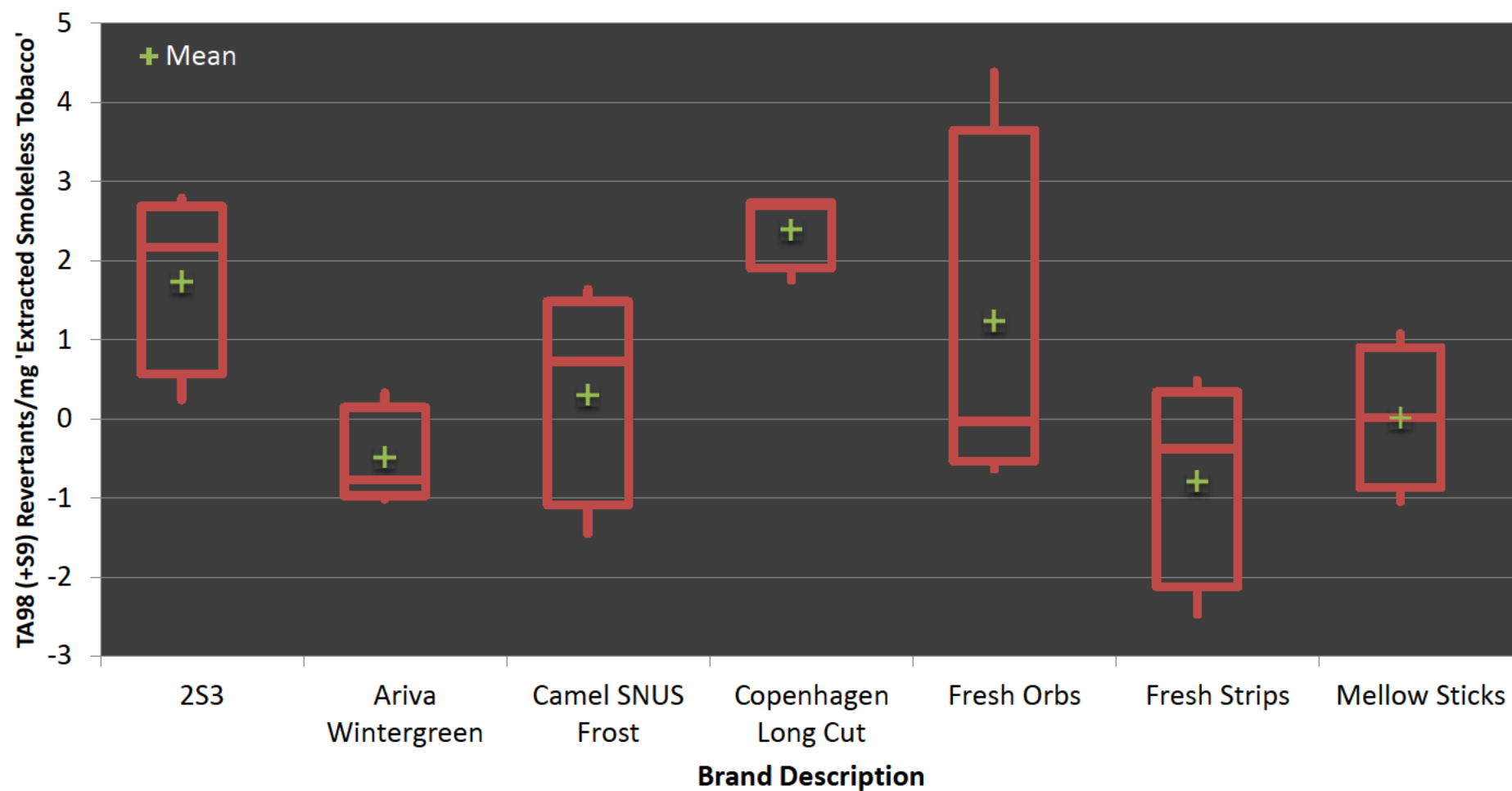




Test Describe - Comparative

Performed by TA98 (+S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

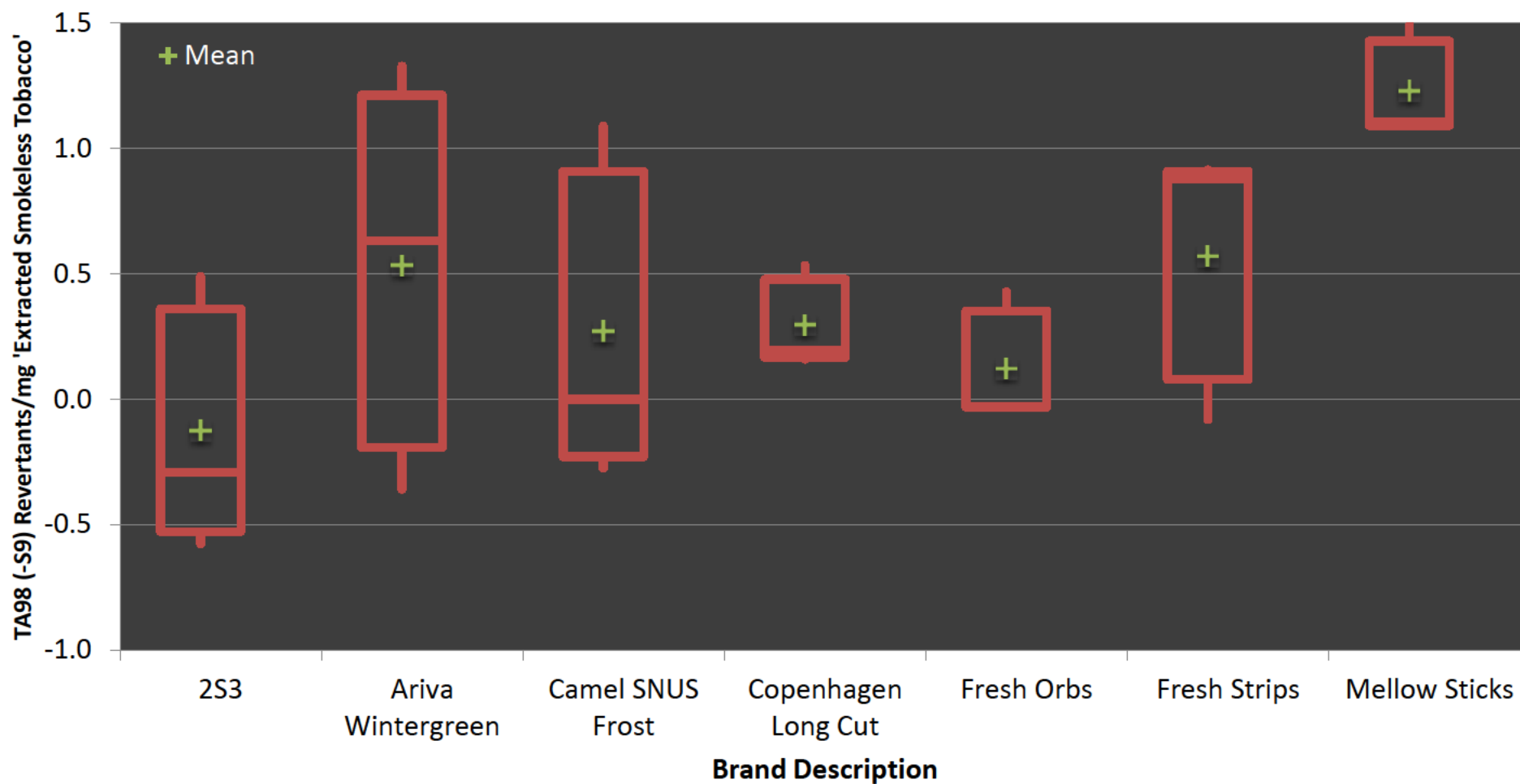
Date 26 October 2009



Test Describe - Comparative

Performed by TA98 (-S9): Revertants/mg 'Extracted Smokeless Tobacco' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009



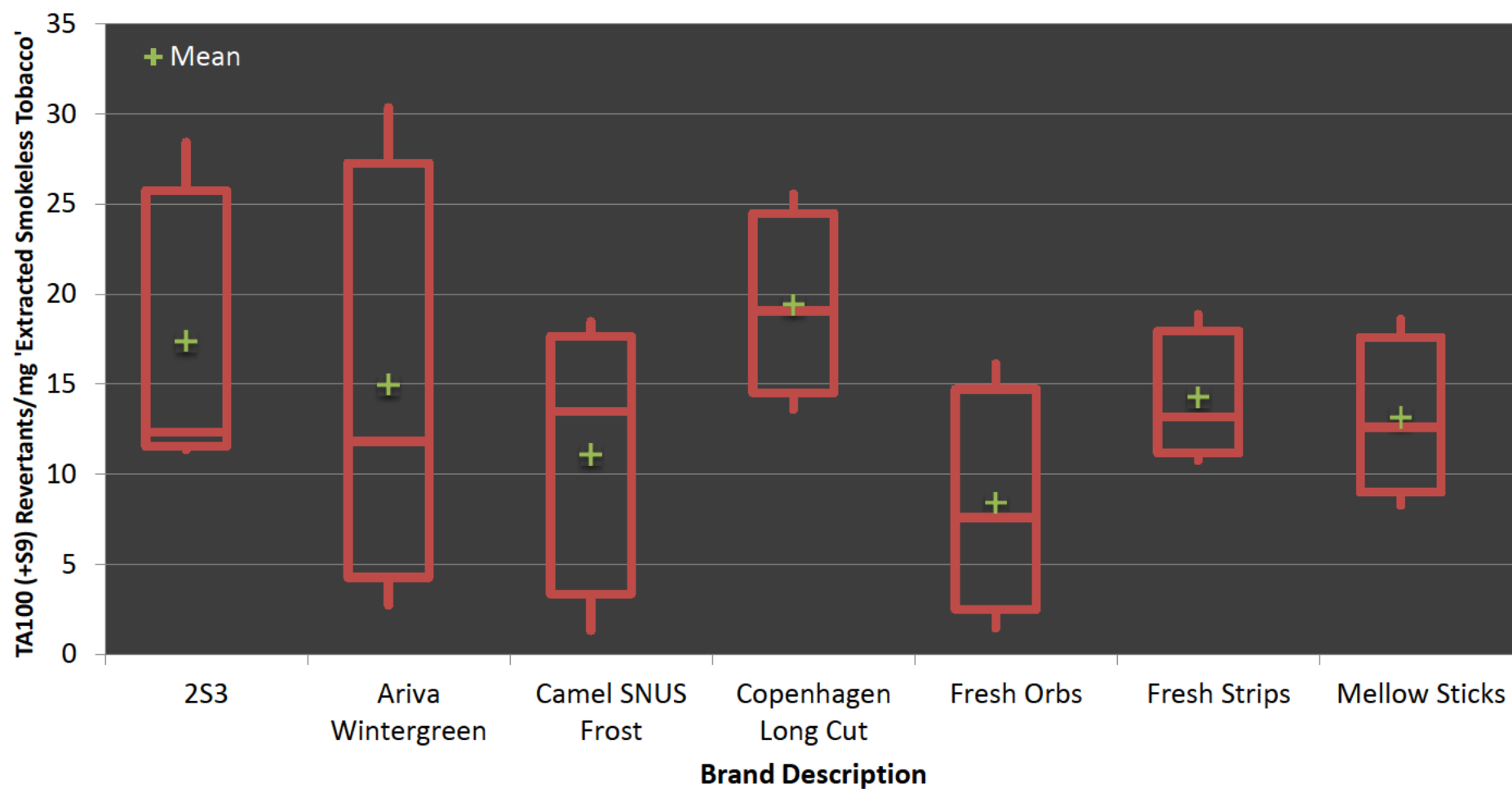
Test Describe - Comparative

Performed by

TA100 (+S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date

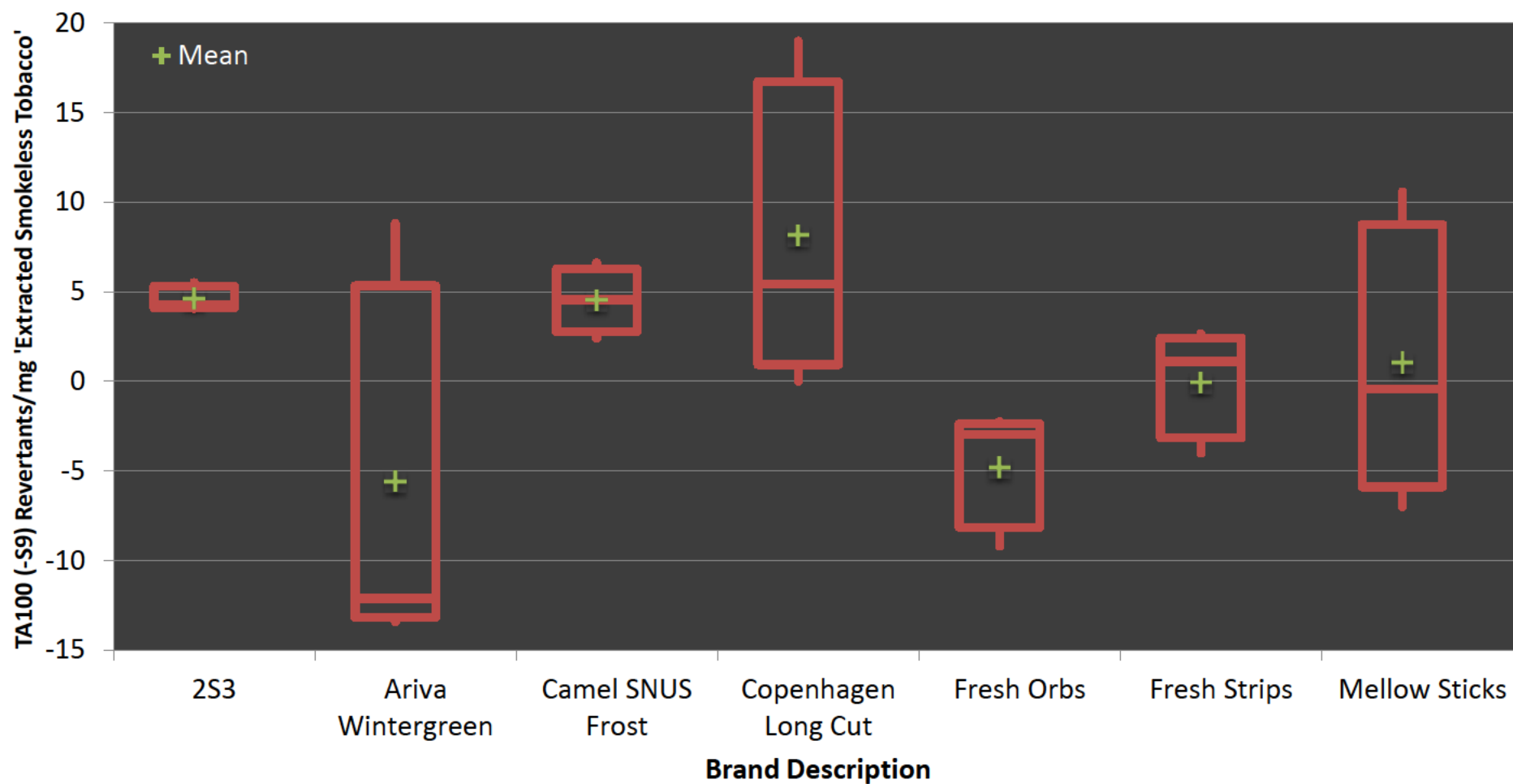
26 October 2009



Test Describe - Comparative

Performed by TA100 (-S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009



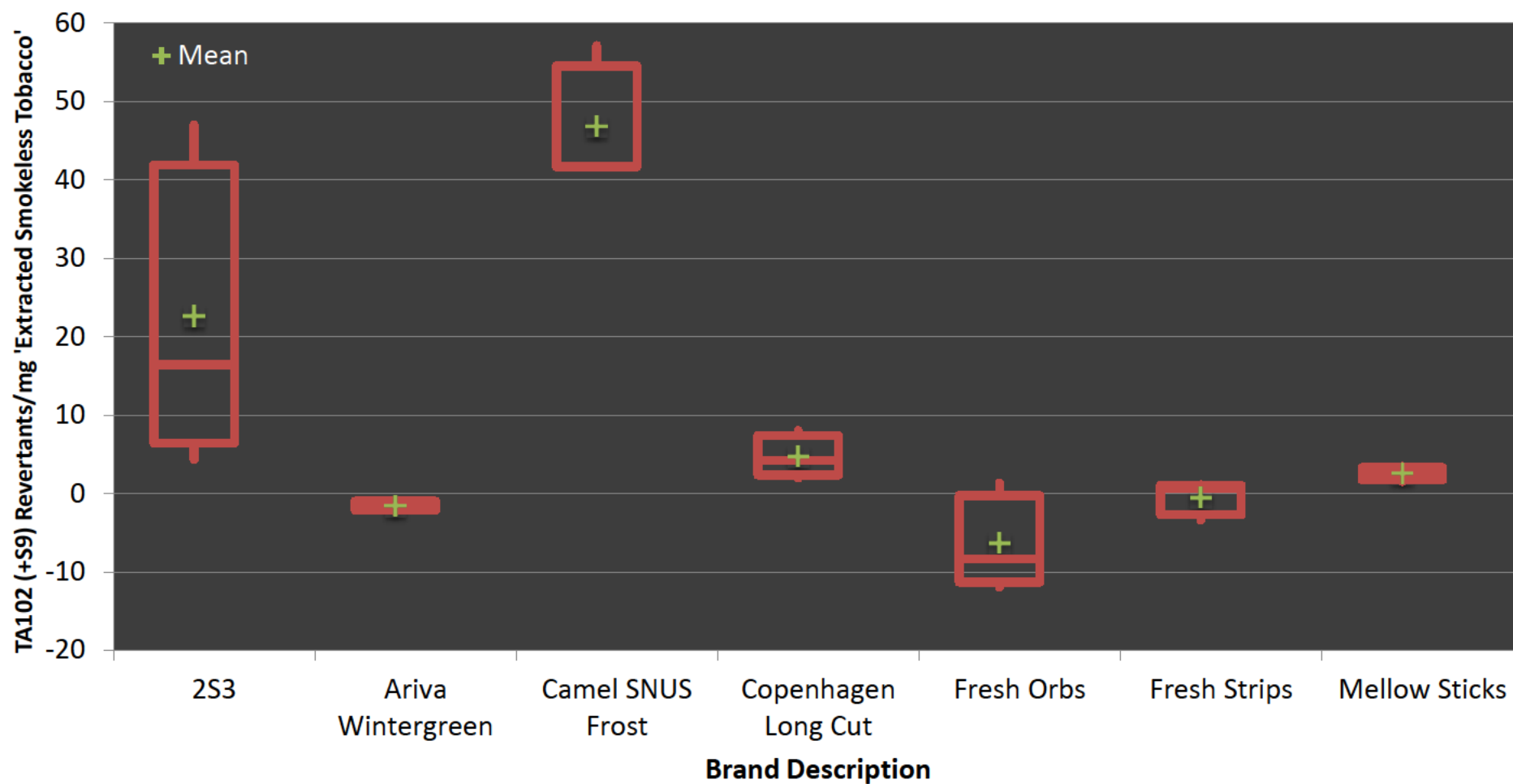
Test Describe - Comparative

Performed by

TA102 (+S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date

26 October 2009



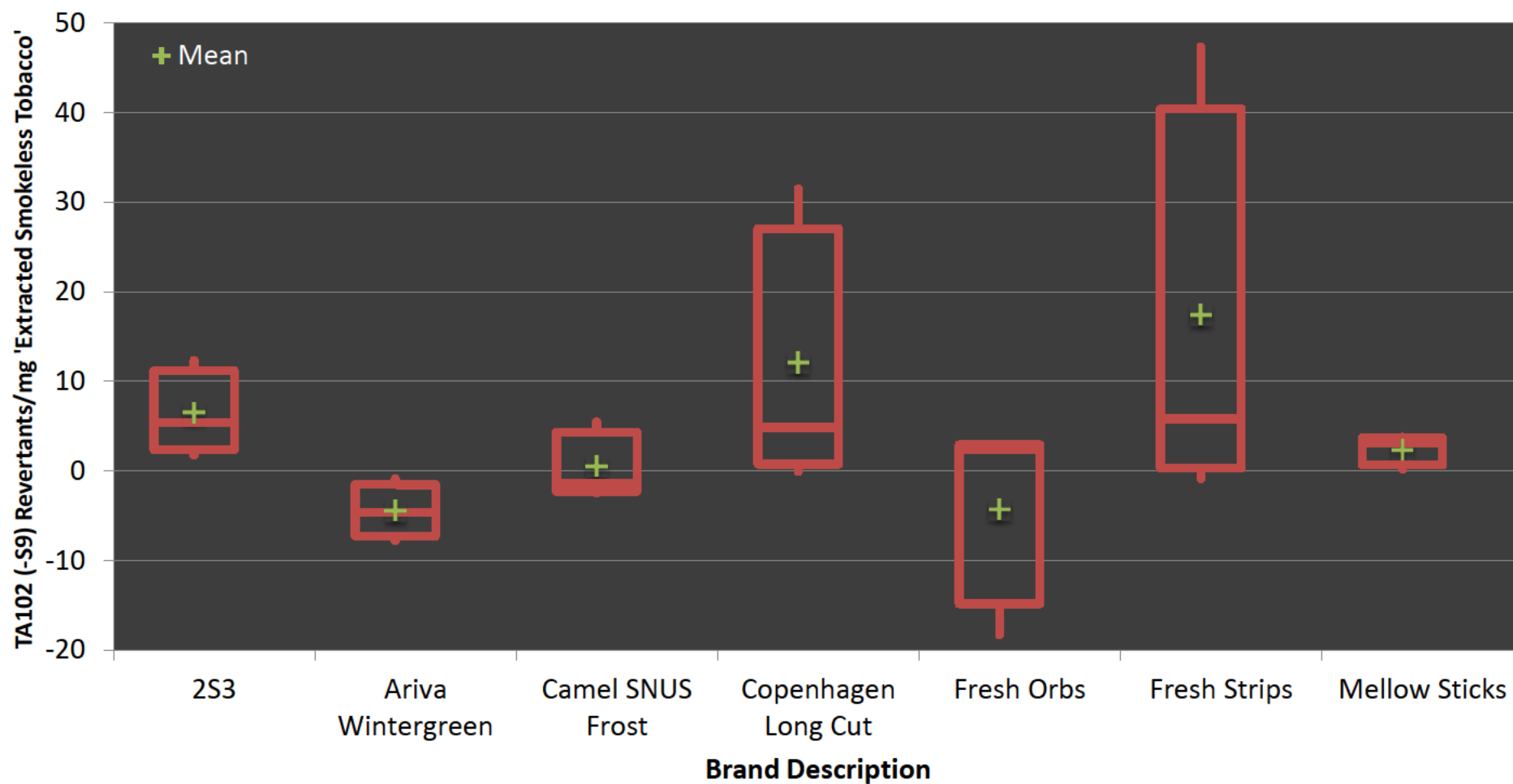
Test Describe - Comparative

Performed by

TA102 (-S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date

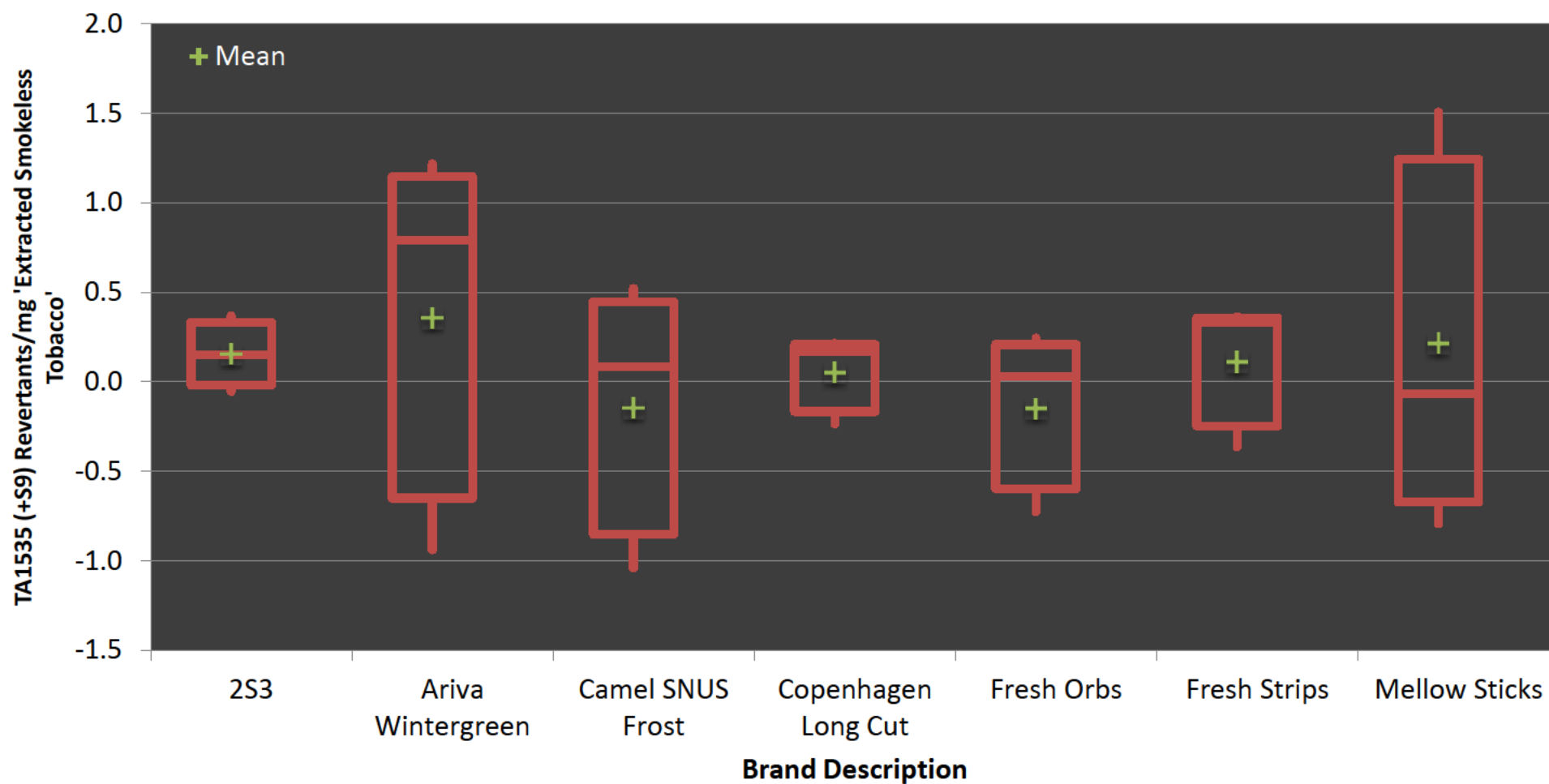
26 October 2009



Test Describe - Comparative

Performed by TA1535 (+S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

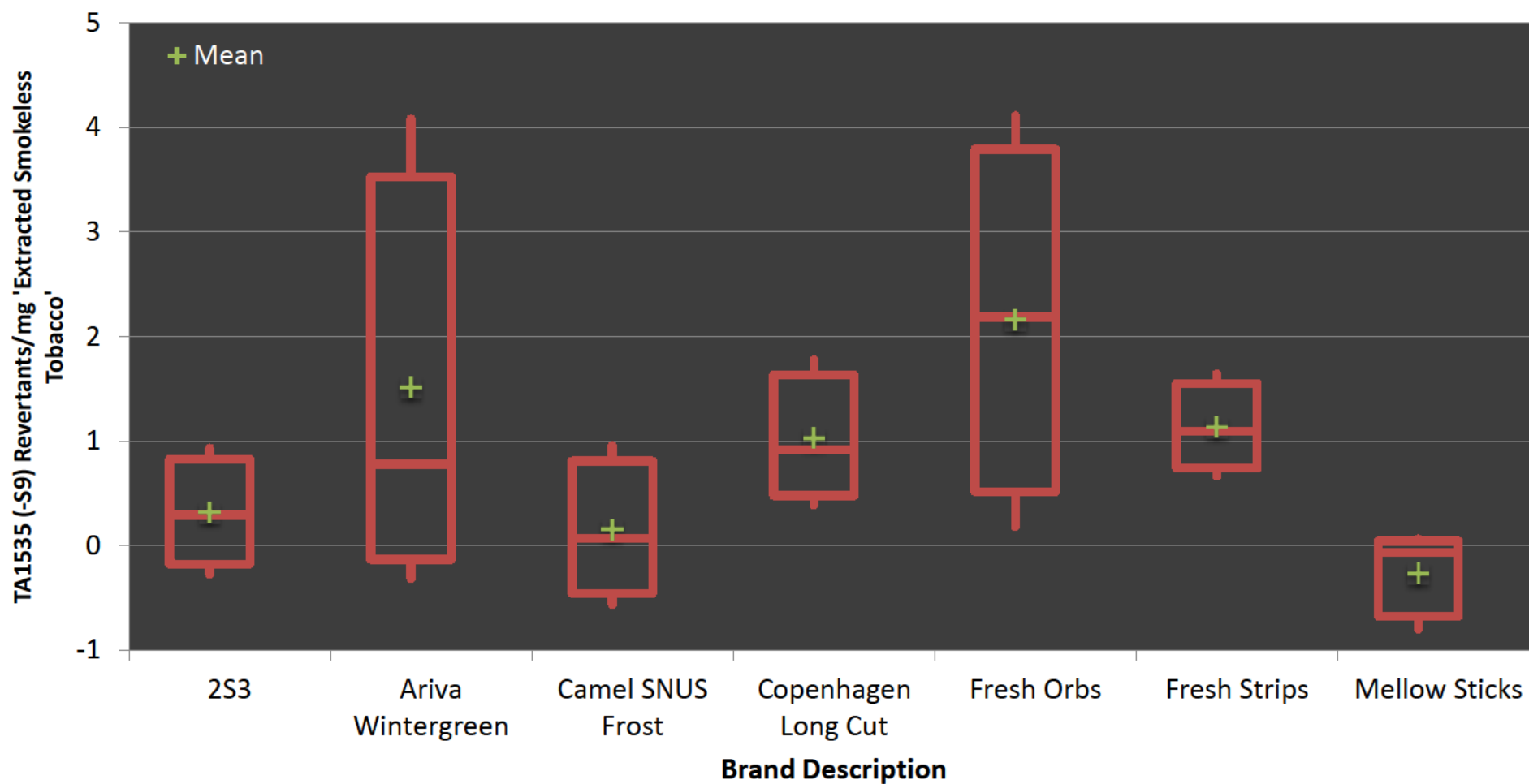
Date 26 October 2009



Test Describe - Comparative

Performed by TA1535 (-S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009

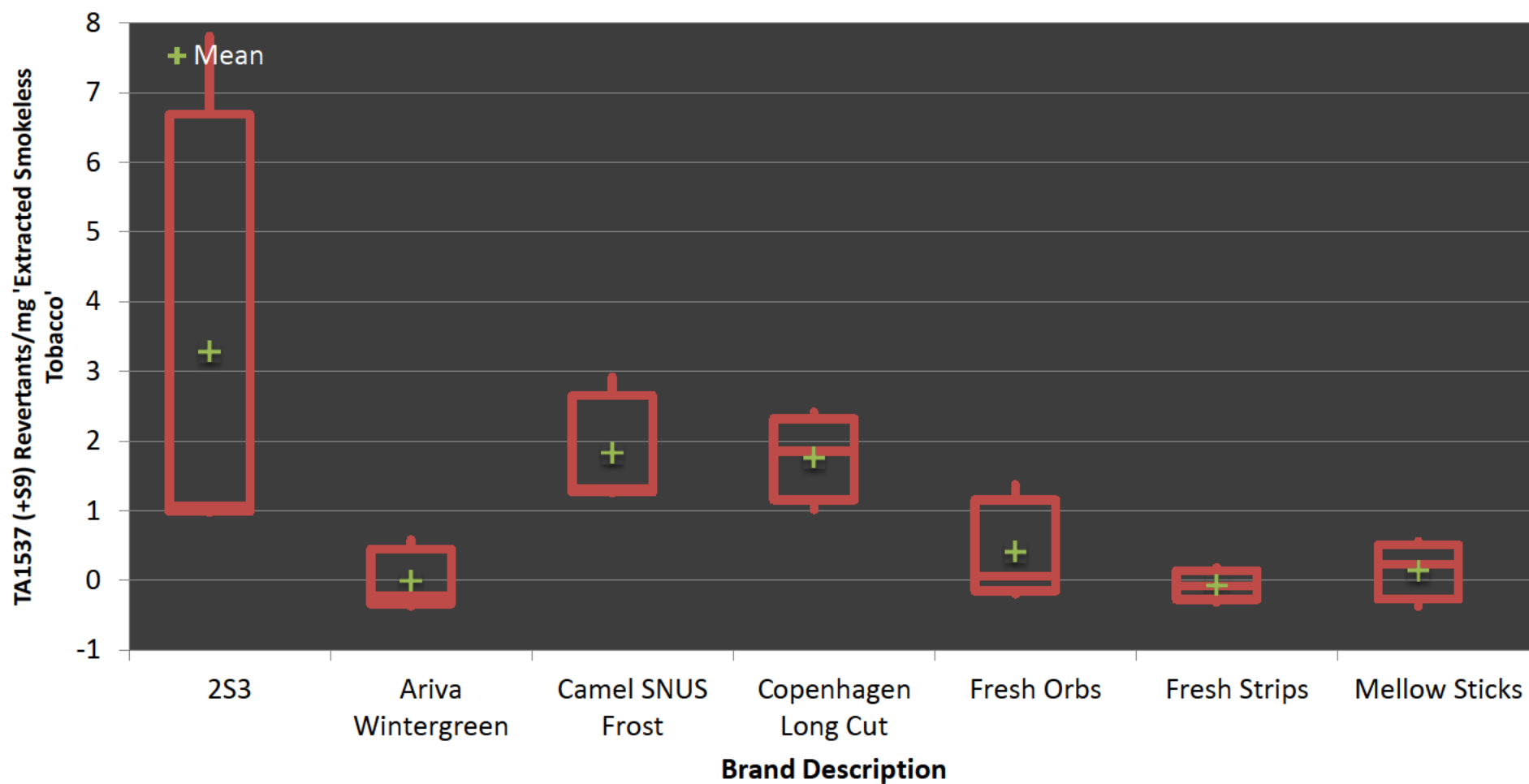




Test Describe - Comparative

Performed by TA1537 (+S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

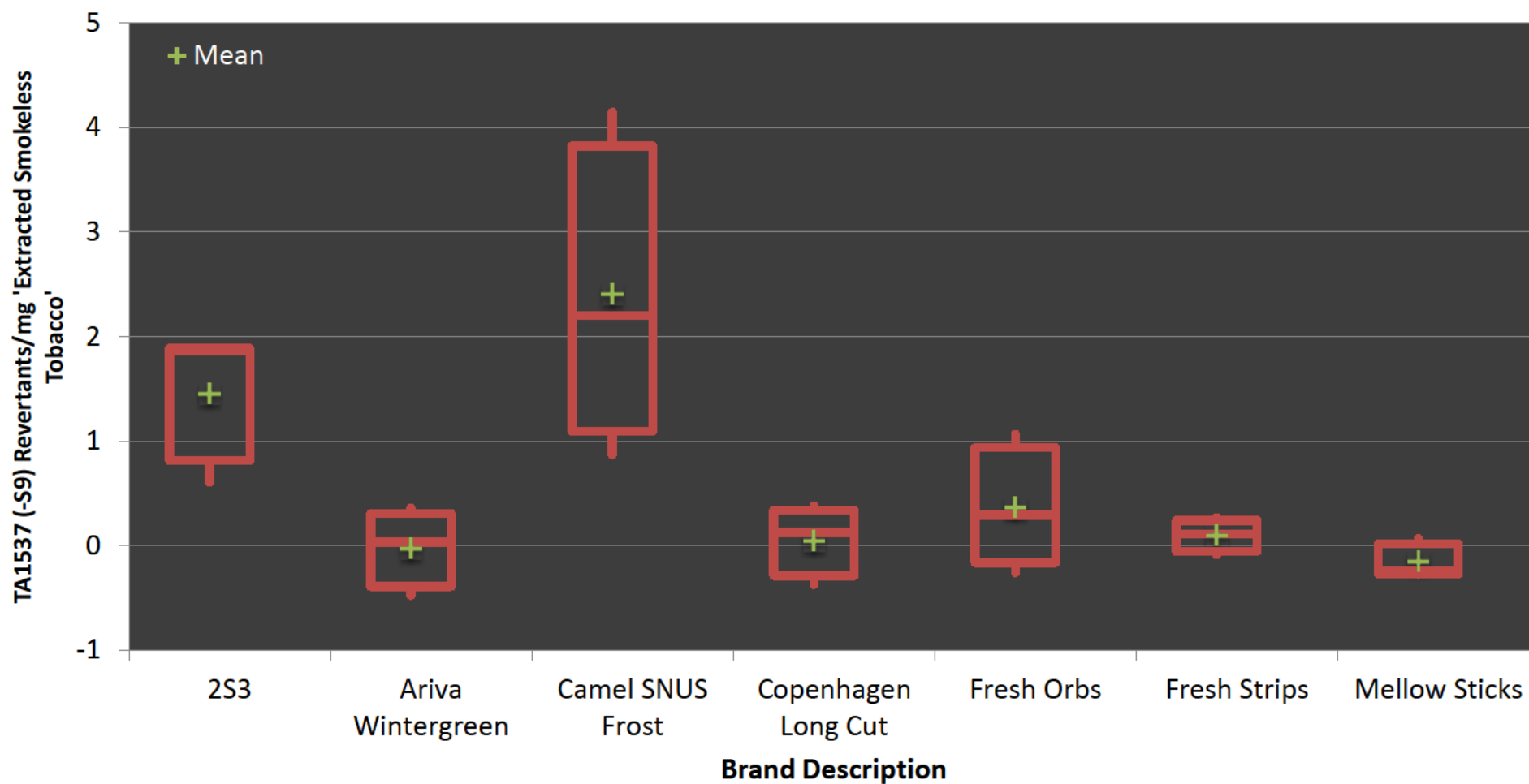
Date 26 October 2009



Test Describe - Comparative

Performed by TA1537 (-S9): Revertants/mg 'Extracted Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

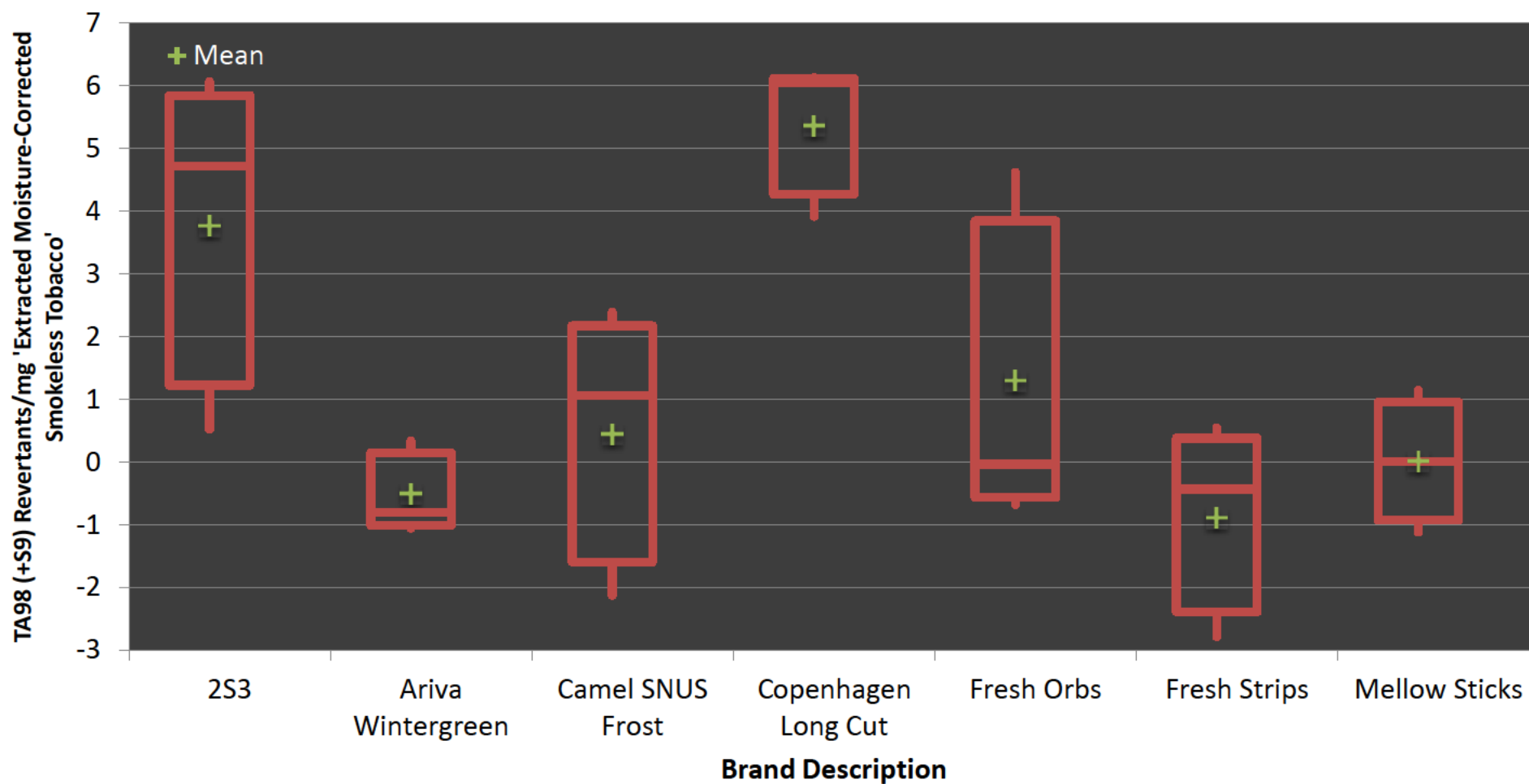
Date 26 October 2009



Test Describe - Comparative

Performed by TA98 (+S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

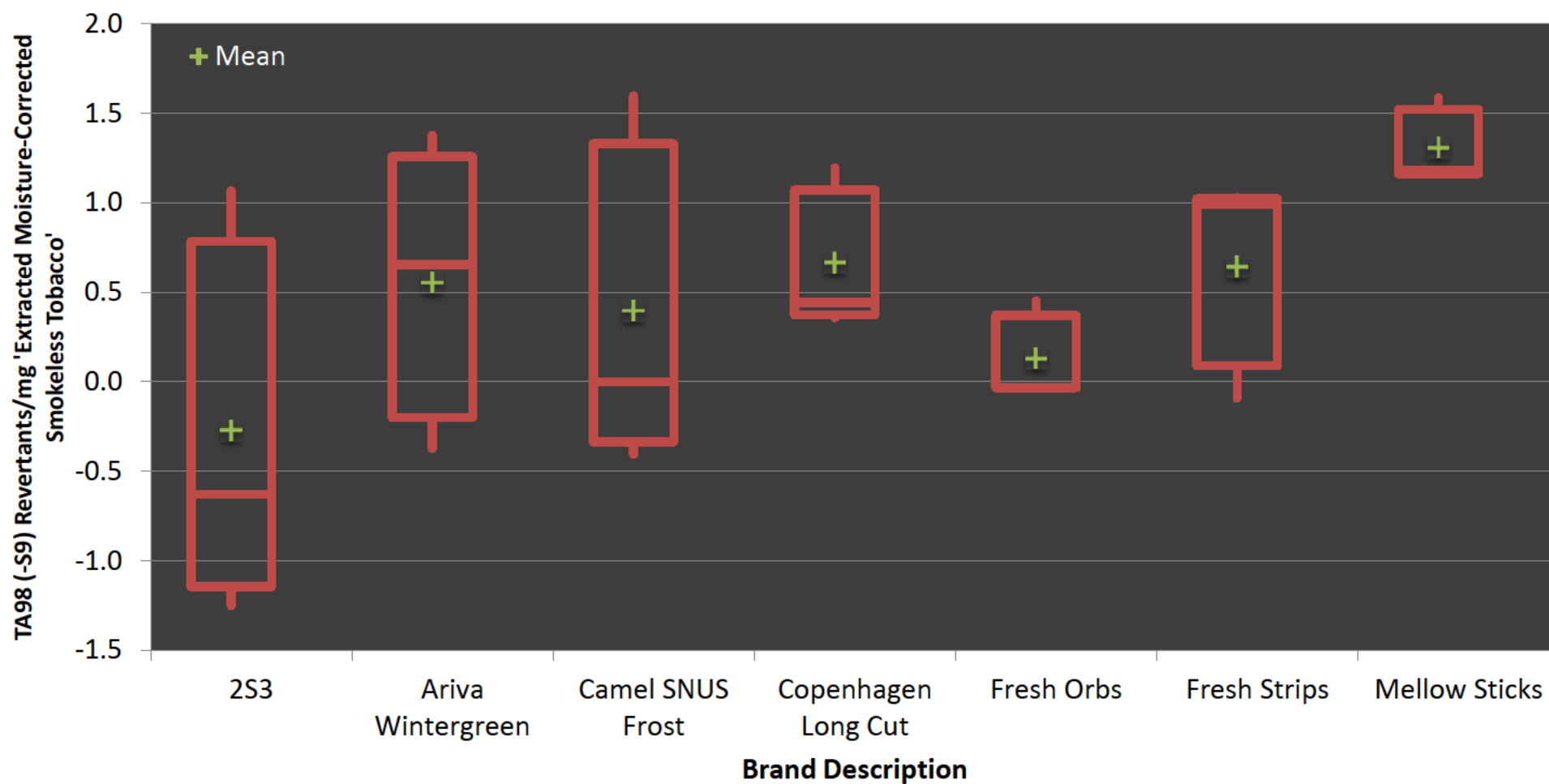
Date 26 October 2009



Test Describe - Comparative

Performed by TA98 (-S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009



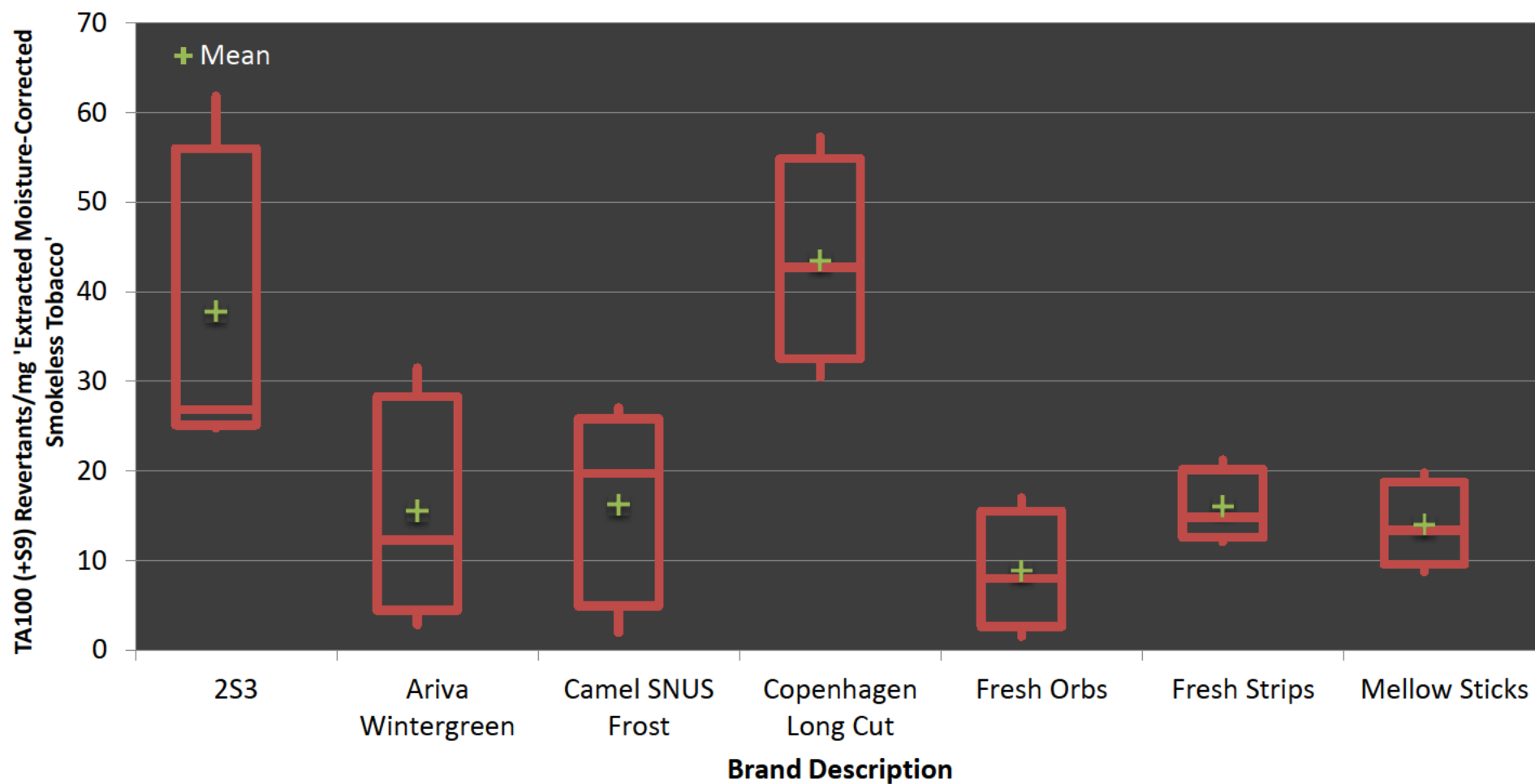
Test Describe - Comparative

Performed by

TA100 (+S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date

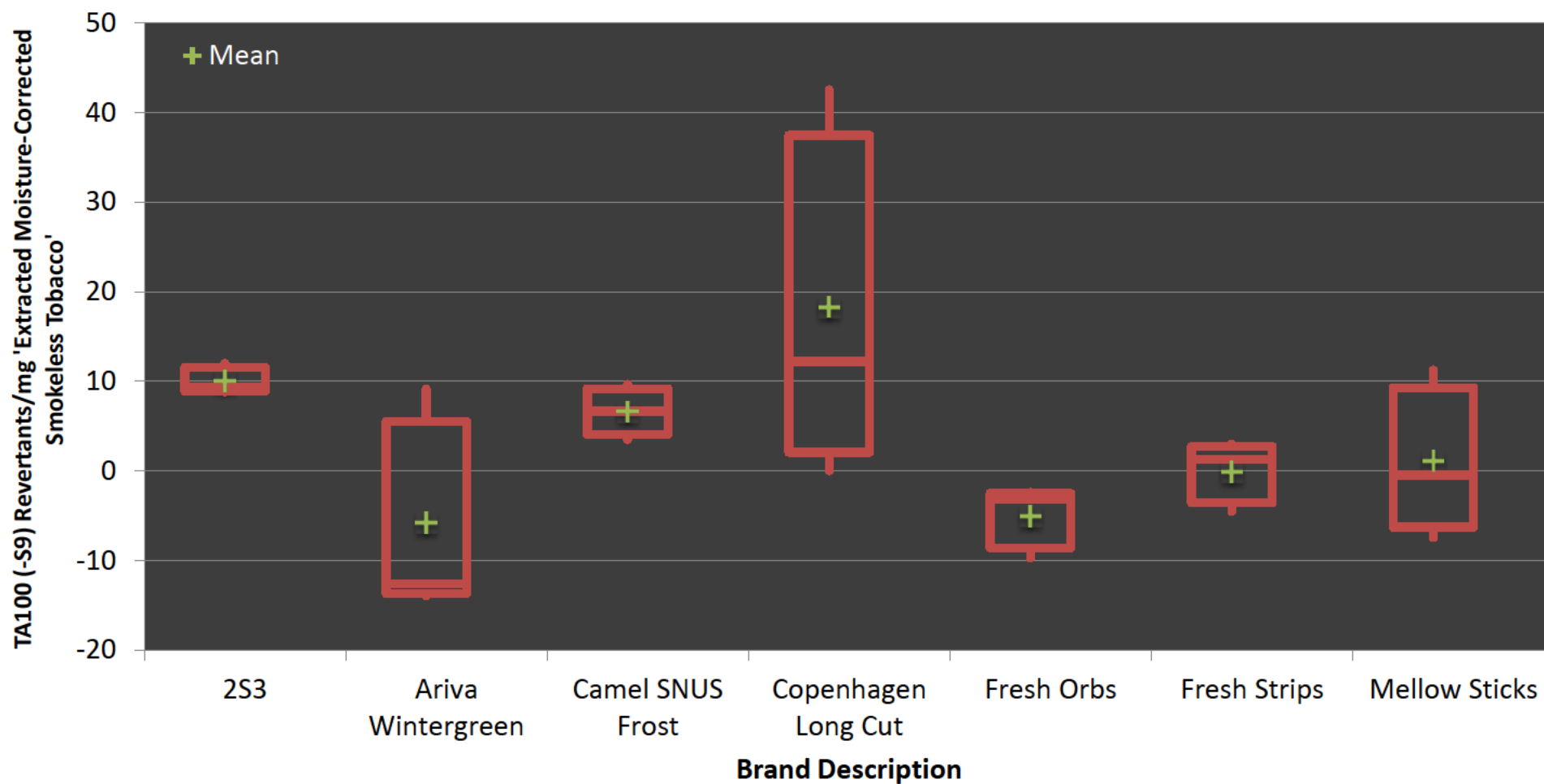
26 October 2009



Test Describe - Comparative

Performed by TA100 (-S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009



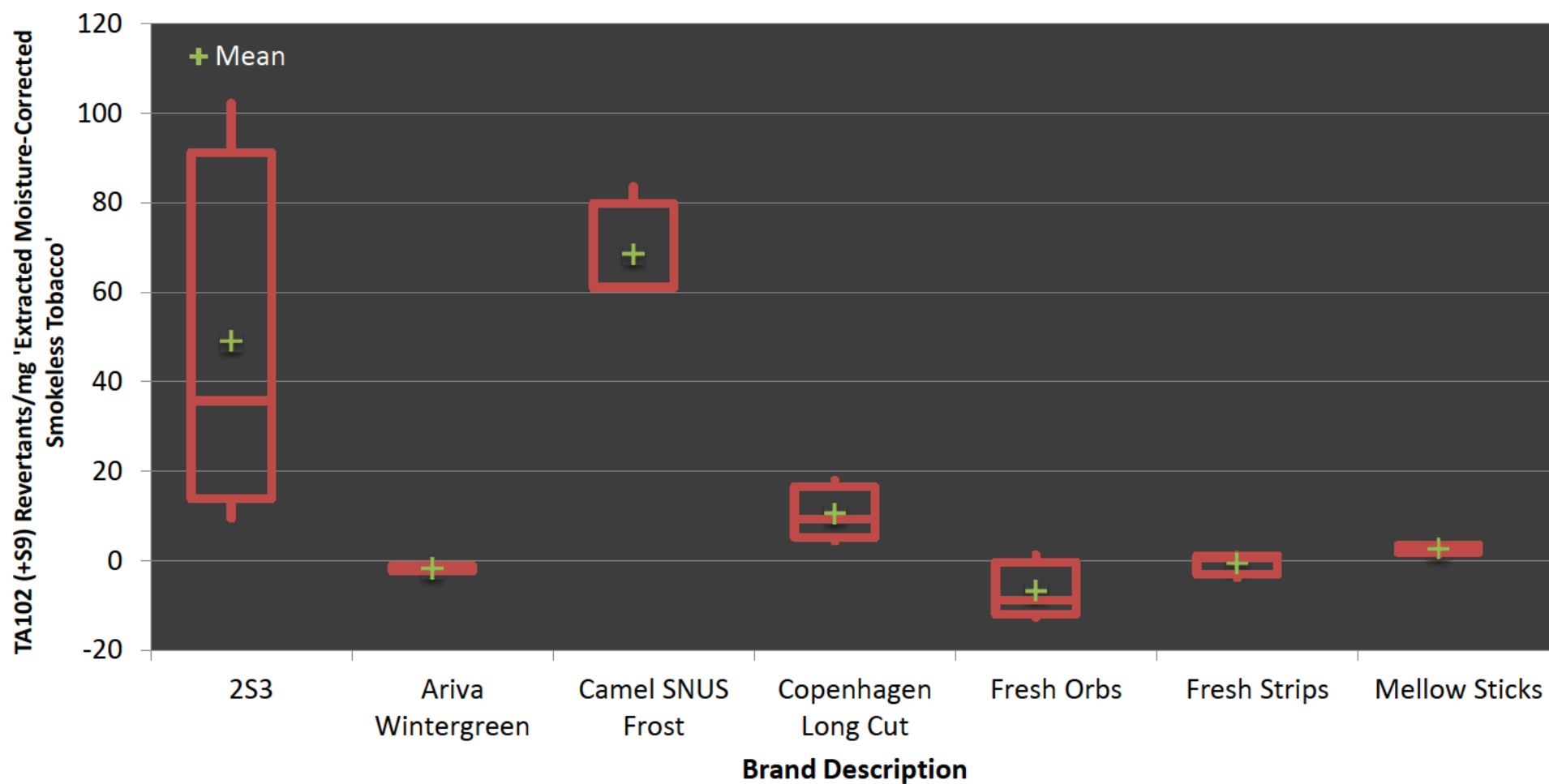
Test Describe - Comparative

Performed by

TA102 (+S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date

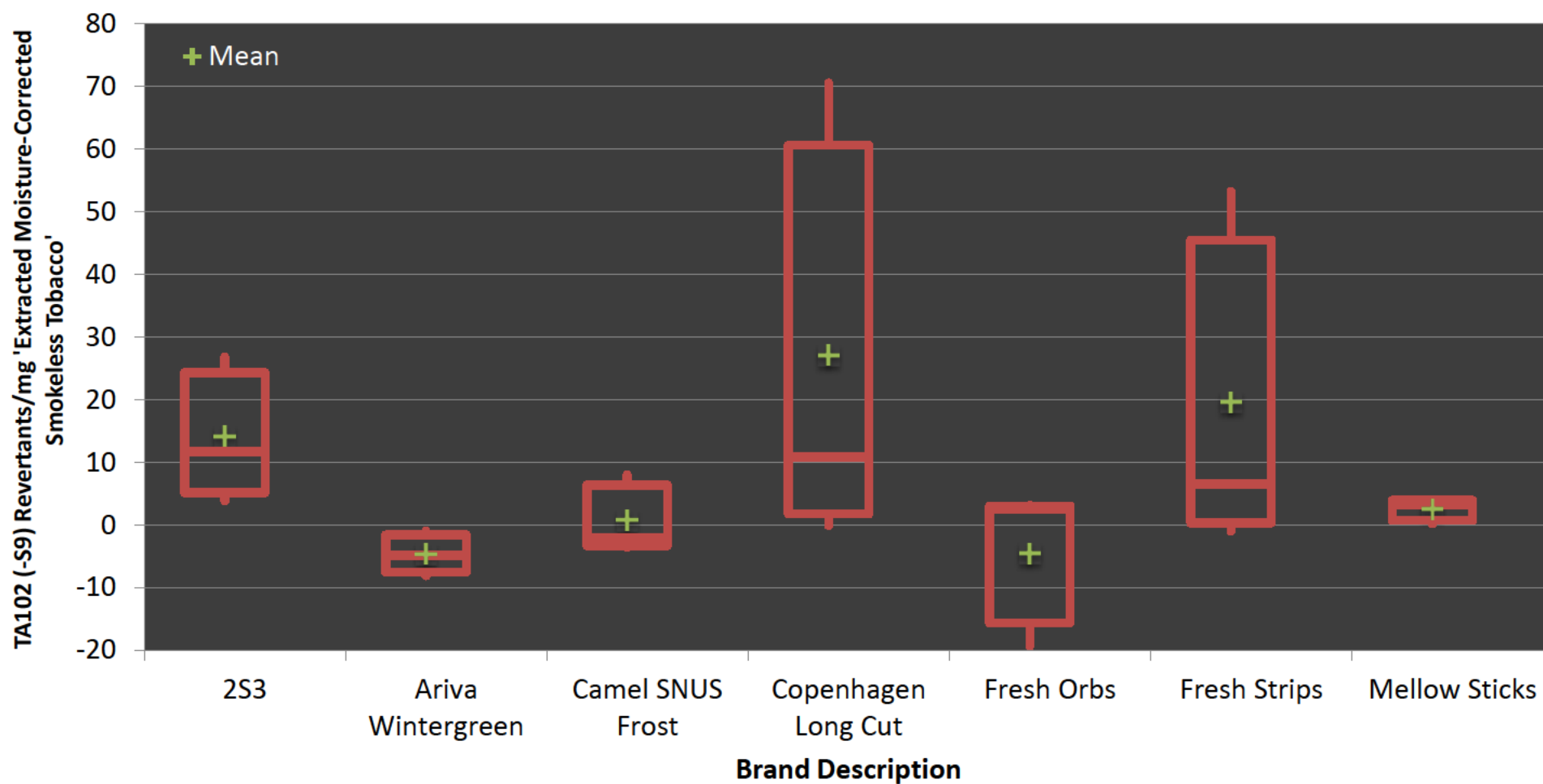
26 October 2009



Test Describe - Comparative

Performed by TA102 (-S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009

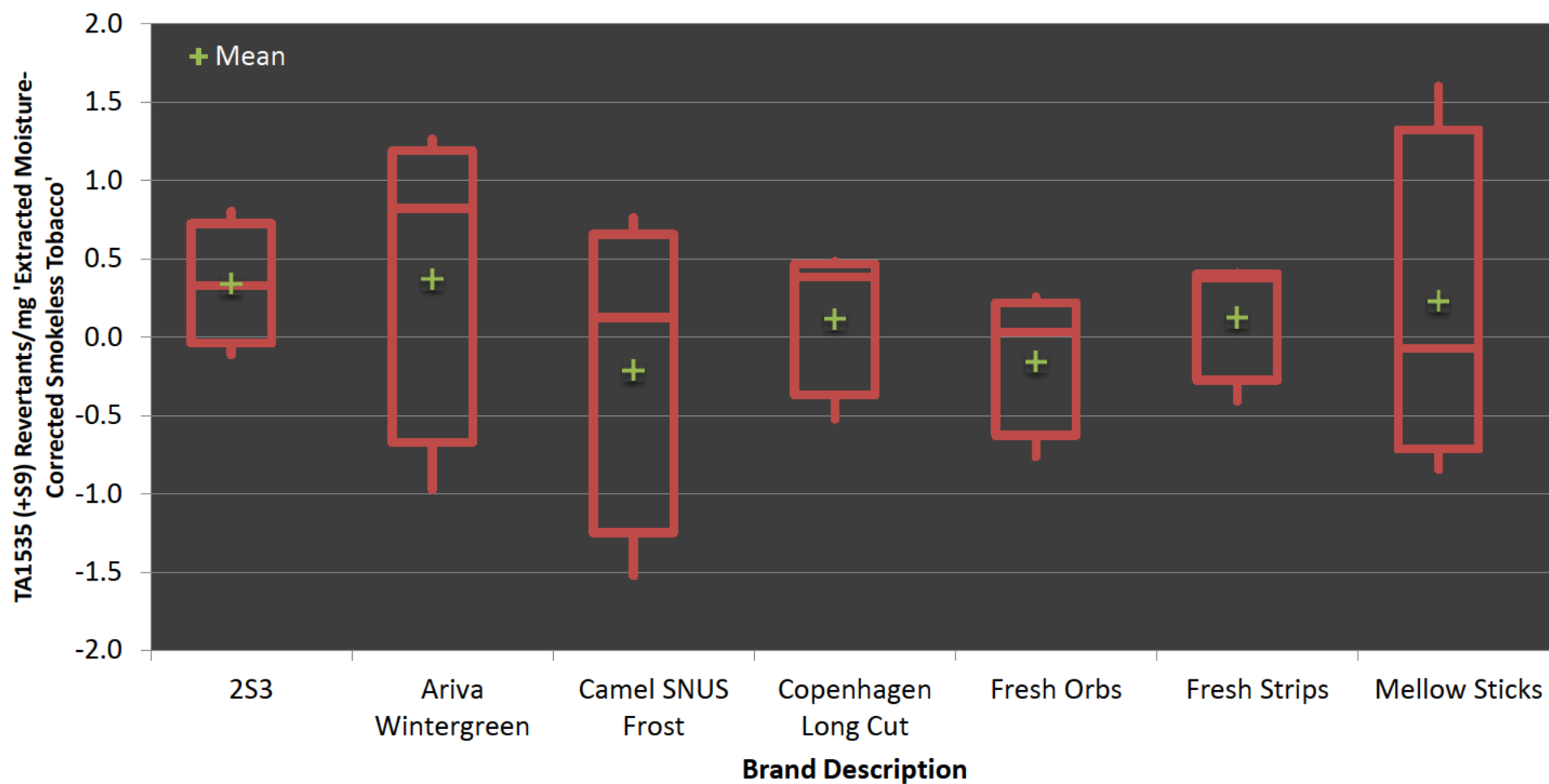




Test Describe - Comparative

Performed by TA1535 (+S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

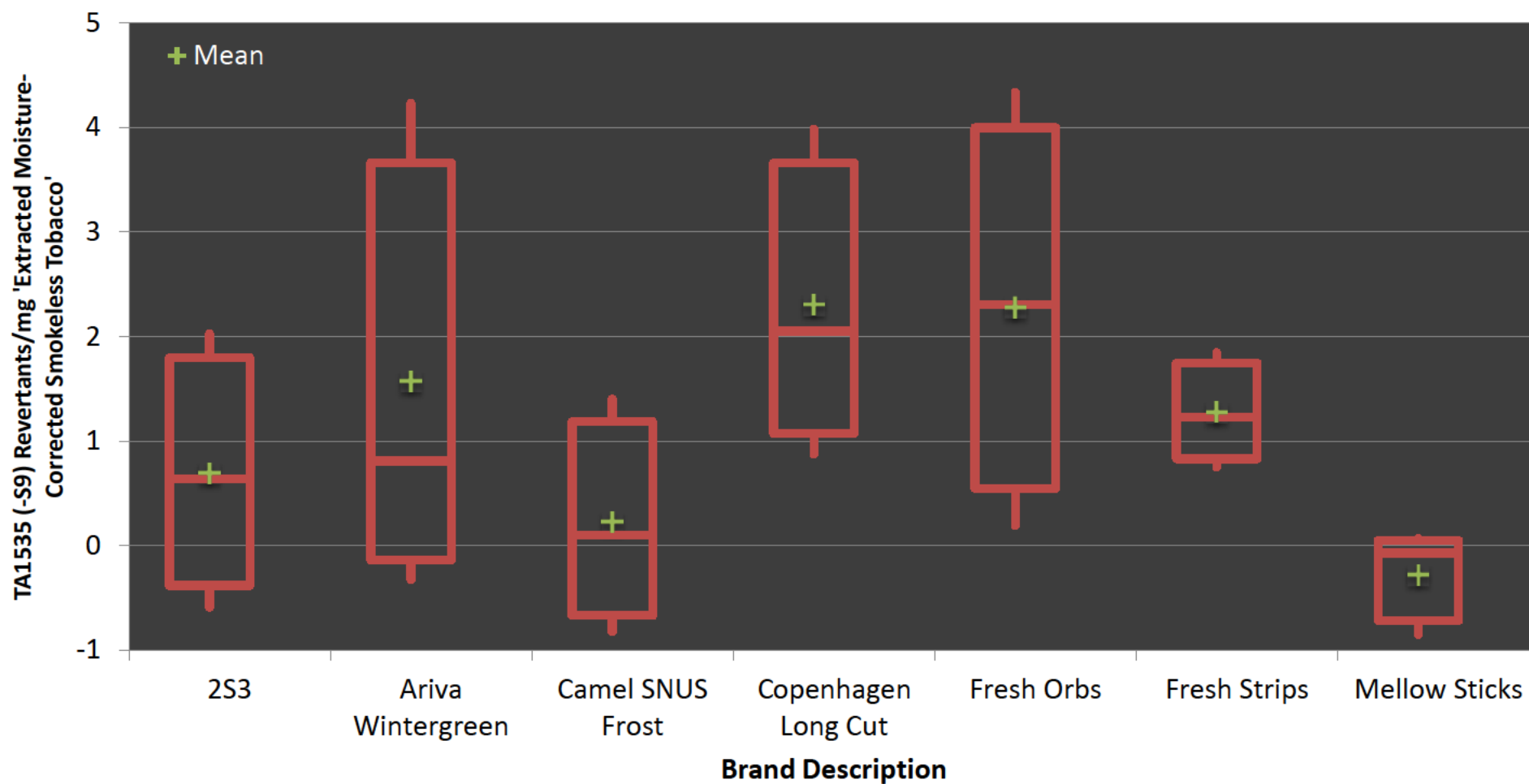
Date 26 October 2009



Test Describe - Comparative

Performed by TA1535 (-S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

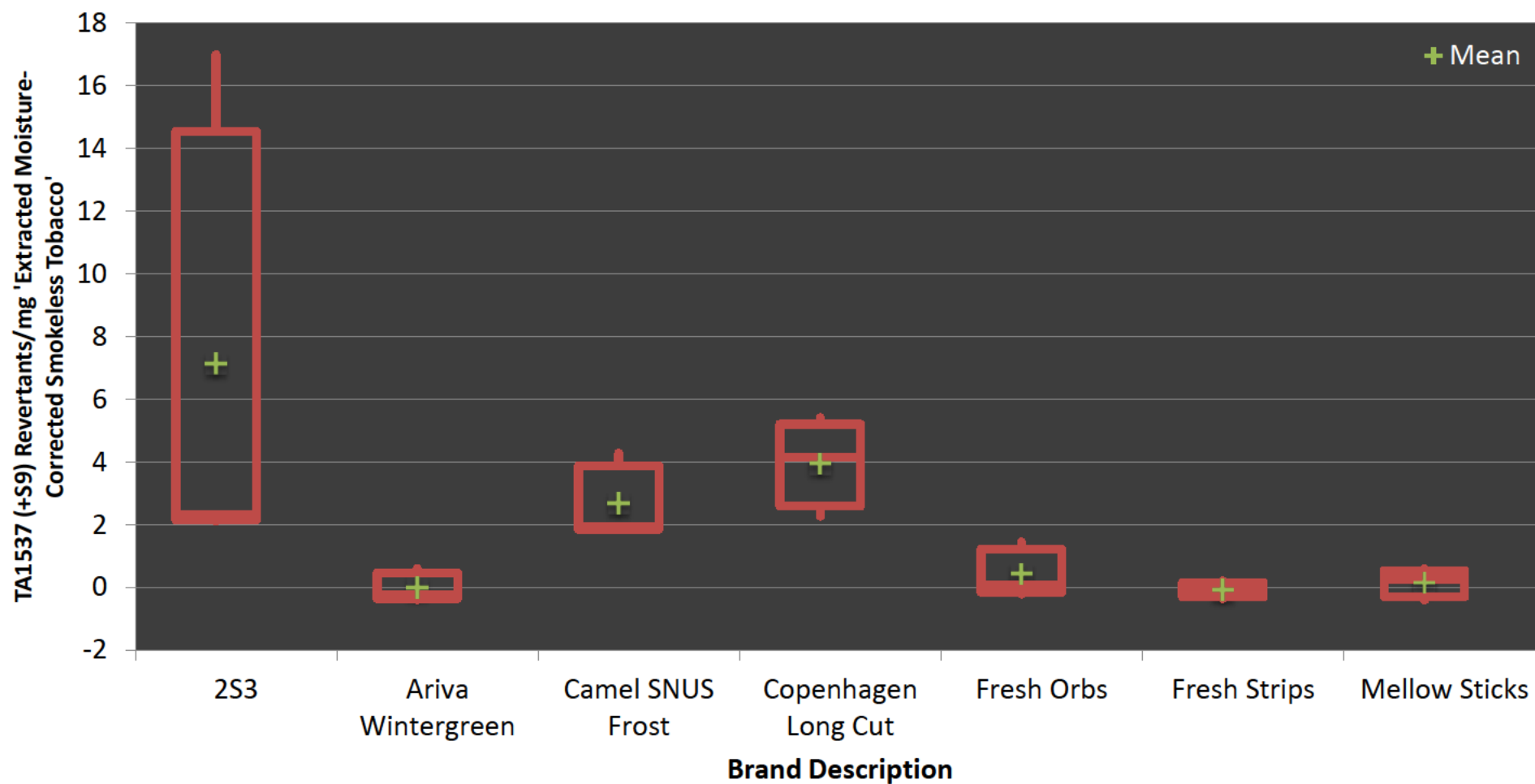
Date 26 October 2009



Test Describe - Comparative

Performed by TA1537 (+S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

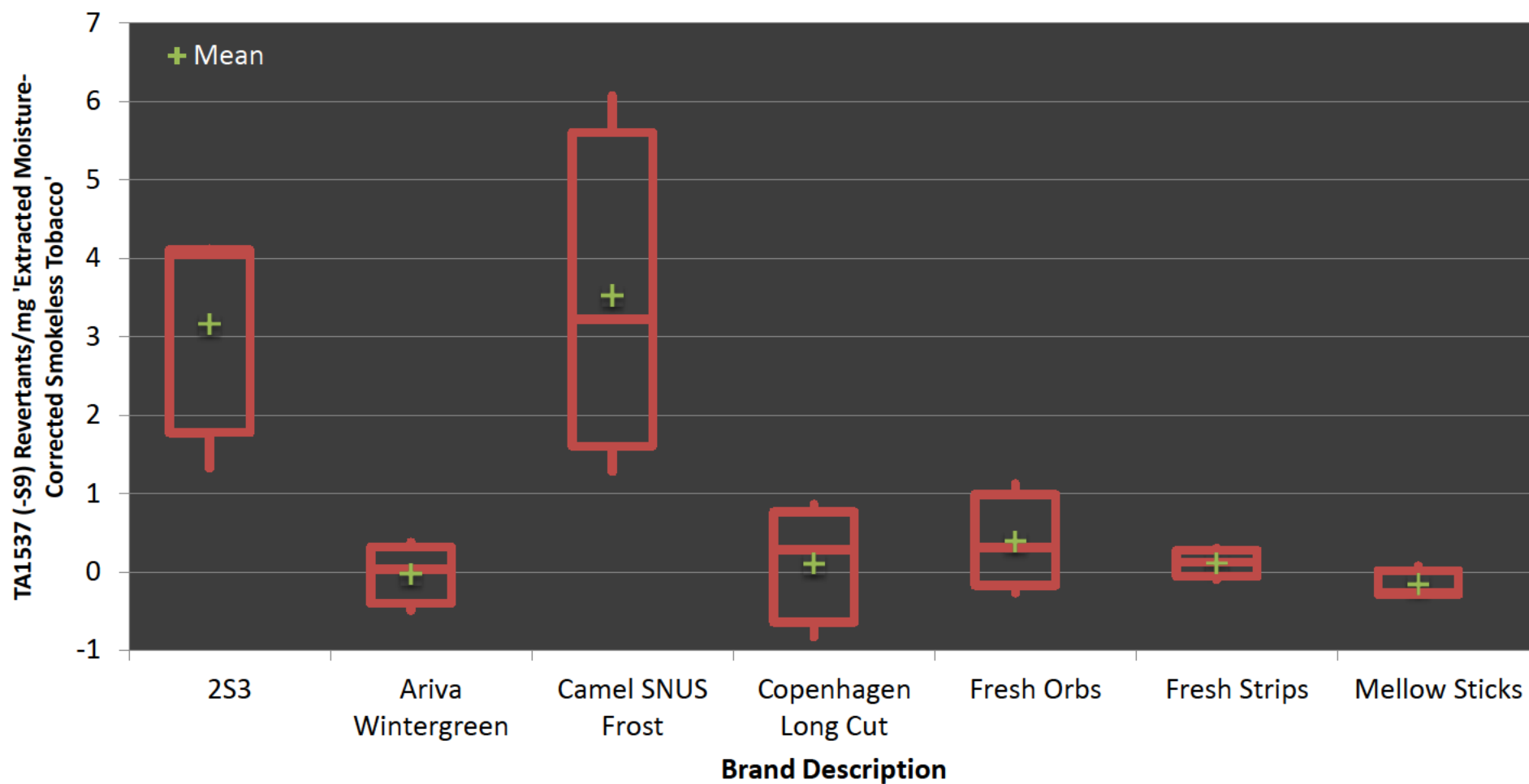
Date 26 October 2009



Test Describe - Comparative

Performed by TA1537 (-S9): Revertants/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' Slope by Brand  
Wendy Wagstaff

Date 26 October 2009



**Slope Analysis of the Linear Portion of the Dose-Response Curve for Smokeless (Revertant Colonies/ $\mu$ g 'Extracted Nicotine in DMSO') and Smoked (Revertant Colonies/ $\mu$ g 'Nicotine in CSC' (KR 2R4F)) Tobacco Products**

| Strain and S9 Activation | Sample ID | Sample Description  | Revertant Colonies/ $\mu$ g 'Extracted Nicotine in DMSO' or Revertant Colonies/ $\mu$ g 'Nicotine in CSC' (KR 2R4F) |        |                       |        |                       |        |   |       |                                    |         |                 |  |
|--------------------------|-----------|---------------------|---|--------|-----------------------|--------|-----------------------|--------|---|-------|------------------------------------|---------|-----------------|--|
|                          |           |                     | Replicate 1   |        | Replicate 2           |        | Replicate 3           |        | Statistics for Replicate 'Nic.' Slope Estimates |       |                                    |         |                 |  |
|                          |           |                     | Dose Range  |        | Dose Range            |        | Dose Range            |        | Standard  |       | t-test p-value ( $H_0$ : mean = 0) |         |                 |  |
|                          |           |                     | ( $\mu$ g Nic./plate)   | slope  | ( $\mu$ g Nic./plate) | slope  | ( $\mu$ g Nic./plate) | slope  | Mean  | Error | 95% C.I.                           | p-value | significance    |  |
| TA98 (+S9)               | 084396    | KR 2R4F             | 0 - 9.4   | 18.118 | 0 - 9.4               | 31.609 | 0 - 9.4               | 28.653 | 26.127  | 4.094 | 8 51 - 43.742                      | 0.024   | significant     |  |
| TA98 (+S9)               | 084394    | Camel SNUS Frost    | 0 - 63.8  | 0.063  | 0 - 71.5              | 0.127  | 0 - 67.2              | -0.120 | 0.023   | 0.074 | 0* - 0.342                         | 0.782   | not significant |  |
| TA98 (+S9)               | 084395    | 2S3                 | 0 - 78  | 0.199  | 0 - 79.7              | 0.017  | 0 - 74.4              | 0.162  | 0.126   | 0.056 | 0* - 0.365                         | 0.152   | not significant |  |
| TA98 (+S9)               | 084454    | Fresh Strips        | 0 - 20  | -0.106 | 0 - 21.6              | 0.124  | 0 - 11.1              | -0.621 | 0*  | 0.220 | 0* - 0.747                         | 0.458   | not significant |  |
| TA98 (+S9)               | 084455    | Mellow Sticks       | 0 - 30.7  | -0.189 | 0 - 29.1              | 0.002  | 0 - 30.9              | 0.193  | 0.002   | 0.110 | 0* - 0.477                         | 0.987   | not significant |  |
| TA98 (+S9)               | 084456    | Copenhagen Long Cut | 0 - 64.6  | 0.235  | 0 - 66.3              | 0.226  | 0 - 67.7              | 0.144  | 0.202   | 0.029 | 0.076 - 0.327                      | 0.020   | significant     |  |
| TA98 (+S9)               | 084457    | Ariva Wintergreen   | 0 - 29.5  | 0.061  | 0 - 30.8              | -0.139 | 0 - 31.8              | -0.177 | 0*  | 0.074 | 0* - 0.233                         | 0.370   | not significant |  |
| TA98 (+S9)               | 084458    | Fresh Orbs          | 0 - 13.1  | -0.014 | 0 - 14.4              | -0.246 | 0 - 7.7               | 1.591  | 0.444   | 0.577 | 0* - 2.928                         | 0.523   | not significant |  |
| TA100 (+S9)              | 084396    | KR 2R4F             | 0 - 18.8  | 8.207  | 0 - 18.8              | 9.973  | 0 - 18.8              | 11.541 | 9.907   | 0.963 | 5.76 - 14.051                      | 0.009   | significant     |  |
| TA100 (+S9)              | 084394    | Camel SNUS Frost    | 0 - 16  | 0.116  | 0 - 17.9              | 1.050  | 0 - 16.8              | 1.528  | 0.898   | 0.414 | 0* - 2.681                         | 0.163   | not significant |  |
| TA100 (+S9)              | 084395    | 2S3                 | 0 - 15.6  | 0.881  | 0 - 15.9              | 1.982  | 0 - 14.9              | 0.852  | 1.238   | 0.372 | 0* - 2.839                         | 0.080   | not significant |  |
| TA100 (+S9)              | 084454    | Fresh Strips        | 0 - 5   | 5.250  | 0 - 10.8              | 2.772  | 0 - 5.5               | 3.314  | 3.779   | 0.752 | 0.542 - 7.015                      | 0.037   | significant     |  |
| TA100 (+S9)              | 084455    | Mellow Sticks       | 0 - 15.3  | 2.282  | 0 - 7.3               | 3.560  | 0 - 15.4              | 1.491  | 2.445   | 0.603 | 0* - 5.037                         | 0.056   | not significant |  |
| TA100 (+S9)              | 084456    | Copenhagen Long Cut | 0 - 32.3  | 1.172  | 0 - 16.6              | 2.143  | 0 - 16.9              | 1.568  | 1.628   | 0.282 | 0.415 - 2.841                      | 0.029   | significant     |  |
| TA100 (+S9)              | 084457    | Ariva Wintergreen   | 0 - 5.9   | 5.725  | 0 - 30.8              | 0.498  | 0 - 7.9               | 2.067  | 2.763   | 1.549 | 0* - 9.426                         | 0.216   | not significant |  |
| TA100 (+S9)              | 084458    | Fresh Orbs          | 0 - 6.6   | 0.628  | 0 - 3.6               | 2.930  | 0 - 3.8               | 5.861  | 3.140   | 1.514 | 0* - 9.655                         | 0.174   | not significant |  |
| TA102 (+S9)              | 084396    | KR 2R4F             | 0 - 37.5  | -0.248 | 0 - 37.5              | 1.030  | 0 - 37.5              | 1.580  | 0.787   | 0.541 | 0* - 3.117                         | 0.283   | not significant |  |
| TA102 (+S9)              | 084394    | Camel SNUS Frost    | 0 - 12.8  | 3.635  | 0 - 17.9              | 4.441  | 0 - 16.8              | 3.444  | 3.840   | 0.306 | 2.525 - 5.155                      | 0.006   | significant     |  |
| TA102 (+S9)              | 084395    | 2S3                 | 0 - 15.6  | 3.351  | 0 - 79.7              | 0.305  | 0 - 18.6              | 1.229  | 1.629   | 0.902 | 0* - 5.508                         | 0.213   | not significant |  |
| TA102 (+S9)              | 084454    | Fresh Strips        | 0 - 20  | 0.309  | 0 - 21.6              | -0.865 | 0 - 22.1              | 0.168  | 0*  | 0.370 | 0* - 1.463                         | 0.760   | not significant |  |
| TA102 (+S9)              | 084455    | Mellow Sticks       | 0 - 30.7  | 0.627  | 0 - 29.1              | 0.293  | 0 - 30.9              | 0.482  | 0.467   | 0.097 | 0.051 - 0.884                      | 0.040   | significant     |  |
| TA102 (+S9)              | 084456    | Copenhagen Long Cut | 0 - 64.6  | 0.691  | 0 - 66.3              | 0.168  | 0 - 67.7              | 0.343  | 0.401   | 0.154 | 0* - 1.063                         | 0.121   | not significant |  |
| TA102 (+S9)              | 084457    | Ariva Wintergreen   | 0 - 29.5  | -0.423 | 0 - 30.8              | -0.151 | 0 - 31.8              | -0.296 | 0*  | 0.079 | 0* - 0.049                         | 0.067   | not significant |  |
| TA102 (+S9)              | 084458    | Fresh Orbs          | 0 - 13.1  | -5.048 | 0 - 14.4              | 0.518  | 0 - 15.3              | -3.032 | 0*  | 1.627 | 0* - 4.48                          | 0.261   | not significant |  |
| TA1535 (+S9)             | 084396    | KR 2R4F             | 0 - 37.5  | 0.186  | 0 - 37.5              | 0.077  | 0 - 37.5              | 0.110  | 0.124   | 0.032 | 0* - 0.263                         | 0.062   | not significant |  |
| TA1535 (+S9)             | 084394    | Camel SNUS Frost    | 0 - 63.8  | 0.007  | 0 - 71.5              | 0.041  | 0 - 67.2              | -0.086 | 0*  | 0.038 | 0* - 0.15                          | 0.770   | not significant |  |
| TA1535 (+S9)             | 084395    | 2S3                 | 0 - 78  | 0.026  | 0 - 79.7              | 0.010  | 0 - 74.4              | -0.004 | 0.011   | 0.009 | 0* - 0.049                         | 0.335   | not significant |  |
| TA1535 (+S9)             | 084454    | Fresh Strips        | 0 - 20  | 0.101  | 0 - 21.6              | 0.086  | 0 - 22.1              | -0.091 | 0.032   | 0.062 | 0* - 0.297                         | 0.656   | not significant |  |
| TA1535 (+S9)             | 084455    | Mellow Sticks       | 0 - 30.7  | -0.012 | 0 - 29.1              | -0.152 | 0 - 15.4              | 0.271  | 0.036   | 0.124 | 0* - 0.57                          | 0.801   | not significant |  |
| TA1535 (+S9)             | 084456    | Copenhagen Long Cut | 0 - 64.6  | 0.015  | 0 - 66.3              | 0.018  | 0 - 67.7              | -0.019 | 0.005   | 0.012 | 0* - 0.056                         | 0.738   | not significant |  |
| TA1535 (+S9)             | 084457    | Ariva Wintergreen   | 0 - 29.5  | 0.230  | 0 - 30.8              | 0.143  | 0 - 31.8              | -0.164 | 0.069   | 0.119 | 0* - 0.583                         | 0.619   | not significant |  |
| TA1535 (+S9)             | 084458    | Fresh Orbs          | 0 - 13.1  | 0.103  | 0 - 14.4              | 0.012  | 0 - 15.3              | -0.262 | 0*  | 0.110 | 0* - 0.424                         | 0.699   | not significant |  |
| TA1537 (+S9)             | 084396    | KR 2R4F             | 0 - 18.8  | 3.985  | 0 - 9.4               | 4.206  | 0 - 9.4               | 4.526  | 4.239   | 0.157 | 3.56 - 4.914                       | 0.001   | significant     |  |
| TA1537 (+S9)             | 084394    | Camel SNUS Frost    | 0 - 31.9  | 0.254  | 0 - 71.5              | 0.098  | 0 - 67.2              | 0.109  | 0.154   | 0.050 | 0* - 0.37                          | 0.093   | not significant |  |
| TA1537 (+S9)             | 084395    | 2S3                 | 0 - 19.5  | 0.557  | 0 - 79.7              | 0.074  | 0 - 74.4              | 0.073  | 0.235   | 0.161 | 0* - 0.928                         | 0.282   | not significant |  |
| TA1537 (+S9)             | 084454    | Fresh Strips        | 0 - 20  | 0.052  | 0 - 21.6              | -0.020 | 0 - 22.1              | -0.077 | 0*  | 0.037 | 0* - 0.146                         | 0.727   | not significant |  |
| TA1537 (+S9)             | 084455    | Mellow Sticks       | 0 - 30.7  | -0.066 | 0 - 29.1              | 0.045  | 0 - 30.9              | 0.101  | 0.027   | 0.049 | 0* - 0.239                         | 0.641   | not significant |  |
| TA1537 (+S9)             | 084456    | Copenhagen Long Cut | 0 - 32.3  | 0.208  | 0 - 33.2              | 0.155  | 0 - 67.7              | 0.084  | 0.149   | 0.036 | 0* - 0.304                         | 0.054   | not significant |  |
| TA1537 (+S9)             | 084457    | Ariva Wintergreen   | 0 - 29.5  | -0.068 | 0 - 30.8              | 0.105  | 0 - 31.8              | -0.039 | 0*  | 0.054 | 0* - 0.23                          | 0.992   | not significant |  |
| TA1537 (+S9)             | 084458    | Fresh Orbs          | 0 - 13.1  | 0.583  | 0 - 14.4              | -0.073 | 0 - 15.3              | 0.022  | 0.177   | 0.205 | 0* - 1.058                         | 0.478   | not significant |  |

0\*: Mean or lower bound of the 95% confidence interval has been truncated at 0.

Cigarette smoke condensate (CSC) test sample with  $\mu$ g 'Nicotine in CSC'/plate dose basis

**Slope Analysis of the Linear Portion of the Dose-Response Curve for Smokeless (Revertant Colonies/ $\mu$ g 'Extracted Nicotine in DMSO') and Smoked (Revertant Colonies/ $\mu$ g 'Nicotine in CSC' (KR 2R4F)) Tobacco Products**

| Strain and S9 Activation | Sample ID | Sample Description  | Revertant Colonies/ $\mu$ g 'Extracted Nicotine in DMSO' or Revertant Colonies/ $\mu$ g 'Nicotine in CSC' (KR 2R4F) |        |                       |        |                       |        |   |       |                                    |         |                 |  |
|--------------------------|-----------|---------------------|---|--------|-----------------------|--------|-----------------------|--------|---|-------|------------------------------------|---------|-----------------|--|
|                          |           |                     | Replicate 1   |        | Replicate 2           |        | Replicate 3           |        | Statistics for Replicate 'Nic.' Slope Estimates |       |                                    |         |                 |  |
|                          |           |                     | Dose Range  |        | Dose Range            |        | Dose Range            |        | Standard  |       | t-test p-value ( $H_0$ : mean = 0) |         |                 |  |
|                          |           |                     | ( $\mu$ g Nic./plate)   | slope  | ( $\mu$ g Nic./plate) | slope  | ( $\mu$ g Nic./plate) | slope  | Mean  | Error | 95% C.I.                           | p-value | significance    |  |
| TA98 (-S9)               | 084396    | KR 2R4F             | 0 - 37.5  | 0.829  | 0 - 37.5              | 1.310  | 0 - 37.5              | 0.674  | 0.938   | 0.192 | 0.113 - 1.762                      | 0.039   | significant     |  |
| TA98 (-S9)               | 084394    | Camel SNUS Frost    | 0 - 63.8  | -0.024 | 0 - 71.5              | 0.085  | 0 - 33.6              | 0.000  | 0.020   | 0.033 | 0* - 0.162                         | 0.601   | not significant |  |
| TA98 (-S9)               | 084395    | 2S3                 | 0 - 78  | 0.035  | 0 - 79.7              | -0.040 | 0 - 37.2              | -0.022 | 0*  | 0.023 | 0* - 0.088                         | 0.731   | not significant |  |
| TA98 (-S9)               | 084454    | Fresh Strips        | 0 - 20  | 0.245  | 0 - 21.6              | -0.021 | 0 - 22.1              | 0.230  | 0.151   | 0.086 | 0* - 0.522                         | 0.221   | not significant |  |
| TA98 (-S9)               | 084455    | Mellow Sticks       | 0 - 30.7  | 0.270  | 0 - 29.1              | 0.212  | 0 - 30.9              | 0.196  | 0.226   | 0.023 | 0.129 - 0.323                      | 0.010   | significant     |  |
| TA98 (-S9)               | 084456    | Copenhagen Long Cut | 0 - 64.6  | 0.014  | 0 - 66.3              | 0.017  | 0 - 67.7              | 0.044  | 0.025   | 0.010 | 0* - 0.066                         | 0.123   | not significant |  |
| TA98 (-S9)               | 084457    | Ariva Wintergreen   | 0 - 29.5  | -0.067 | 0 - 15.4              | 0.240  | 0 - 31.8              | 0.110  | 0.094   | 0.089 | 0* - 0.477                         | 0.401   | not significant |  |
| TA98 (-S9)               | 084458    | Fresh Orbs          | 0 - 13.1  | -0.012 | 0 - 14.4              | 0.165  | 0 - 15.3              | -0.011 | 0.047   | 0.059 | 0* - 0.301                         | 0.505   | not significant |  |
| TA100 (-S9)              | 084396    | KR 2R4F             | 0 - 9.4   | 4.450  | 0 - 9.4               | 3.677  | 0 - 18.8              | 1.966  | 3.364   | 0.734 | 0.208 - 6.521                      | 0.044   | significant     |  |
| TA100 (-S9)              | 084394    | Camel SNUS Frost    | 0 - 63.8  | 0.210  | 0 - 71.5              | 0.355  | 0 - 67.2              | 0.547  | 0.371   | 0.098 | 0* - 0.791                         | 0.063   | not significant |  |
| TA100 (-S9)              | 084395    | 2S3                 | 0 - 39  | 0.290  | 0 - 79.7              | 0.299  | 0 - 74.4              | 0.413  | 0.334   | 0.039 | 0.164 - 0.504                      | 0.014   | significant     |  |
| TA100 (-S9)              | 084454    | Fresh Strips        | 0 - 20  | -1.111 | 0 - 21.6              | 0.290  | 0 - 11.1              | 0.671  | 0*  | 0.542 | 0* - 2.282                         | 0.935   | not significant |  |
| TA100 (-S9)              | 084455    | Mellow Sticks       | 0 - 15.3  | 1.917  | 0 - 29.1              | -0.080 | 0 - 30.9              | -1.255 | 0.194   | 0.926 | 0* - 4.178                         | 0.854   | not significant |  |
| TA100 (-S9)              | 084456    | Copenhagen Long Cut | 0 - 32.3  | 1.634  | 0 - 33.2              | 0.003  | 0 - 33.8              | 0.448  | 0.695   | 0.487 | 0* - 2.789                         | 0.290   | not significant |  |
| TA100 (-S9)              | 084457    | Ariva Wintergreen   | 0 - 29.5  | 1.663  | 0 - 30.8              | -2.186 | 0 - 31.8              | -2.339 | 0*  | 1.309 | 0* - 4.68                          | 0.542   | not significant |  |
| TA100 (-S9)              | 084458    | Fresh Orbs          | 0 - 13.1  | -1.250 | 0 - 14.4              | -3.537 | 0 - 15.3              | -0.813 | 0*  | 0.845 | 0* - 1.767                         | 0.158   | not significant |  |
| TA102 (-S9)              | 084396    | KR 2R4F             | 0 - 37.5  | -0.731 | 0 - 9.4               | 2.606  | 0 - 37.5              | 0.485  | 0.786   | 0.975 | 0* - 4.982                         | 0.505   | not significant |  |
| TA102 (-S9)              | 084394    | Camel SNUS Frost    | 0 - 63.8  | -0.212 | 0 - 35.7              | 0.427  | 0 - 67.2              | -0.117 | 0.033   | 0.199 | 0* - 0.89                          | 0.885   | not significant |  |
| TA102 (-S9)              | 084395    | 2S3                 | 0 - 78  | 0.127  | 0 - 79.7              | 0.376  | 0 - 74.4              | 0.923  | 0.475   | 0.235 | 0* - 1.486                         | 0.180   | not significant |  |
| TA102 (-S9)              | 084454    | Fresh Strips        | 0 - 20  | -0.223 | 0 - 21.6              | 1.500  | 0 - 5.5               | 11.888 | 4.388   | 3.783 | 0* - 20.664                        | 0.366   | not significant |  |
| TA102 (-S9)              | 084455    | Mellow Sticks       | 0 - 15.3  | 0.687  | 0 - 29.1              | 0.595  | 0 - 30.9              | 0.041  | 0.441   | 0.202 | 0* - 1.309                         | 0.161   | not significant |  |
| TA102 (-S9)              | 084456    | Copenhagen Long Cut | 0 - 64.6  | -0.002 | 0 - 66.3              | 0.408  | 0 - 33.8              | 2.587  | 0.998   | 0.803 | 0* - 4.455                         | 0.340   | not significant |  |
| TA102 (-S9)              | 084457    | Ariva Wintergreen   | 0 - 29.5  | -0.871 | 0 - 30.8              | -1.401 | 0 - 31.8              | -0.152 | 0*  | 0.362 | 0* - 0.748                         | 0.155   | not significant |  |
| TA102 (-S9)              | 084458    | Fresh Orbs          | 0 - 13.1  | -7.725 | 0 - 14.4              | 0.930  | 0 - 15.3              | 1.099  | 0*  | 2.913 | 0* - 10.637                        | 0.581   | not significant |  |
| TA1535 (-S9)             | 084396    | KR 2R4F             | 0 - 37.5  | 0.017  | 0 - 37.5              | 0.121  | 0 - 37.5              | 0.026  | 0.055   | 0.033 | 0* - 0.198                         | 0.240   | not significant |  |
| TA1535 (-S9)             | 084394    | Camel SNUS Frost    | 0 - 63.8  | 0.006  | 0 - 71.5              | 0.074  | 0 - 67.2              | -0.046 | 0.011   | 0.035 | 0* - 0.162                         | 0.776   | not significant |  |
| TA1535 (-S9)             | 084395    | 2S3                 | 0 - 78  | -0.019 | 0 - 79.7              | 0.020  | 0 - 74.4              | 0.070  | 0.024   | 0.026 | 0* - 0.134                         | 0.455   | not significant |  |
| TA1535 (-S9)             | 084454    | Fresh Strips        | 0 - 10  | 0.186  | 0 - 10.8              | 0.422  | 0 - 11.1              | 0.275  | 0.295   | 0.069 | 0* - 0.59                          | 0.050   | not significant |  |
| TA1535 (-S9)             | 084455    | Mellow Sticks       | 0 - 30.7  | -0.144 | 0 - 29.1              | 0.013  | 0 - 30.9              | -0.011 | 0*  | 0.049 | 0* - 0.162                         | 0.432   | not significant |  |
| TA1535 (-S9)             | 084456    | Copenhagen Long Cut | 0 - 64.6  | 0.034  | 0 - 66.3              | 0.077  | 0 - 33.8              | 0.146  | 0.086   | 0.033 | 0* - 0.226                         | 0.120   | not significant |  |
| TA1535 (-S9)             | 084457    | Ariva Wintergreen   | 0 - 7.4   | 0.769  | 0 - 30.8              | 0.141  | 0 - 31.8              | -0.054 | 0.285   | 0.249 | 0* - 1.355                         | 0.370   | not significant |  |
| TA1535 (-S9)             | 084458    | Fresh Orbs          | 0 - 3.3   | 1.741  | 0 - 7.2               | 0.842  | 0 - 15.3              | 0.067  | 0.884   | 0.484 | 0* - 2.965                         | 0.209   | not significant |  |
| TA1537 (-S9)             | 084396    | KR 2R4F             | 0 - 18.8  | 0.196  | 0 - 18.8              | 0.231  | 0 - 9.4               | 0.523  | 0.317   | 0.104 | 0* - 0.763                         | 0.092   | not significant |  |
| TA1537 (-S9)             | 084394    | Camel SNUS Frost    | 0 - 16  | 0.361  | 0 - 71.5              | 0.068  | 0 - 33.6              | 0.182  | 0.204   | 0.085 | 0* - 0.571                         | 0.140   | not significant |  |
| TA1537 (-S9)             | 084395    | 2S3                 | 0 - 78  | 0.133  | 0 - 39.9              | 0.132  | 0 - 37.2              | 0.045  | 0.103   | 0.029 | 0* - 0.228                         | 0.070   | not significant |  |
| TA1537 (-S9)             | 084454    | Fresh Strips        | 0 - 20  | -0.024 | 0 - 21.6              | 0.069  | 0 - 22.1              | 0.028  | 0.024   | 0.027 | 0* - 0.14                          | 0.458   | not significant |  |
| TA1537 (-S9)             | 084455    | Mellow Sticks       | 0 - 30.7  | 0.013  | 0 - 29.1              | -0.053 | 0 - 30.9              | -0.044 | 0*  | 0.020 | 0* - 0.06                          | 0.304   | not significant |  |
| TA1537 (-S9)             | 084456    | Copenhagen Long Cut | 0 - 64.6  | 0.011  | 0 - 66.3              | -0.031 | 0 - 67.7              | 0.032  | 0.004   | 0.018 | 0* - 0.083                         | 0.854   | not significant |  |
| TA1537 (-S9)             | 084457    | Ariva Wintergreen   | 0 - 29.5  | 0.006  | 0 - 30.8              | -0.085 | 0 - 31.8              | 0.063  | 0*  | 0.043 | 0* - 0.181                         | 0.914   | not significant |  |
| TA1537 (-S9)             | 084458    | Fresh Orbs          | 0 - 6.6   | 0.452  | 0 - 14.4              | 0.112  | 0 - 15.3              | -0.093 | 0.157   | 0.159 | 0* - 0.84                          | 0.426   | not significant |  |

0\*: Mean or lower bound of the 95% confidence interval has been truncated at 0.

Cigarette smoke condensate (CSC) test sample with  $\mu$ g 'Nicotine in CSC'/plate dose basis

**One-Way ANOVA of Mean 'Extracted Nicotine' and 'Nicotine in CSC'  
Slope Estimates Among Test Samples**

TA98 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 1782.6084      | 7  | 254.65834   | 39.5    | <b>0.000</b> |
| Within Samples | 103.02679      | 16 | 6.4391745   |         |              |
| Total (Corr.)  | 1216.5009      | 23 |             |         |              |

TA98 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 2.0611403      | 7  | 0.2944486   | 13.6    | <b>0.000</b> |
| Within Samples | 0.34615        | 16 | 0.0216344   |         |              |
| Total (Corr.)  | 2.4072903      | 23 |             |         |              |

TA100 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 173.10833      | 7  | 24.729762   | 9.51    | <b>0.000</b> |
| Within Samples | 41.623451      | 16 | 2.6014657   |         |              |
| Total (Corr.)  | 142.55837      | 23 |             |         |              |

TA100 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 47.82619       | 7  | 6.8323129   | 4.17    | <b>0.009</b> |
| Within Samples | 26.190404      | 16 | 1.6369003   |         |              |
| Total (Corr.)  | 74.016594      | 23 |             |         |              |

TA102 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 67.985595      | 7  | 9.7122278   | 6.44    | <b>0.001</b> |
| Within Samples | 24.138367      | 16 | 1.508648    |         |              |
| Total (Corr.)  | 90.958932      | 23 |             |         |              |

TA102 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 69.345731      | 7  | 9.906533    | 1.07    | 0.425   |
| Within Samples | 147.95201      | 16 | 9.2470009   |         |         |
| Total (Corr.)  | 217.29774      | 23 |             |         |         |

TA1535 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.058412       | 7  | 0.0083446   | 0.461   | 0.848   |
| Within Samples | 0.2893065      | 16 | 0.0180817   |         |         |
| Total (Corr.)  | 0.3405169      | 23 |             |         |         |

TA1535 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 1.9366563      | 7  | 0.2766652   | 2.40    | 0.069   |
| Within Samples | 1.8414342      | 16 | 0.1150896   |         |         |
| Total (Corr.)  | 3.7780905      | 23 |             |         |         |

TA1537 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 45.058986      | 7  | 6.4369979   | 167     | <b>0.000</b> |
| Within Samples | 0.6180467      | 16 | 0.0386279   |         |              |
| Total (Corr.)  | 29.763859      | 23 |             |         |              |

TA1537 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.3102492      | 7  | 0.0443213   | 2.49    | 0.062   |
| Within Samples | 0.2843007      | 16 | 0.0177688   |         |         |
| Total (Corr.)  | 0.59455        | 23 |             |         |         |

One-way ANOVA analysis indicates significant differences (at  $\alpha = 0.05$ ) among mean 'Nicotine' specific activity slope estimates for test samples with TA98(+S9), TA98(-S9), TA100(+S9), TA100(-S9), TA102(+S9) and TA1537(+S9).

**Evaluation of Ratio (Max ÷ Min) of Standard Deviations of  
'Extracted Nicotine' and 'Nicotine in CSC' Slope Estimates  
and Corresponding Method of Comparison**

| <b>Strain and<br/>S9 Activation</b> | <b>Std. Dev. Ratio<br/>(Max ÷ Min)</b> | <b>Method of<br/>Comparison</b>    |
|-------------------------------------|--|------------------------------------|
| TA98 (+S9)                          | 140.4                                  | Pairwise T-test (unequal variance) |
| TA98 (-S9)                          | 20.0                                   | Pairwise T-test (unequal variance) |
| TA100 (+S9)                         | 5.5                                    | ANOVA (equal variance)             |
| TA100 (-S9)                         | 33.2                                   | Pairwise T-test (unequal variance) |
| TA102 (+S9)                         | 20.7                                   | Pairwise T-test (unequal variance) |
| TA102 (-S9)                         | 19.0                                   | Pairwise T-test (unequal variance) |
| TA1535 (+S9)                        | 14.2                                   | ANOVA (equal variance)             |
| TA1535 (-S9)                        | 18.8                                   | Pairwise T-test (unequal variance) |
| TA1537 (+S9)                        | 5.7                                    | ANOVA (equal variance)             |
| TA1537 (-S9)                        | 8.6                                    | ANOVA (equal variance)             |



**ANOVA-Based Comparisons of Smokeless Tobacco Mean 'Extracted Nicotine' Slope to Control Brand KR 2R4F (084396)  
Mean 'Nicotine in CSC' Slope using Bonferroni-adjusted p-values**

| ANOVA-Based Comparison | TA98 (+S9) |         |                                 | TA100 (+S9) |         |                                 | TA102 (+S9) |         |                                 | TA1535 (+S9) |         |                                 | TA1537 (+S9) |         |                                 |
|------------------------|------------|---------|---------------------------------|-------------|---------|---------------------------------|-------------|---------|---------------------------------|--------------|---------|---------------------------------|--------------|---------|---------------------------------|
|                        | f-ratio    | p-value | significance at $\alpha = 0.05$ | f-ratio     | p-value | significance at $\alpha = 0.05$ | f-ratio     | p-value | significance at $\alpha = 0.05$ | f-ratio      | p-value | significance at $\alpha = 0.05$ | f-ratio      | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084396      | 158.73     | 1.0E-09 | significant                     | 46.799      | 4.0E-06 | significant                     | 9.2648      | 0.0077  | not significant                 | 1.5546       | 0.2304  | not significant                 | 648.03       | 2.3E-14 | significant                     |
| 084395 vs. 084396      | 157.48     | 1.1E-09 | significant                     | 43.335      | 6.3E-06 | significant                     | 0.7037      | 0.4139  | not significant                 | 1.0634       | 0.3178  | not significant                 | 622.57       | 3.1E-14 | significant                     |
| 084454 vs. 084396      | 161.46     | 8.9E-10 | significant                     | 21.656      | 2.6E-04 | significant                     | 0.8357      | 0.3742  | not significant                 | 0.7065       | 0.4130  | not significant                 | 702.65       | 1.2E-14 | significant                     |
| 084455 vs. 084396      | 158.99     | 1.0E-09 | significant                     | 32.111      | 3.5E-05 | significant                     | 0.1019      | 0.7537  | not significant                 | 0.6490       | 0.4323  | not significant                 | 688.91       | 1.4E-14 | significant                     |
| 084456 vs. 084396      | 156.56     | 1.1E-09 | significant                     | 39.527      | 1.1E-05 | significant                     | 0.1487      | 0.7048  | not significant                 | 1.1874       | 0.2920  | not significant                 | 649.50       | 2.2E-14 | significant                     |
| 084457 vs. 084396      | 160.05     | 9.5E-10 | significant                     | 29.428      | 5.6E-05 | significant                     | 1.1541      | 0.2986  | not significant                 | 0.2485       | 0.6249  | not significant                 | 697.91       | 1.3E-14 | significant                     |
| 084458 vs. 084396      | 153.66     | 1.3E-09 | significant                     | 26.409      | 9.9E-05 | significant                     | 10.879      | 0.0045  | significant                     | 2.4898       | 0.1342  | not significant                 | 640.62       | 2.5E-14 | significant                     |

| ANOVA-Based Comparison | TA98 (-S9) |         |                                 | TA100 (-S9) |         |                                 | TA102 (-S9) |         |                                 | TA1535 (-S9) |         |                                 | TA1537 (-S9) |         |                                 |
|------------------------|------------|---------|---------------------------------|-------------|---------|---------------------------------|-------------|---------|---------------------------------|--------------|---------|---------------------------------|--------------|---------|---------------------------------|
|                        | f-ratio    | p-value | significance at $\alpha = 0.05$ | f-ratio     | p-value | significance at $\alpha = 0.05$ | f-ratio     | p-value | significance at $\alpha = 0.05$ | f-ratio      | p-value | significance at $\alpha = 0.05$ | f-ratio      | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084396      | 58.363     | 1.0E-06 | significant                     | 8.2139      | 0.0112  | not significant                 | 0.0922      | 0.7653  | not significant                 | 0.0247       | 0.8772  | not significant                 | 1.081        | 0.3139  | not significant                 |
| 084395 vs. 084396      | 62.137     | 6.7E-07 | significant                     | 8.4154      | 0.0104  | not significant                 | 0.0157      | 0.9019  | not significant                 | 0.0127       | 0.9117  | not significant                 | 3.849        | 0.0674  | not significant                 |
| 084454 vs. 084396      | 42.883     | 6.7E-06 | significant                     | 10.683      | 0.0048  | significant                     | 2.1045      | 0.1662  | not significant                 | 0.7487       | 0.3997  | not significant                 | 7.220        | 0.0162  | not significant                 |
| 084455 vs. 084396      | 35.130     | 2.1E-05 | significant                     | 9.2118      | 0.0079  | not significant                 | 0.0194      | 0.8910  | not significant                 | 0.1365       | 0.7166  | not significant                 | 10.043       | 0.0060  | significant                     |
| 084456 vs. 084396      | 57.798     | 1.1E-06 | significant                     | 6.5308      | 0.0212  | not significant                 | 0.0072      | 0.9332  | not significant                 | 0.0123       | 0.9131  | not significant                 | 8.272        | 0.0110  | not significant                 |
| 084457 vs. 084396      | 49.338     | 2.9E-06 | significant                     | 17.088      | 0.0008  | significant                     | 0.4125      | 0.5298  | not significant                 | 0.6914       | 0.4179  | not significant                 | 8.760        | 0.0092  | not significant                 |
| 084458 vs. 084396      | 54.968     | 1.5E-06 | significant                     | 25.079      | 0.0001  | significant                     | 1.1696      | 0.2955  | not significant                 | 8.9507       | 0.0086  | not significant                 | 2.155        | 0.1615  | not significant                 |

Some ANOVA-based comparison p-values for tester strains TA98(+S9), TA100(+S9), TA102(+S9), TA1537(+S9), TA98(-S9), TA100(-S9) and TA1537(-S9) were significant at  $\alpha = 0.05$ .

Significant differences between the mean 'Nicotine in CSC' specific activity slope of the KR 2R4F control sample and the mean 'Extracted Nicotine' specific activity slope of the various smokeless tobacco test samples are summarized below:

**TA98(+S9), TA100(+S9), TA1537(+S9) and TA98(-S9):**

- KR 2R4F (084396) specific activity is significantly different from that of each of the 7 smokeless tobacco test samples

**TA102(+S9)**

- KR 2R4F (084396) and Fresh Orbs (084458)

**TA100(-S9)**

- KR 2R4F (084396) and each of {Fresh Strips (084454), Ariva Wintergreen (084457), Fresh Orbs (084458)}

**TA1537(-S9)**

- KR 2R4F (084396) and Mellow Sticks (084455)

**Pairwise T-test Comparisons of Smokeless Tobacco Mean 'Extracted Nicotine' Slope to Control Brand KR 2R4F (084396)  
Mean 'Nicotine in CSC' Slope using Bonferroni-adjusted p-values**

| Pairwise T-test Comparison | TA98 (+S9)  |         |                                 | TA100 (+S9) |         |                                 | TA102 (+S9) |         |                                 | TA1535 (+S9) |         |                                 | TA1537 (+S9) |         |                                 |
|----------------------------|-------------|---------|---------------------------------|-------------|---------|---------------------------------|-------------|---------|---------------------------------|--------------|---------|---------------------------------|--------------|---------|---------------------------------|
|                            | t-statistic | p-value | significance at $\alpha = 0.05$ | t-statistic | p-value | significance at $\alpha = 0.05$ | t-statistic | p-value | significance at $\alpha = 0.05$ | t-statistic  | p-value | significance at $\alpha = 0.05$ | t-statistic  | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084396          | 6.375       | 0.0031  | significant                     |             |         |                                 | 4.911       | 0.0080  | not significant                 |              |         |                                 |              |         |                                 |
| 084395 vs. 084396          | 6.350       | 0.0032  | significant                     |             |         |                                 | 0.800       | 0.4686  | not significant                 |              |         |                                 |              |         |                                 |
| 084454 vs. 084396          | 6.421       | 0.0030  | significant                     |             |         |                                 | 1.398       | 0.2347  | not significant                 |              |         |                                 |              |         |                                 |
| 084455 vs. 084396          | 6.379       | 0.0031  | significant                     |             |         |                                 | 0.582       | 0.5918  | not significant                 |              |         |                                 |              |         |                                 |
| 084456 vs. 084396          | 6.332       | 0.0032  | significant                     |             |         |                                 | 0.687       | 0.5297  | not significant                 |              |         |                                 |              |         |                                 |
| 084457 vs. 084396          | 6.401       | 0.0031  | significant                     |             |         |                                 | 1.969       | 0.1203  | not significant                 |              |         |                                 |              |         |                                 |
| 084458 vs. 084396          | 6.212       | 0.0034  | significant                     |             |         |                                 | 1.929       | 0.1260  | not significant                 |              |         |                                 |              |         |                                 |

| Pairwise T-test Comparison | TA98 (-S9)  |         |                                 | TA100 (-S9) |         |                                 | TA102 (-S9) |         |                                 | TA1535 (-S9) |         |                                 | TA1537 (-S9) |         |                                 |
|----------------------------|-------------|---------|---------------------------------|-------------|---------|---------------------------------|-------------|---------|---------------------------------|--------------|---------|---------------------------------|--------------|---------|---------------------------------|
|                            | t-statistic | p-value | significance at $\alpha = 0.05$ | t-statistic | p-value | significance at $\alpha = 0.05$ | t-statistic | p-value | significance at $\alpha = 0.05$ | t-statistic  | p-value | significance at $\alpha = 0.05$ | t-statistic  | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084396          | 4.720       | 0.0092  | not significant                 | 4.045       | 0.0155  | not significant                 | 0.758       | 0.4909  | not significant                 | 0.902        | 0.4182  | not significant                 |              |         |                                 |
| 084395 vs. 084396          | 4.908       | 0.0080  | not significant                 | 4.124       | 0.0146  | not significant                 | 0.310       | 0.7719  | not significant                 | 0.743        | 0.4989  | not significant                 |              |         |                                 |
| 084454 vs. 084396          | 3.744       | 0.0200  | not significant                 | 3.743       | 0.0201  | not significant                 | 0.922       | 0.4087  | not significant                 | 3.138        | 0.0349  | not significant                 |              |         |                                 |
| 084455 vs. 084396          | 3.690       | 0.0210  | not significant                 | 2.684       | 0.0550  | not significant                 | 0.347       | 0.7459  | not significant                 | 1.738        | 0.1572  | not significant                 |              |         |                                 |
| 084456 vs. 084396          | 4.760       | 0.0089  | not significant                 | 3.032       | 0.0387  | not significant                 | 0.167       | 0.8752  | not significant                 | 0.658        | 0.5462  | not significant                 |              |         |                                 |
| 084457 vs. 084396          | 3.994       | 0.0162  | not significant                 | 2.877       | 0.0451  | not significant                 | 1.533       | 0.2000  | not significant                 | 0.919        | 0.4103  | not significant                 |              |         |                                 |
| 084458 vs. 084396          | 4.443       | 0.0113  | not significant                 | 4.676       | 0.0095  | not significant                 | 0.874       | 0.4314  | not significant                 | 1.709        | 0.1626  | not significant                 |              |         |                                 |

Some pairwise t-test comparison p-values for tester strain TA98(+S9) were significant at  $\alpha = 0.05$ .

Significant differences between the mean 'Nicotine in CSC' specific activity slope of the KR 2R4F control sample and the mean 'Extracted Nicotine' specific activity slope of the various smokeless tobacco test samples are summarized below:

**TA98 (+S9):**

- KR 2R4F (084396) specific activity is significantly different from that of each of the 7 smokeless tobacco test samples

**Number of Mean 'Nicotine' Slope Estimates (Including Control Brand KR 2R4F)  
Significantly Greater than Zero (0), the Corresponding Number of Paired  
Comparisons and Comparison Method**

| <b>Strain and<br/>S9 Activation</b> | <b># Significant Slopes<br/>(Including KR 2R4F)</b> | <b>Number of<br/>Comparisons</b> | <b>Std. Dev. Ratio<br/>(Max ÷ Min)</b> | <b>Method of<br/>Comparison</b>    |
|-------------------------------------|---|----------------------------------|--|------------------------------------|
| TA98 (+S9)                          | 2   | 1                                | 140.4                                  | Pairwise T-test (unequal variance) |
| TA98 (-S9)                          | 2   | 1                                | 8.5                                    | ANOVA (equal variance)             |
| TA100 (+S9)                         | 3   | 2                                | 3.4                                    | ANOVA (equal variance)             |
| TA100 (-S9)                         | 2   | 1                                | 18.6                                   | Pairwise T-test (unequal variance) |
| TA102 (+S9)                         | 0   | 0                                |  |                                    |
| TA102 (-S9)                         | 0   | 0                                |  |                                    |
| TA1535 (+S9)                        | 0   | 0                                |  |                                    |
| TA1535 (-S9)                        | 0   | 0                                |  |                                    |
| TA1537 (+S9)                        | 1   | 0                                |  |                                    |
| TA1537 (-S9)                        | 0   | 0                                |  |                                    |

# **One-Way ANOVA and ANOVA-Based Comparisons of Mean 'Nicotine' Slope Estimates Between KR 2R4F and Smokeless Tobacco Samples that are Significantly Greater than Zero (0)**

TA98 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 1008.14        | 1  | 1008.14     | 40.1    | <b>0.003</b> |
| Within Samples | 100.58         | 4  | 25.14       |         |              |

| TA98 (+S9)                 |             |         |                                 |
|----------------------------|-------------|---------|---------------------------------|
| Pairwise T-test Comparison | t-statistic | p-value | significance at $\alpha = 0.05$ |
| 084456 vs. 084396          | 6.33        | 0.0032  | <b>significant</b>              |

TA98 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 0.760          | 1  | 0.760       | 13.6    | <b>0.021</b> |
| Within Samples | 0.223          | 4  | 0.056       |         |              |

| TA98 (-S9)             |         |         |                                 |
|------------------------|---------|---------|---------------------------------|
| ANOVA-Based Comparison | f-ratio | p-value | significance at $\alpha = 0.05$ |
| 084455 vs. 084396      | 13.62   | 0.0210  | <b>significant</b>              |

TA100 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 110.74         | 2  | 55.37       | 35.2    | <b>0.000</b> |
| Within Samples | 9.44           | 6  | 1.57        |         |              |

| TA100 (+S9)            |         |         |                                 |
|------------------------|---------|---------|---------------------------------|
| ANOVA-Based Comparison | f-ratio | p-value | significance at $\alpha = 0.05$ |
| 084454 vs. 084396      | 35.82   | 0.0010  | <b>significant</b>              |
| 084456 vs. 084396      | 65.38   | 0.0002  | <b>significant</b>              |

TA100 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 13.78          | 1  | 13.78       | 17.0    | <b>0.015</b> |
| Within Samples | 3.24           | 4  | 0.81        |         |              |

| TA100 (-S9)                |             |         |                                 |
|----------------------------|-------------|---------|---------------------------------|
| Pairwise T-test Comparison | t-statistic | p-value | significance at $\alpha = 0.05$ |
| 084395 vs. 084396          | 4.12        | 0.0146  | <b>significant</b>              |

Each of TA98 (+S9), TA98 (-S9), TA100 (+S9) and TA100 (-S9) strains have the mean 'nicotine in CSC' specific activity slope of the KR 2R4F and at least one smokeless tobacco test sample mean 'extracted nicotine' specific activity slope estimate being greater than zero (0) .

## **TA98 (+S9):**

A significant difference between mean 'Nicotine' specific activity slope estimates was detected in TA98 (+S9) between **KR 2R4F** and **084456 (Copenhagen Long Cut)**

## **TA98 (-S9):**

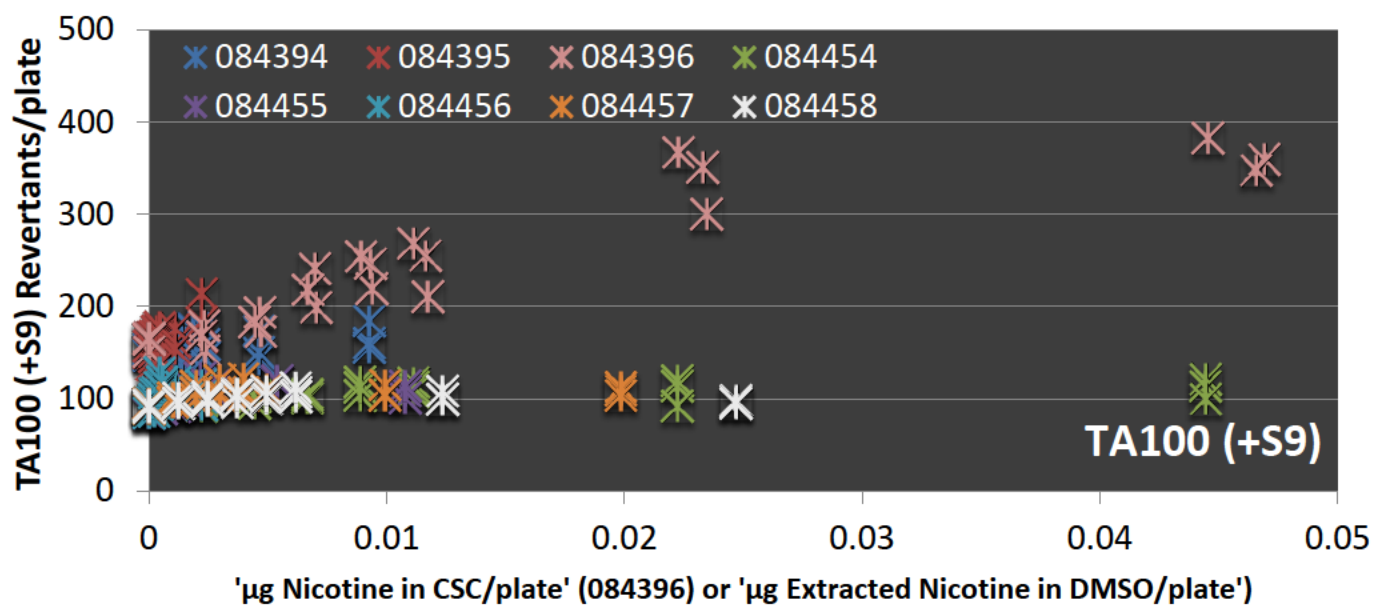
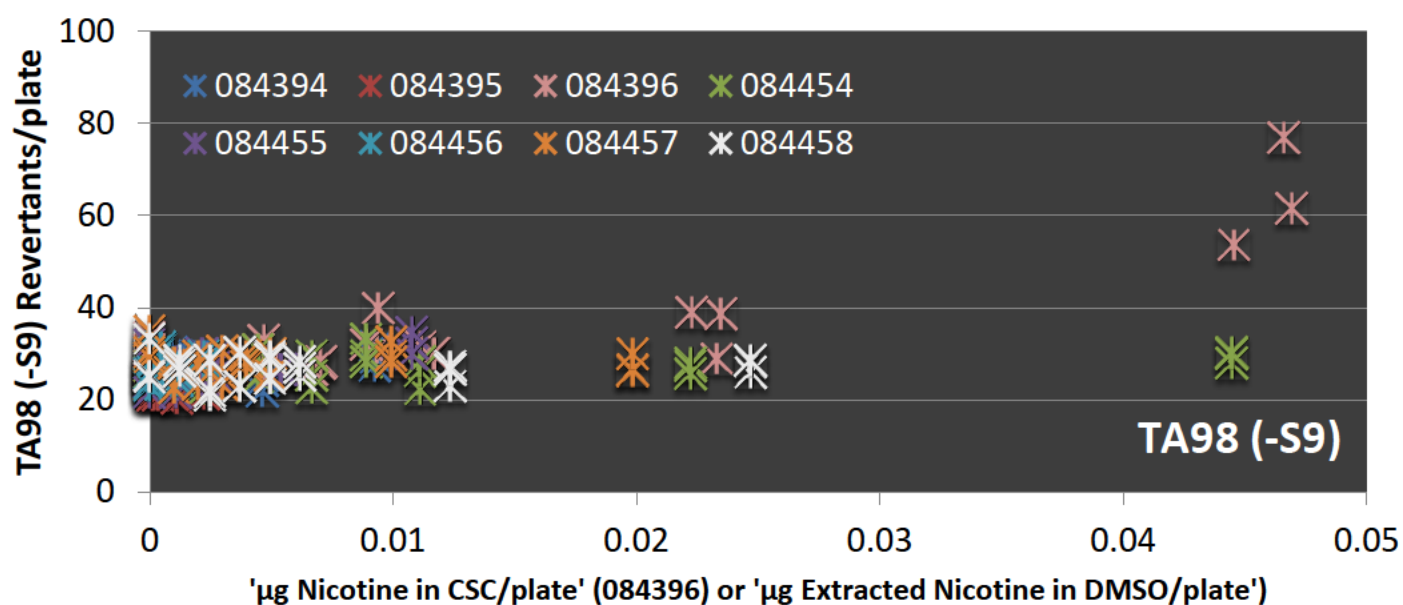
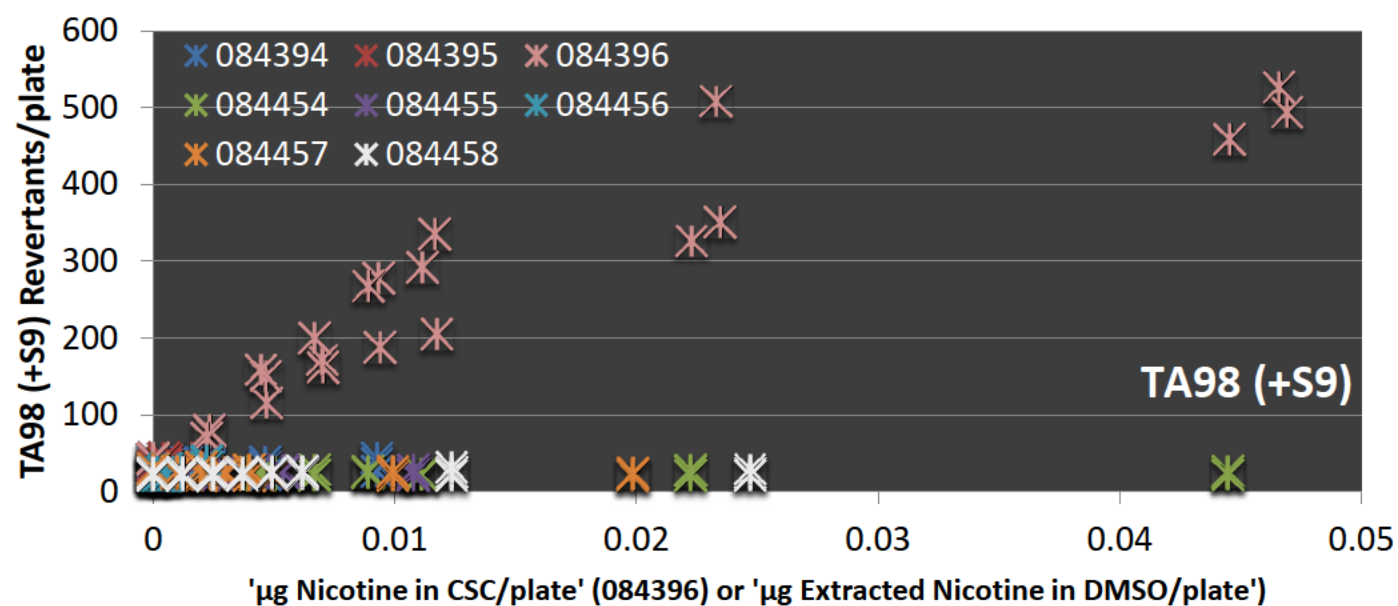
A significant difference between mean 'Nicotine' specific activity slope estimates was detected in TA98 (-S9) between **KR 2R4F** and **084455 (Mellow Sticks)**

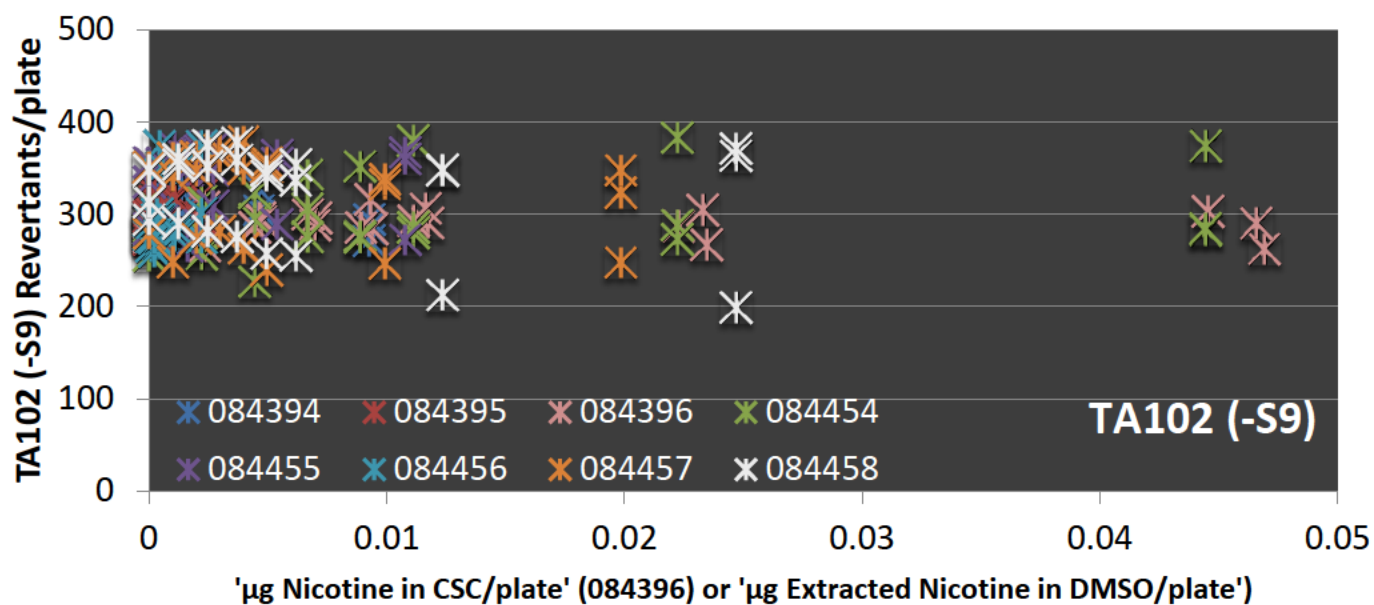
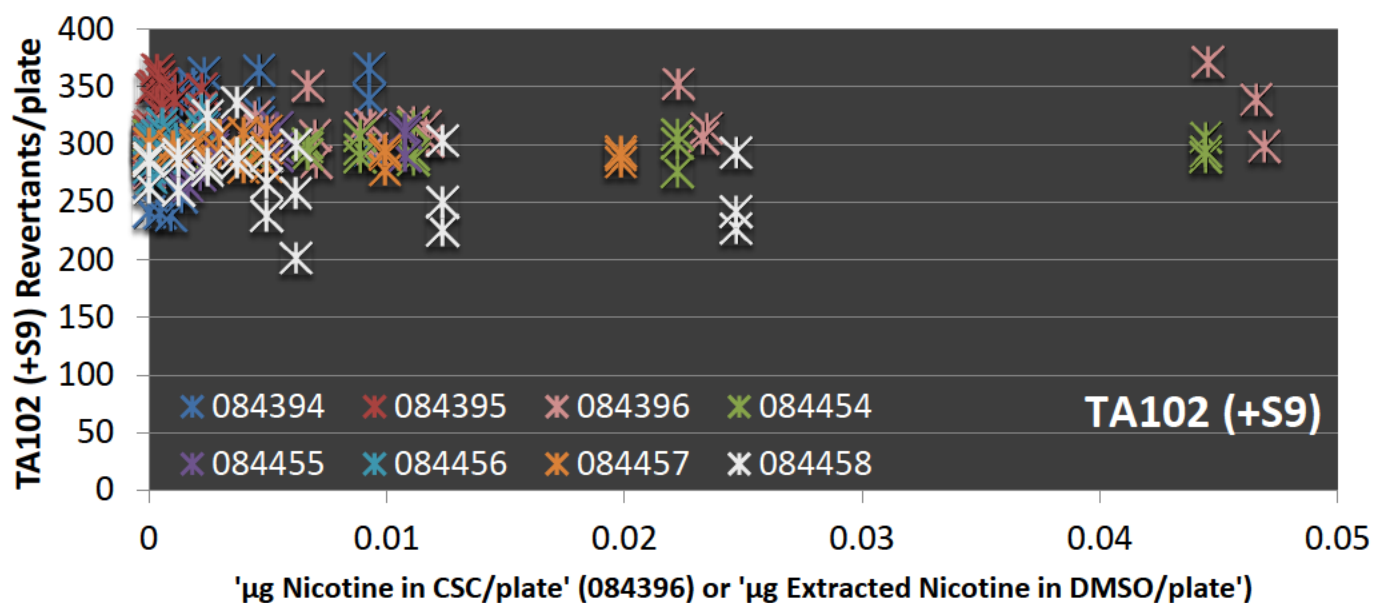
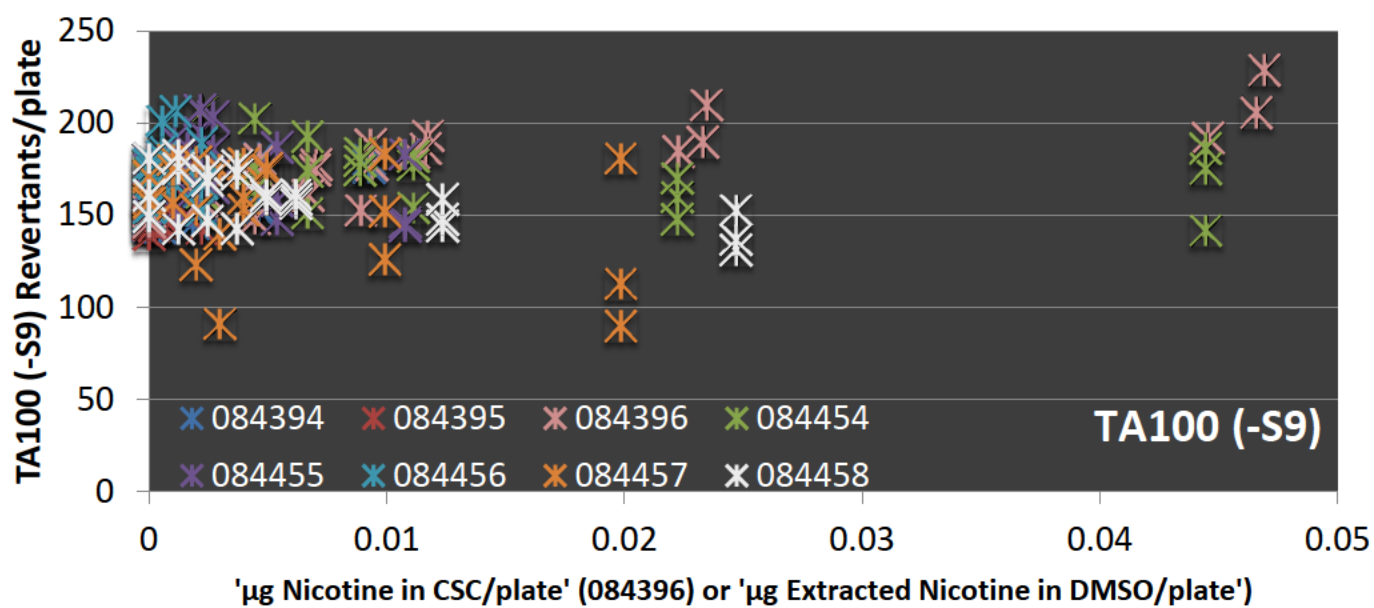
## **TA100 (+S9)**

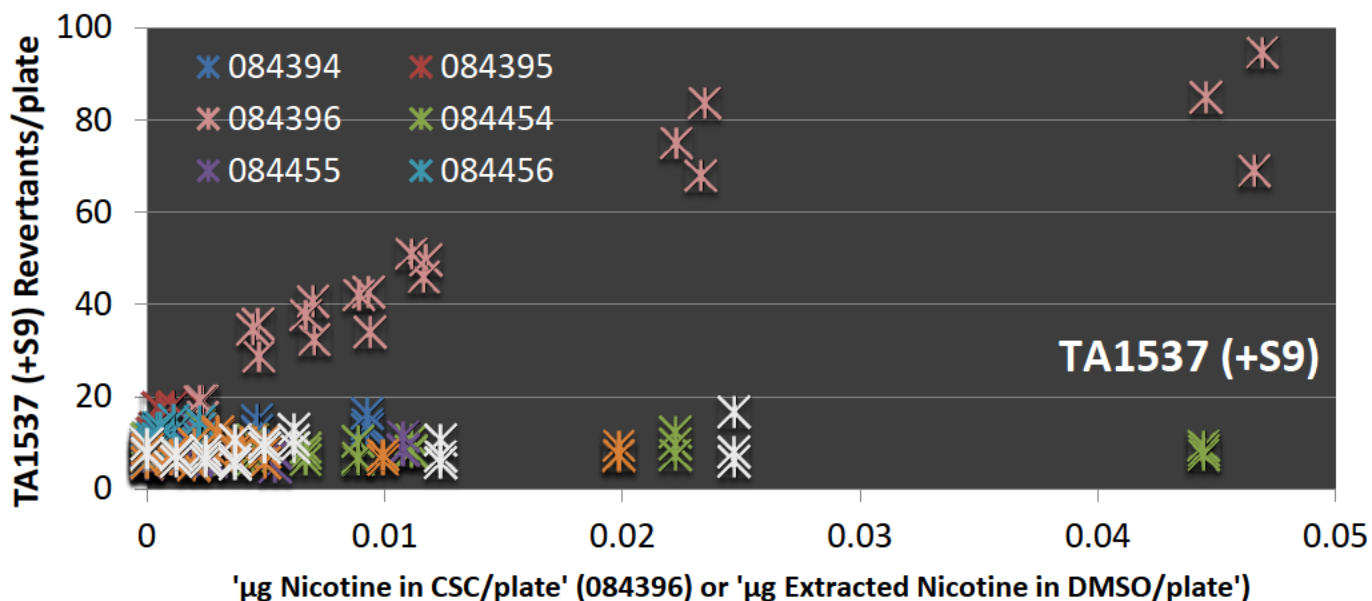
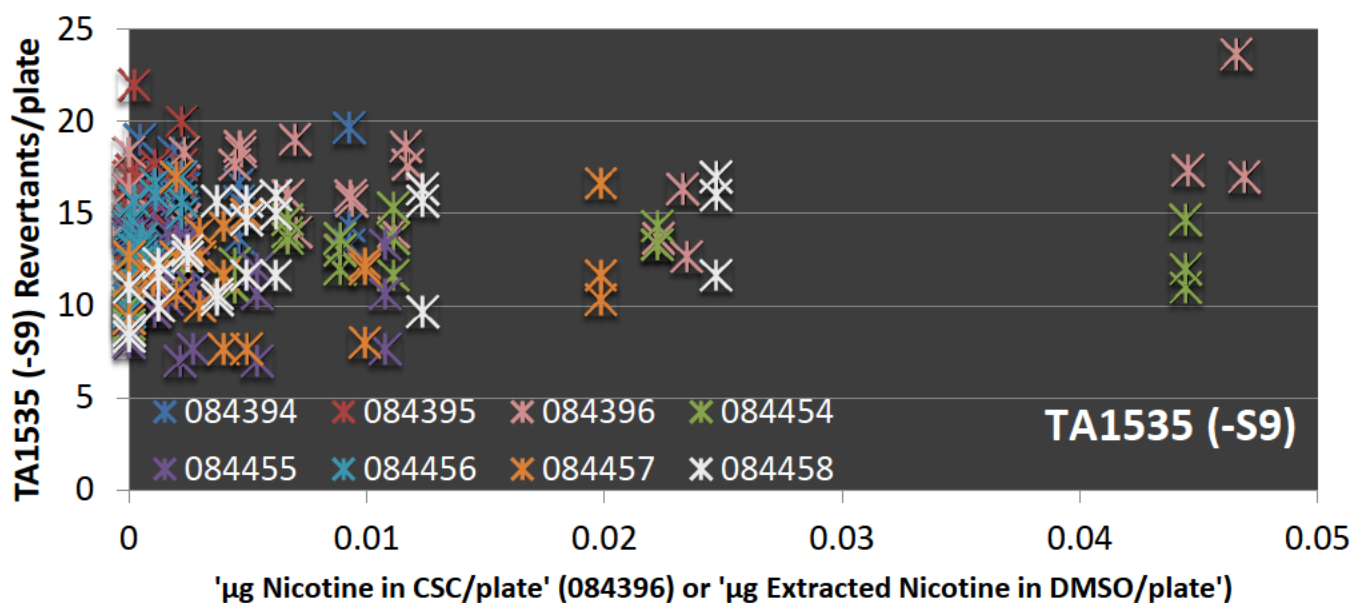
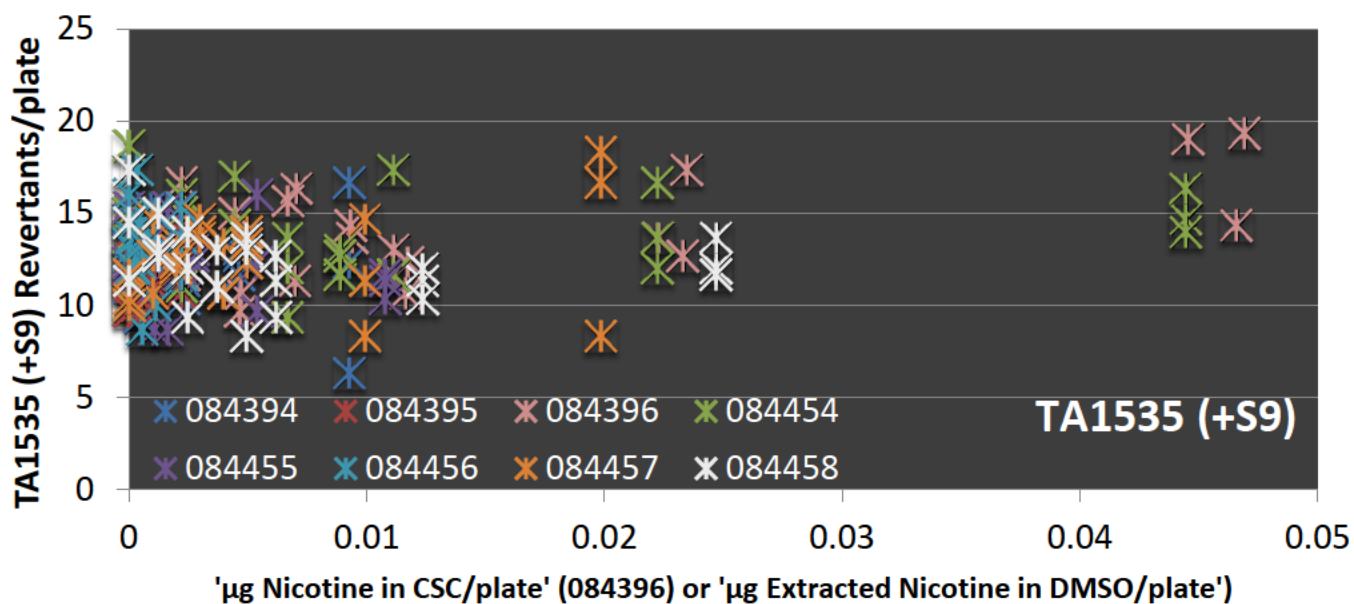
A significant difference between mean 'Nicotine' specific activity slope estimates was detected in TA100 (+S9) between **KR 2R4F** and each of **{084454 (Fresh Strips), 084456 (Copenhagen Long Cut)}**

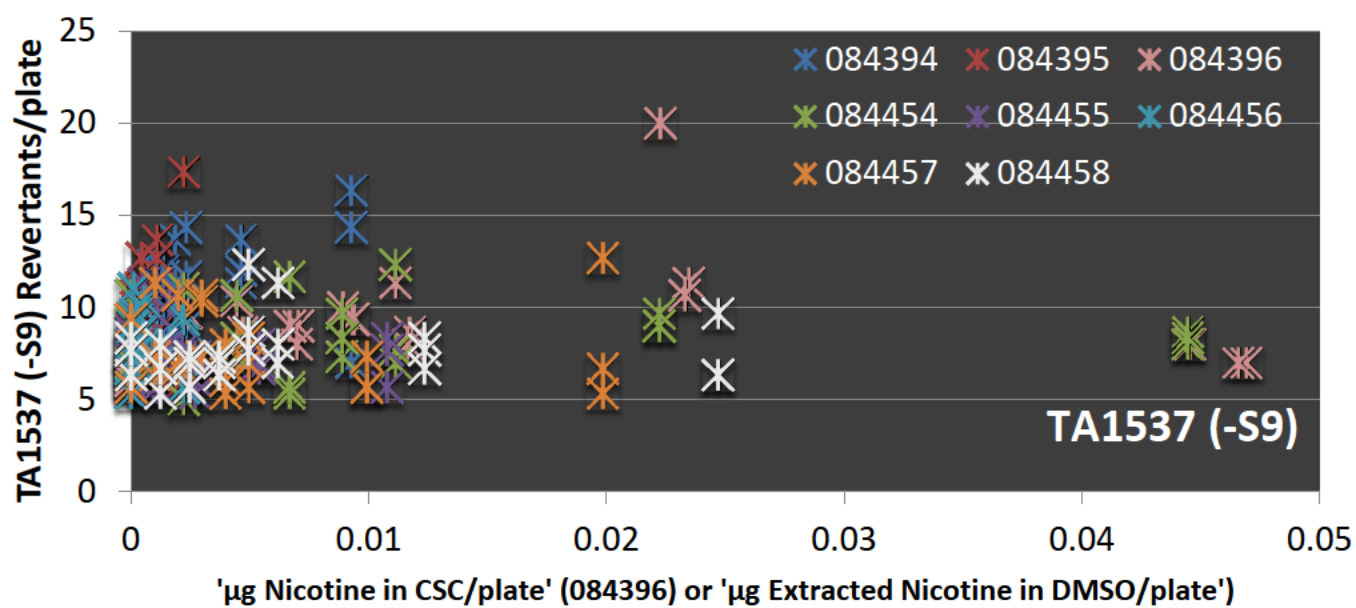
## **TA100 (-S9)**

A significant difference between mean 'Nicotine' specific activity slope estimates was detected in TA100 (-S9) between **KR 2R4F** and **084395 (2S3)**











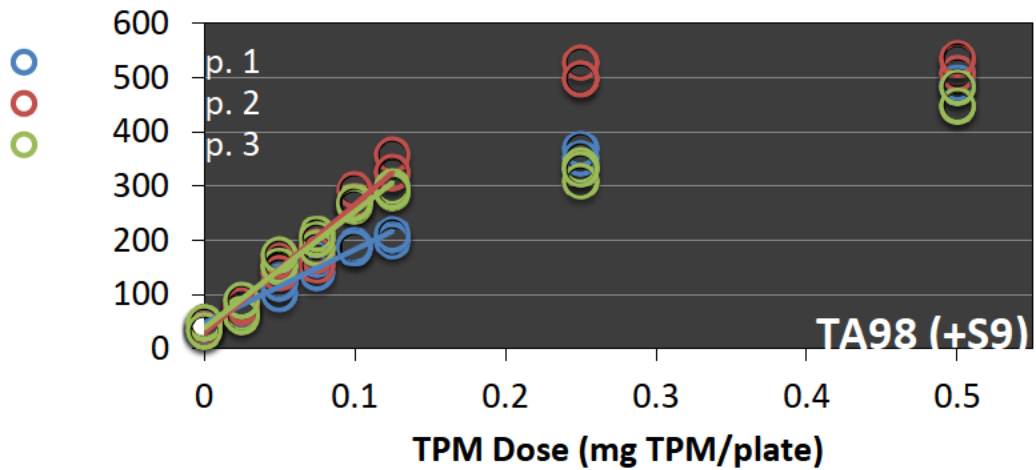
**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/mg TPM)**

| Strain and<br>S9 Activation | Sample<br>ID | Sample<br>Description | Number of Revertant Colonies/mg TPM |       |                |       |                |       |  |       |            |   |                    |
|-----------------------------|--------------|-----------------------|-------------------------------------|-------|----------------|-------|----------------|-------|--|-------|------------|---|--------------------|
|                             |              |                       | Replicate 1                         |       | Replicate 2    |       | Replicate 3    |       | Statistics for Replicate TPM Slope Estimates |       |            |   |                    |
|                             |              |                       | Dose Range                          |       | Dose Range     |       | Dose Range     |       | Standard                                     |       |            | t-test p-value (H <sub>0</sub> : mean= 0) |                    |
|                             |              |                       | (mg TPM/plate)                      | slope | (mg TPM/plate) | slope | (mg TPM/plate) | slope | Mean   | Error | 95% C.I.   | p-value                                   | significance       |
| TA98 (+S9)                  | 084396       | KR 2R4F               | 0 - 0.125                           | 1359  | 0 - 0.125      | 2371  | 0 - 0.125      | 2149  | 1959   | 307   | 638 - 3281 | 0.024                                     | <b>significant</b> |
| TA98 (-S9)                  | 084396       | KR 2R4F               | 0 - 0.500                           | 62.2  | 0 - 0.500      | 98.3  | 0 - 0.500      | 50.5  | 70.3   | 14.4  | 8.51 - 132 | 0.039                                     | <b>significant</b> |
| TA100 (+S9)                 | 084396       | KR 2R4F               | 0 - 0.250                           | 616   | 0 - 0.250      | 748   | 0 - 0.250      | 866   | 743  | 72    | 432 - 1054 | 0.009                                     | <b>significant</b> |
| TA100 (-S9)                 | 084396       | KR 2R4F               | 0 - 0.125                           | 334   | 0 - 0.125      | 276   | 0 - 0.250      | 147   | 252  | 55    | 15.6 - 489 | 0.044                                     | <b>significant</b> |
| TA102 (+S9)                 | 084396       | KR 2R4F               | 0 - 0.500                           | -18.6 | 0 - 0.500      | 77.3  | 0 - 0.500      | 118   | 59.1   | 40.6  | 0* - 234   | 0.283                                     | not significant    |
| TA102 (-S9)                 | 084396       | KR 2R4F               | 0 - 0.500                           | -54.9 | 0 - 0.125      | 195   | 0 - 0.500      | 36.4  | 59.0   | 73.1  | 0* - 374   | 0.505                                     | not significant    |
| TA1535 (+S9)                | 084396       | KR 2R4F               | 0 - 0.500                           | 14.0  | 0 - 0.500      | 5.75  | 0 - 0.500      | 8.25  | 9.32   | 2.43  | 0* - 19.8  | 0.062                                     | not significant    |
| TA1535 (-S9)                | 084396       | KR 2R4F               | 0 - 0.500                           | 1.29  | 0 - 0.500      | 9.08  | 0 - 0.500      | 1.97  | 4.12   | 2.49  | 0* - 14.8  | 0.240                                     | not significant    |
| TA1537 (+S9)                | 084396       | KR 2R4F               | 0 - 0.250                           | 299   | 0 - 0.125      | 315   | 0 - 0.125      | 339   | 318  | 12    | 267 - 369  | 0.001                                     | <b>significant</b> |
| TA1537 (-S9)                | 084396       | KR 2R4F               | 0 - 0.250                           | 14.7  | 0 - 0.250      | 17.3  | 0 - 0.125      | 39.2  | 23.8   | 7.8   | 0* - 57.2  | 0.092                                     | not significant    |

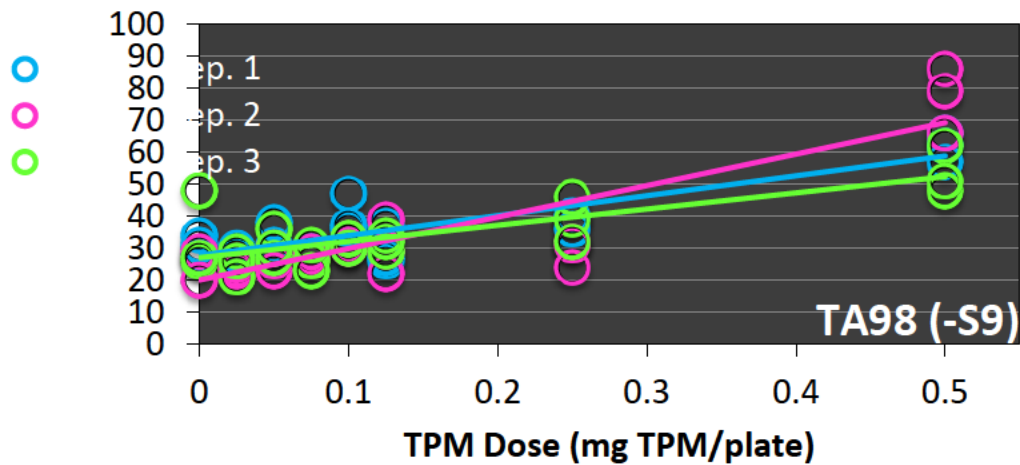
t-test analysis indicates mean specific activity TPM slope is greater than zero at  $\alpha = 0.05$  for strains TA98 (+S9), TA98 (-S9), TA100 (+S9), TA100 (-S9) and TA1537 (+S9).

0\*: Lower bound of the 95% confidence interval has been truncated at 0.

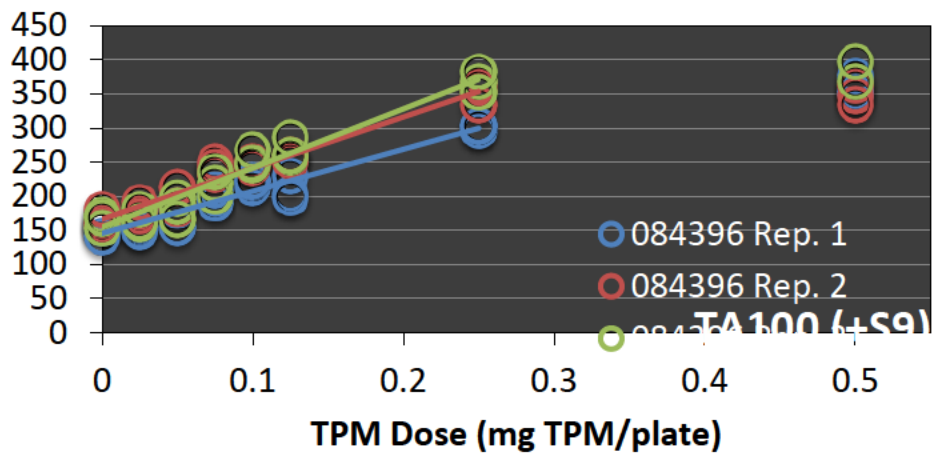
TA98 (+S9) Revertants/plate



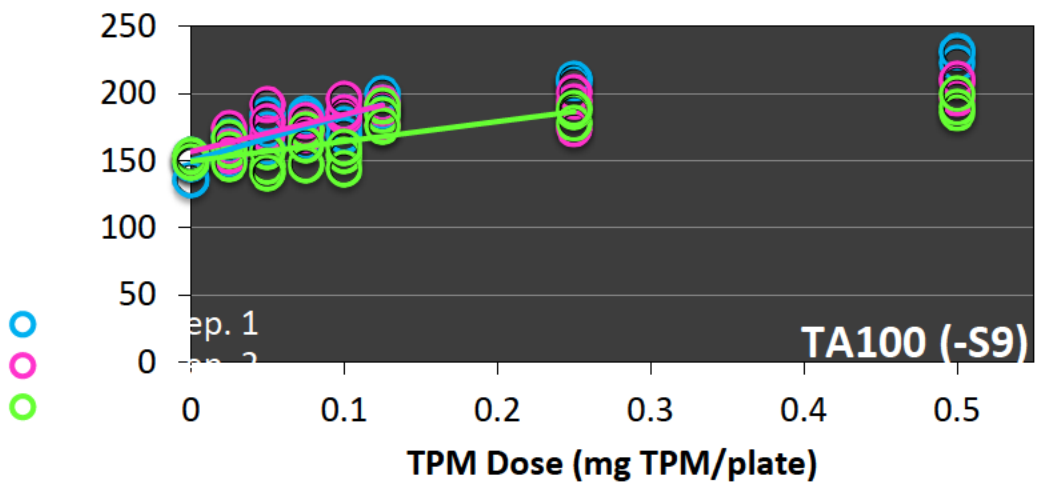
TA98 (-S9) Revertants/plate



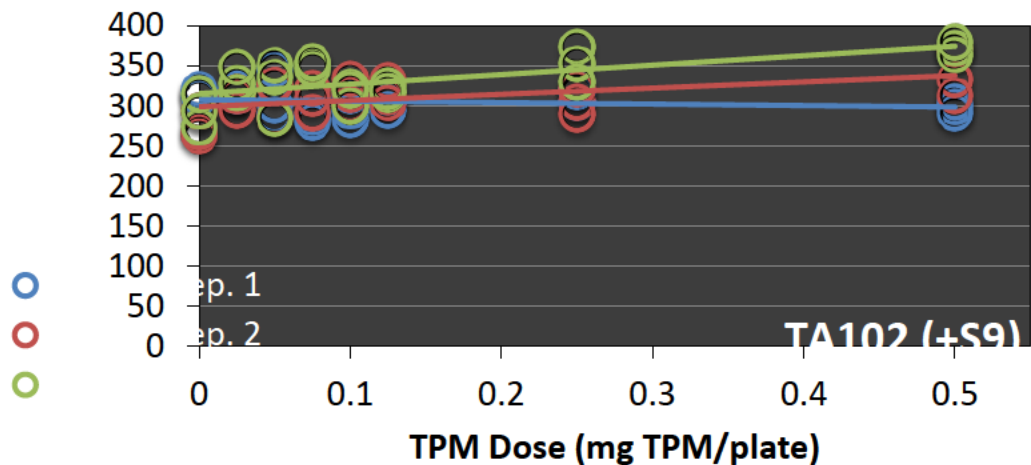
TA100 (+S9) Revertants/plate



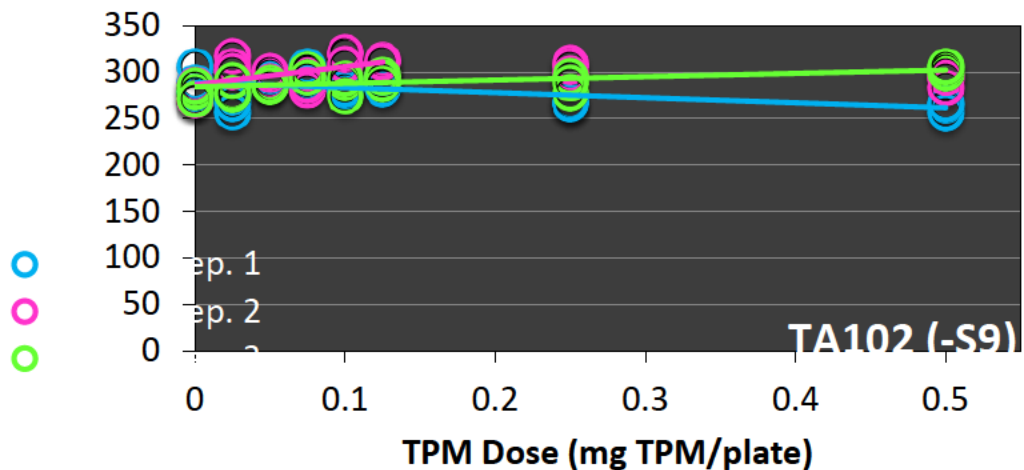
TA100 (-S9) Revertants/plate

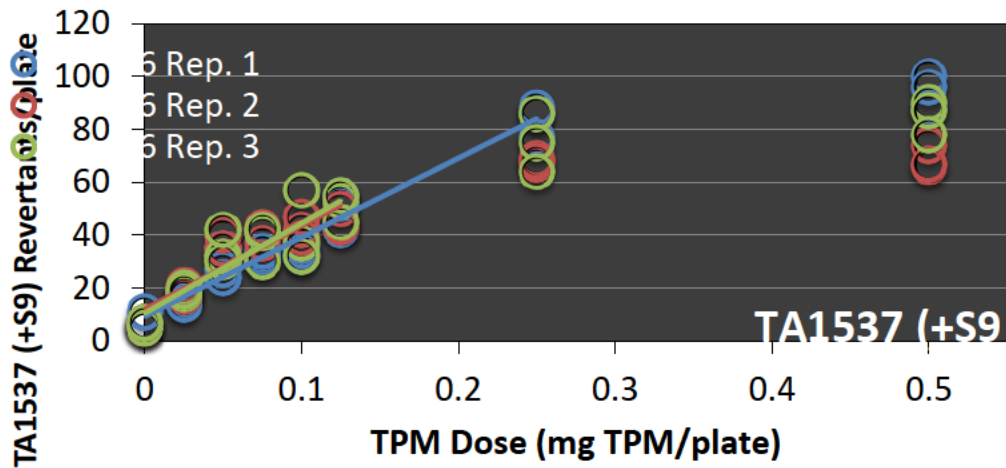
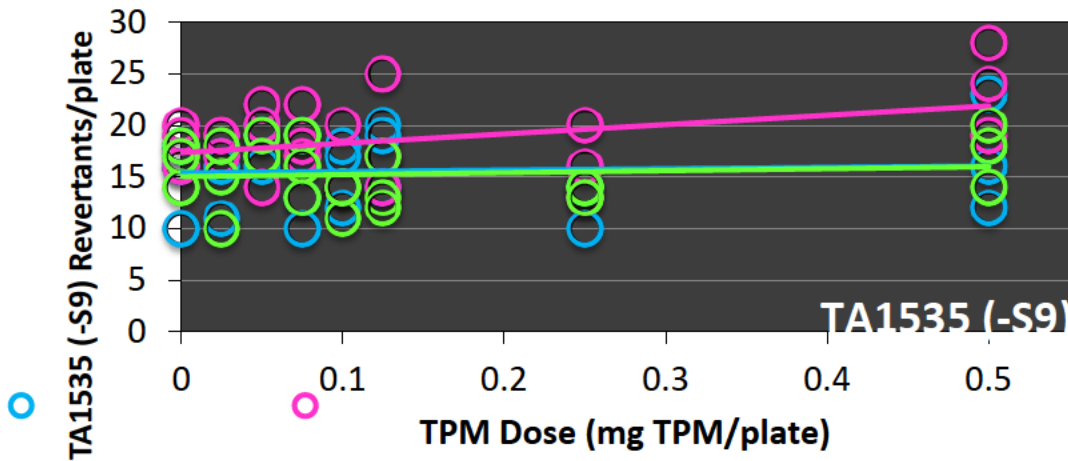
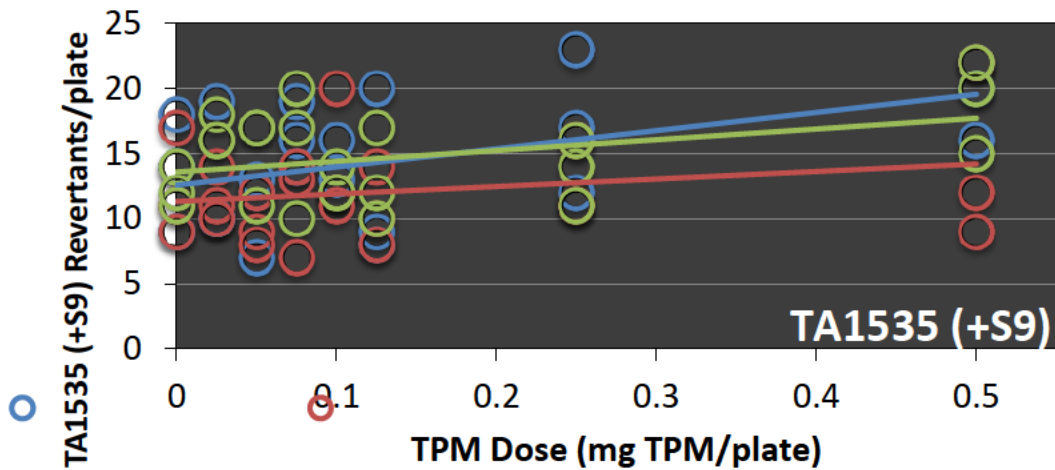


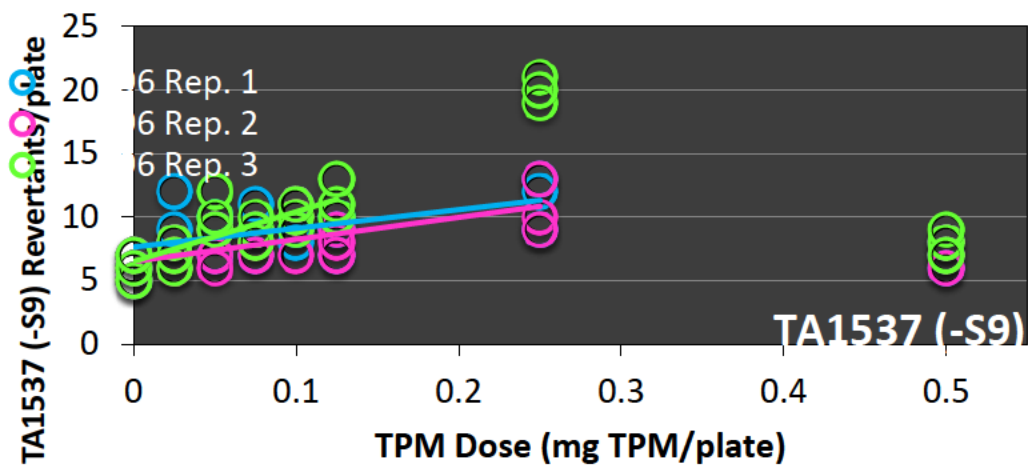
TA102 (+S9) Revertants/plate



TA102 (-S9) Revertants/plate







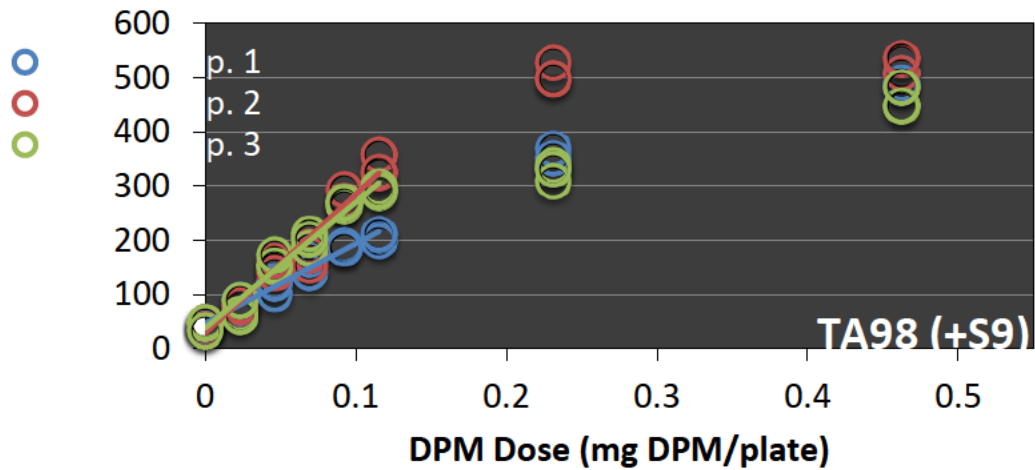
**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/mg Dry Particulate Matter (DPM))**

| Strain and<br>S9 Activation | Sample<br>ID | Sample<br>Description | Number of Revertant Colonies/mg DPM |       |                              |       |                              |       |  |       |                                   |         |                 |
|-----------------------------|--------------|-----------------------|-------------------------------------|-------|------------------------------|-------|------------------------------|-------|--|-------|-----------------------------------|---------|-----------------|
|                             |              |                       | Replicate 1                         |       | Replicate 2                  |       | Replicate 3                  |       | Statistics for Replicate Slope Estimates |       |                                   |         |                 |
|                             |              |                       | Dose Range<br>(mg DPM/plate)        |       | Dose Range<br>(mg DPM/plate) |       | Dose Range<br>(mg DPM/plate) |       | Standard                                 |       | t-test p-value ( $H_0$ : mean= 0) |         |                 |
|                             |              |                       |                                     | slope |                              | slope |                              | slope | Mean                                     | Error | 95% C.I.                          | p-value | significance    |
| TA98 (+S9)                  | 084396       | KR 2R4F               | 0 - 0.116                           | 1469  | 0 - 0.116                    | 2563  | 0 - 0.116                    | 2323  | 2118                                     | 332   | 690 - 3547                        | 0.024   | significant     |
| TA98 (-S9)                  | 084396       | KR 2R4F               | 0 - 0.463                           | 67.2  | 0 - 0.463                    | 106   | 0 - 0.463                    | 54.6  | 76.0                                     | 15.5  | 9.2 - 143                         | 0.039   | significant     |
| TA100 (+S9)                 | 084396       | KR 2R4F               | 0 - 0.231                           | 665   | 0 - 0.231                    | 809   | 0 - 0.231                    | 936   | 803                                      | 78    | 467 - 1139                        | 0.009   | significant     |
| TA100 (-S9)                 | 084396       | KR 2R4F               | 0 - 0.116                           | 361   | 0 - 0.116                    | 298   | 0 - 0.231                    | 159   | 273                                      | 59    | 16.8 - 529                        | 0.044   | significant     |
| TA102 (+S9)                 | 084396       | KR 2R4F               | 0 - 0.463                           | -20.1 | 0 - 0.463                    | 83.5  | 0 - 0.463                    | 128   | 63.8                                     | 43.9  | 0* - 253                          | 0.283   | not significant |
| TA102 (-S9)                 | 084396       | KR 2R4F               | 0 - 0.463                           | -59.3 | 0 - 0.116                    | 211   | 0 - 0.463                    | 39.3  | 63.8                                     | 79.1  | 0* - 404                          | 0.505   | not significant |
| TA1535 (+S9)                | 084396       | KR 2R4F               | 0 - 0.463                           | 15.1  | 0 - 0.463                    | 6.21  | 0 - 0.463                    | 8.92  | 10.07                                    | 2.62  | 0* - 21.4                         | 0.062   | not significant |
| TA1535 (-S9)                | 084396       | KR 2R4F               | 0 - 0.463                           | 1.4   | 0 - 0.463                    | 9.82  | 0 - 0.463                    | 2.13  | 4.45                                     | 2.69  | 0* - 16                           | 0.240   | not significant |
| TA1537 (+S9)                | 084396       | KR 2R4F               | 0 - 0.231                           | 323   | 0 - 0.116                    | 341   | 0 - 0.116                    | 367   | 344                                      | 13    | 289 - 398                         | 0.001   | significant     |
| TA1537 (-S9)                | 084396       | KR 2R4F               | 0 - 0.231                           | 15.9  | 0 - 0.231                    | 18.7  | 0 - 0.116                    | 42.4  | 25.7                                     | 8.4   | 0* - 61.8                         | 0.092   | not significant |

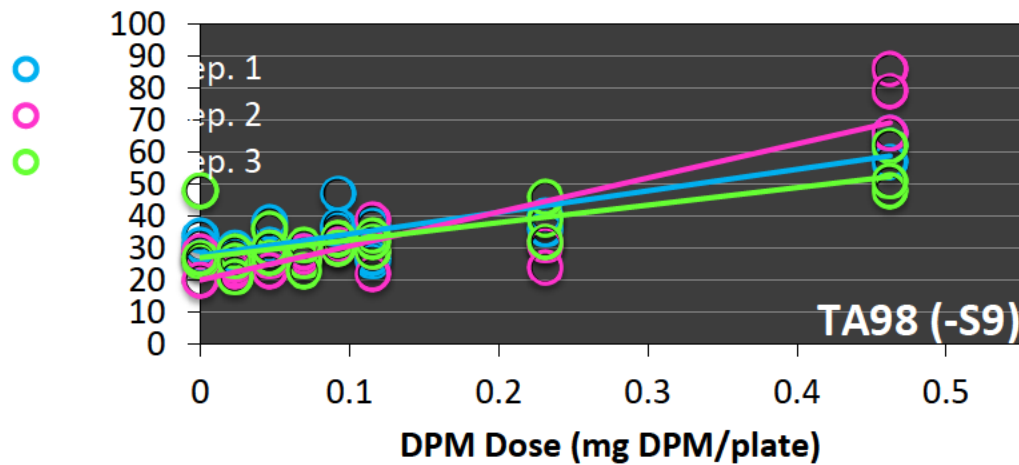
t-test analysis indicates mean specific activity DPM slope is greater than zero at  $\alpha = 0.05$  for strains TA98 (+S9), TA98 (-S9), TA100 (+S9), TA100 (-S9) and TA1537 (+S9).

0\*: Lower bound of the 95% confidence interval has been truncated at 0.

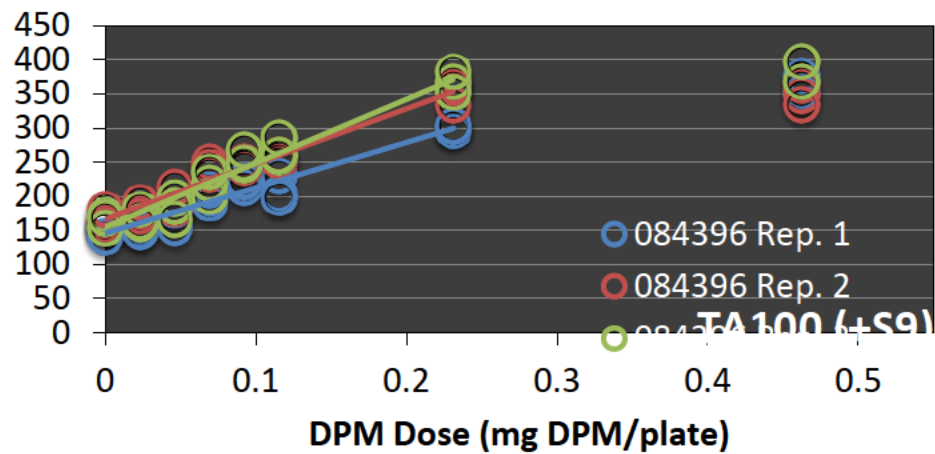
TA98 (+S9) Revertants/plate



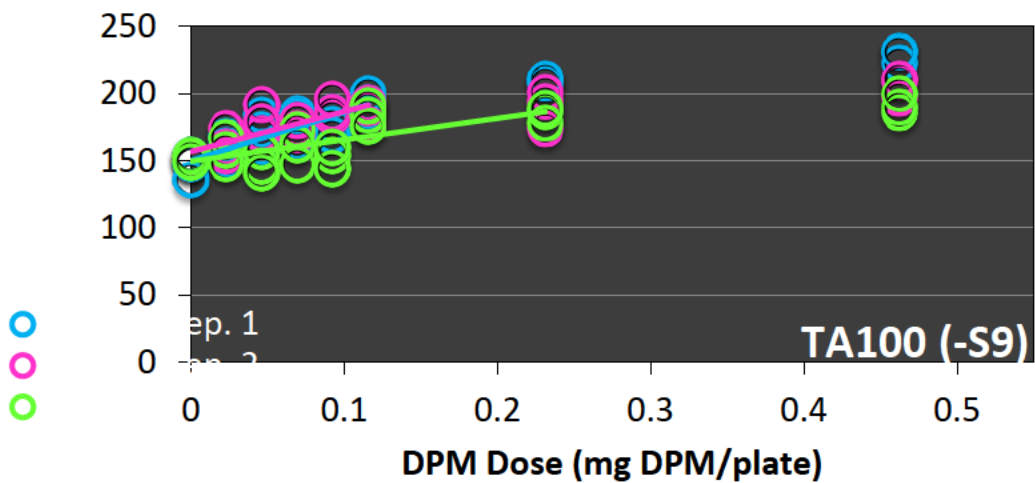
TA98 (-S9) Revertants/plate



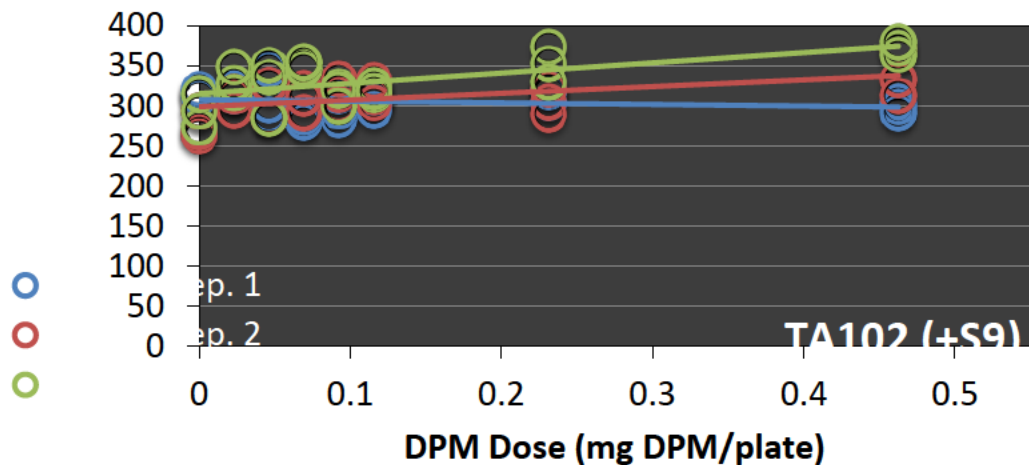
TA100 (+S9) Revertants/plate



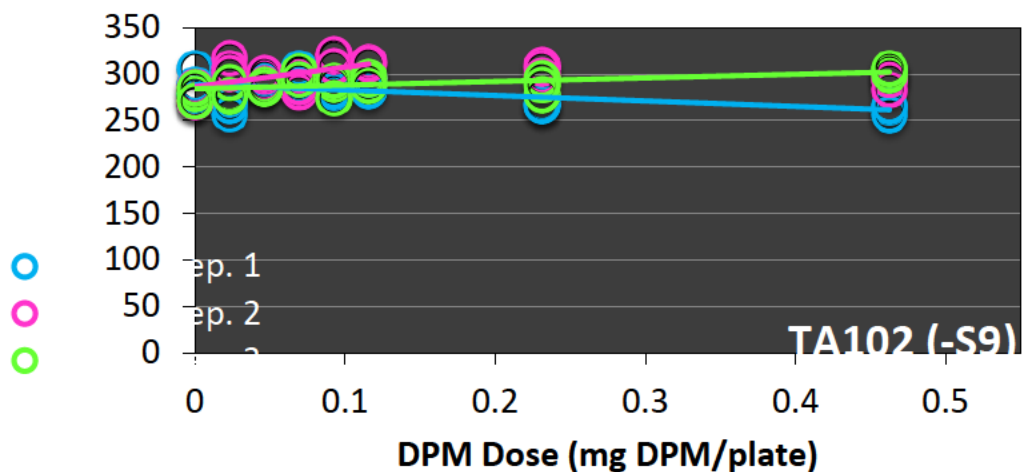
TA100 (-S9) Revertants/plate



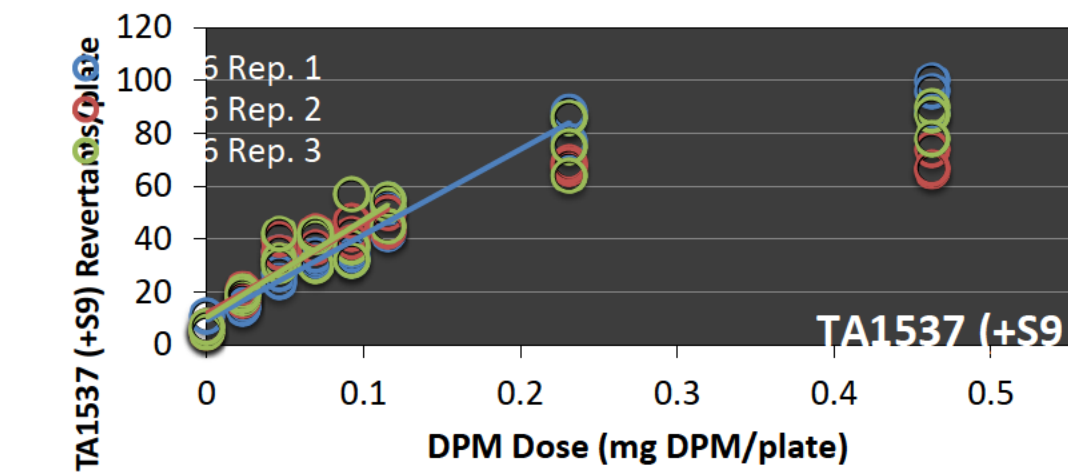
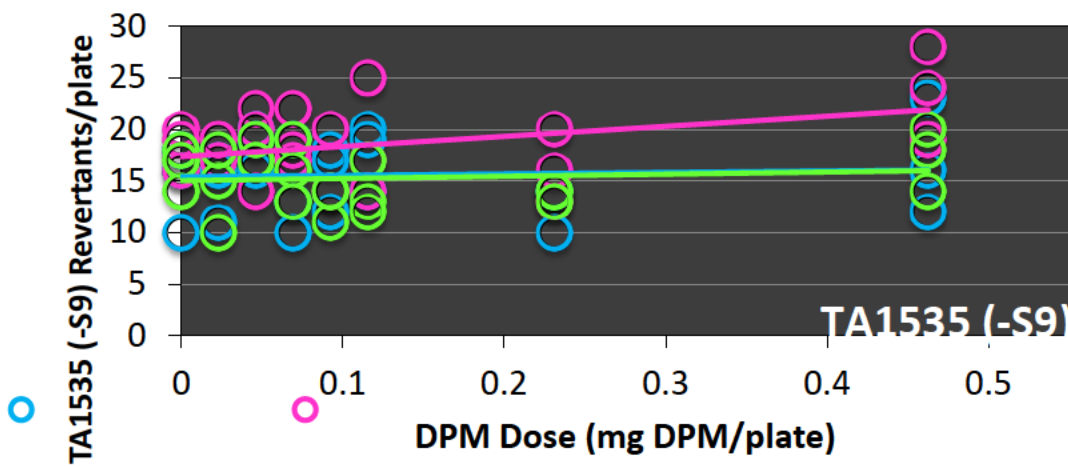
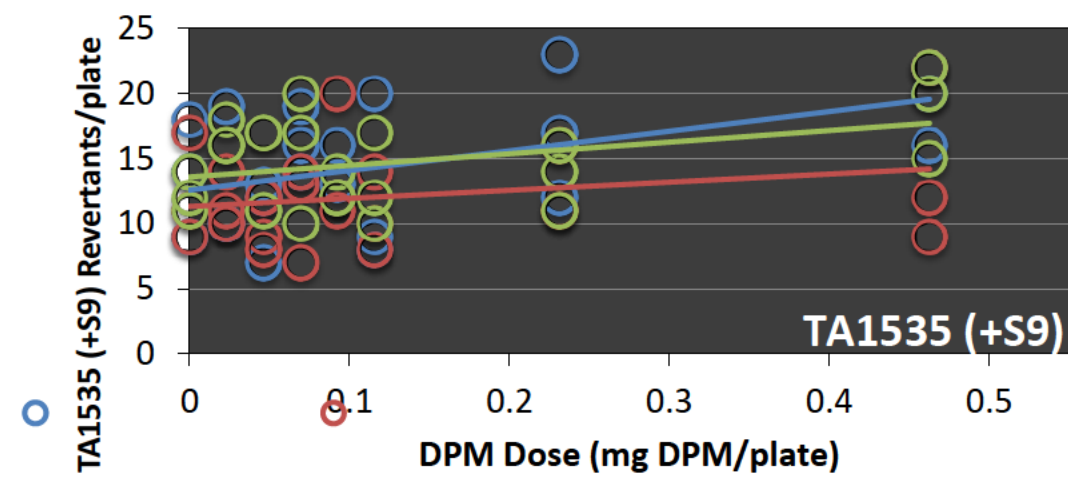
TA102 (+S9) Revertants/plate

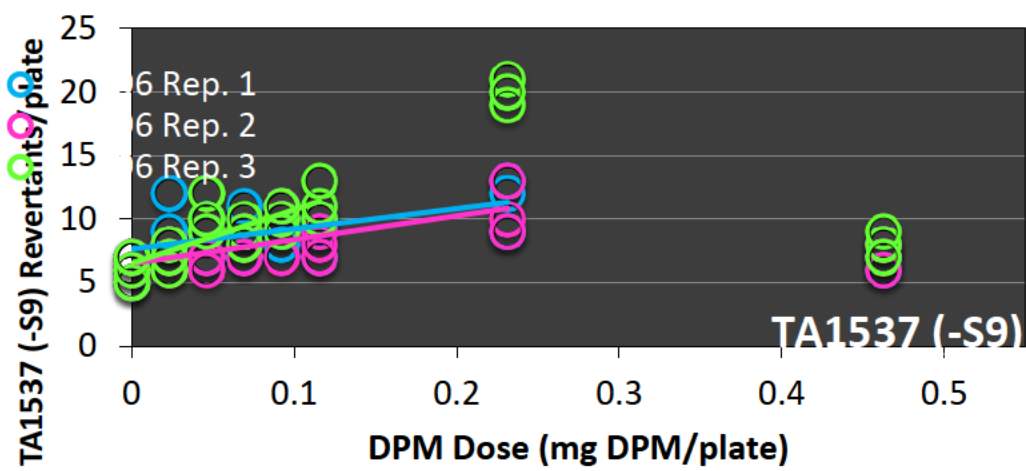


TA102 (-S9) Revertants/plate









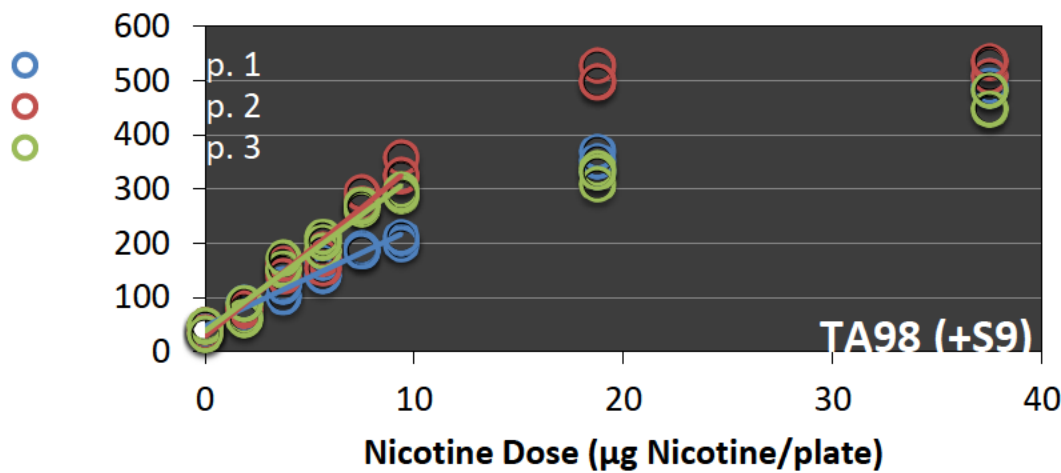
**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/ $\mu$ g Nicotine (Nic.))**

|               |        |             | Number of Revertant Colonies/μg Nicotine |        |                 |       |                 |       |  |       |              |   |                 |
|---------------|--------|-------------|--|--------|-----------------|-------|-----------------|-------|--|-------|--------------|---|-----------------|
| Strain and    | Sample | Sample      | Replicate 1                              |        | Replicate 2     |       | Replicate 3     |       | Statistics for Replicate Slope Estimates |       |              |   |                 |
|               |        |             | Dose Range                               |        | Dose Range      |       | Dose Range      |       | Standard                                 |       |              | t-test p-value (H <sub>0</sub> : mean= 0) |                 |
| S9 Activation | ID     | Description | (μg Nic./plate)                          | slope  | (μg Nic./plate) | slope | (μg Nic./plate) | slope | Mean                                     | Error | 95% C.I.     | p-value                                   | significance    |
| TA98 (+S9)    | 084396 | KR 2R4F     | 0 - 9.38                                 | 18.1   | 0 - 9.38        | 31.61 | 0 - 9.38        | 28.65 | 26.1                                     | 4.1   | 8.51 - 43.7  | 0.024                                     | significant     |
| TA98 (-S9)    | 084396 | KR 2R4F     | 0 - 37.5                                 | 0.829  | 0 - 37.5        | 1.31  | 0 - 37.5        | 0.674 | 0.938                                    | 0.192 | 0.113 - 1.76 | 0.039                                     | significant     |
| TA100 (+S9)   | 084396 | KR 2R4F     | 0 - 18.8                                 | 8.21   | 0 - 18.8        | 9.973 | 0 - 18.8        | 11.54 | 9.91                                     | 0.96  | 5.76 - 14.1  | 0.009                                     | significant     |
| TA100 (-S9)   | 084396 | KR 2R4F     | 0 - 9.38                                 | 4.45   | 0 - 9.38        | 3.677 | 0 - 18.8        | 1.966 | 3.36                                     | 0.73  | 0.208 - 6.52 | 0.044                                     | significant     |
| TA102 (+S9)   | 084396 | KR 2R4F     | 0 - 37.5                                 | -0.248 | 0 - 37.5        | 1.03  | 0 - 37.5        | 1.58  | 0.787                                    | 0.541 | 0* - 3.12    | 0.283                                     | not significant |
| TA102 (-S9)   | 084396 | KR 2R4F     | 0 - 37.5                                 | -0.731 | 0 - 9.38        | 2.606 | 0 - 37.5        | 0.485 | 0.786                                    | 0.975 | 0* - 4.98    | 0.505                                     | not significant |
| TA1535 (+S9)  | 084396 | KR 2R4F     | 0 - 37.5                                 | 0.186  | 0 - 37.5        | 0.077 | 0 - 37.5        | 0.110 | 0.124                                    | 0.032 | 0* - 0.263   | 0.062                                     | not significant |
| TA1535 (-S9)  | 084396 | KR 2R4F     | 0 - 37.5                                 | 0.017  | 0 - 37.5        | 0.121 | 0 - 37.5        | 0.026 | 0.055                                    | 0.033 | 0* - 0.198   | 0.240                                     | not significant |
| TA1537 (+S9)  | 084396 | KR 2R4F     | 0 - 18.8                                 | 3.98   | 0 - 9.38        | 4.206 | 0 - 9.38        | 4.526 | 4.24                                     | 0.16  | 3.56 - 4.91  | 0.001                                     | significant     |
| TA1537 (-S9)  | 084396 | KR 2R4F     | 0 - 18.8                                 | 0.196  | 0 - 18.8        | 0.231 | 0 - 9.38        | 0.523 | 0.317                                    | 0.104 | 0* - 0.763   | 0.092                                     | not significant |

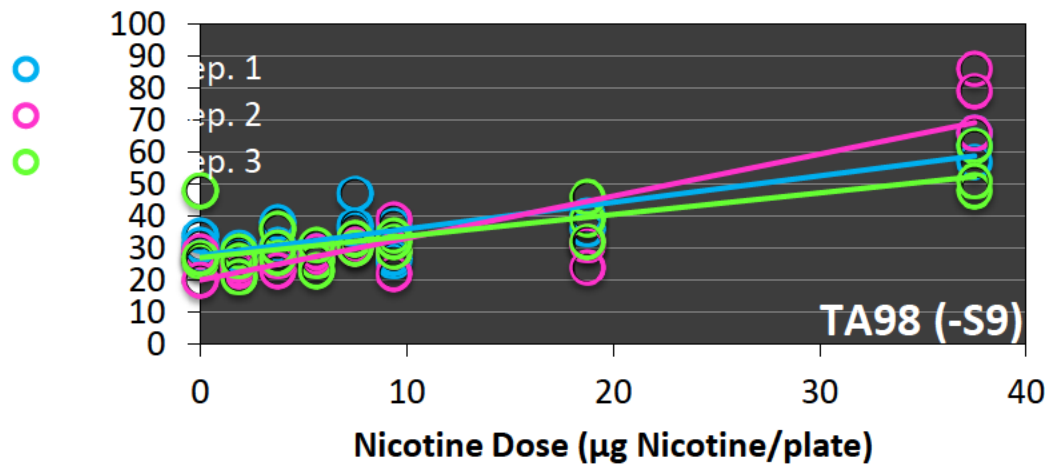
t-test analysis indicates mean specific activity Nicotine slope is greater than zero at  $\alpha = 0.05$  for strains TA98 (+S9), TA98 (-S9), TA100 (+S9), TA100 (-S9) and TA1537 (+S9).

0\*: Lower bound of the 95% confidence interval has been truncated at 0.

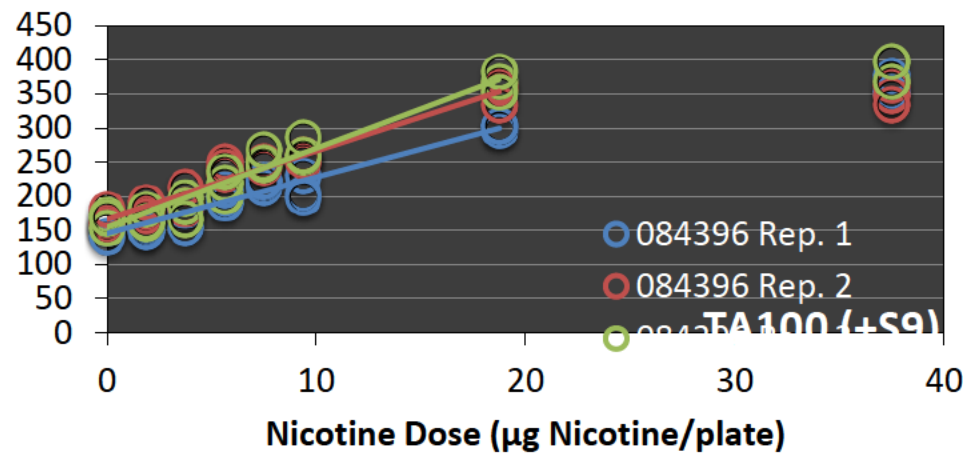
TA98 (+S9) Revertants/plate



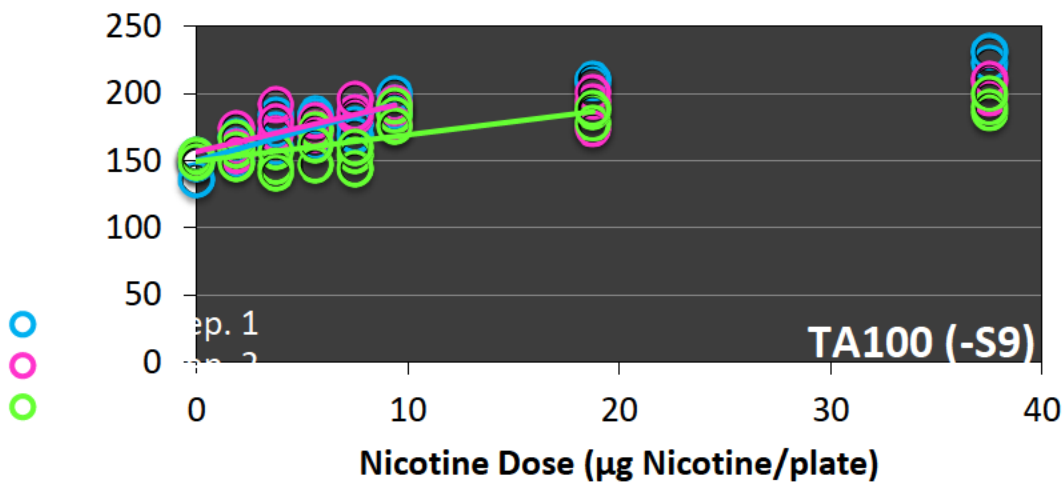
TA98 (-S9) Revertants/plate



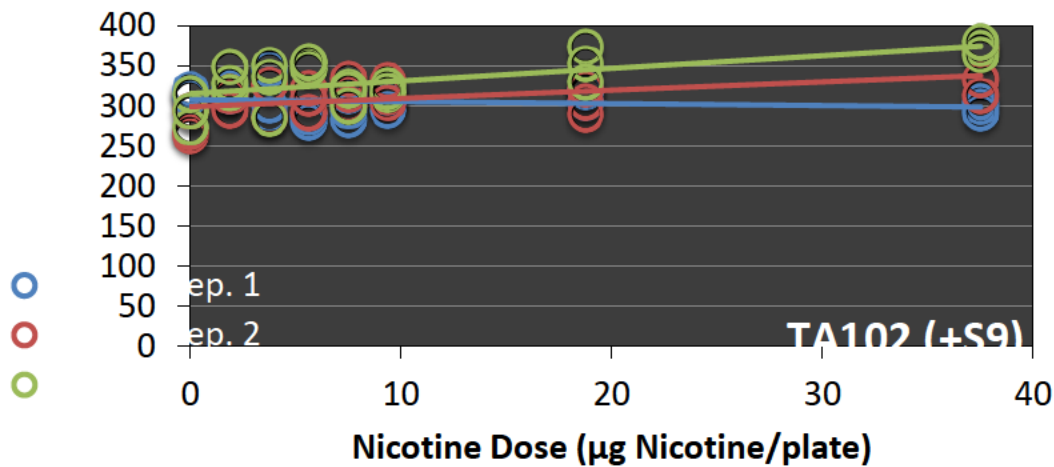
TA100 (+S9) Revertants/plate



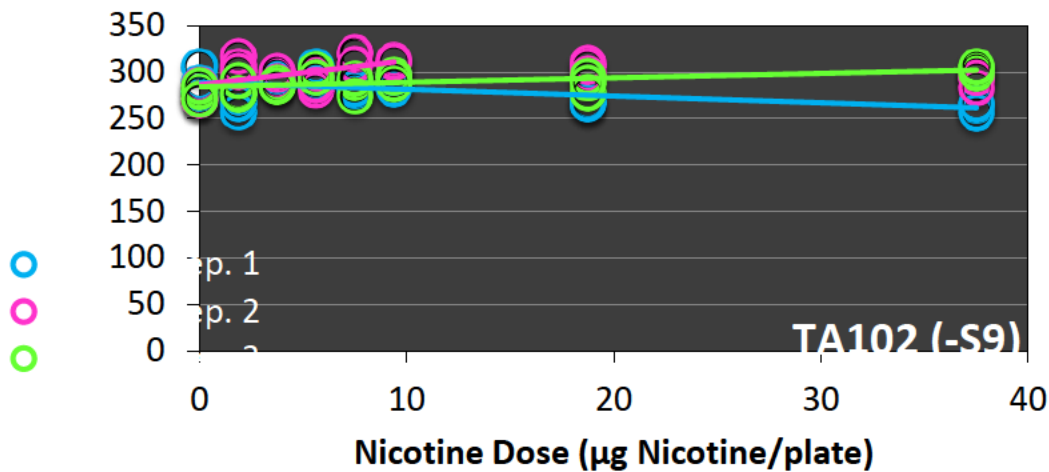
TA100 (-S9) Revertants/plate

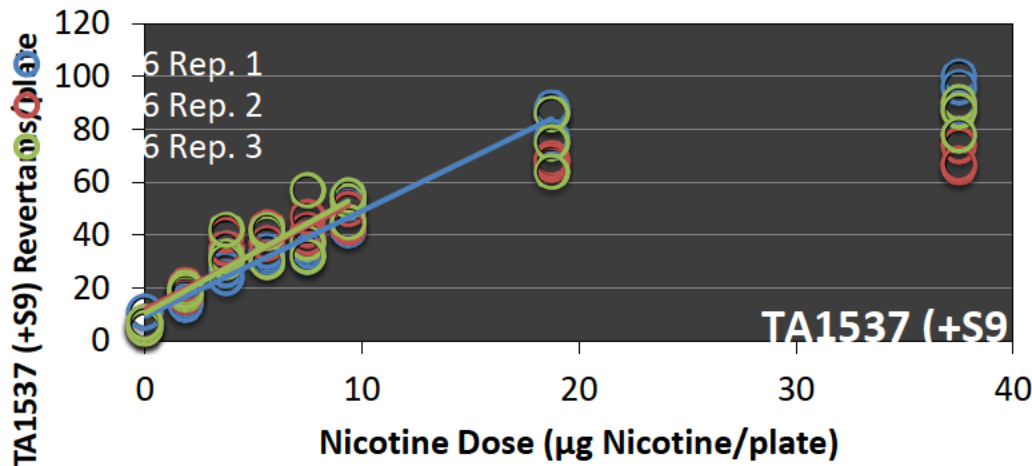
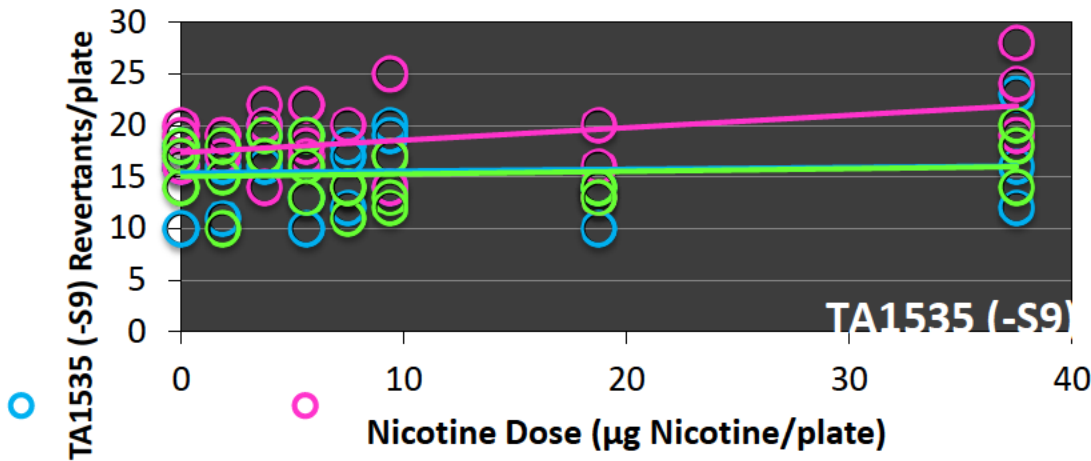
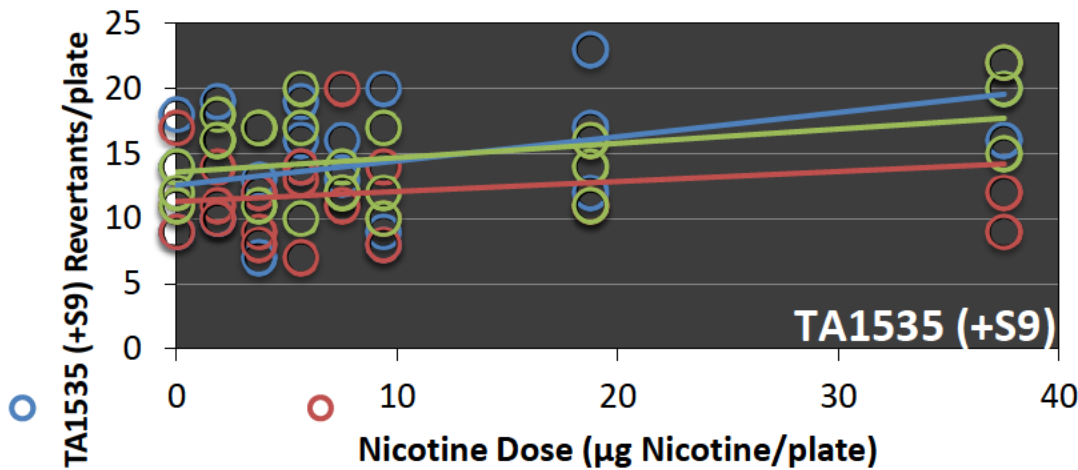


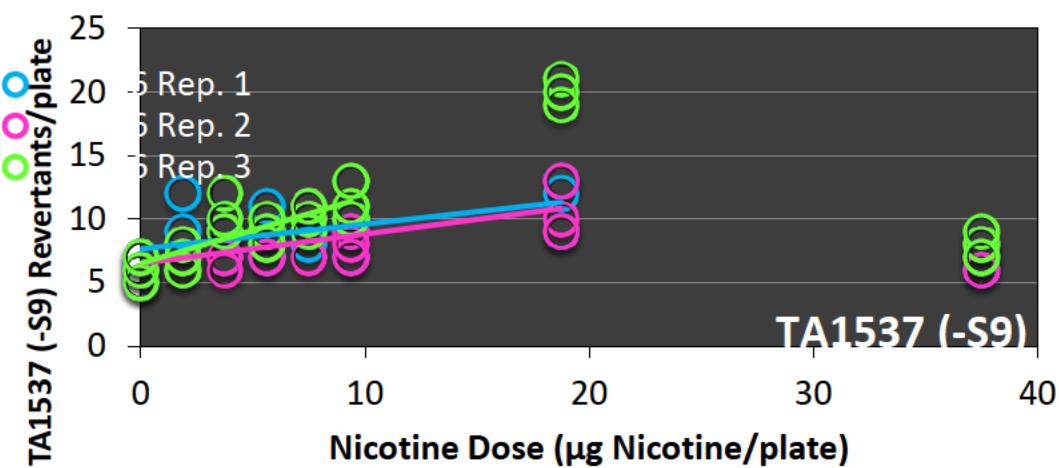
TA102 (+S9) Revertants/plate



TA102 (-S9) Revertants/plate







**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/ $\mu$ g 'Extracted Nicotine in DMSO' (Nic))**

| Strain and<br>S9 Activation | Sample<br>ID | Sample<br>Description | Number of Revertant Colonies/ $\mu$ g 'Extracted Nicotine in DMSO' |        |                       |        |                       |        |   |       |                                    |         |                    |
|-----------------------------|--------------|-----------------------|--|--------|-----------------------|--------|-----------------------|--------|---|-------|------------------------------------|---------|--------------------|
|                             |              |                       | Replicate 1  |        | Replicate 2           |        | Replicate 3           |        | Statistics for Replicate 'Nic.' Slope Estimates |       |                                    |         |                    |
|                             |              |                       | Dose Range   |        | Dose Range            |        | Dose Range            |        | Standard  |       | t-test p-value ( $H_0$ : mean = 0) |         |                    |
|                             |              |                       | ( $\mu$ g Nic./plate)  | slope  | ( $\mu$ g Nic./plate) | slope  | ( $\mu$ g Nic./plate) | slope  | Mean  | Error | 95% C.I.                           | p-value | significance       |
| TA98 (+S9)                  | 084394       | Camel SNUS Frost      | 0 - 63.8   | 0.063  | 0 - 71.5              | 0.127  | 0 - 67.2              | -0.120 | 0.023   | 0.074 | 0* - 0.342                         | 0.782   | not significant    |
| TA98 (+S9)                  | 084395       | 2S3                   | 0 - 78   | 0.199  | 0 - 79.7              | 0.017  | 0 - 74.4              | 0.162  | 0.126   | 0.056 | 0* - 0.365                         | 0.152   | not significant    |
| TA98 (+S9)                  | 084454       | Fresh Strips          | 0 - 20   | -0.106 | 0 - 21.6              | 0.124  | 0 - 11.1              | -0.621 | 0*  | 0.220 | 0* - 0.747                         | 0.458   | not significant    |
| TA98 (+S9)                  | 084455       | Mellow Sticks         | 0 - 30.7   | -0.189 | 0 - 29.1              | 0.002  | 0 - 30.9              | 0.193  | 0.002   | 0.110 | 0* - 0.477                         | 0.987   | not significant    |
| TA98 (+S9)                  | 084456       | Copenhagen Long Cut   | 0 - 64.6   | 0.235  | 0 - 66.3              | 0.226  | 0 - 67.7              | 0.144  | 0.202   | 0.029 | 0.076 - 0.327                      | 0.020   | <b>significant</b> |
| TA98 (+S9)                  | 084457       | Ariva Wintergreen     | 0 - 29.5   | 0.061  | 0 - 30.8              | -0.139 | 0 - 31.8              | -0.177 | 0*  | 0.074 | 0* - 0.233                         | 0.370   | not significant    |
| TA98 (+S9)                  | 084458       | Fresh Orbs            | 0 - 13.1   | -0.014 | 0 - 14.4              | -0.246 | 0 - 7.7               | 1.59   | 0.444   | 0.58  | 0* - 2.928                         | 0.523   | not significant    |
| TA98 (-S9)                  | 084394       | Camel SNUS Frost      | 0 - 63.8   | -0.024 | 0 - 71.5              | 0.085  | 0 - 33.6              | 0.000  | 0.020   | 0.033 | 0* - 0.162                         | 0.601   | not significant    |
| TA98 (-S9)                  | 084395       | 2S3                   | 0 - 78   | 0.035  | 0 - 79.7              | -0.040 | 0 - 37.2              | -0.022 | 0*  | 0.023 | 0* - 0.088                         | 0.731   | not significant    |
| TA98 (-S9)                  | 084454       | Fresh Strips          | 0 - 20   | 0.245  | 0 - 21.6              | -0.021 | 0 - 22.1              | 0.230  | 0.151   | 0.086 | 0* - 0.522                         | 0.221   | not significant    |
| TA98 (-S9)                  | 084455       | Mellow Sticks         | 0 - 30.7   | 0.270  | 0 - 29.1              | 0.212  | 0 - 30.9              | 0.196  | 0.226   | 0.023 | 0.129 - 0.323                      | 0.010   | <b>significant</b> |
| TA98 (-S9)                  | 084456       | Copenhagen Long Cut   | 0 - 64.6   | 0.014  | 0 - 66.3              | 0.017  | 0 - 67.7              | 0.044  | 0.025   | 0.010 | 0* - 0.066                         | 0.123   | not significant    |
| TA98 (-S9)                  | 084457       | Ariva Wintergreen     | 0 - 29.5   | -0.067 | 0 - 15.4              | 0.240  | 0 - 31.8              | 0.110  | 0.094   | 0.089 | 0* - 0.477                         | 0.401   | not significant    |
| TA98 (-S9)                  | 084458       | Fresh Orbs            | 0 - 13.1   | -0.012 | 0 - 14.4              | 0.165  | 0 - 15.3              | -0.011 | 0.047   | 0.059 | 0* - 0.301                         | 0.505   | not significant    |
| TA100 (+S9)                 | 084394       | Camel SNUS Frost      | 0 - 16   | 0.116  | 0 - 17.9              | 1.05   | 0 - 16.8              | 1.53   | 0.898   | 0.41  | 0* - 2.681                         | 0.163   | not significant    |
| TA100 (+S9)                 | 084395       | 2S3                   | 0 - 15.6   | 0.881  | 0 - 15.9              | 1.98   | 0 - 14.9              | 0.852  | 1.24  | 0.37  | 0* - 2.839                         | 0.080   | not significant    |
| TA100 (+S9)                 | 084454       | Fresh Strips          | 0 - 5  | 5.25   | 0 - 10.8              | 2.77   | 0 - 5.5               | 3.31   | 3.78  | 0.75  | 0.542 - 7.015                      | 0.037   | <b>significant</b> |
| TA100 (+S9)                 | 084455       | Mellow Sticks         | 0 - 15.3   | 2.28   | 0 - 7.3               | 3.56   | 0 - 15.4              | 1.49   | 2.44  | 0.60  | 0* - 5.037                         | 0.056   | not significant    |
| TA100 (+S9)                 | 084456       | Copenhagen Long Cut   | 0 - 32.3   | 1.17   | 0 - 16.6              | 2.14   | 0 - 16.9              | 1.57   | 1.63  | 0.28  | 0.415 - 2.841                      | 0.029   | <b>significant</b> |
| TA100 (+S9)                 | 084457       | Ariva Wintergreen     | 0 - 5.9  | 5.73   | 0 - 30.8              | 0.498  | 0 - 7.9               | 2.07   | 2.76  | 1.55  | 0* - 9.426                         | 0.216   | not significant    |
| TA100 (+S9)                 | 084458       | Fresh Orbs            | 0 - 6.6  | 0.628  | 0 - 3.6               | 2.93   | 0 - 3.8               | 5.86   | 3.14  | 1.51  | 0* - 9.655                         | 0.174   | not significant    |
| TA100 (-S9)                 | 084394       | Camel SNUS Frost      | 0 - 63.8   | 0.210  | 0 - 71.5              | 0.355  | 0 - 67.2              | 0.547  | 0.371   | 0.10  | 0* - 0.791                         | 0.063   | not significant    |
| TA100 (-S9)                 | 084395       | 2S3                   | 0 - 39   | 0.290  | 0 - 79.7              | 0.299  | 0 - 74.4              | 0.413  | 0.334   | 0.039 | 0.164 - 0.504                      | 0.014   | <b>significant</b> |
| TA100 (-S9)                 | 084454       | Fresh Strips          | 0 - 20   | -1.11  | 0 - 21.6              | 0.290  | 0 - 11.1              | 0.671  | 0*  | 0.54  | 0* - 2.282                         | 0.935   | not significant    |
| TA100 (-S9)                 | 084455       | Mellow Sticks         | 0 - 15.3   | 1.92   | 0 - 29.1              | -0.080 | 0 - 30.9              | -1.26  | 0.194   | 0.93  | 0* - 4.178                         | 0.854   | not significant    |
| TA100 (-S9)                 | 084456       | Copenhagen Long Cut   | 0 - 32.3   | 1.63   | 0 - 33.2              | 0.003  | 0 - 33.8              | 0.448  | 0.695   | 0.49  | 0* - 2.789                         | 0.290   | not significant    |
| TA100 (-S9)                 | 084457       | Ariva Wintergreen     | 0 - 29.5   | 1.66   | 0 - 30.8              | -2.19  | 0 - 31.8              | -2.34  | 0*  | 1.31  | 0* - 4.68                          | 0.542   | not significant    |
| TA100 (-S9)                 | 084458       | Fresh Orbs            | 0 - 13.1   | -1.25  | 0 - 14.4              | -3.54  | 0 - 15.3              | -0.813 | 0*  | 0.84  | 0* - 1.767                         | 0.158   | not significant    |
| TA102 (+S9)                 | 084394       | Camel SNUS Frost      | 0 - 12.8   | 3.64   | 0 - 17.9              | 4.44   | 0 - 16.8              | 3.44   | 3.84  | 0.31  | 2.525 - 5.155                      | 0.006   | <b>significant</b> |
| TA102 (+S9)                 | 084395       | 2S3                   | 0 - 15.6   | 3.35   | 0 - 79.7              | 0.305  | 0 - 18.6              | 1.23   | 1.63  | 0.9   | 0* - 5.508                         | 0.213   | not significant    |
| TA102 (+S9)                 | 084454       | Fresh Strips          | 0 - 20   | 0.309  | 0 - 21.6              | -0.865 | 0 - 22.1              | 0.168  | 0*  | 0.37  | 0* - 1.463                         | 0.760   | not significant    |
| TA102 (+S9)                 | 084455       | Mellow Sticks         | 0 - 30.7   | 0.627  | 0 - 29.1              | 0.293  | 0 - 30.9              | 0.482  | 0.467   | 0.097 | 0.051 - 0.884                      | 0.040   | <b>significant</b> |
| TA102 (+S9)                 | 084456       | Copenhagen Long Cut   | 0 - 64.6   | 0.691  | 0 - 66.3              | 0.168  | 0 - 67.7              | 0.343  | 0.401   | 0.15  | 0* - 1.063                         | 0.121   | not significant    |
| TA102 (+S9)                 | 084457       | Ariva Wintergreen     | 0 - 29.5   | -0.423 | 0 - 30.8              | -0.151 | 0 - 31.8              | -0.296 | 0*  | 0.079 | 0* - 0.049                         | 0.067   | not significant    |
| TA102 (+S9)                 | 084458       | Fresh Orbs            | 0 - 13.1   | -5.05  | 0 - 14.4              | 0.518  | 0 - 15.3              | -3.03  | 0*  | 1.63  | 0* - 4.48                          | 0.261   | not significant    |
| TA102 (-S9)                 | 084394       | Camel SNUS Frost      | 0 - 63.8   | -0.212 | 0 - 35.7              | 0.427  | 0 - 67.2              | -0.117 | 0.033   | 0.20  | 0* - 0.89                          | 0.885   | not significant    |
| TA102 (-S9)                 | 084395       | 2S3                   | 0 - 78   | 0.127  | 0 - 79.7              | 0.376  | 0 - 74.4              | 0.923  | 0.475   | 0.23  | 0* - 1.486                         | 0.180   | not significant    |



**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/ $\mu$ g 'Extracted Nicotine in DMSO' (Nic))**

| Strain and<br>S9 Activation | Sample<br>ID | Sample<br>Description | Number of Revertant Colonies/ $\mu$ g 'Extracted Nicotine in DMSO' |        |                       |        |                       |        |   |       |                                    |         |                 |
|-----------------------------|--------------|-----------------------|--|--------|-----------------------|--------|-----------------------|--------|---|-------|------------------------------------|---------|-----------------|
|                             |              |                       | Replicate 1  |        | Replicate 2           |        | Replicate 3           |        | Statistics for Replicate 'Nic.' Slope Estimates |       |                                    |         |                 |
|                             |              |                       | Dose Range   |        | Dose Range            |        | Dose Range            |        | Standard  |       | t-test p-value ( $H_0$ : mean = 0) |         |                 |
|                             |              |                       | ( $\mu$ g Nic./plate)  | slope  | ( $\mu$ g Nic./plate) | slope  | ( $\mu$ g Nic./plate) | slope  | Mean  | Error | 95% C.I.                           | p-value | significance    |
| TA102 (-S9)                 | 084454       | Fresh Strips          | 0 - 20   | -0.223 | 0 - 21.6              | 1.50   | 0 - 5.5               | 11.9   | 4.39  | 3.8   | 0* - 20.664                        | 0.366   | not significant |
| TA102 (-S9)                 | 084455       | Mellow Sticks         | 0 - 15.3   | 0.687  | 0 - 29.1              | 0.595  | 0 - 30.9              | 0.041  | 0.441   | 0.20  | 0* - 1.309                         | 0.161   | not significant |
| TA102 (-S9)                 | 084456       | Copenhagen Long Cut   | 0 - 64.6   | -0.002 | 0 - 66.3              | 0.408  | 0 - 33.8              | 2.59   | 0.998   | 0.80  | 0* - 4.455                         | 0.340   | not significant |
| TA102 (-S9)                 | 084457       | Ariva Wintergreen     | 0 - 29.5   | -0.871 | 0 - 30.8              | -1.40  | 0 - 31.8              | -0.152 | 0*  | 0.36  | 0* - 0.748                         | 0.155   | not significant |
| TA102 (-S9)                 | 084458       | Fresh Orbs            | 0 - 13.1   | -7.72  | 0 - 14.4              | 0.930  | 0 - 15.3              | 1.10   | 0*  | 2.91  | 0* - 10.637                        | 0.581   | not significant |
| TA1535 (+S9)                | 084394       | Camel SNUS Frost      | 0 - 63.8   | 0.007  | 0 - 71.5              | 0.041  | 0 - 67.2              | -0.086 | 0*  | 0.038 | 0* - 0.15                          | 0.770   | not significant |
| TA1535 (+S9)                | 084395       | 2S3                   | 0 - 78   | 0.026  | 0 - 79.7              | 0.010  | 0 - 74.4              | -0.004 | 0.011   | 0.009 | 0* - 0.049                         | 0.335   | not significant |
| TA1535 (+S9)                | 084454       | Fresh Strips          | 0 - 20   | 0.101  | 0 - 21.6              | 0.086  | 0 - 22.1              | -0.091 | 0.032   | 0.062 | 0* - 0.297                         | 0.656   | not significant |
| TA1535 (+S9)                | 084455       | Mellow Sticks         | 0 - 30.7   | -0.012 | 0 - 29.1              | -0.152 | 0 - 15.4              | 0.271  | 0.036   | 0.124 | 0* - 0.57                          | 0.801   | not significant |
| TA1535 (+S9)                | 084456       | Copenhagen Long Cut   | 0 - 64.6   | 0.015  | 0 - 66.3              | 0.018  | 0 - 67.7              | -0.019 | 0.005   | 0.012 | 0* - 0.056                         | 0.738   | not significant |
| TA1535 (+S9)                | 084457       | Ariva Wintergreen     | 0 - 29.5   | 0.230  | 0 - 30.8              | 0.143  | 0 - 31.8              | -0.164 | 0.069   | 0.119 | 0* - 0.583                         | 0.619   | not significant |
| TA1535 (+S9)                | 084458       | Fresh Orbs            | 0 - 13.1   | 0.103  | 0 - 14.4              | 0.012  | 0 - 15.3              | -0.262 | 0*  | 0.110 | 0* - 0.424                         | 0.699   | not significant |
| TA1535 (-S9)                | 084394       | Camel SNUS Frost      | 0 - 63.8   | 0.006  | 0 - 71.5              | 0.074  | 0 - 67.2              | -0.046 | 0.011   | 0.035 | 0* - 0.162                         | 0.776   | not significant |
| TA1535 (-S9)                | 084395       | 2S3                   | 0 - 78   | -0.019 | 0 - 79.7              | 0.020  | 0 - 74.4              | 0.070  | 0.024   | 0.026 | 0* - 0.134                         | 0.455   | not significant |
| TA1535 (-S9)                | 084454       | Fresh Strips          | 0 - 10   | 0.186  | 0 - 10.8              | 0.422  | 0 - 11.1              | 0.275  | 0.295   | 0.069 | 0* - 0.59                          | 0.050   | not significant |
| TA1535 (-S9)                | 084455       | Mellow Sticks         | 0 - 30.7   | -0.144 | 0 - 29.1              | 0.013  | 0 - 30.9              | -0.011 | 0*  | 0.049 | 0* - 0.162                         | 0.432   | not significant |
| TA1535 (-S9)                | 084456       | Copenhagen Long Cut   | 0 - 64.6   | 0.034  | 0 - 66.3              | 0.077  | 0 - 33.8              | 0.146  | 0.086   | 0.033 | 0* - 0.226                         | 0.120   | not significant |
| TA1535 (-S9)                | 084457       | Ariva Wintergreen     | 0 - 7.4  | 0.769  | 0 - 30.8              | 0.141  | 0 - 31.8              | -0.054 | 0.285   | 0.25  | 0* - 1.355                         | 0.370   | not significant |
| TA1535 (-S9)                | 084458       | Fresh Orbs            | 0 - 3.3  | 1.74   | 0 - 7.2               | 0.842  | 0 - 15.3              | 0.067  | 0.884   | 0.48  | 0* - 2.965                         | 0.209   | not significant |
| TA1537 (+S9)                | 084394       | Camel SNUS Frost      | 0 - 31.9   | 0.254  | 0 - 71.5              | 0.098  | 0 - 67.2              | 0.109  | 0.154   | 0.050 | 0* - 0.37                          | 0.093   | not significant |
| TA1537 (+S9)                | 084395       | 2S3                   | 0 - 19.5   | 0.557  | 0 - 79.7              | 0.074  | 0 - 74.4              | 0.073  | 0.235   | 0.16  | 0* - 0.928                         | 0.282   | not significant |
| TA1537 (+S9)                | 084454       | Fresh Strips          | 0 - 20   | 0.052  | 0 - 21.6              | -0.020 | 0 - 22.1              | -0.077 | 0*  | 0.037 | 0* - 0.146                         | 0.727   | not significant |
| TA1537 (+S9)                | 084455       | Mellow Sticks         | 0 - 30.7   | -0.066 | 0 - 29.1              | 0.045  | 0 - 30.9              | 0.101  | 0.027   | 0.049 | 0* - 0.239                         | 0.641   | not significant |
| TA1537 (+S9)                | 084456       | Copenhagen Long Cut   | 0 - 32.3   | 0.208  | 0 - 33.2              | 0.155  | 0 - 67.7              | 0.084  | 0.149   | 0.036 | 0* - 0.304                         | 0.054   | not significant |
| TA1537 (+S9)                | 084457       | Ariva Wintergreen     | 0 - 29.5   | -0.068 | 0 - 30.8              | 0.105  | 0 - 31.8              | -0.039 | 0*  | 0.054 | 0* - 0.23                          | 0.992   | not significant |
| TA1537 (+S9)                | 084458       | Fresh Orbs            | 0 - 13.1   | 0.583  | 0 - 14.4              | -0.073 | 0 - 15.3              | 0.022  | 0.177   | 0.205 | 0* - 1.058                         | 0.478   | not significant |
| TA1537 (-S9)                | 084394       | Camel SNUS Frost      | 0 - 16   | 0.361  | 0 - 71.5              | 0.068  | 0 - 33.6              | 0.182  | 0.204   | 0.085 | 0* - 0.571                         | 0.140   | not significant |
| TA1537 (-S9)                | 084395       | 2S3                   | 0 - 78   | 0.133  | 0 - 39.9              | 0.132  | 0 - 37.2              | 0.045  | 0.103   | 0.029 | 0* - 0.228                         | 0.070   | not significant |
| TA1537 (-S9)                | 084454       | Fresh Strips          | 0 - 20   | -0.024 | 0 - 21.6              | 0.069  | 0 - 22.1              | 0.028  | 0.024   | 0.027 | 0* - 0.14                          | 0.458   | not significant |
| TA1537 (-S9)                | 084455       | Mellow Sticks         | 0 - 30.7   | 0.013  | 0 - 29.1              | -0.053 | 0 - 30.9              | -0.044 | 0*  | 0.020 | 0* - 0.06                          | 0.304   | not significant |
| TA1537 (-S9)                | 084456       | Copenhagen Long Cut   | 0 - 64.6   | 0.011  | 0 - 66.3              | -0.031 | 0 - 67.7              | 0.032  | 0.004   | 0.018 | 0* - 0.083                         | 0.854   | not significant |
| TA1537 (-S9)                | 084457       | Ariva Wintergreen     | 0 - 29.5   | 0.006  | 0 - 30.8              | -0.085 | 0 - 31.8              | 0.063  | 0*  | 0.043 | 0* - 0.181                         | 0.914   | not significant |
| TA1537 (-S9)                | 084458       | Fresh Orbs            | 0 - 6.6  | 0.452  | 0 - 14.4              | 0.112  | 0 - 15.3              | -0.093 | 0.157   | 0.159 | 0* - 0.84                          | 0.426   | not significant |

0\*: Mean or lower bound of the 95% confidence interval has been truncated at 0.

**One-Way ANOVA of Mean 'Extracted Nicotine'  
Slope Estimates Among Test Samples**

TA98 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.792327199    | 6  | 0.132054533 | 0.753   | 0.617   |
| Within Samples | 2.453979328    | 14 | 0.175284238 |         |         |
| Total (Corr.)  | 3.246306527    | 20 |             |         |         |

TA100 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 19.99759742    | 6  | 3.332932903 | 1.294   | 0.322   |
| Within Samples | 36.05876745    | 14 | 2.575626247 |         |         |
| Total (Corr.)  | 56.05636487    | 20 |             |         |         |

TA102 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 67.74594643    | 6  | 11.29099107 | 7.063   | <b>0.001</b> |
| Within Samples | 22.37982339    | 14 | 1.598558814 |         |              |
| Total (Corr.)  | 90.12576982    | 20 |             |         |              |

TA1535 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.025947952    | 6  | 0.004324659 | 0.214   | 0.966   |
| Within Samples | 0.283019515    | 14 | 0.02021568  |         |         |
| Total (Corr.)  | 0.308967467    | 20 |             |         |         |

TA1537 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.173991565    | 6  | 0.028998594 | 0.863   | 0.544   |
| Within Samples | 0.470180994    | 14 | 0.033584357 |         |         |
| Total (Corr.)  | 0.64417256     | 20 |             |         |         |

**One-Way ANOVA of Mean 'Extracted Nicotine'  
Slope Estimates Among Test Samples**

TA98 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.126526575    | 6  | 0.021087762 | 2.344   | 0.089   |
| Within Samples | 0.125944491    | 14 | 0.008996035 |         |         |
| Total (Corr.)  | 0.252471066    | 20 |             |         |         |

TA100 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 14.80174676    | 6  | 2.466957793 | 1.504   | 0.247   |
| Within Samples | 22.96043495    | 14 | 1.640031068 |         |         |
| Total (Corr.)  | 37.76218171    | 20 |             |         |         |

TA102 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 69.15694637    | 6  | 11.52615773 | 1.134   | 0.393   |
| Within Samples | 142.2476686    | 14 | 10.16054776 |         |         |
| Total (Corr.)  | 211.404615     | 20 |             |         |         |

TA1535 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 1.865520022    | 6  | 0.310920004 | 2.372   | 0.086   |
| Within Samples | 1.834813937    | 14 | 0.131058138 |         |         |
| Total (Corr.)  | 3.700333959    | 20 |             |         |         |

TA1537 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.144493408    | 6  | 0.024082235 | 1.534   | 0.238   |
| Within Samples | 0.219854302    | 14 | 0.015703879 |         |         |
| Total (Corr.)  | 0.36434771     | 20 |             |         |         |

One-way ANOVA analysis indicates significant differences (at  $\alpha = 0.05$ ) among mean 'Extracted Nicotine' specific activity slope estimates for test samples with TA102 (+S9).

**Evaluation of Ratio (Max ÷ Min) of Standard Deviations of  
'Nicotine in Smokeless Tobacco' Slope Estimates and  
Corresponding Method of Comparison**

| <b>Strain and<br/>S9 Activation</b> | <b>Std. Dev. Ratio<br/>(Max ÷ Min)</b> | <b>Method of<br/>Comparison</b>    |
|-------------------------------------|--|------------------------------------|
| TA98 (+S9)                          | 19.8                                   | Pairwise T-test (unequal variance) |
| TA98 (-S9)                          | 9.3                                    | ANOVA (equal variance)             |
| TA100 (+S9)                         | 5.5                                    | ANOVA (equal variance)             |
| TA100 (-S9)                         | 33.2                                   | Pairwise T-test (unequal variance) |
| TA102 (+S9)                         | 20.7                                   | Pairwise T-test (unequal variance) |
| TA102 (-S9)                         | 19.0                                   | Pairwise T-test (unequal variance) |
| TA1535 (+S9)                        | 14.2                                   | ANOVA (equal variance)             |
| TA1535 (-S9)                        | 18.8                                   | Pairwise T-test (unequal variance) |
| TA1537 (+S9)                        | 5.7                                    | ANOVA (equal variance)             |
| TA1537 (-S9)                        | 8.6                                    | ANOVA (equal variance)             |

**Evaluation of Ratio (Max ÷ Min) of Standard Deviations of  
'Nicotine in Smokeless Tobacco' Slope Estimates and  
Corresponding Method of Comparison**

**ANOVA-Based Comparison Tests of Mean 'Extracted Nicotine' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| ANOVA-Based<br>Comparison | TA98 (+S9) |         |                                    | TA100 (+S9) |         |                                    | TA102 (+S9) |         |                                    | TA1535 (+S9) |         |                                    | TA1537 (+S9) |         |                                    |
|---------------------------|------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                           | f-ratio    | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395         | 0.0900     | 0.7686  | not significant                    | 0.07        | 0.7991  | not significant                    | 4.5884      | 0.0503  | not significant                    | 0.0416       | 0.8413  | not significant                    | 0.2934       | 0.5966  | not significant                    |
| <b>084394 vs. 084454</b>  | 0.4302     | 0.5225  | not significant                    | 4.8325      | 0.0452  | not significant                    | 14.784      | 0.0018  | <b>significant</b>                 | 0.1477       | 0.7065  | not significant                    | 1.2707       | 0.2786  | not significant                    |
| 084394 vs. 084455         | 0.0039     | 0.9510  | not significant                    | 1.3929      | 0.2576  | not significant                    | 10.673      | 0.0056  | not significant                    | 0.1741       | 0.6828  | not significant                    | 0.7191       | 0.4107  | not significant                    |
| 084394 vs. 084456         | 0.27       | 0.6100  | not significant                    | 0.31        | 0.5865  | not significant                    | 11.100      | 0.0049  | not significant                    | 0.0221       | 0.8839  | not significant                    | 0.0010       | 0.9758  | not significant                    |
| <b>084394 vs. 084457</b>  | 0.1004     | 0.7560  | not significant                    | 2.0257      | 0.1766  | not significant                    | 16.005      | 0.0013  | <b>significant</b>                 | 0.5010       | 0.4907  | not significant                    | 1.0633       | 0.3199  | not significant                    |
| <b>084394 vs. 084458</b>  | 1.5108     | 0.2393  | not significant                    | 2.9261      | 0.1092  | not significant                    | 37.961      | 0.0000  | <b>significant</b>                 | 0.0980       | 0.7588  | not significant                    | 0.0245       | 0.8778  | not significant                    |
| 084395 vs. 084454         | 0.91       | 0.3554  | not significant                    | 3.76        | 0.0729  | not significant                    | 2.9002      | 0.1107  | not significant                    | 0.0325       | 0.8594  | not significant                    | 2.7853       | 0.1173  | not significant                    |
| 084395 vs. 084455         | 0.1314     | 0.7224  | not significant                    | 0.85        | 0.3727  | not significant                    | 1.2655      | 0.2795  | not significant                    | 0.0455       | 0.8341  | not significant                    | 1.9312       | 0.1863  | not significant                    |
| 084395 vs. 084456         | 0.0492     | 0.8277  | not significant                    | 0.0884      | 0.7706  | not significant                    | 1.4151      | 0.2540  | not significant                    | 0.0031       | 0.9567  | not significant                    | 0.3278       | 0.5760  | not significant                    |
| 084395 vs. 084457         | 0.38       | 0.5472  | not significant                    | 1.35        | 0.2639  | not significant                    | 3.4542      | 0.0842  | not significant                    | 0.2539       | 0.6222  | not significant                    | 2.4739       | 0.1381  | not significant                    |
| <b>084395 vs. 084458</b>  | 0.8634     | 0.3685  | not significant                    | 2.11        | 0.1688  | not significant                    | 16.154      | 0.0013  | <b>significant</b>                 | 0.2673       | 0.6132  | not significant                    | 0.1483       | 0.7059  | not significant                    |
| 084454 vs. 084455         | 0.3521     | 0.5624  | not significant                    | 1.0365      | 0.3259  | not significant                    | 0.3341      | 0.5724  | not significant                    | 0.0011       | 0.9742  | not significant                    | 0.0780       | 0.7841  | not significant                    |
| 084454 vs. 084456         | 1.39       | 0.2586  | not significant                    | 2.69        | 0.1229  | not significant                    | 0.2636      | 0.6157  | not significant                    | 0.0555       | 0.8171  | not significant                    | 1.2020       | 0.2914  | not significant                    |
| 084454 vs. 084457         | 0.1149     | 0.7396  | not significant                    | 0.6006      | 0.4512  | not significant                    | 0.0242      | 0.8786  | not significant                    | 0.1047       | 0.7511  | not significant                    | 0.0092       | 0.9248  | not significant                    |
| 084454 vs. 084458         | 3.5533     | 0.0804  | not significant                    | 0.2378      | 0.6333  | not significant                    | 5.3646      | 0.0362  | not significant                    | 0.4863       | 0.4970  | not significant                    | 1.6481       | 0.2201  | not significant                    |
| 084455 vs. 084456         | 0.34       | 0.5684  | not significant                    | 0.39        | 0.5430  | not significant                    | 0.0042      | 0.9494  | not significant                    | 0.0722       | 0.7921  | not significant                    | 0.6676       | 0.4276  | not significant                    |
| 084455 vs. 084457         | 0.0647     | 0.8029  | not significant                    | 0.0591      | 0.8115  | not significant                    | 0.5382      | 0.4753  | not significant                    | 0.0844       | 0.7757  | not significant                    | 0.0336       | 0.8573  | not significant                    |
| 084455 vs. 084458         | 1.6683     | 0.2174  | not significant                    | 0.2813      | 0.6041  | not significant                    | 8.3764      | 0.0118  | not significant                    | 0.5334       | 0.4772  | not significant                    | 1.0091       | 0.3322  | not significant                    |
| 084456 vs. 084457         | 0.70       | 0.4158  | not significant                    | 0.75        | 0.4008  | not significant                    | 0.4475      | 0.5144  | not significant                    | 0.3126       | 0.5849  | not significant                    | 1.0005       | 0.3342  | not significant                    |
| 084456 vs. 084458         | 0.50       | 0.4909  | not significant                    | 1.33        | 0.2679  | not significant                    | 8.0065      | 0.0134  | not significant                    | 0.2132       | 0.6514  | not significant                    | 0.0351       | 0.8540  | not significant                    |
| 084457 vs. 084458         | 2.3902     | 0.1444  | not significant                    | 0.0825      | 0.7781  | not significant                    | 4.6682      | 0.0485  | not significant                    | 1.0422       | 0.3246  | not significant                    | 1.4107       | 0.2547  | not significant                    |

**ANOVA-Based Comparison Tests of Mean 'Extracted Nicotine' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| ANOVA-Based<br>Comparison | TA98 (-S9) |         |                                    | TA100 (-S9) |         |                                    | TA102 (-S9) |         |                                    | TA1535 (-S9) |         |                                    | TA1537 (-S9) |         |                                    |
|---------------------------|------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                           | f-ratio    | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395         | 0.1421     | 0.7118  | not significant                    | 0.0012      | 0.9726  | not significant                    | 0.0289      | 0.8673  | not significant                    | 0.0017       | 0.9674  | not significant                    | 0.9621       | 0.3433  | not significant                    |
| 084394 vs. 084454         | 2.8627     | 0.1128  | not significant                    | 0.1616      | 0.6937  | not significant                    | 2.8009      | 0.1164  | not significant                    | 0.9178       | 0.3543  | not significant                    | 3.070        | 0.1016  | not significant                    |
| 084394 vs. 084455         | 7.0529     | 0.0188  | not significant                    | 0.0285      | 0.8683  | not significant                    | 0.0246      | 0.8776  | not significant                    | 0.0396       | 0.8451  | not significant                    | 5.129        | 0.0399  | not significant                    |
| 084394 vs. 084456         | 0.0033     | 0.9550  | not significant                    | 0.0962      | 0.7610  | not significant                    | 0.1376      | 0.7163  | not significant                    | 0.0630       | 0.8054  | not significant                    | 3.815        | 0.0711  | not significant                    |
| 084394 vs. 084457         | 0.9109     | 0.3561  | not significant                    | 1.6042      | 0.2260  | not significant                    | 0.1044      | 0.7514  | not significant                    | 0.8582       | 0.3699  | not significant                    | 4.170        | 0.0604  | not significant                    |
| 084394 vs. 084458         | 0.1223     | 0.7318  | not significant                    | 4.5788      | 0.0505  | not significant                    | 0.5506      | 0.4703  | not significant                    | 8.7072       | 0.0105  | not significant                    | 0.207        | 0.6558  | not significant                    |
| 084395 vs. 084454         | 4.2806     | 0.0575  | not significant                    | 0.1348      | 0.7190  | not significant                    | 2.2604      | 0.1549  | not significant                    | 0.8398       | 0.3750  | not significant                    | 0.59         | 0.4534  | not significant                    |
| 084395 vs. 084455         | 9.1976     | 0.0090  | not significant                    | 0.0180      | 0.8953  | not significant                    | 0.0002      | 0.9896  | not significant                    | 0.0579       | 0.8133  | not significant                    | 1.65         | 0.2200  | not significant                    |
| 084395 vs. 084456         | 0.1888     | 0.6705  | not significant                    | 0.1191      | 0.7352  | not significant                    | 0.0403      | 0.8438  | not significant                    | 0.0439       | 0.8371  | not significant                    | 0.95         | 0.3474  | not significant                    |
| 084395 vs. 084457         | 1.7727     | 0.2043  | not significant                    | 1.5170      | 0.2384  | not significant                    | 0.2432      | 0.6295  | not significant                    | 0.7829       | 0.3912  | not significant                    | 1.13         | 0.3065  | not significant                    |
| 084395 vs. 084458         | 0.5282     | 0.4794  | not significant                    | 4.4306      | 0.0538  | not significant                    | 0.8321      | 0.3771  | not significant                    | 8.4633       | 0.0114  | not significant                    | 0.28         | 0.6075  | not significant                    |
| 084454 vs. 084455         | 0.9289     | 0.3515  | not significant                    | 0.0543      | 0.8190  | not significant                    | 2.3007      | 0.1516  | not significant                    | 1.3389       | 0.2666  | not significant                    | 0.2629       | 0.6161  | not significant                    |
| 084454 vs. 084456         | 2.6715     | 0.1244  | not significant                    | 0.5072      | 0.4880  | not significant                    | 1.6971      | 0.2137  | not significant                    | 0.4998       | 0.4912  | not significant                    | 0.0404       | 0.8435  | not significant                    |
| 084454 vs. 084457         | 0.5440     | 0.4730  | not significant                    | 0.7474      | 0.4019  | not significant                    | 3.9866      | 0.0657  | not significant                    | 0.0010       | 0.9752  | not significant                    | 0.0842       | 0.7760  | not significant                    |
| 084454 vs. 084458         | 1.8016     | 0.2009  | not significant                    | 3.0198      | 0.1042  | not significant                    | 5.8353      | 0.0300  | not significant                    | 3.9712       | 0.0662  | not significant                    | 1.6814       | 0.2157  | not significant                    |
| 084455 vs. 084456         | 6.7509     | 0.0210  | not significant                    | 0.2295      | 0.6393  | not significant                    | 0.0458      | 0.8336  | not significant                    | 0.2026       | 0.6595  | not significant                    | 0.0971       | 0.7599  | not significant                    |
| 084455 vs. 084457         | 2.8945     | 0.1110  | not significant                    | 1.2048      | 0.2909  | not significant                    | 0.2303      | 0.6387  | not significant                    | 1.2667       | 0.2793  | not significant                    | 0.0496       | 0.8270  | not significant                    |
| 084455 vs. 084458         | 5.3177     | 0.0369  | not significant                    | 3.8844      | 0.0688  | not significant                    | 0.8079      | 0.3839  | not significant                    | 9.9217       | 0.0071  | not significant                    | 3.2740       | 0.0919  | not significant                    |
| 084456 vs. 084457         | 0.8045     | 0.3849  | not significant                    | 2.4860      | 0.1372  | not significant                    | 0.4815      | 0.4991  | not significant                    | 0.4561       | 0.5104  | not significant                    | 0.0079       | 0.9303  | not significant                    |
| 084456 vs. 084458         | 0.0854     | 0.7744  | not significant                    | 6.0023      | 0.0280  | not significant                    | 1.2386      | 0.2845  | not significant                    | 7.2886       | 0.0173  | not significant                    | 2.2433       | 0.1564  | not significant                    |
| 084457 vs. 084458         | 0.3656     | 0.5551  | not significant                    | 0.7626      | 0.3973  | not significant                    | 0.1756      | 0.6816  | not significant                    | 4.0981       | 0.0624  | not significant                    | 2.5179       | 0.1349  | not significant                    |

Some ANOVA-based comparison p-values for tester strains TA102 (+S9) and TA1537 (-S9) were significant at  $\alpha = 0.05$ .

Significant differences in mean 'Extracted Nicotine' specific activity slope were detected in TA102 (+S9) between Camel SNUS Frost (084394) and each of {Fresh Strips (084454), Ariva Wintergreen (084457), Fresh Orbs (084458)} and between 2S3 Research Moist Snuff (084395) and Fresh Orbs (084458).

**Pairwise T-Test Comparisons of Mean 'Extracted Nicotine' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| Pairwise T-test<br>Comparison | TA98 (+S9)  |         |                                    | TA100 (+S9) |         |                                    | TA102 (+S9) |         |                                    | TA1535 (+S9) |         |                                    | TA1537 (+S9) |         |                                    |
|-------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                               | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395             | 1.107904    | 0.3300  | not significant                    |             |         |                                    | 2.322649    | 0.0809  | not significant                    |              |         |                                    |              |         |                                    |
| <b>084394 vs. 084454</b>      | 0.96473     | 0.3893  | not significant                    |             |         |                                    | 8.270391    | 0.0012  | <b>significant</b>                 |              |         |                                    |              |         |                                    |
| <b>084394 vs. 084455</b>      | 0.160766    | 0.8801  | not significant                    |             |         |                                    | 10.5229     | 0.0005  | <b>significant</b>                 |              |         |                                    |              |         |                                    |
| <b>084394 vs. 084456</b>      | 2.242299    | 0.0884  | not significant                    |             |         |                                    | 10.054      | 0.0006  | <b>significant</b>                 |              |         |                                    |              |         |                                    |
| <b>084394 vs. 084457</b>      | 1.035582    | 0.3589  | not significant                    |             |         |                                    | 13.08978    | 0.0002  | <b>significant</b>                 |              |         |                                    |              |         |                                    |
| 084394 vs. 084458             | 0.721793    | 0.5104  | not significant                    |             |         |                                    | 3.842052    | 0.0184  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084454             | 1.438034    | 0.2238  | not significant                    |             |         |                                    | 1.80363     | 0.1456  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084455             | 1.002409    | 0.3729  | not significant                    |             |         |                                    | 1.280537    | 0.2696  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084456             | 1.207692    | 0.2937  | not significant                    |             |         |                                    | 1.342492    | 0.2506  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084457             | 2.279653    | 0.0848  | not significant                    |             |         |                                    | 2.119697    | 0.1014  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084458             | 0.547582    | 0.6131  | not significant                    |             |         |                                    | 2.230461    | 0.0896  | not significant                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084455             | 0.823143    | 0.4567  | not significant                    |             |         |                                    | 1.559599    | 0.1939  | not significant                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084456             | 1.811397    | 0.1443  | not significant                    |             |         |                                    | 1.32213     | 0.2567  | not significant                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084457             | 0.498693    | 0.6442  | not significant                    |             |         |                                    | 0.424339    | 0.6931  | not significant                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084458             | 1.042686    | 0.3560  | not significant                    |             |         |                                    | 1.432955    | 0.2252  | not significant                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084456             | 1.748984    | 0.1552  | not significant                    |             |         |                                    | 0.366923    | 0.7323  | not significant                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084457             | 0.654449    | 0.5485  | not significant                    |             |         |                                    | 6.064888    | 0.0037  | not significant                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084458             | 0.751095    | 0.4944  | not significant                    |             |         |                                    | 1.833083    | 0.1407  | not significant                    |              |         |                                    |              |         |                                    |
| 084456 vs. 084457             | 3.607046    | 0.0226  | not significant                    |             |         |                                    | 3.994206    | 0.0162  | not significant                    |              |         |                                    |              |         |                                    |
| 084456 vs. 084458             | 0.418283    | 0.6972  | not significant                    |             |         |                                    | 1.78734     | 0.1484  | not significant                    |              |         |                                    |              |         |                                    |
| 084457 vs. 084458             | 0.907888    | 0.4153  | not significant                    |             |         |                                    | 1.369265    | 0.2428  | not significant                    |              |         |                                    |              |         |                                    |



**Pairwise T-Test Comparisons of Mean 'Extracted Nicotine' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| Pairwise T-test<br>Comparison | TA98 (-S9)  |         |                                    | TA100 (-S9) |         |                                    | TA102 (-S9) |         |                                    | TA1535 (-S9) |         |                                    | TA1537 (-S9) |         |                                    |
|-------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                               | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395             |             |         |                                    | 0.346383    | 0.7465  | not significant                    | 1.437174    | 0.2240  | not significant                    | 0.283278     | 0.7910  | not significant                    |              |         |                                    |
| 084394 vs. 084454             |             |         |                                    | 0.763552    | 0.4877  | not significant                    | 1.149923    | 0.3143  | not significant                    | 3.669446     | 0.0214  | not significant                    |              |         |                                    |
| 084394 vs. 084455             |             |         |                                    | 0.189722    | 0.8588  | not significant                    | 1.439236    | 0.2235  | not significant                    | 0.982292     | 0.3816  | not significant                    |              |         |                                    |
| 084394 vs. 084456             |             |         |                                    | 0.653188    | 0.5493  | not significant                    | 1.16606     | 0.3084  | not significant                    | 1.549086     | 0.1963  | not significant                    |              |         |                                    |
| 084394 vs. 084457             |             |         |                                    | 1.008708    | 0.3702  | not significant                    | 2.035651    | 0.1115  | not significant                    | 1.091021     | 0.3366  | not significant                    |              |         |                                    |
| 084394 vs. 084458             |             |         |                                    | 2.631482    | 0.0581  | not significant                    | 0.661351    | 0.5445  | not significant                    | 1.79847      | 0.1465  | not significant                    |              |         |                                    |
| 084395 vs. 084454             |             |         |                                    | 0.706615    | 0.5188  | not significant                    | 1.032464    | 0.3602  | not significant                    | 3.688684     | 0.0210  | not significant                    |              |         |                                    |
| 084395 vs. 084455             |             |         |                                    | 0.151208    | 0.8871  | not significant                    | 0.11205     | 0.9162  | not significant                    | 1.293404     | 0.2655  | not significant                    |              |         |                                    |
| 084395 vs. 084456             |             |         |                                    | 0.738798    | 0.5010  | not significant                    | 0.624118    | 0.5664  | not significant                    | 1.487539     | 0.2111  | not significant                    |              |         |                                    |
| 084395 vs. 084457             |             |         |                                    | 0.983182    | 0.3812  | not significant                    | 2.97552     | 0.0409  | not significant                    | 1.046693     | 0.3543  | not significant                    |              |         |                                    |
| 084395 vs. 084458             |             |         |                                    | 2.602967    | 0.0599  | not significant                    | 0.81225     | 0.4622  | not significant                    | 1.775228     | 0.1505  | not significant                    |              |         |                                    |
| 084454 vs. 084455             |             |         |                                    | 0.227202    | 0.8314  | not significant                    | 1.042147    | 0.3562  | not significant                    | 4.060383     | 0.0153  | not significant                    |              |         |                                    |
| 084454 vs. 084456             |             |         |                                    | 1.0224      | 0.3644  | not significant                    | 0.876775    | 0.4301  | not significant                    | 2.743654     | 0.0517  | not significant                    |              |         |                                    |
| 084454 vs. 084457             |             |         |                                    | 0.637951    | 0.5582  | not significant                    | 1.367552    | 0.2433  | not significant                    | 0.03622      | 0.9728  | not significant                    |              |         |                                    |
| 084454 vs. 084458             |             |         |                                    | 1.810734    | 0.1444  | not significant                    | 1.316788    | 0.2583  | not significant                    | 1.205618     | 0.2944  | not significant                    |              |         |                                    |
| 084455 vs. 084456             |             |         |                                    | 0.478868    | 0.6570  | not significant                    | 0.672578    | 0.5381  | not significant                    | 2.27029      | 0.0857  | not significant                    |              |         |                                    |
| 084455 vs. 084457             |             |         |                                    | 0.715698    | 0.5137  | not significant                    | 3.015153    | 0.0394  | not significant                    | 1.313646     | 0.2592  | not significant                    |              |         |                                    |
| 084455 vs. 084458             |             |         |                                    | 1.644287    | 0.1755  | not significant                    | 0.80106     | 0.4680  | not significant                    | 1.915173     | 0.1280  | not significant                    |              |         |                                    |
| 084456 vs. 084457             |             |         |                                    | 1.180273    | 0.3033  | not significant                    | 2.049669    | 0.1097  | not significant                    | 0.796347     | 0.4704  | not significant                    |              |         |                                    |
| 084456 vs. 084458             |             |         |                                    | 2.627824    | 0.0583  | not significant                    | 0.958438    | 0.3921  | not significant                    | 1.646001     | 0.1751  | not significant                    |              |         |                                    |
| 084457 vs. 084458             |             |         |                                    | 0.586035    | 0.5893  | not significant                    | 0.371449    | 0.7291  | not significant                    | 1.100309     | 0.3330  | not significant                    |              |         |                                    |

Pairwise t-test comparison p-values less than the Bonferroni-adjusted  $\alpha = 0.05$  indicate that significant differences in mean 'Extracted Nicotine' specific activity slope were as follows for strain TA102 (+S9):

**TA102 (+S9): Camel SNUS Frost (084394) was significantly different from each of {Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456), Ariva Wintergreen (084457)}**

**Number of Mean 'Extracted Nicotine' Slope Estimates  
Significantly Greater than Zero (0), the Corresponding Number  
of Paired Comparisons and Comparison Method**

| Strain and<br>S9 Activation | # of Significant<br>Mean Slopes | Number of<br>Comparisons | Std. Dev. Ratio<br>(Max ÷ Min) | Method of<br>Comparison |
|-----------------------------|---------------------------------|--------------------------|--------------------------------|-------------------------|
| TA98 (+S9)                  | 1                               | 0                        |                                |                         |
| TA98 (-S9)                  | 1                               | 0                        |                                |                         |
| TA100 (+S9)                 | 2                               | 1                        | 2.7                            | ANOVA (equal variance)  |
| TA100 (-S9)                 | 1                               | 0                        |                                |                         |
| TA102 (+S9)                 | 2                               | 1                        | 3.2                            | ANOVA (equal variance)  |
| TA102 (-S9)                 | 0                               | 0                        |                                |                         |
| TA1535 (+S9)                | 0                               | 0                        |                                |                         |
| TA1535 (-S9)                | 0                               | 0                        |                                |                         |
| TA1537 (+S9)                | 0                               | 0                        |                                |                         |
| TA1537 (-S9)                | 0                               | 0                        |                                |                         |

**One-Way ANOVA and ANOVA-Based Comparisons Among  
Test Samples of Mean 'Extracted Nicotine' Slope Estimates  
that are Significantly Greater than Zero (0)**

TA100 (+S9)

| Source         | Sum of<br>Squares | Df | Mean<br>Square | F-Ratio | P-Value |
|----------------|-------------------|----|----------------|---------|---------|
| Among Samples  | 6.941             | 1  | 6.941          | 7.170   | 0.055   |
| Within Samples | 3.872             | 4  | 0.968          |         |         |
| Total (Corr.)  | 10.813            | 5  |                |         |         |

| TA100 (+S9)               |         |         |                                    |
|---------------------------|---------|---------|------------------------------------|
| ANOVA-Based<br>Comparison | f-ratio | p-value | significance<br>at $\alpha = 0.05$ |
| 084454 vs. 084456         | 7.17    | 0.0554  | not significant                    |

TA102 (+S9)

| Source         | Sum of<br>Squares | Df | Mean<br>Square | F-Ratio | P-Value      |
|----------------|-------------------|----|----------------|---------|--------------|
| Among Samples  | 17.062            | 1  | 17.06          | 110.73  | <b>0.000</b> |
| Within Samples | 0.616             | 4  | 0.154          |         |              |
| Total (Corr.)  | 17.678            | 5  |                |         |              |

| TA102 (+S9)               |         |         |                                    |
|---------------------------|---------|---------|------------------------------------|
| ANOVA-Based<br>Comparison | f-ratio | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084455         | 110.73  | 0.0005  | <b>significant</b>                 |

Both TA100 (+S9) and TA102 (+S9) strains have more than one test sample for which the mean 'extracted nicotine' specific activity slope estimate is greater than zero (0) .

**TA100 (+S9):**

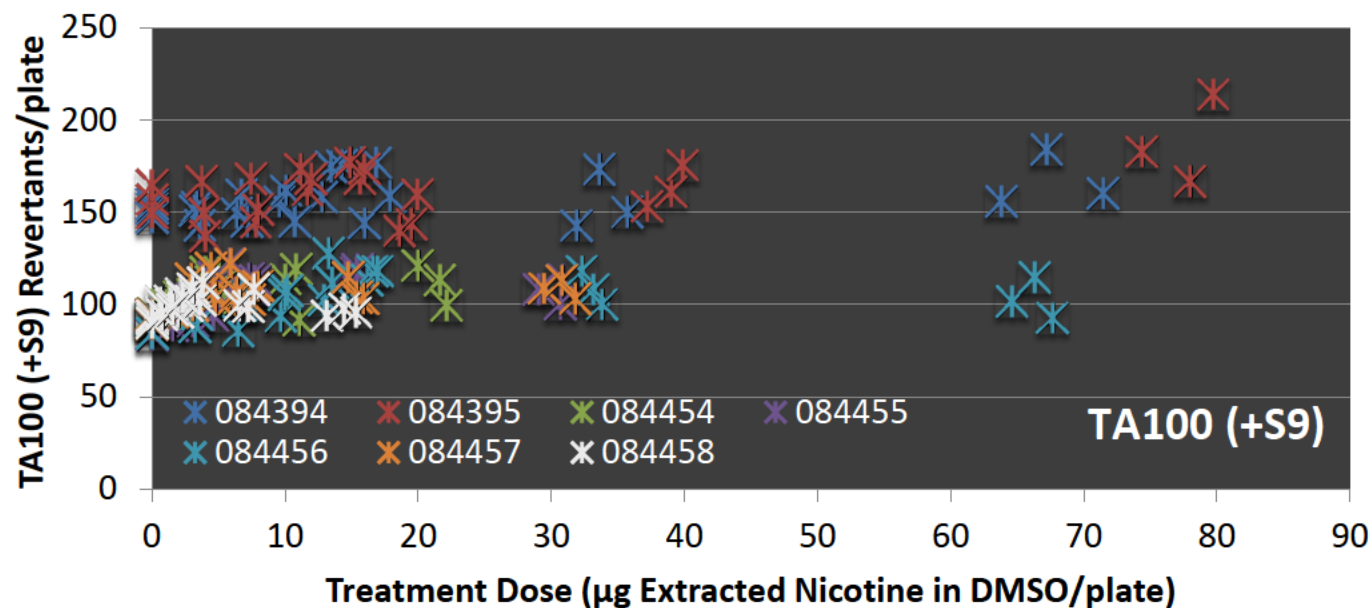
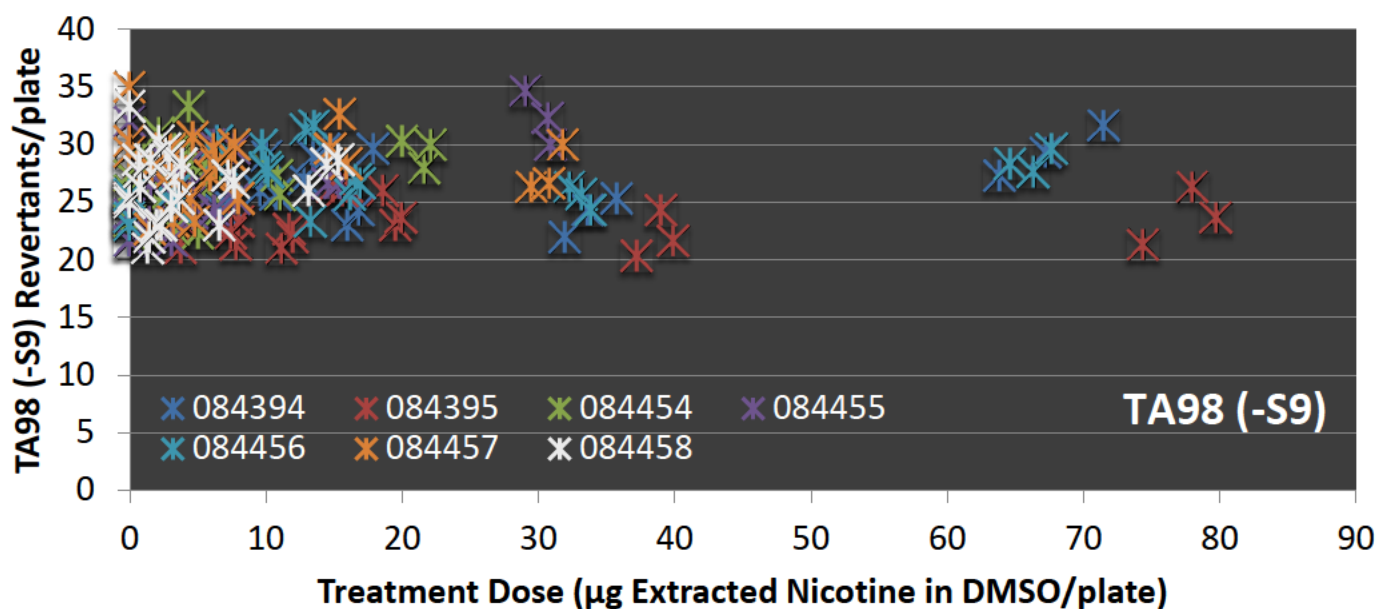
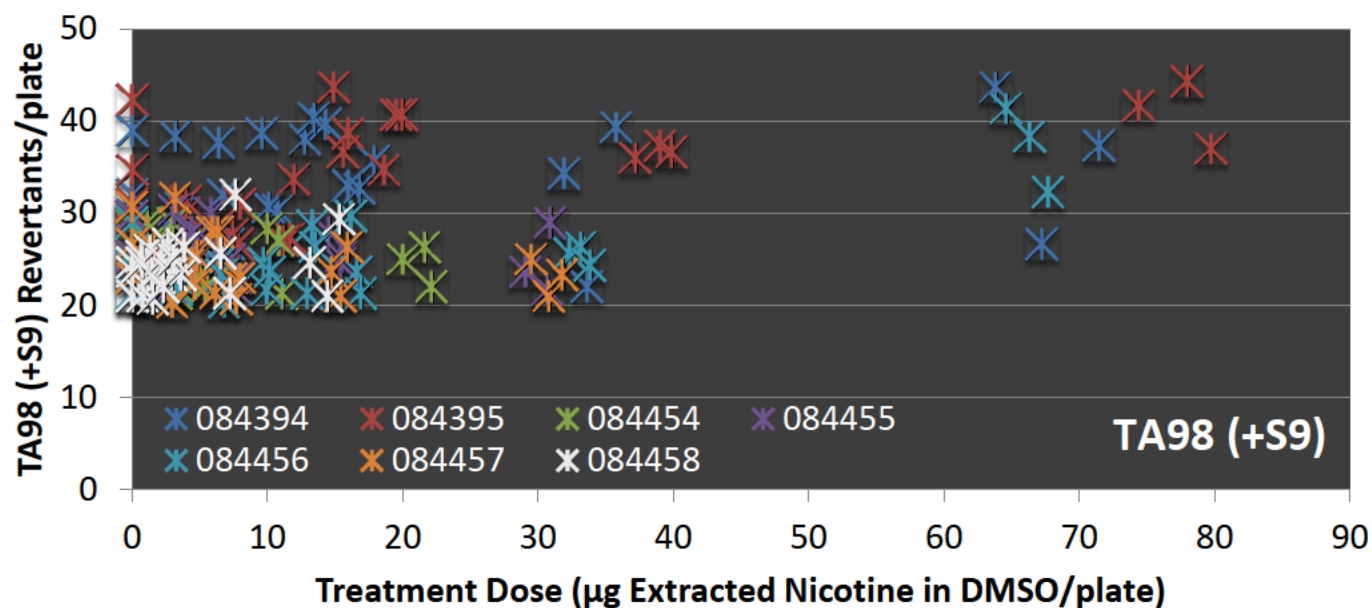
No significant differences among mean 'Extracted Nicotine' specific activity slope estimates were detected in TA100 (+S9) between test samples 084454 (Fresh Strips) and 084456 (Copenhagen Long Cut).

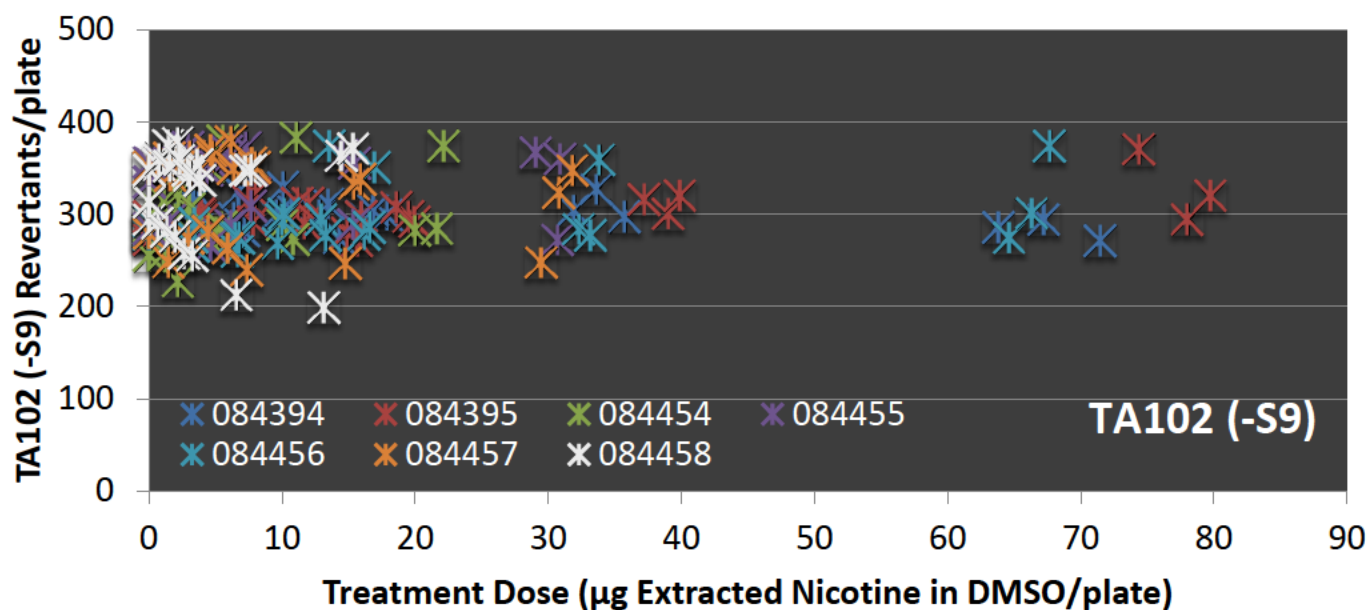
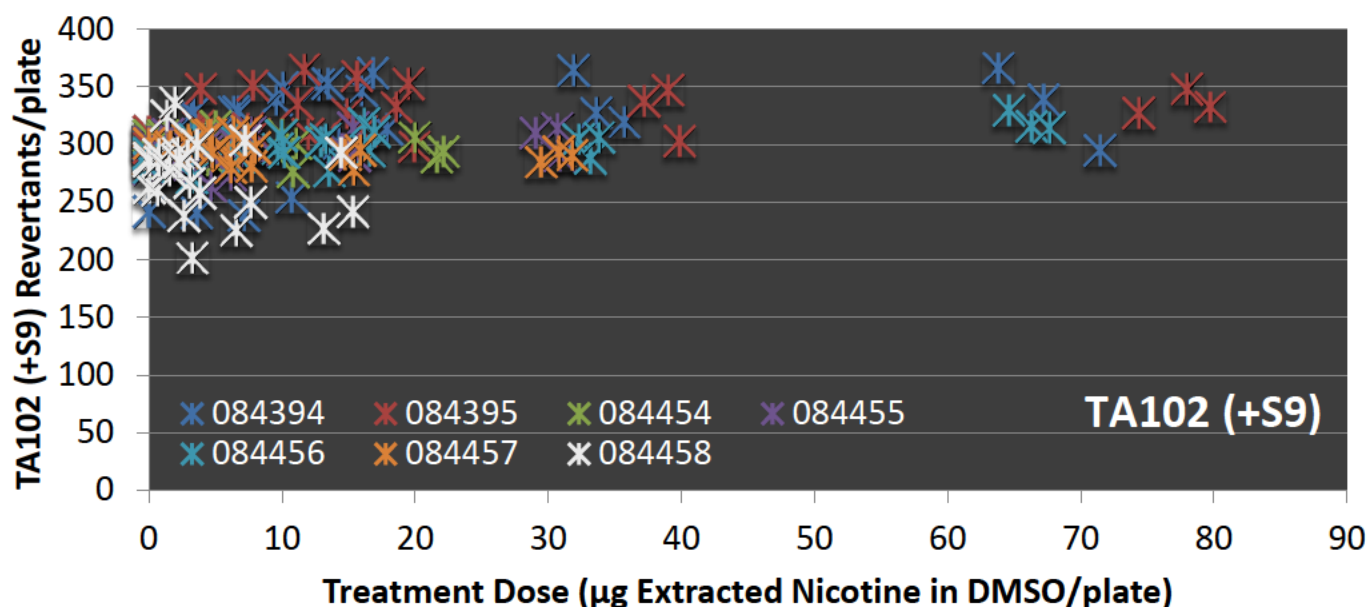
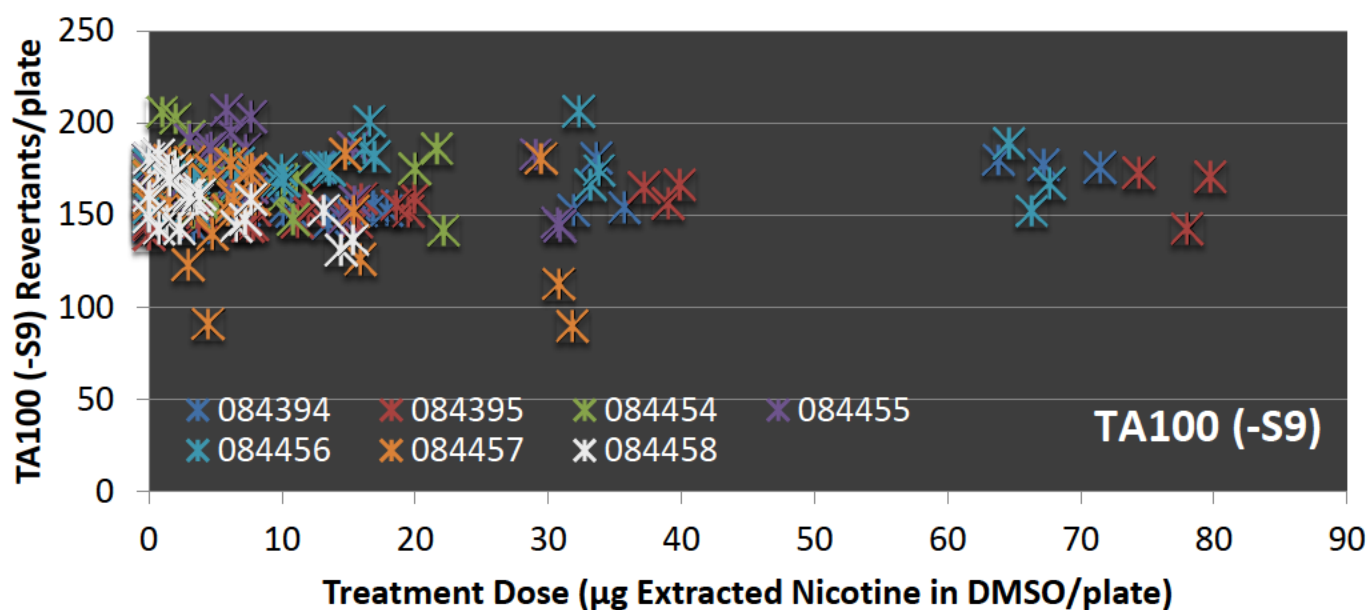
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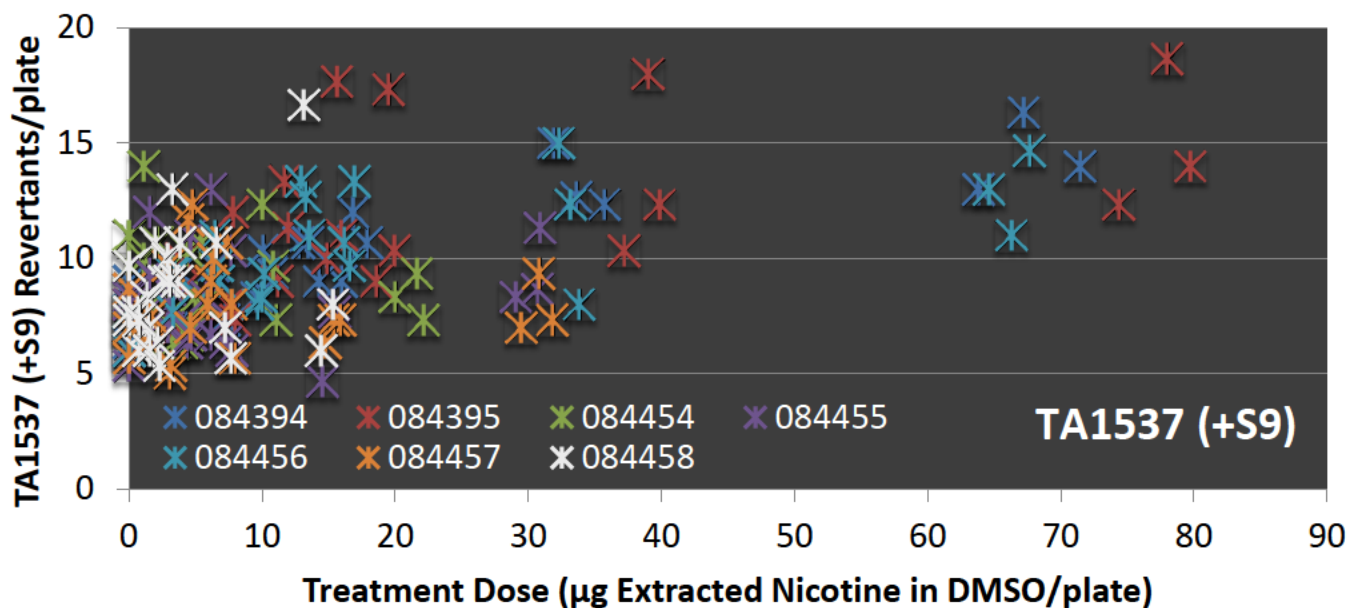
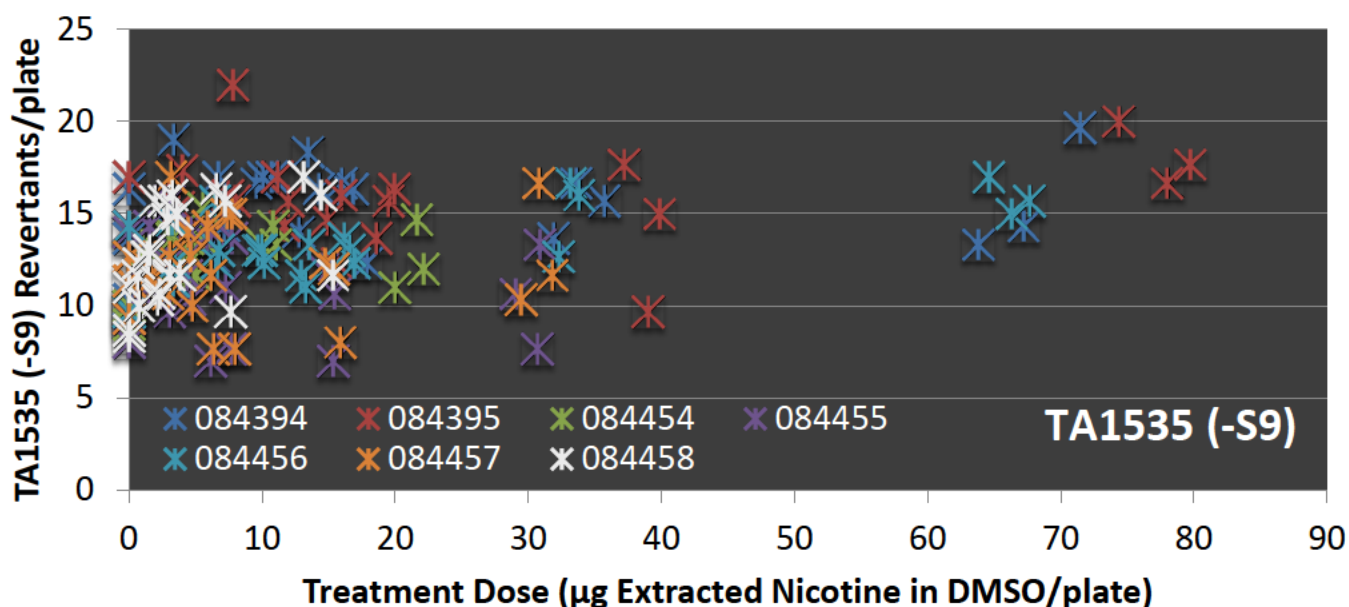
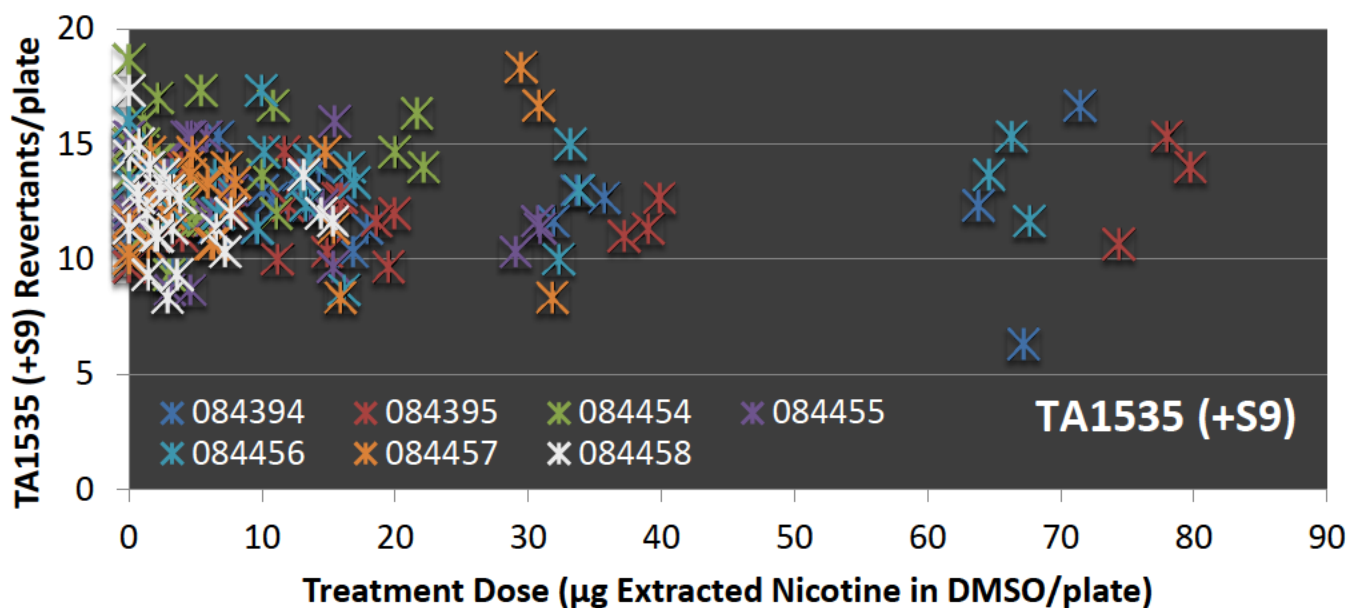
Significant differences among mean 'Extracted Nicotine' specific activity slope estimates were detected in TA102 (+S9) between test samples 084394 (Camel SNUS Frost) and 084455 (Mellow Sticks).

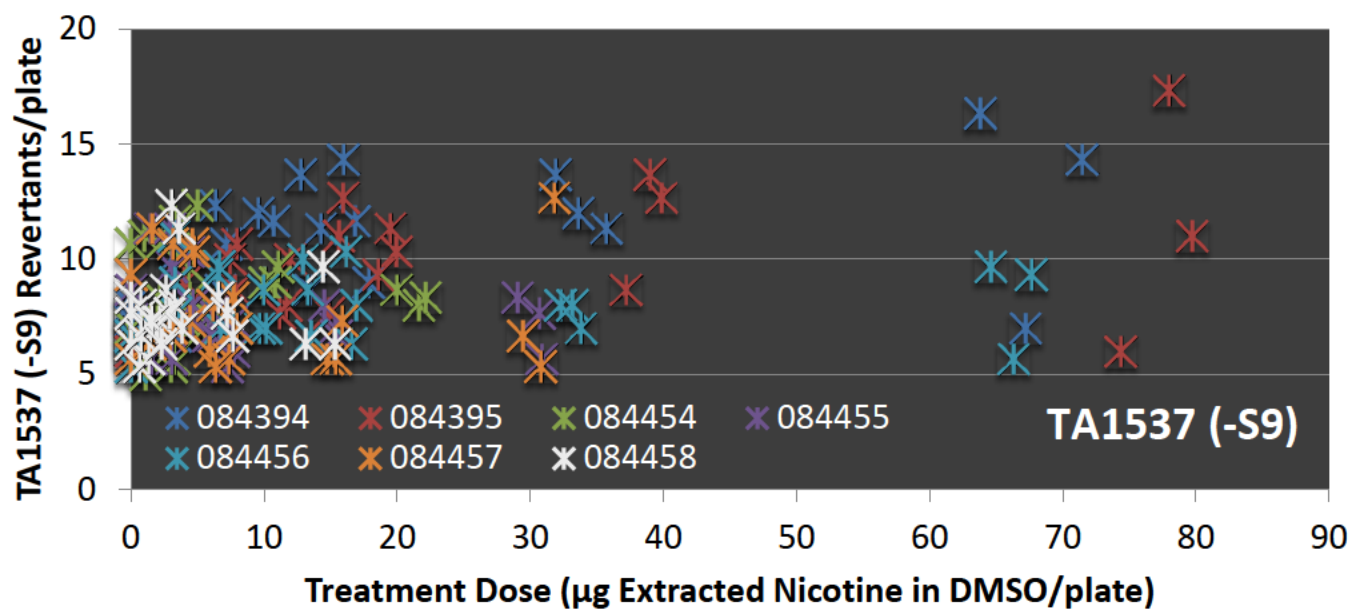
**Number of Mean 'Extracted Nicotine' Slope Estimates  
Significantly Greater than Zero (0), the Corresponding Number  
of Paired Comparisons and Comparison Method**

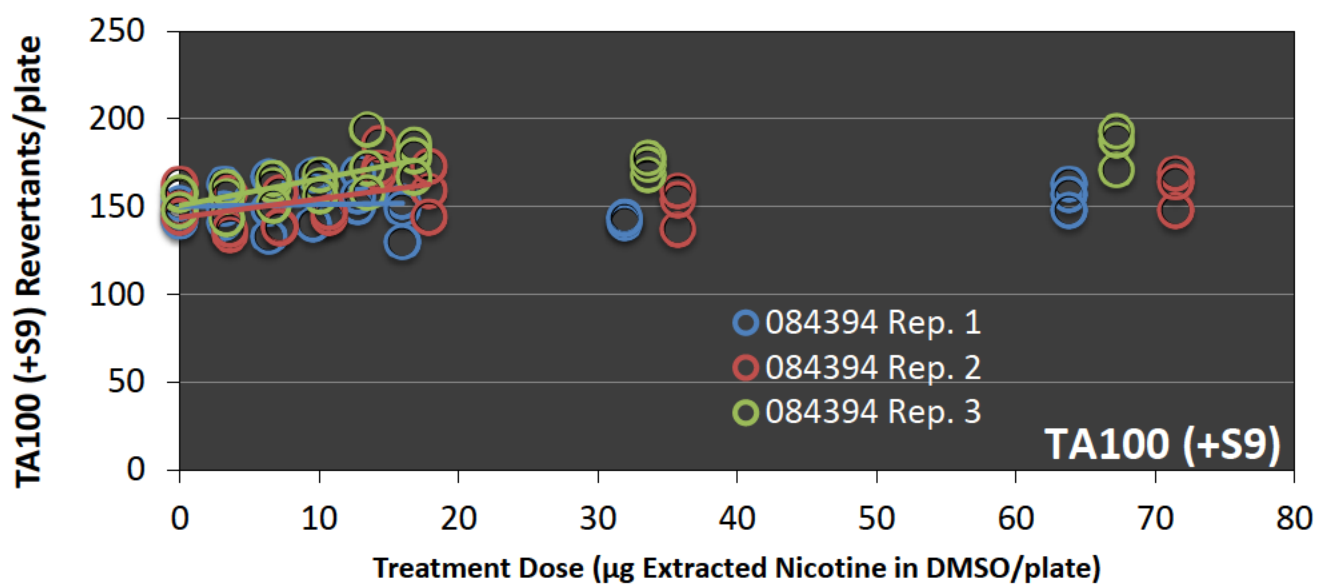
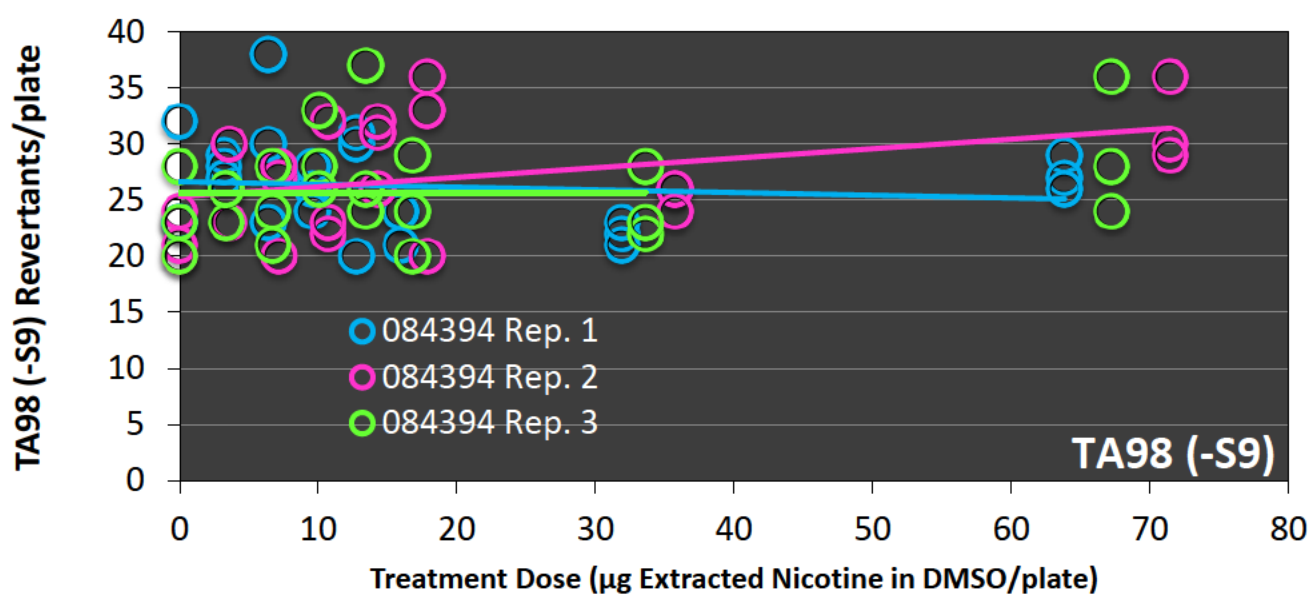
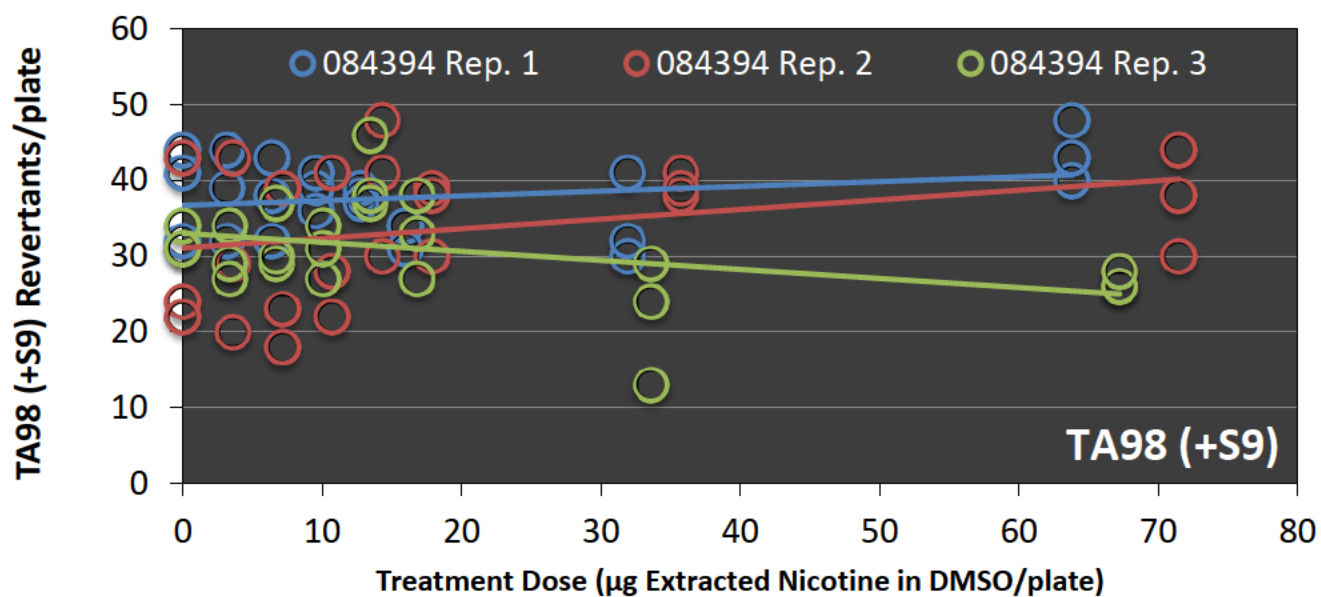
**One-Way ANOVA and ANOVA-Based Comparisons Among  
Test Samples of Mean 'Extracted Nicotine' Slope Estimates  
that are Significantly Greater than Zero (0)**



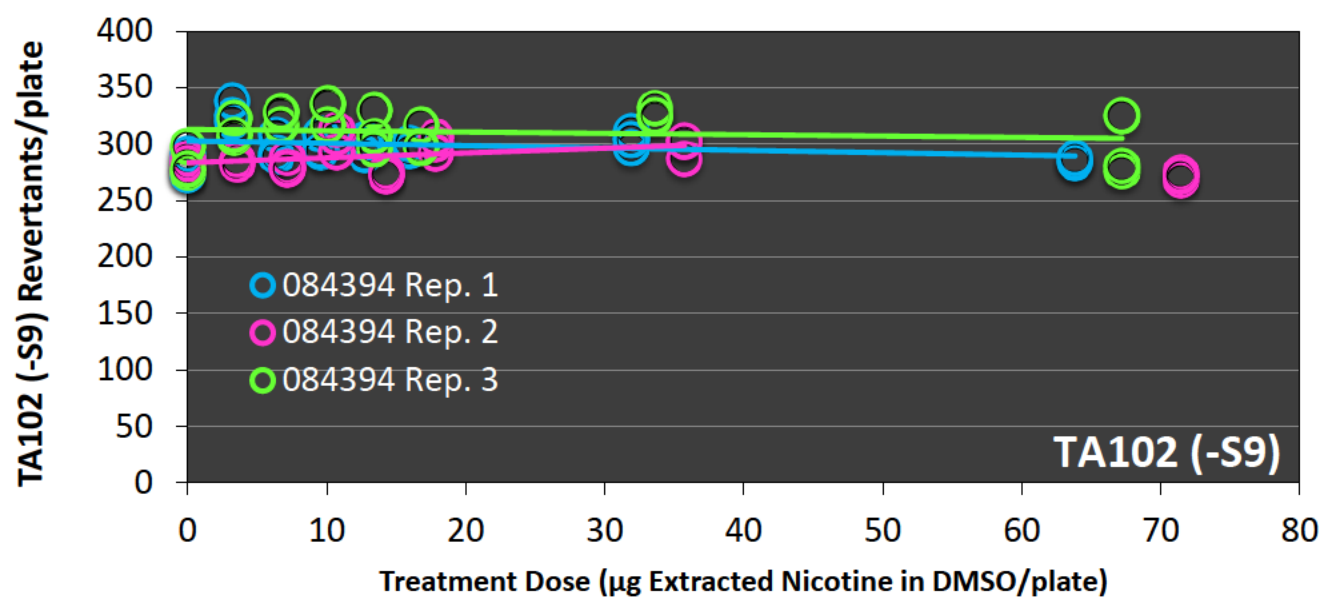
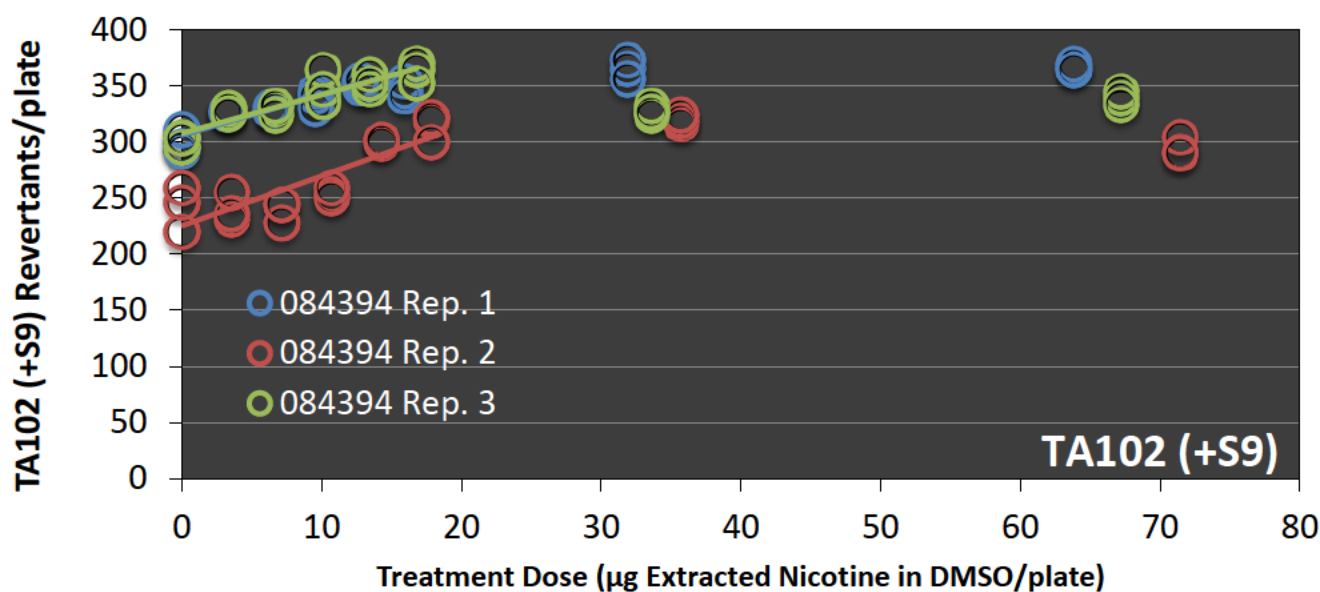
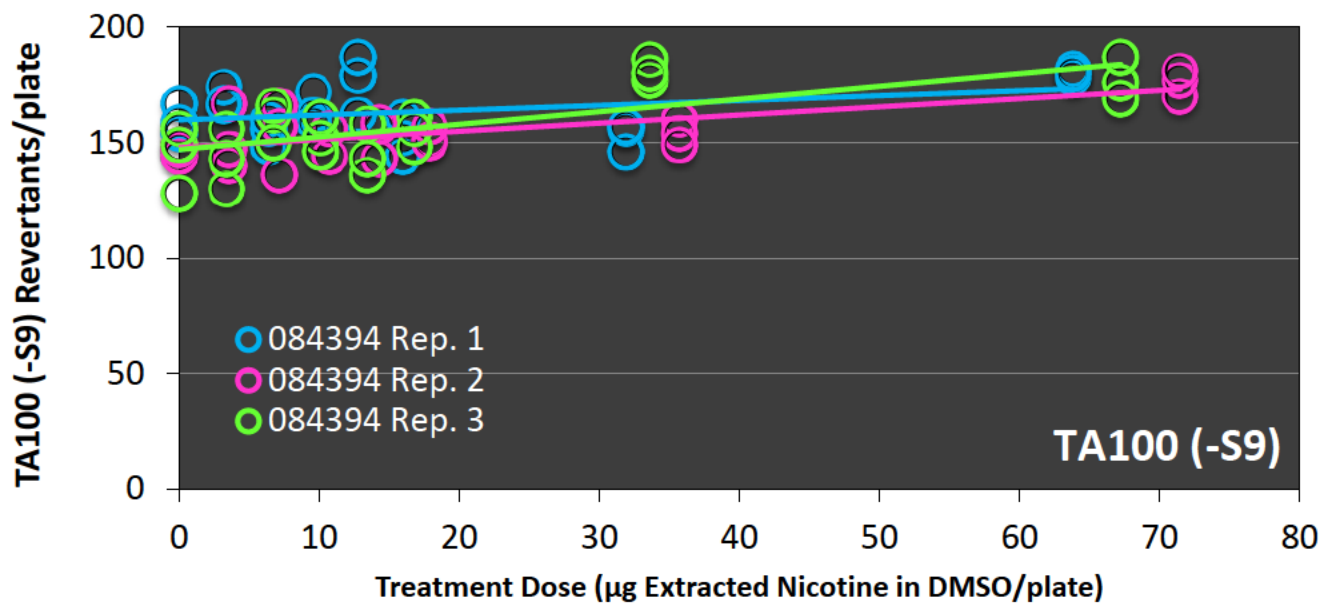


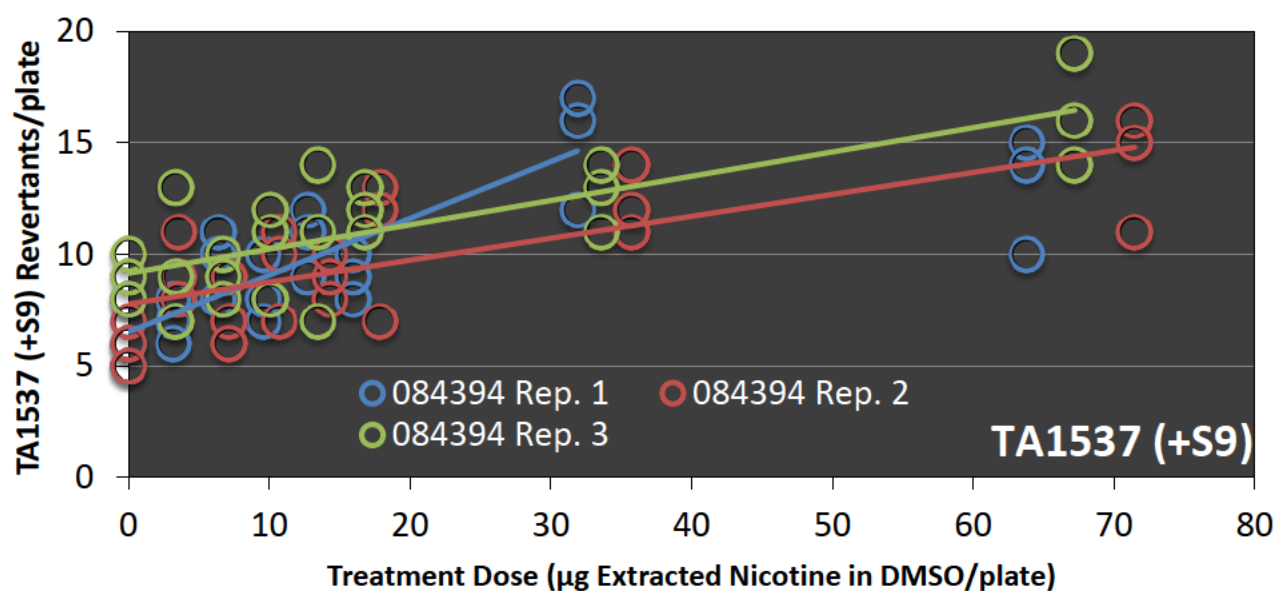
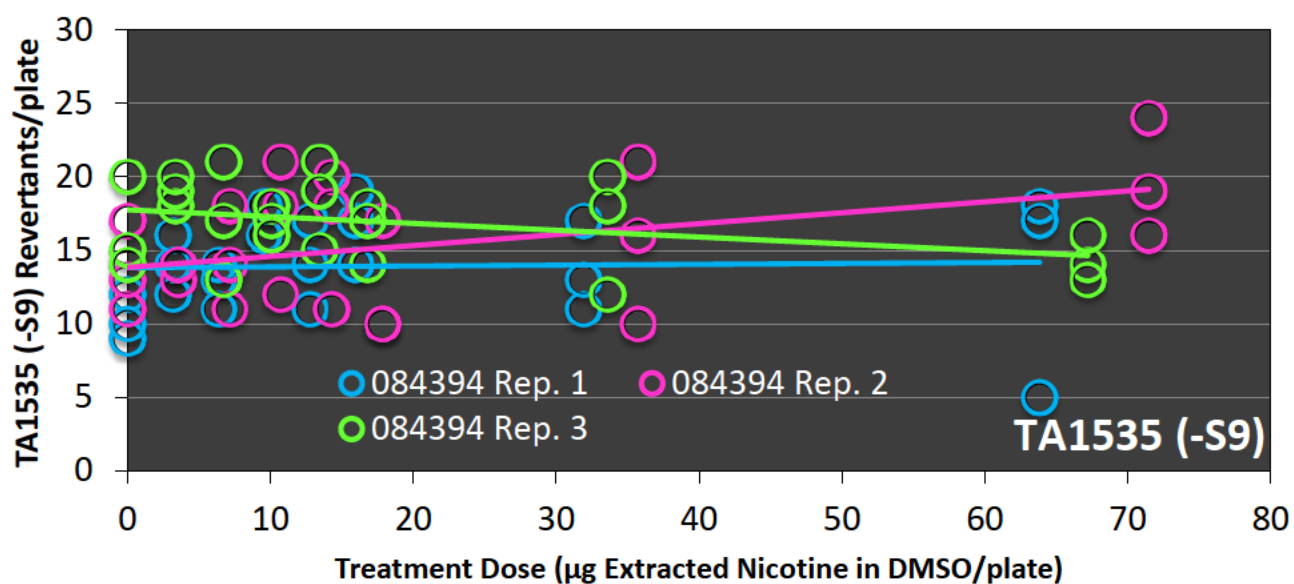
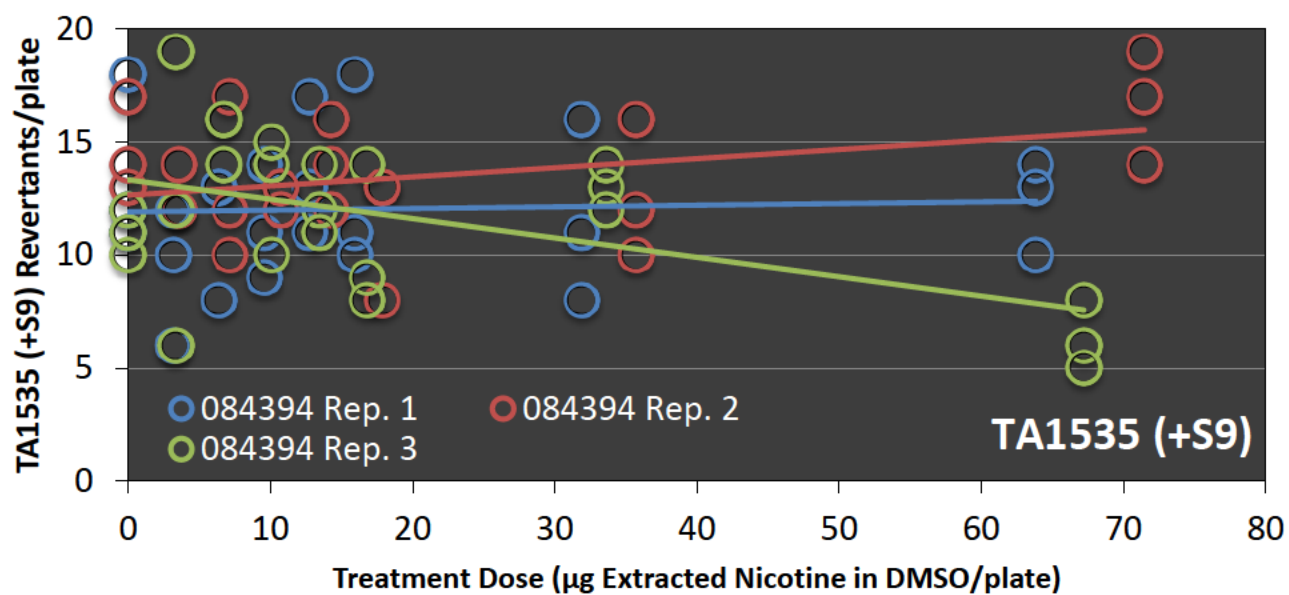


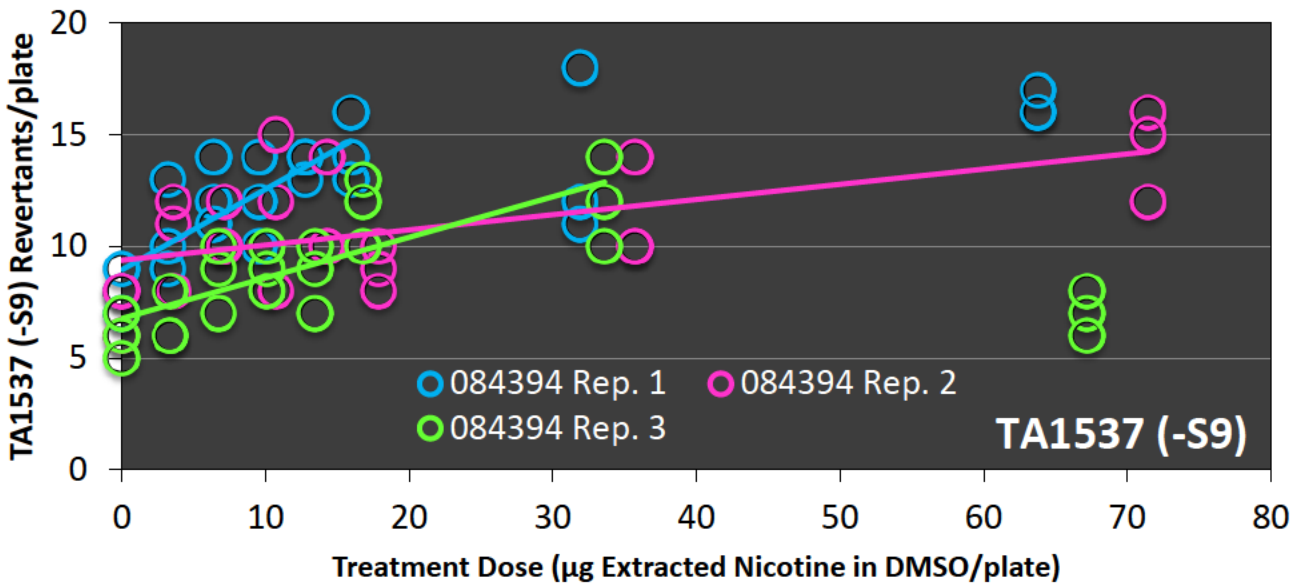


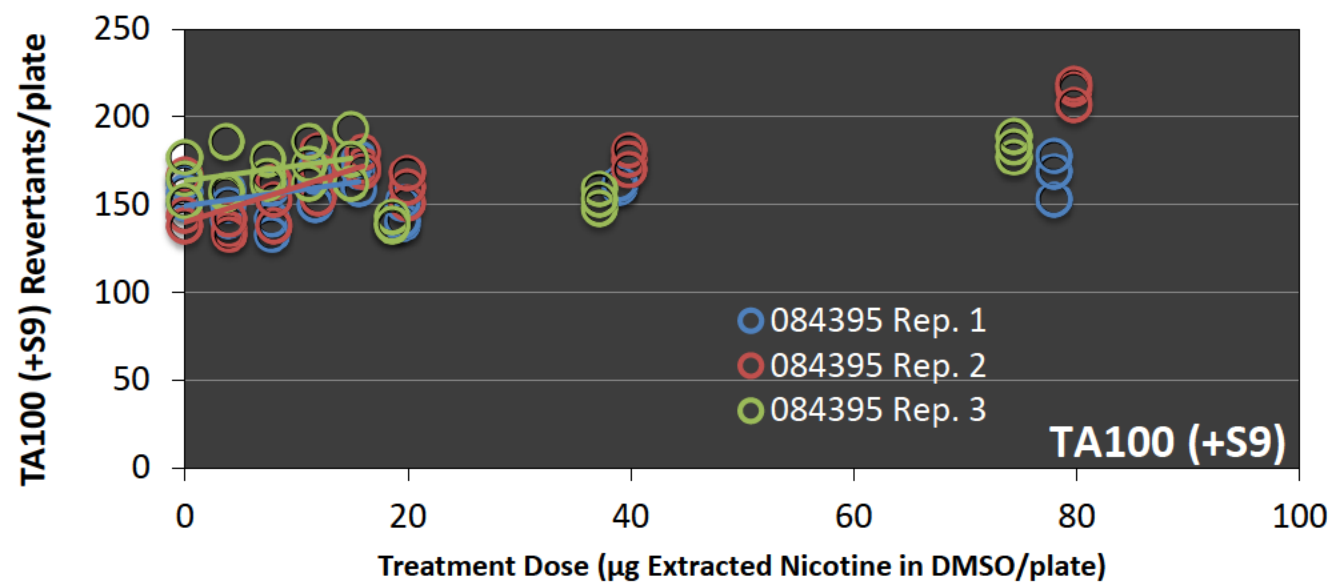
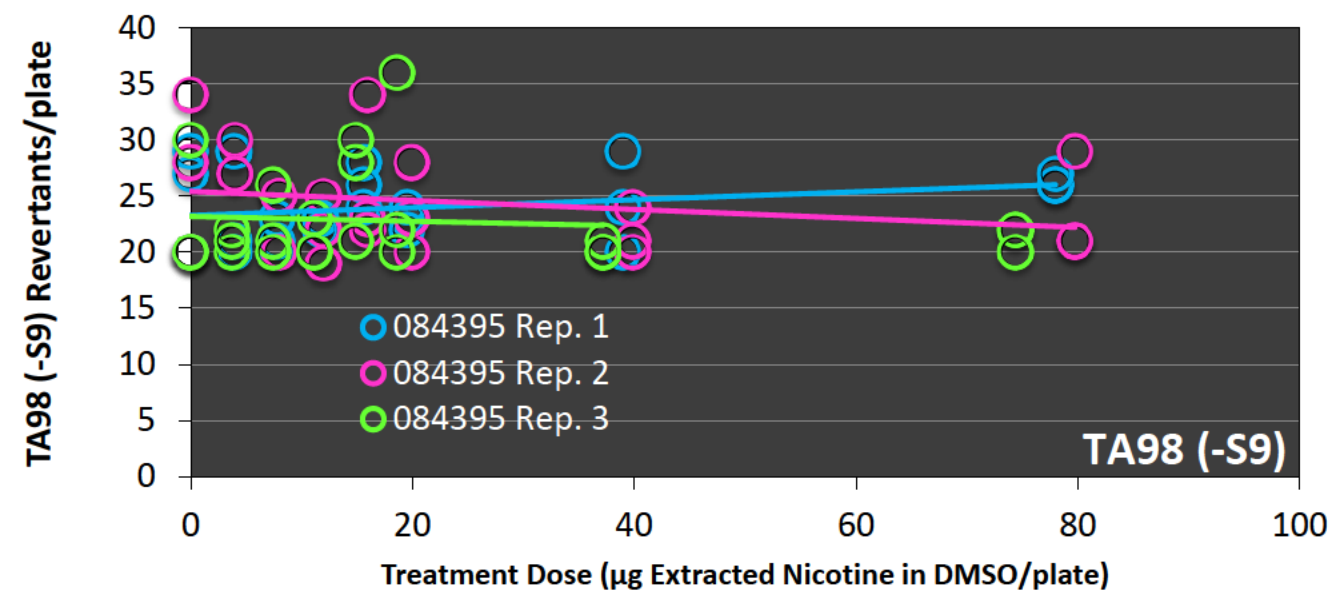
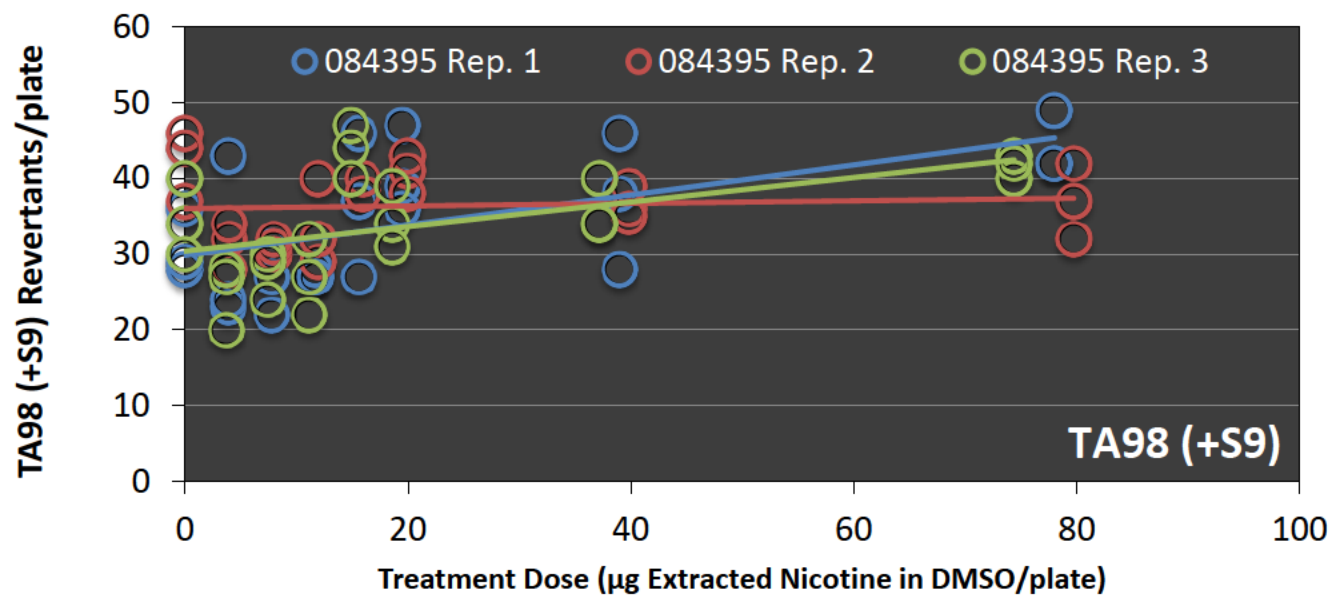


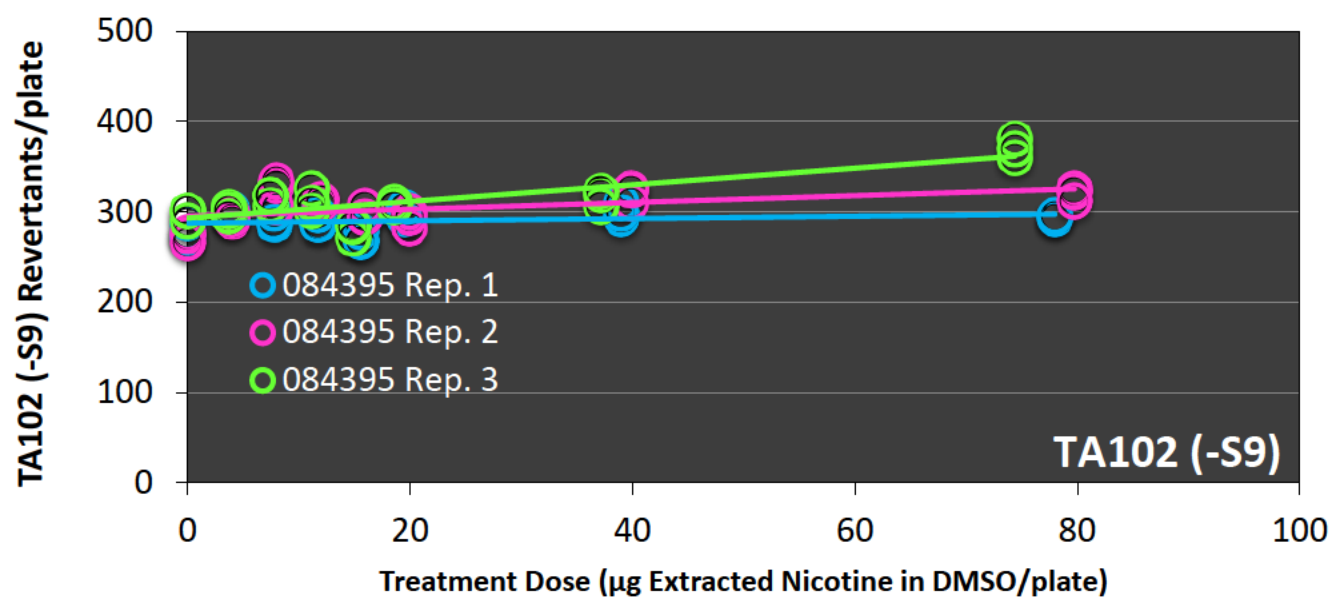
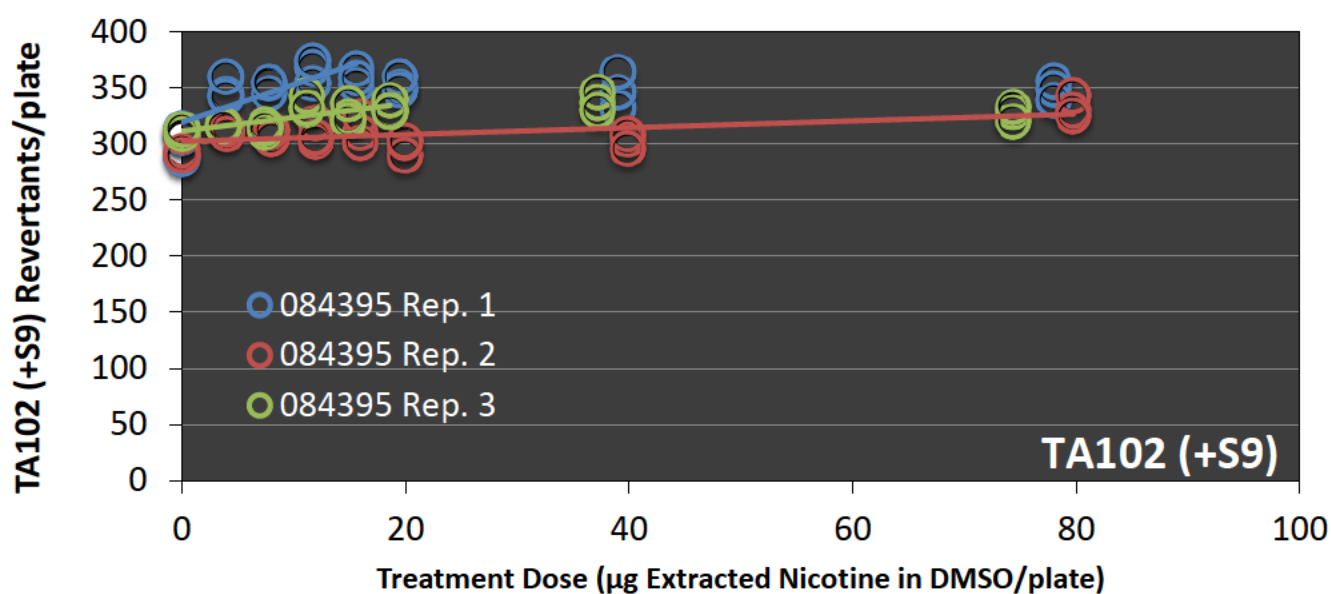
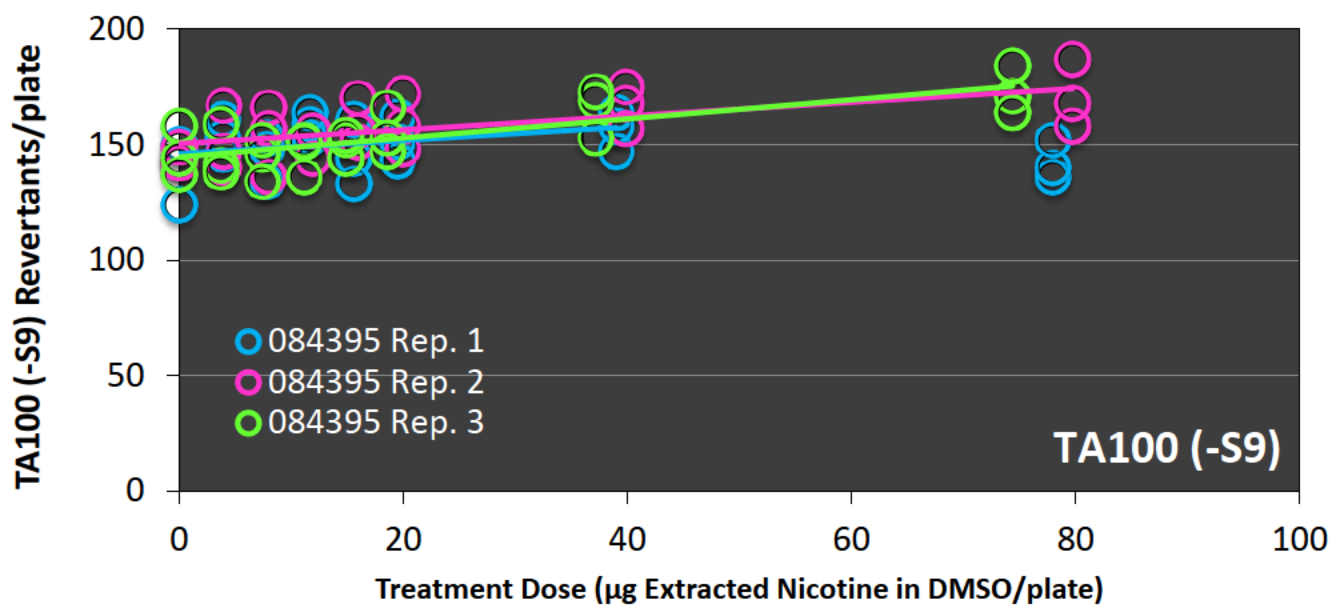


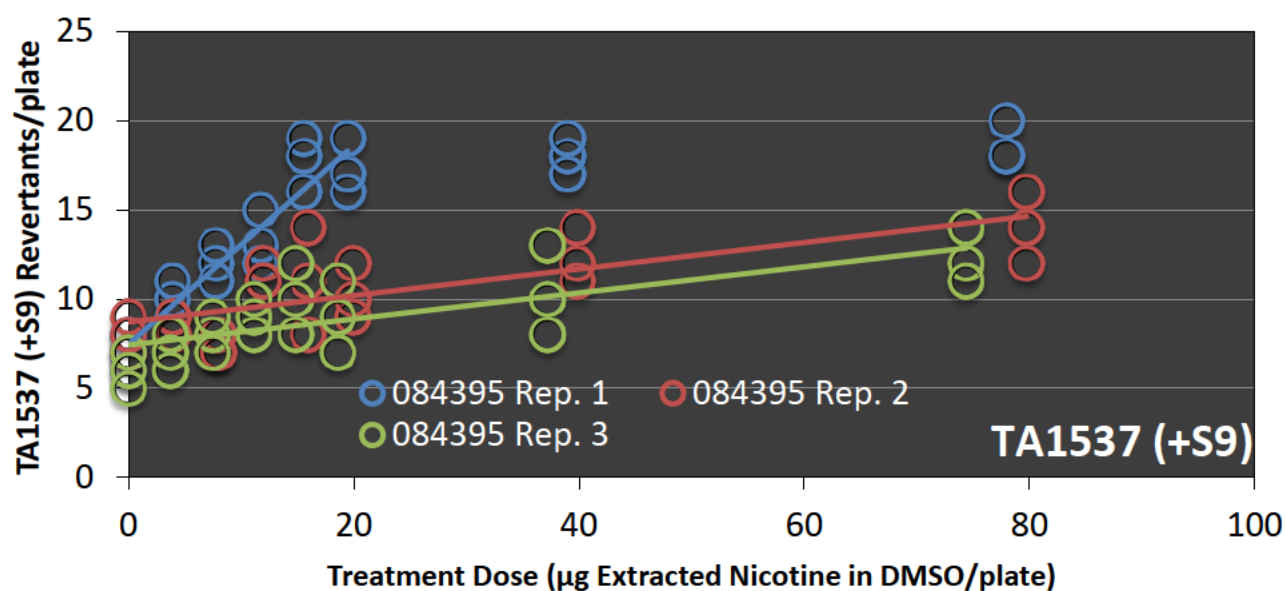
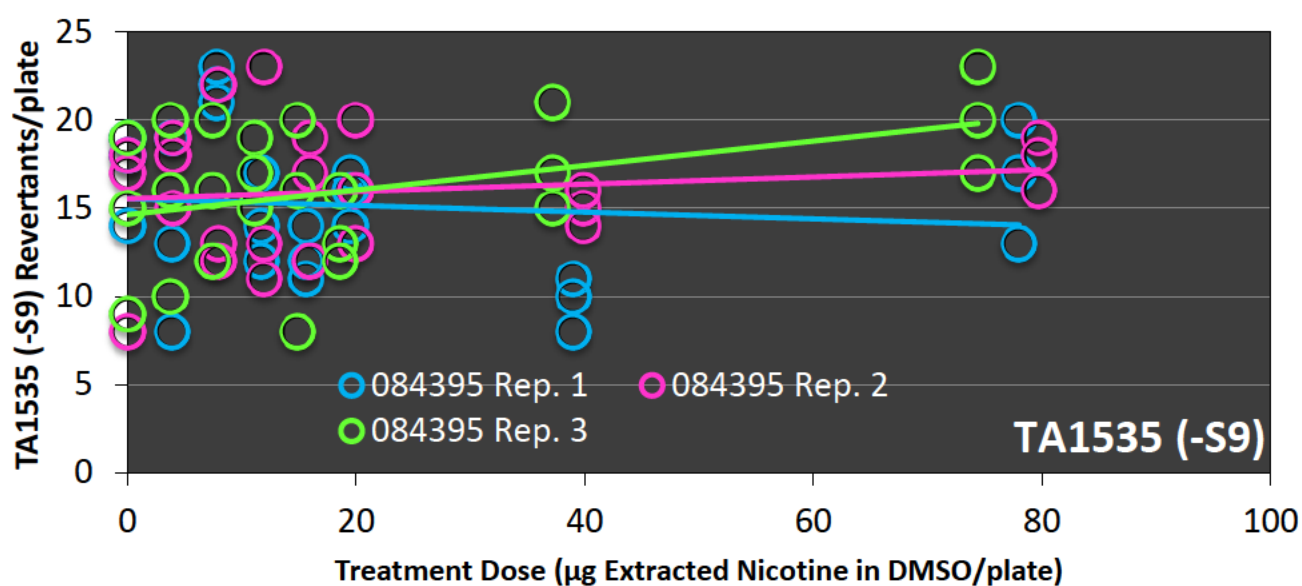
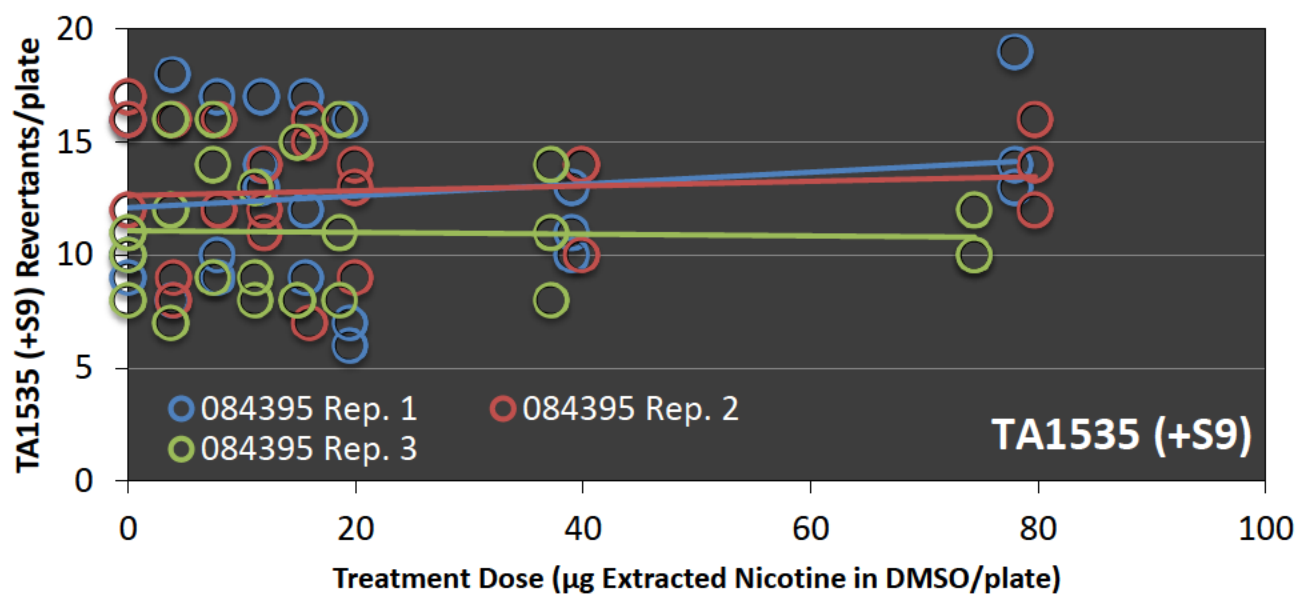


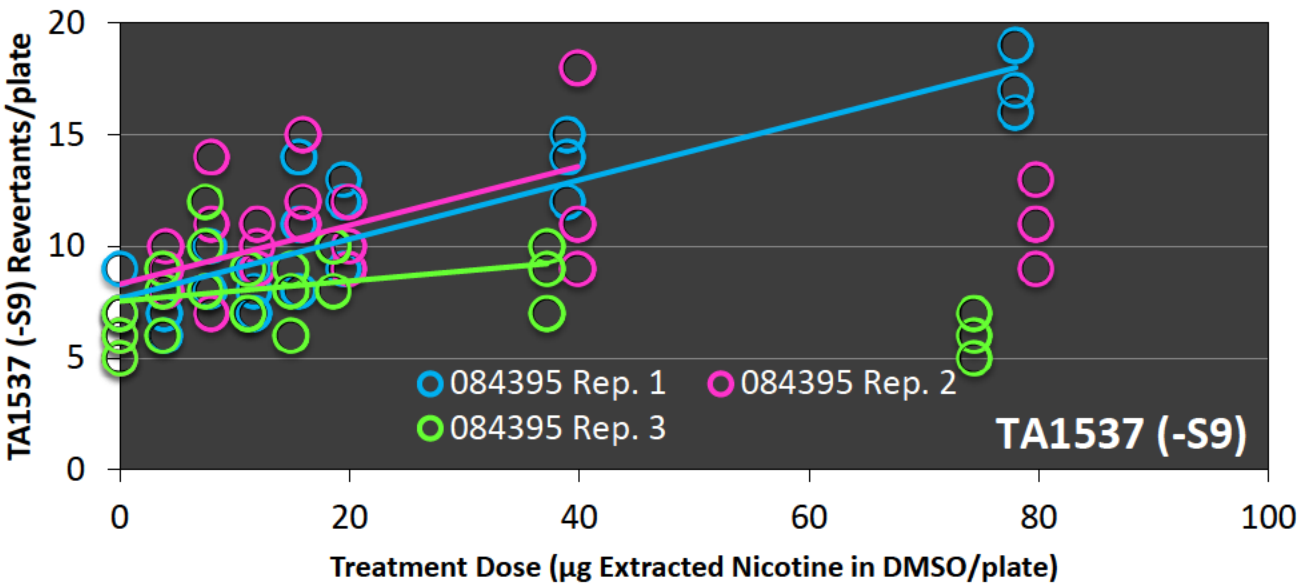




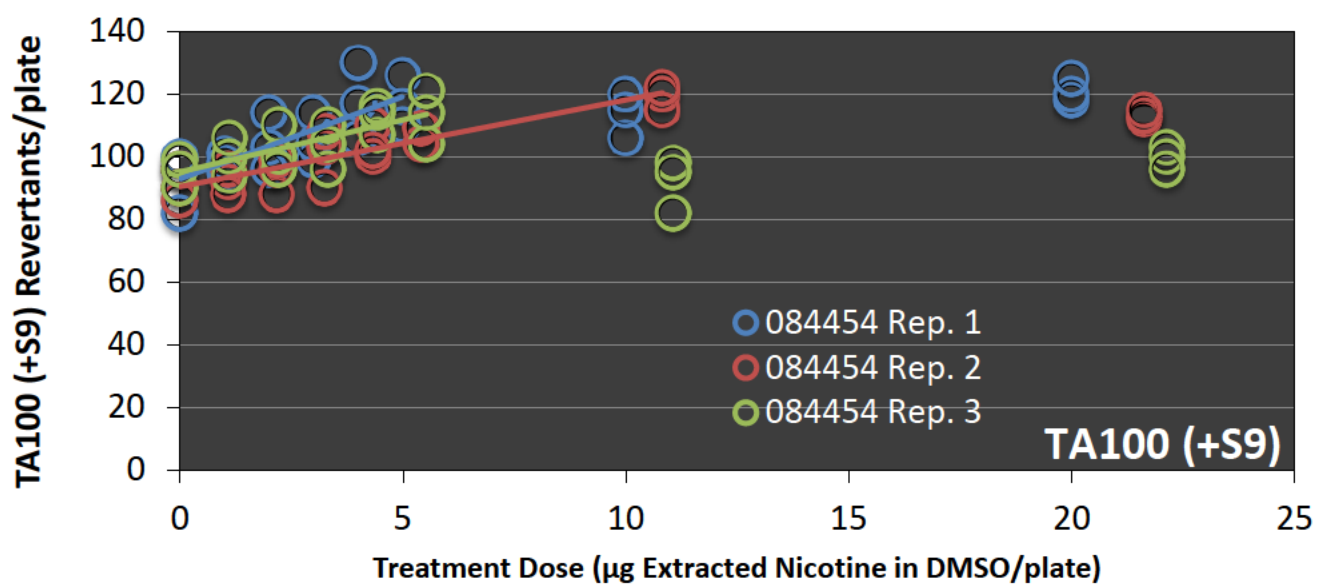
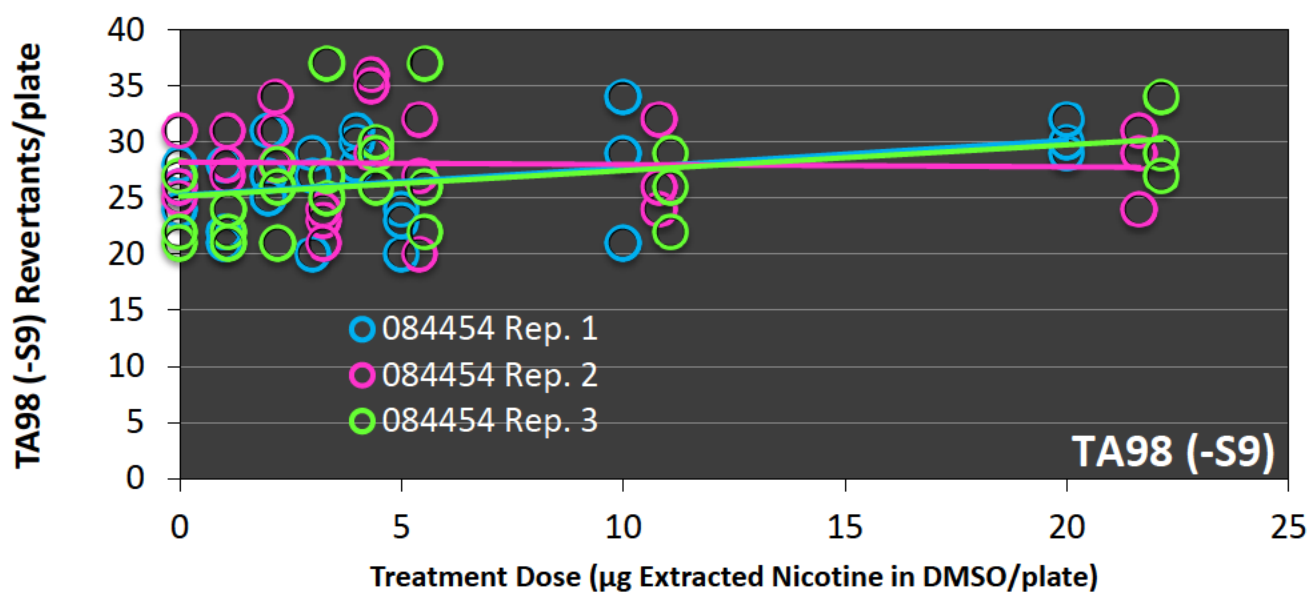
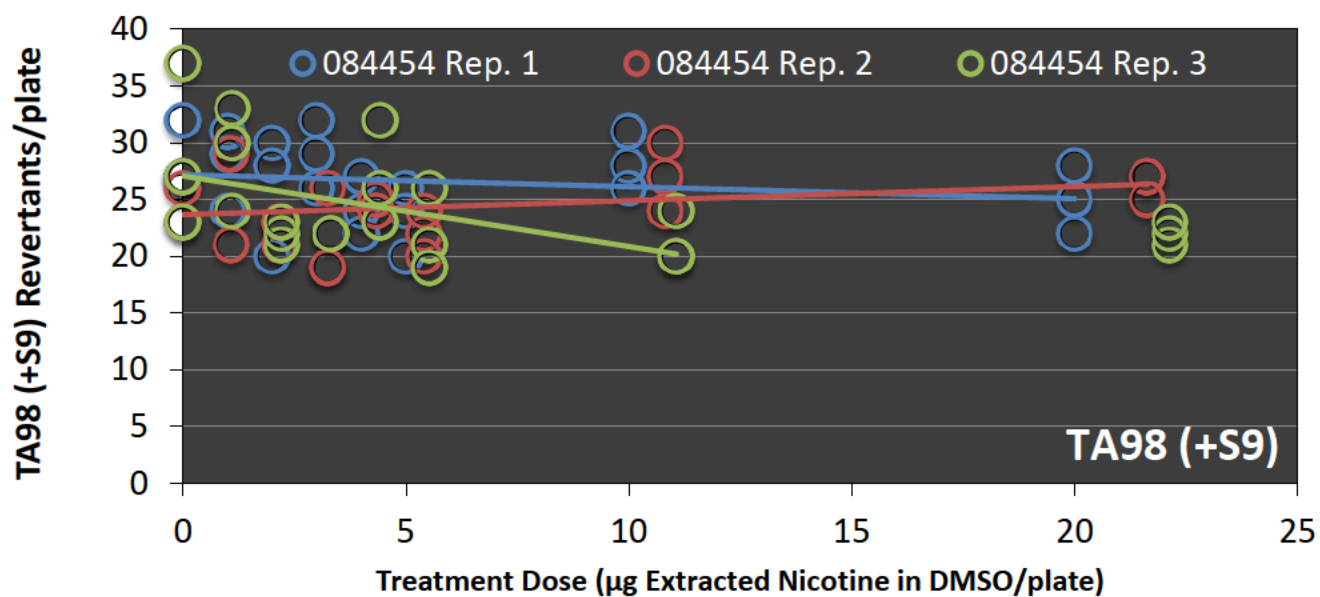




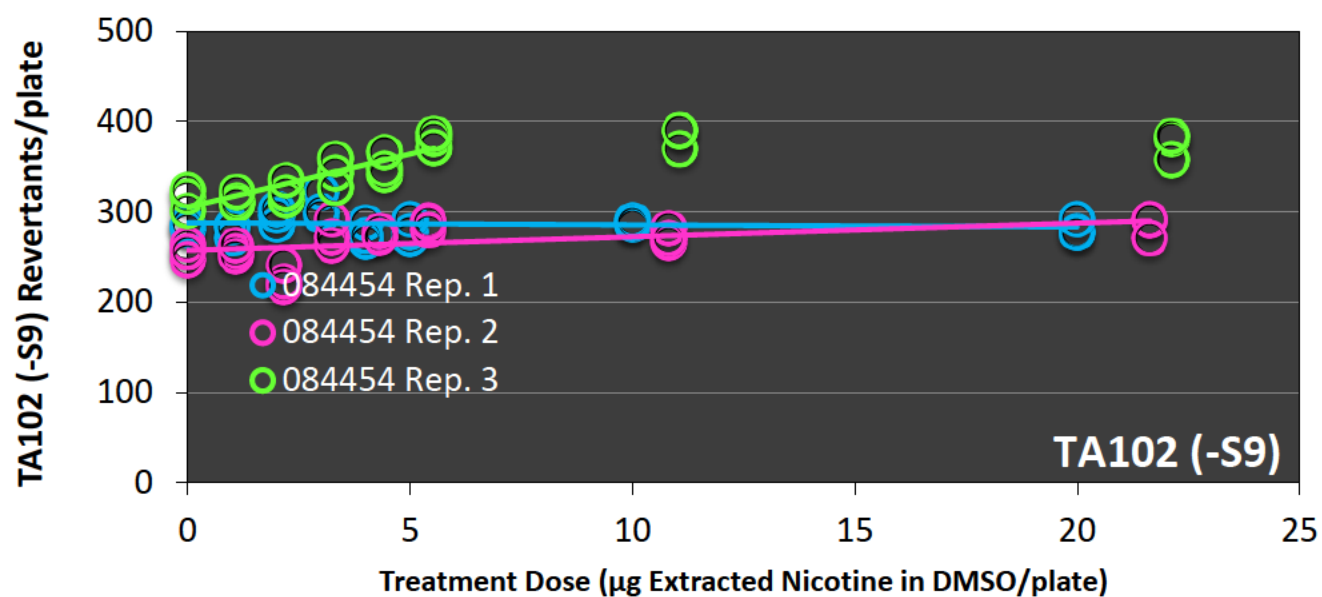
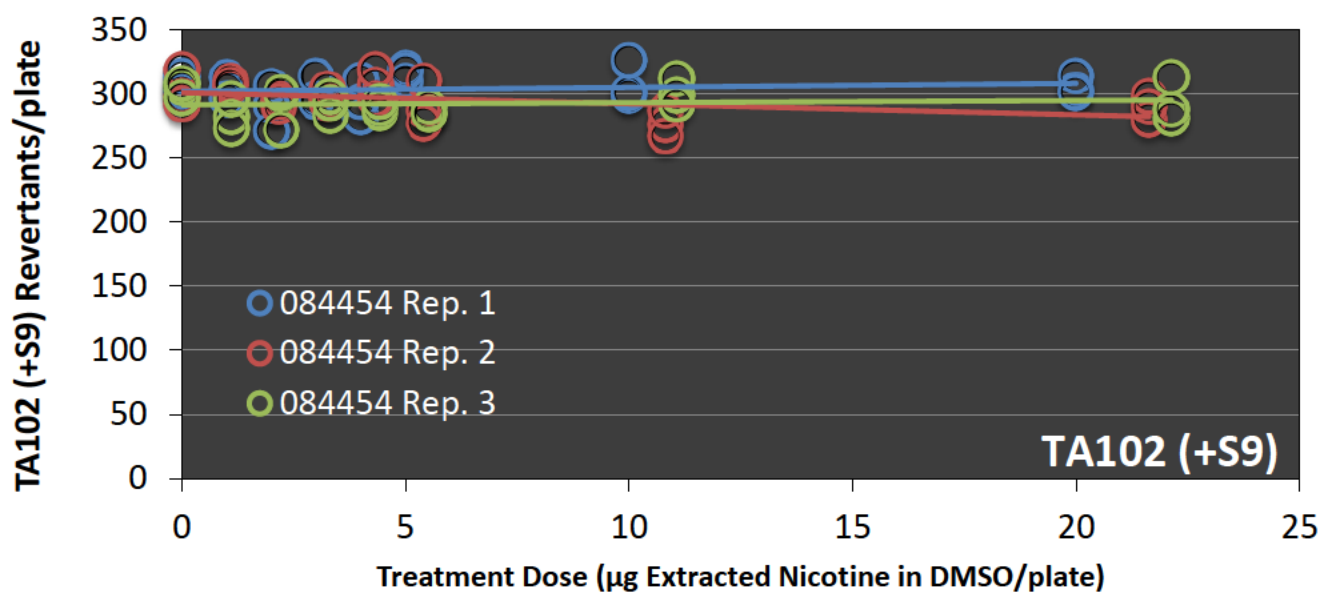
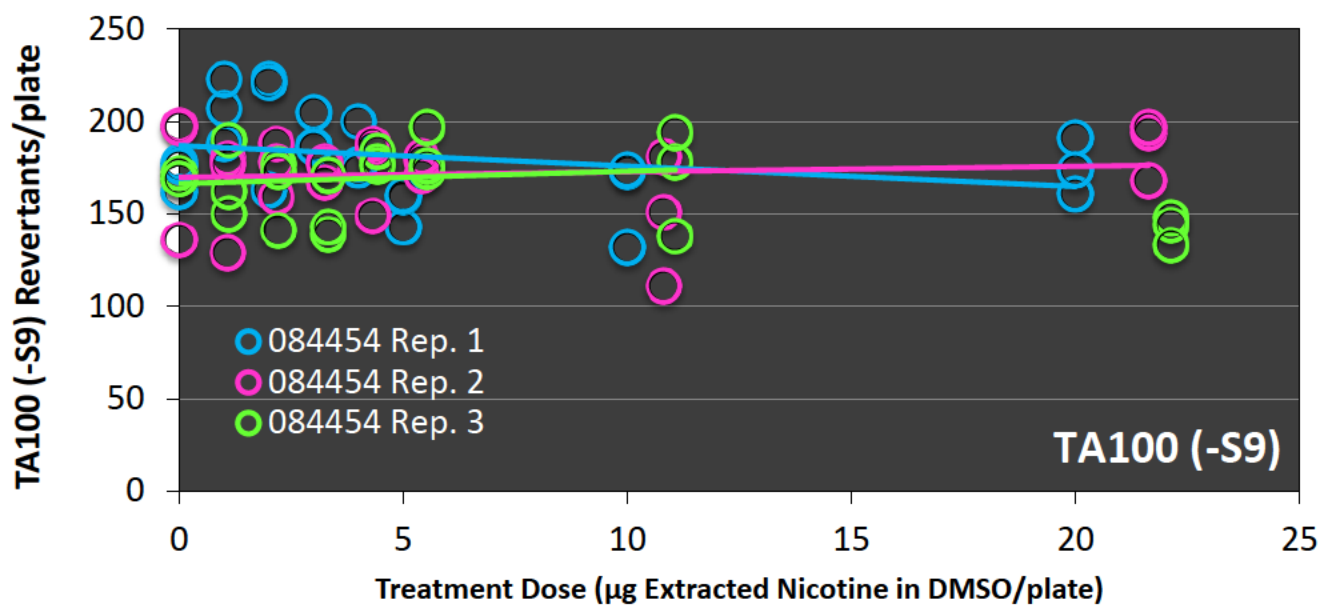


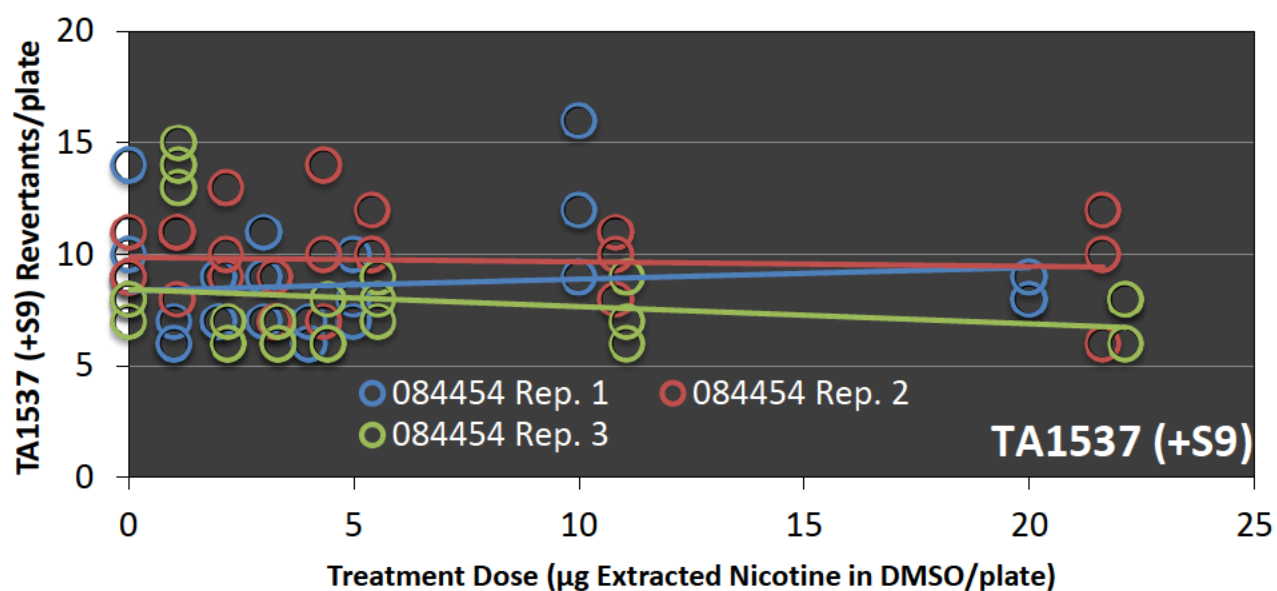
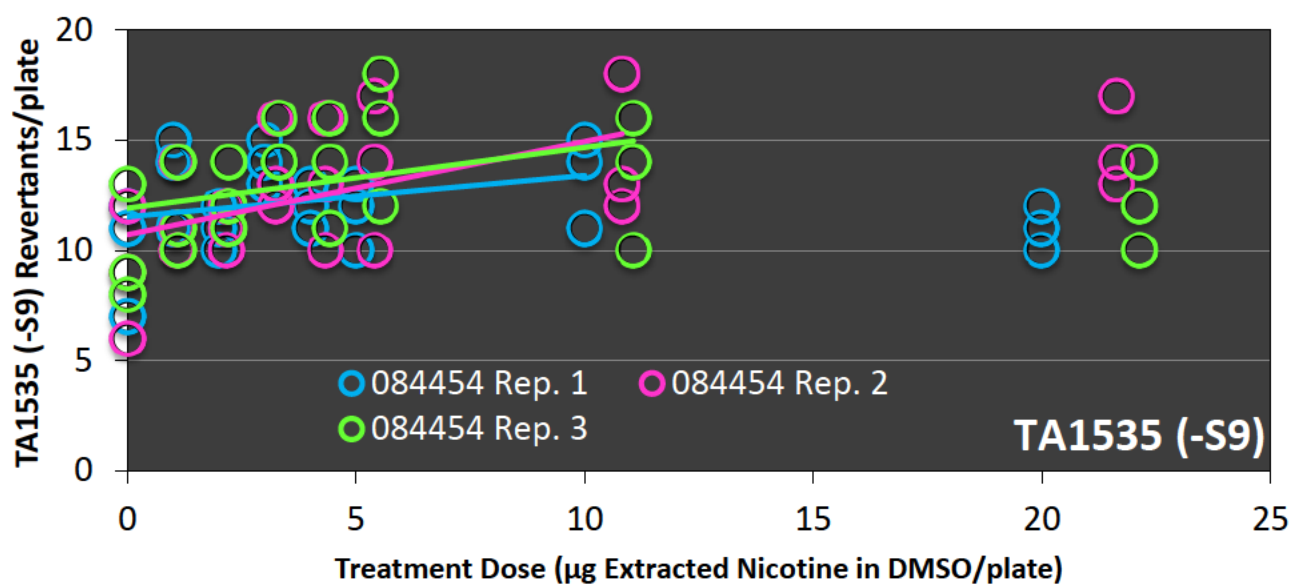
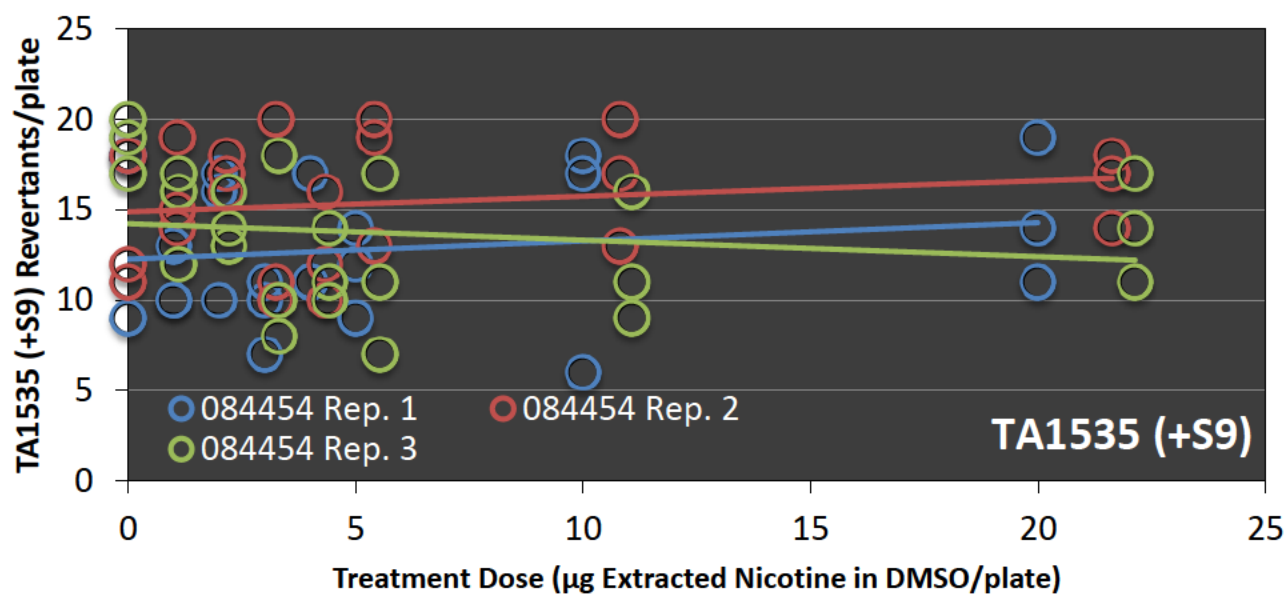


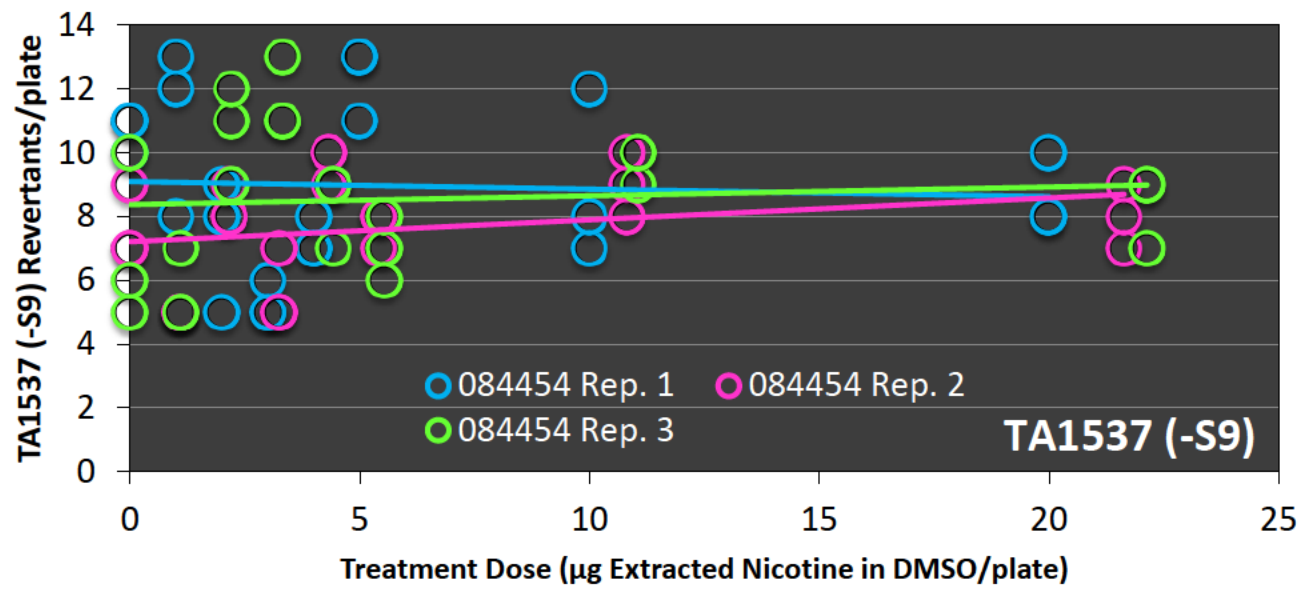


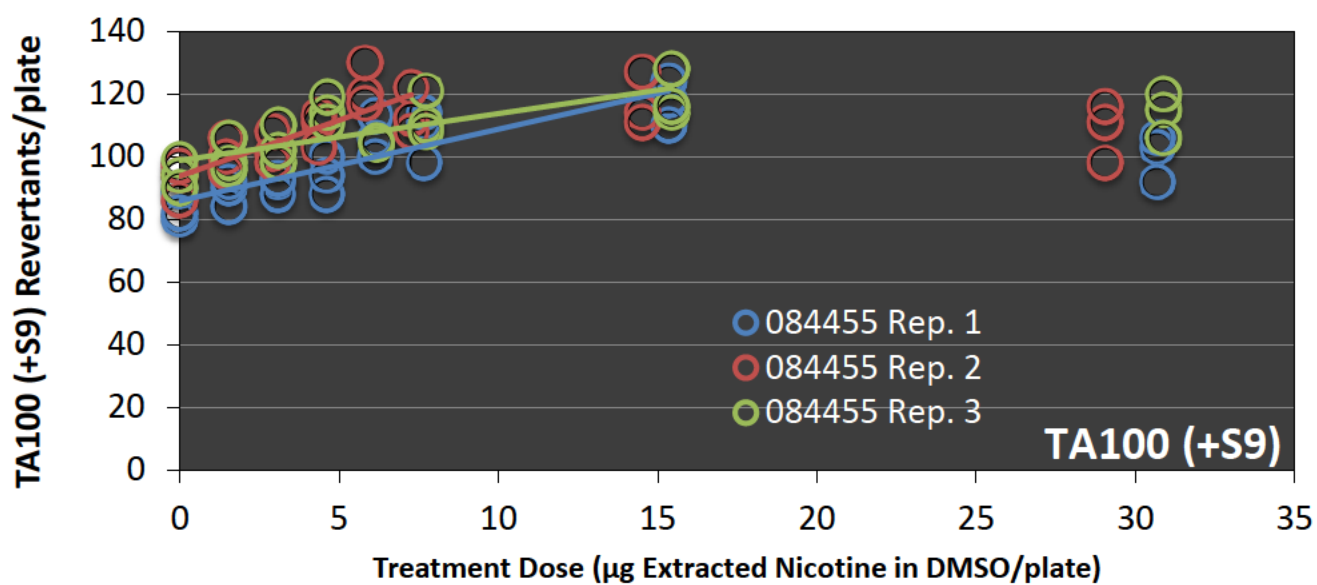
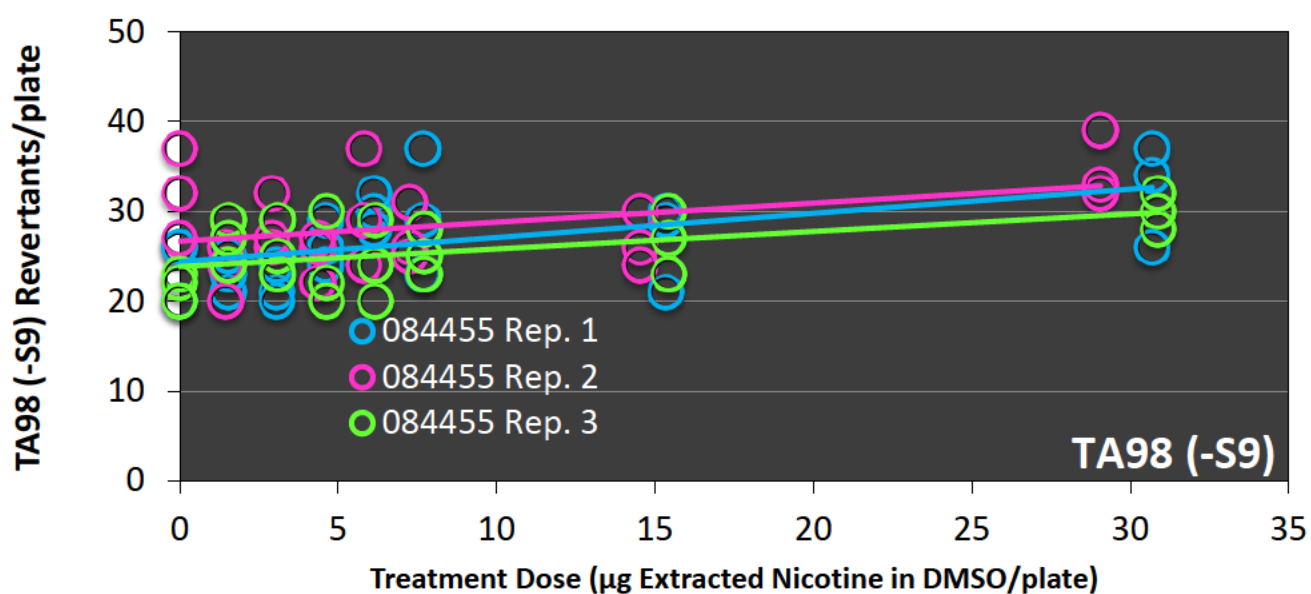
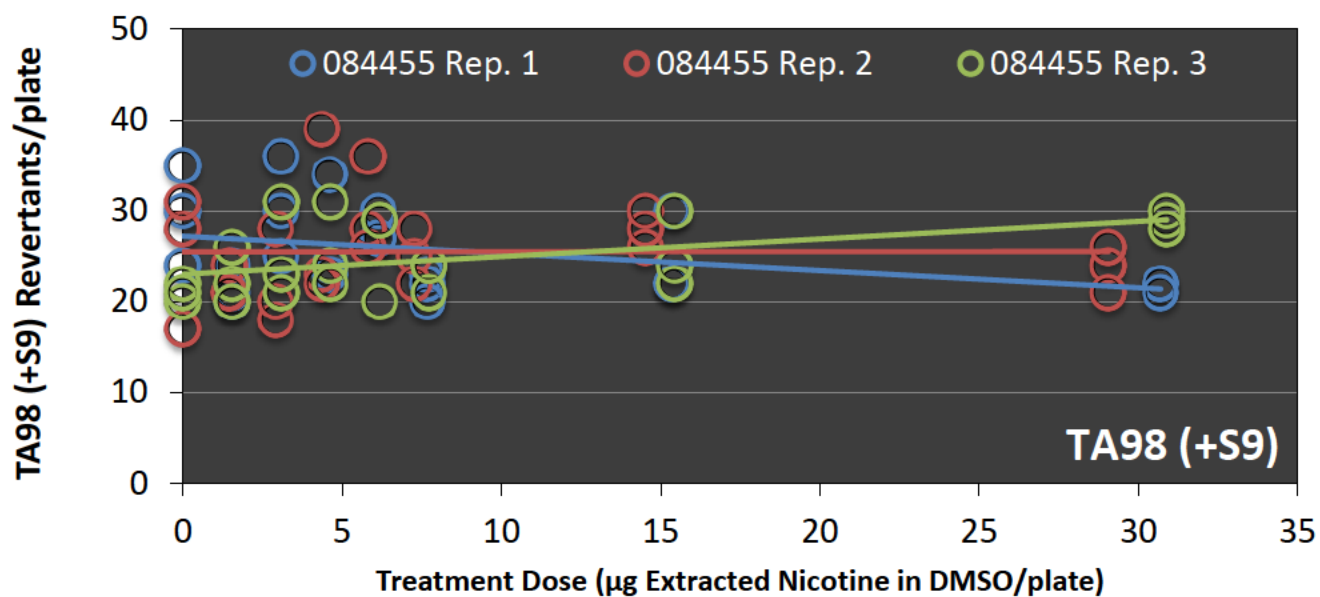


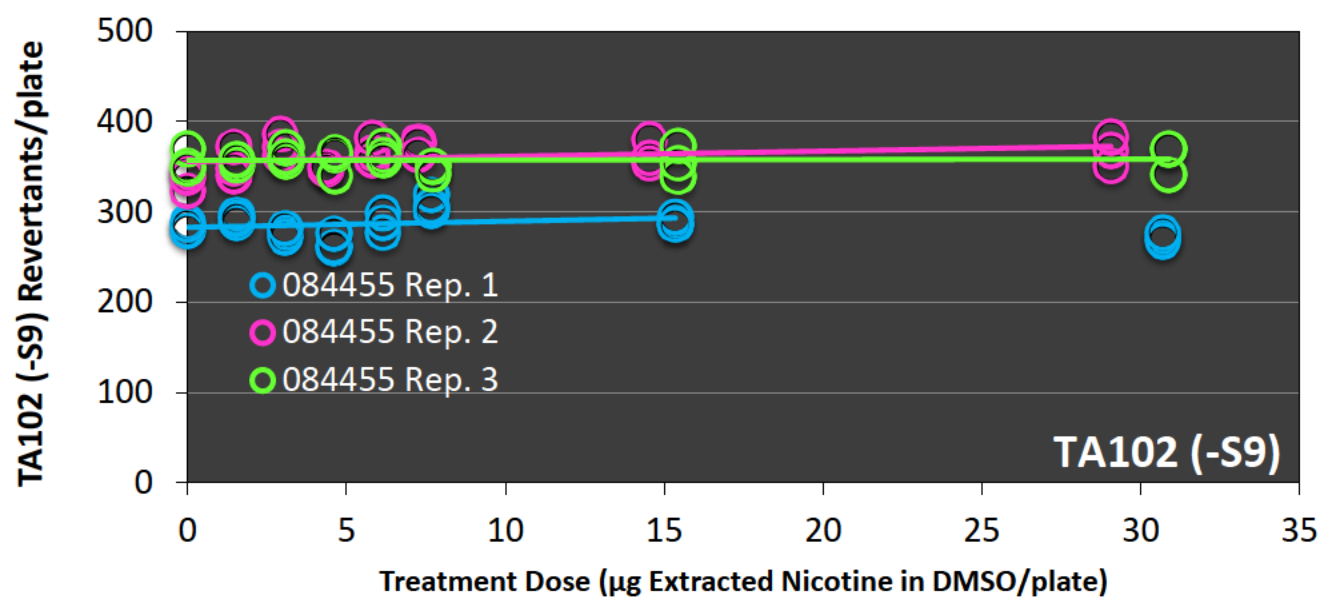
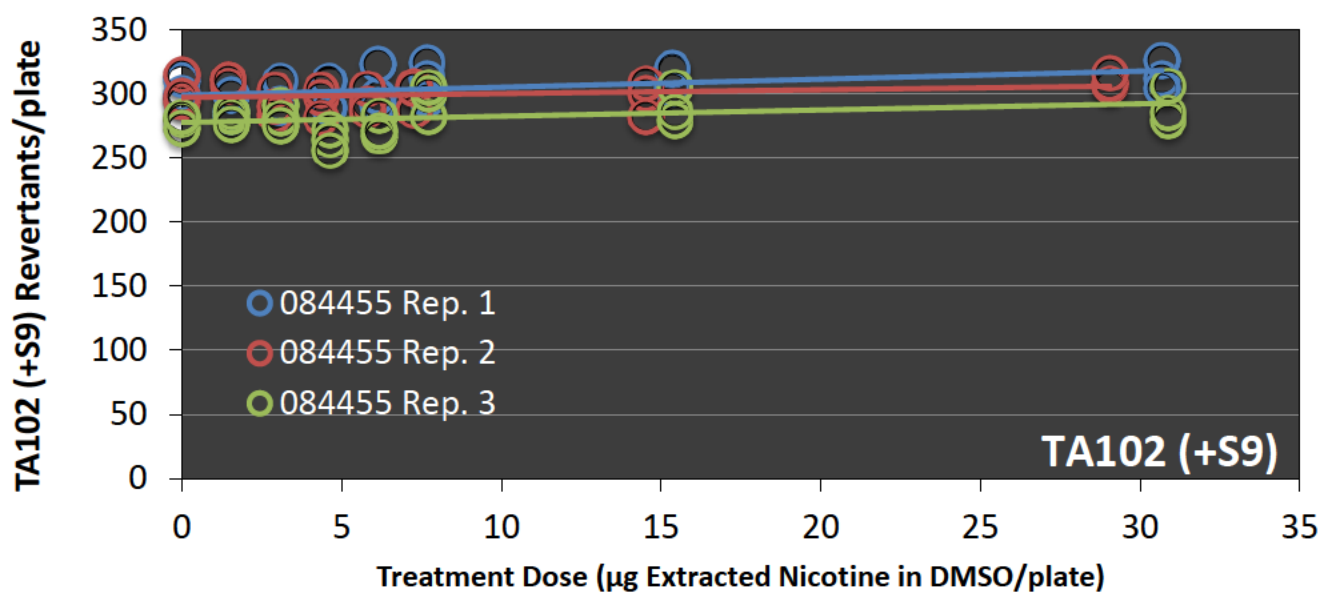
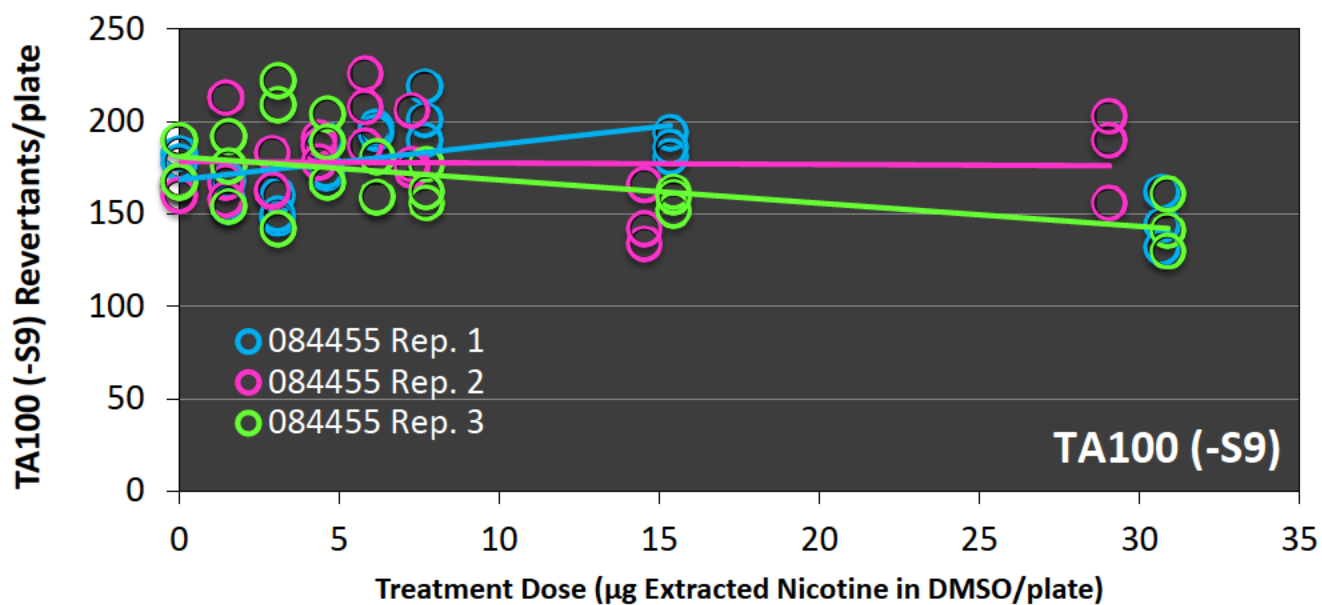


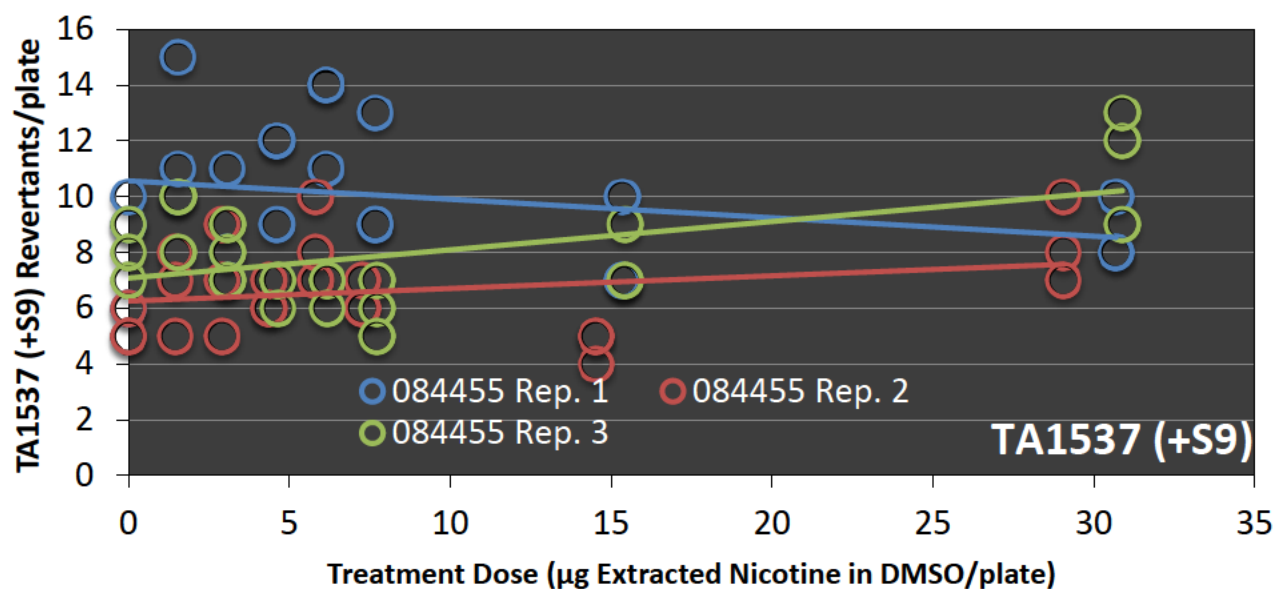
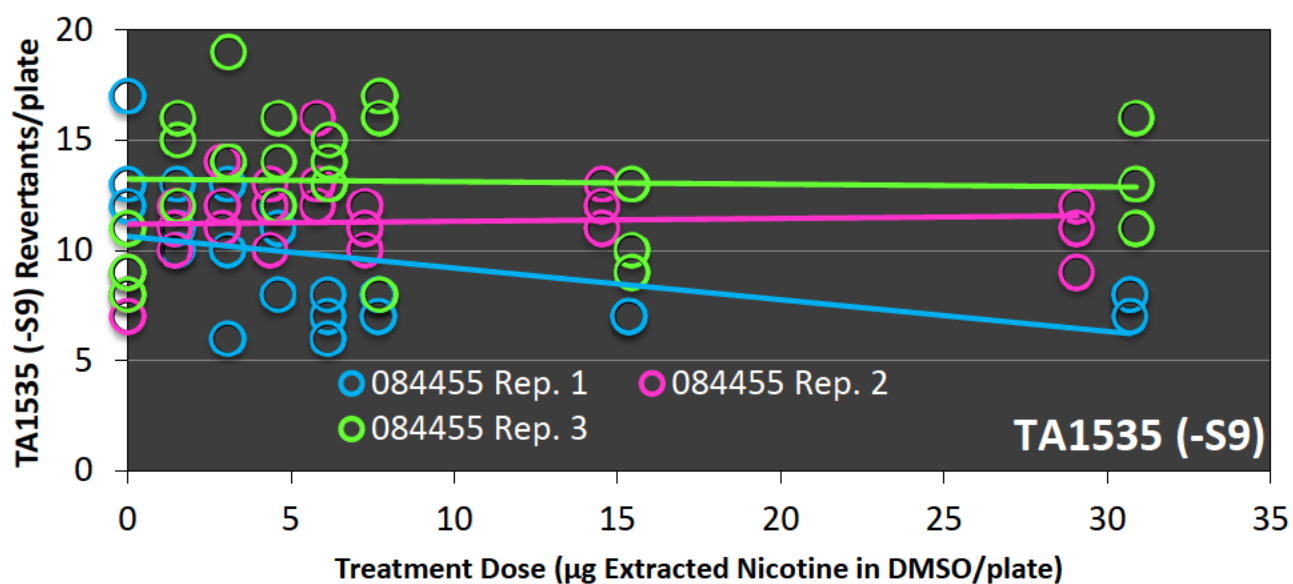
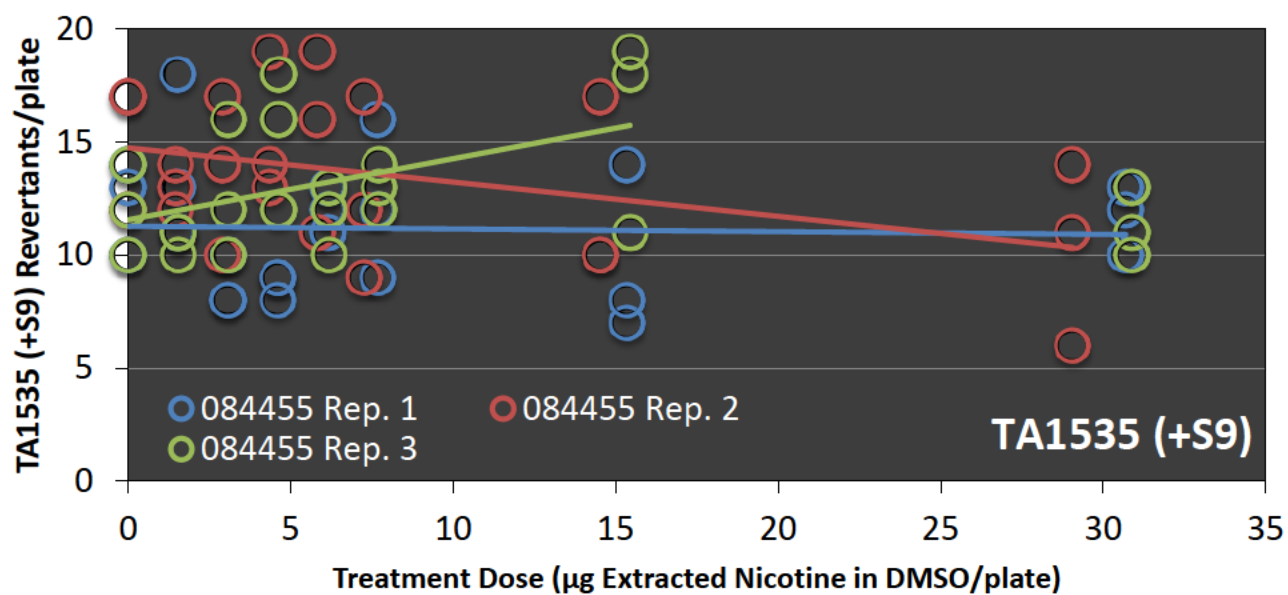


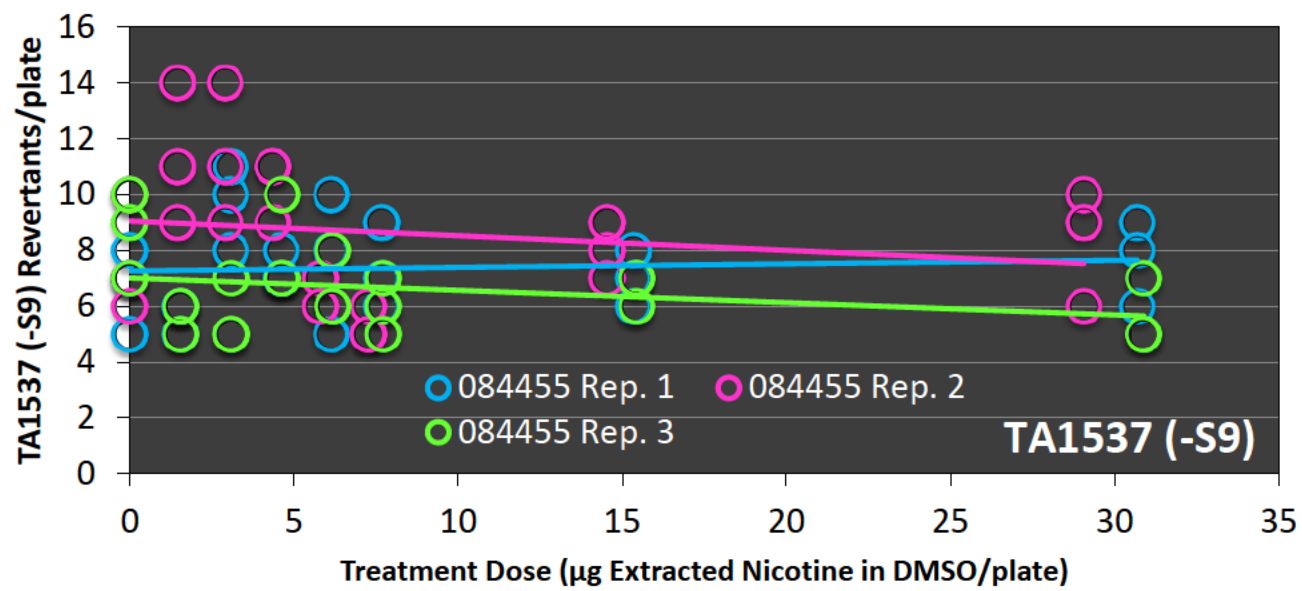




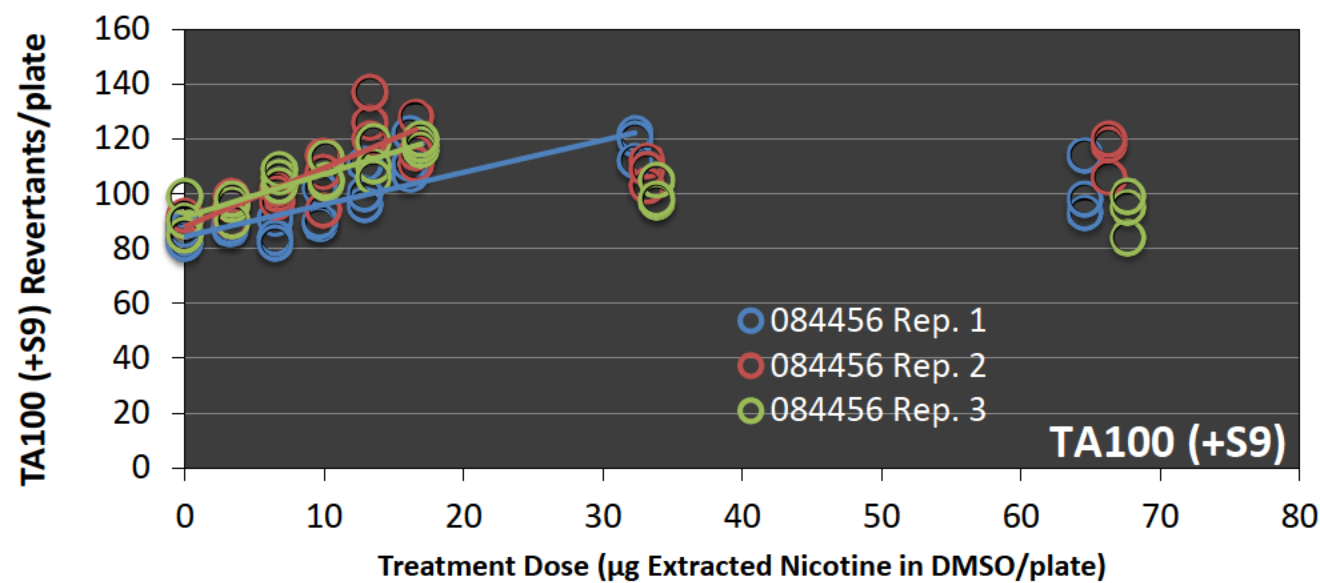
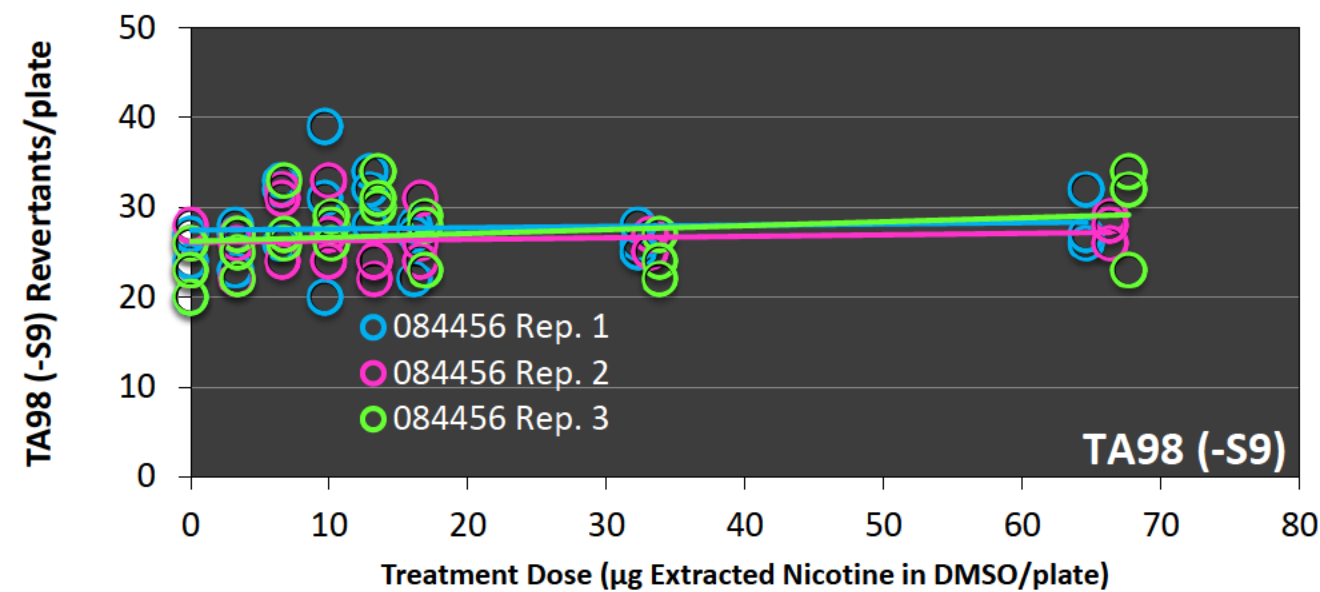
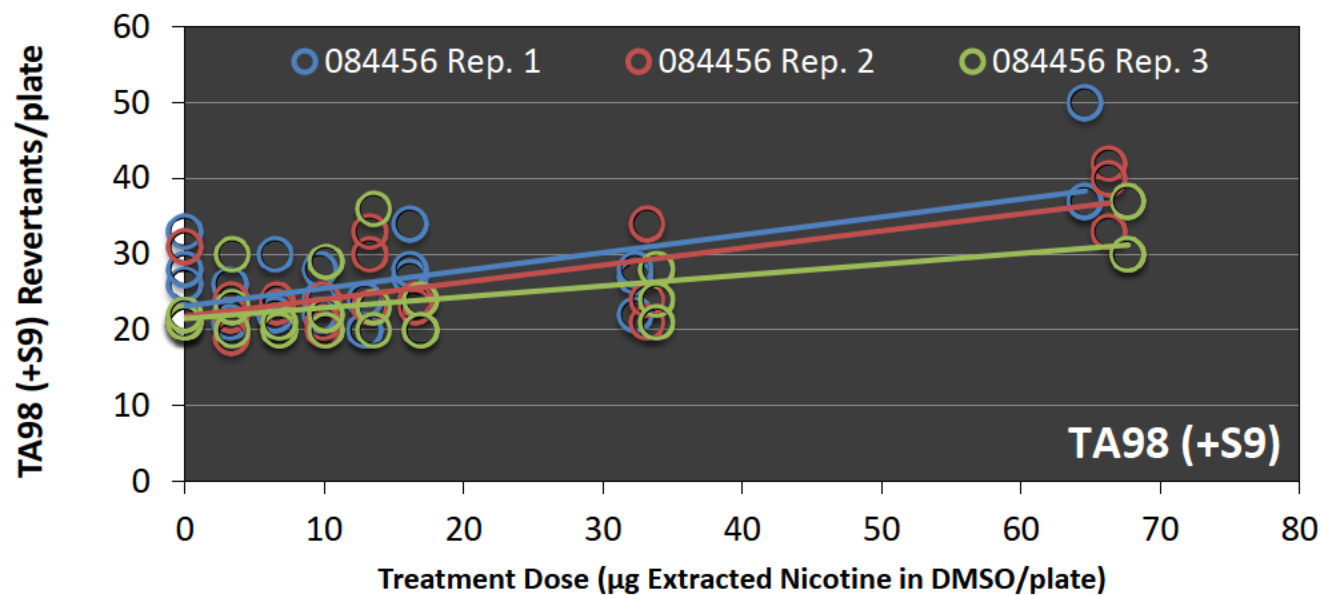




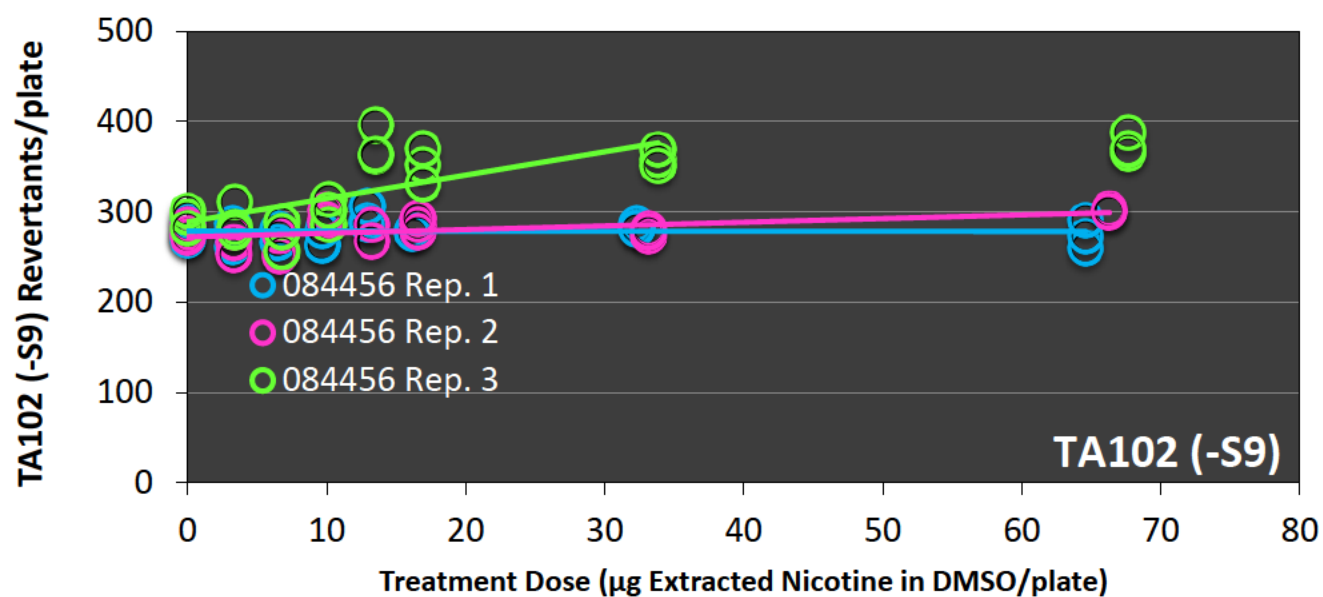
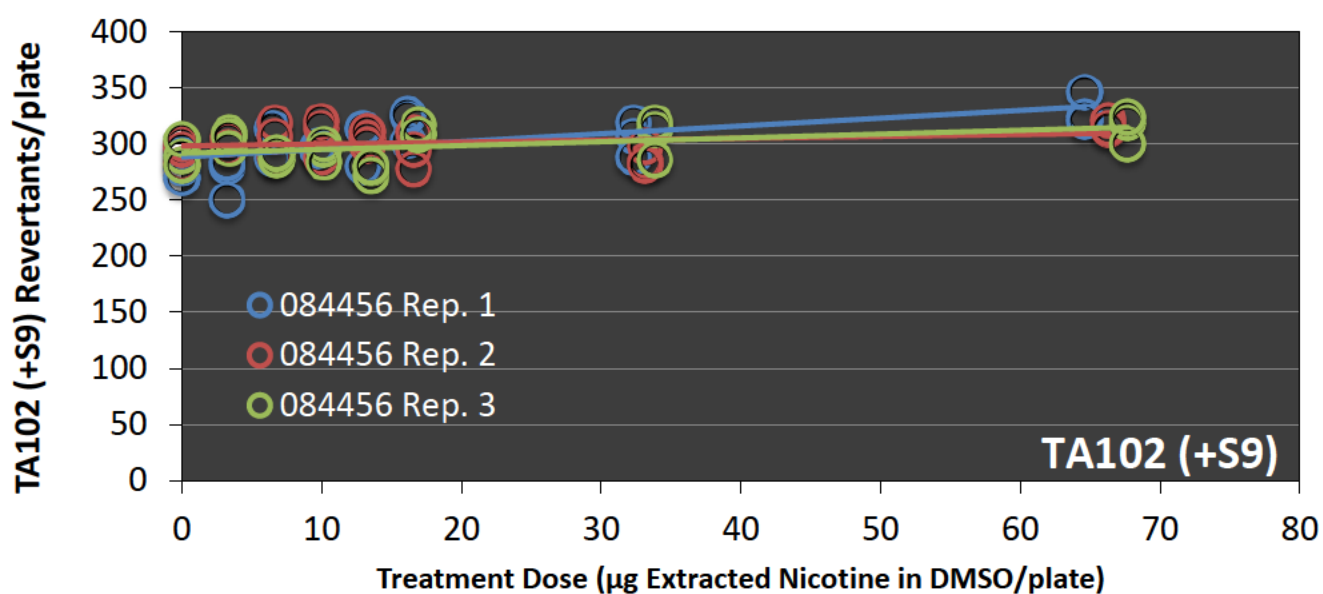
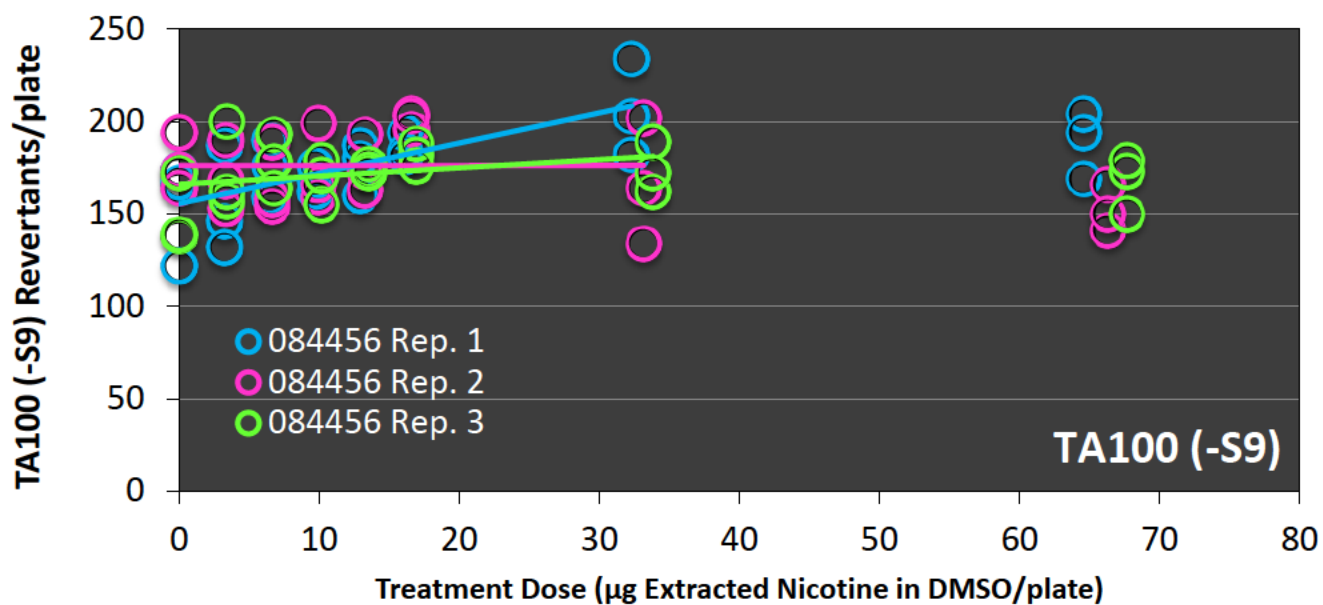


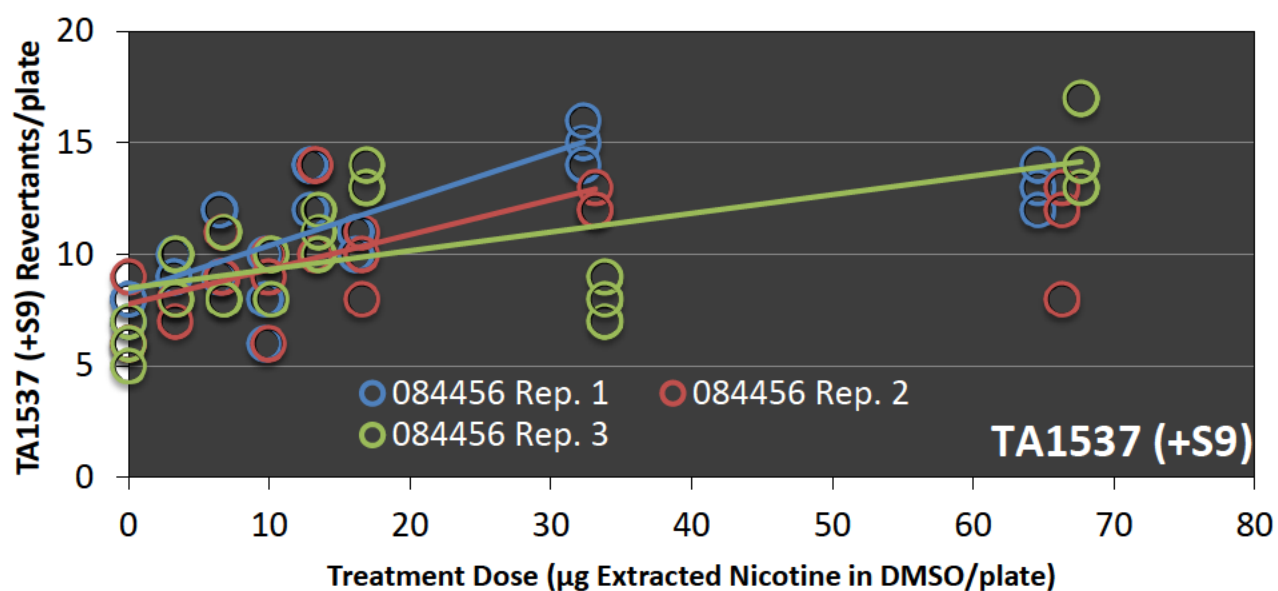
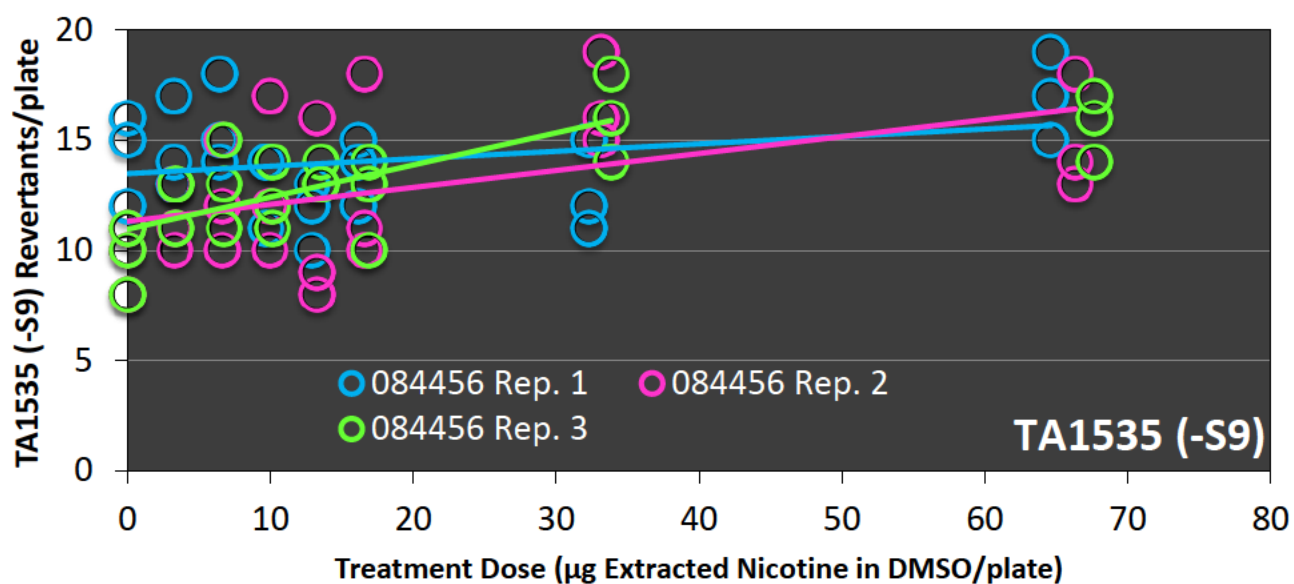
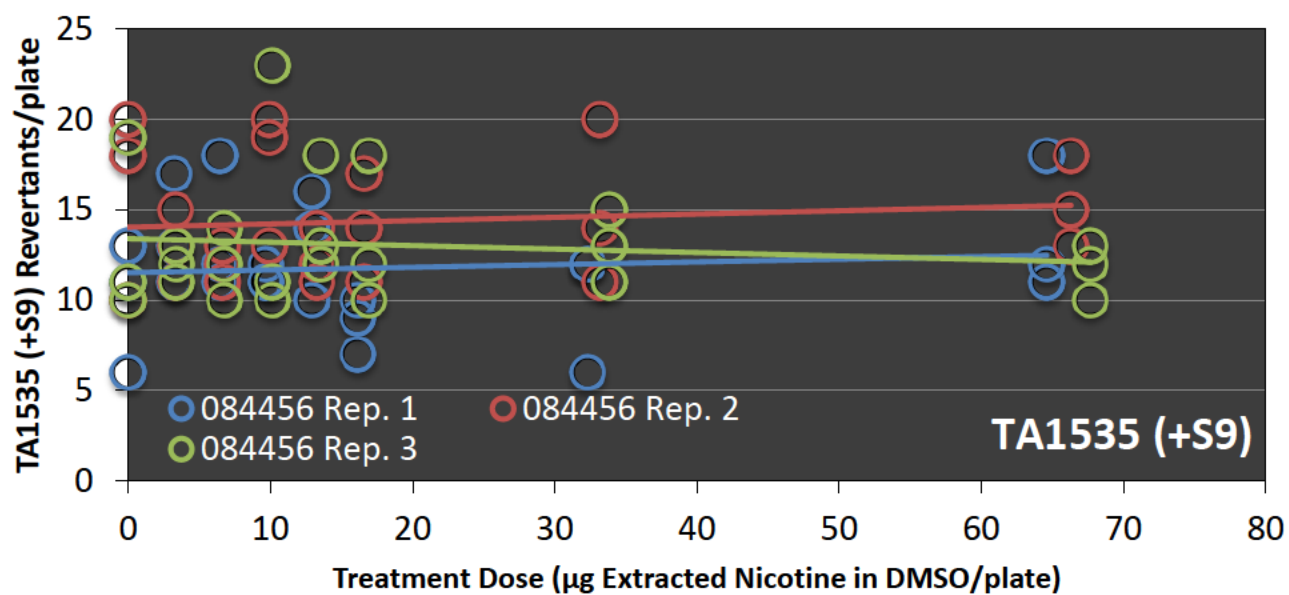


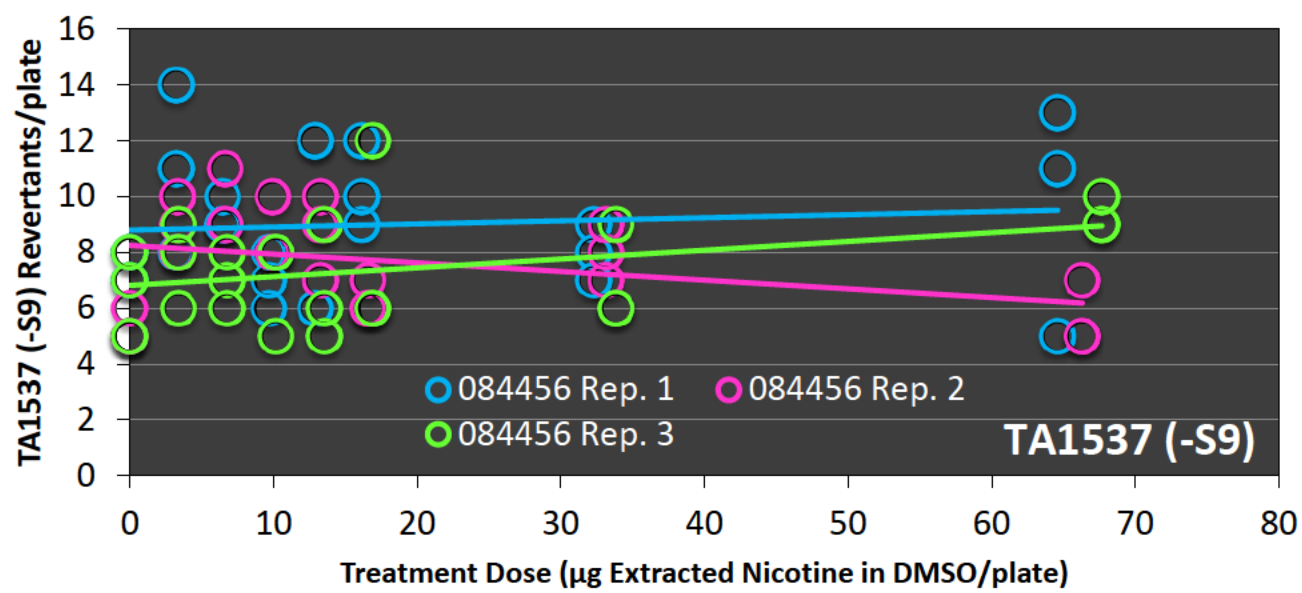


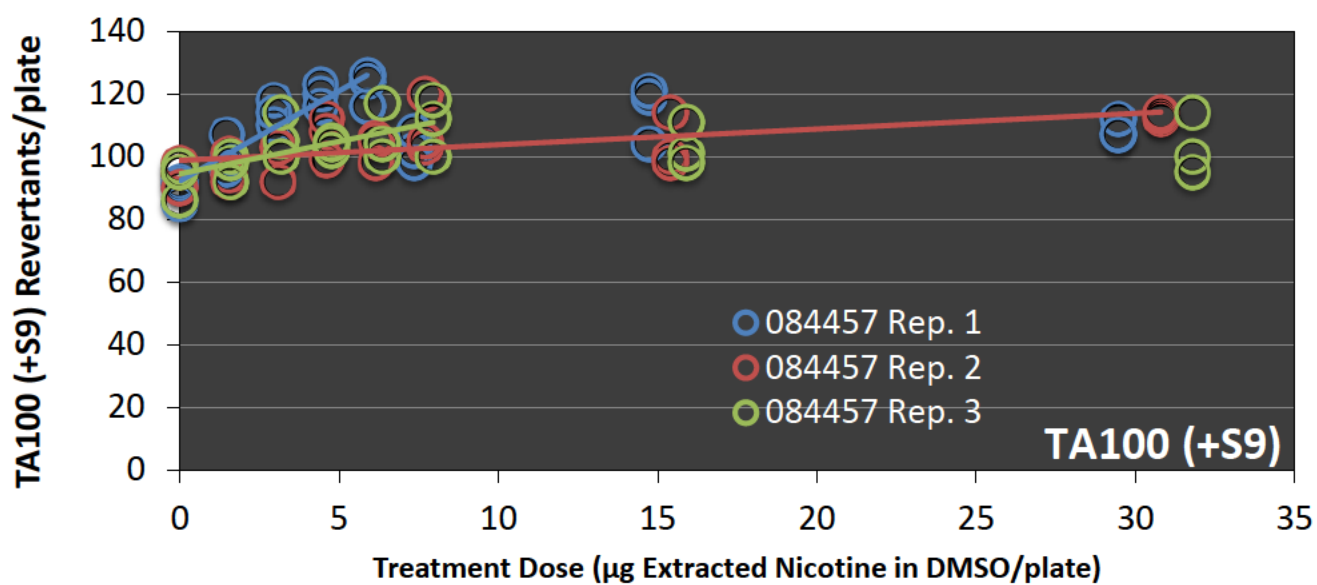
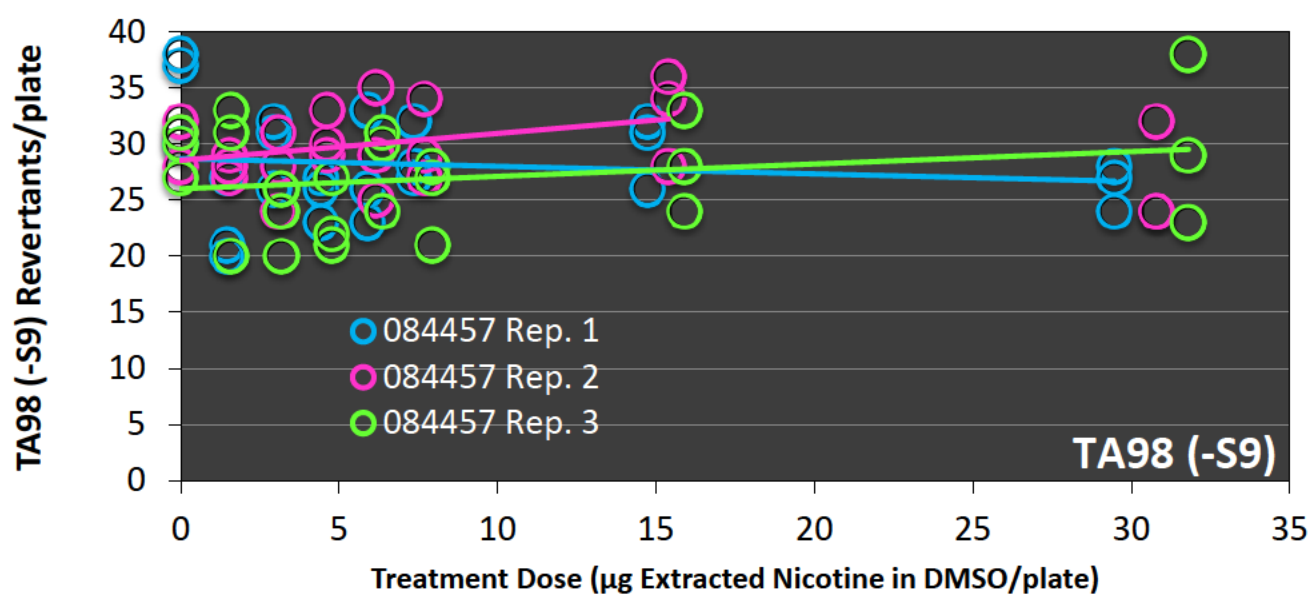
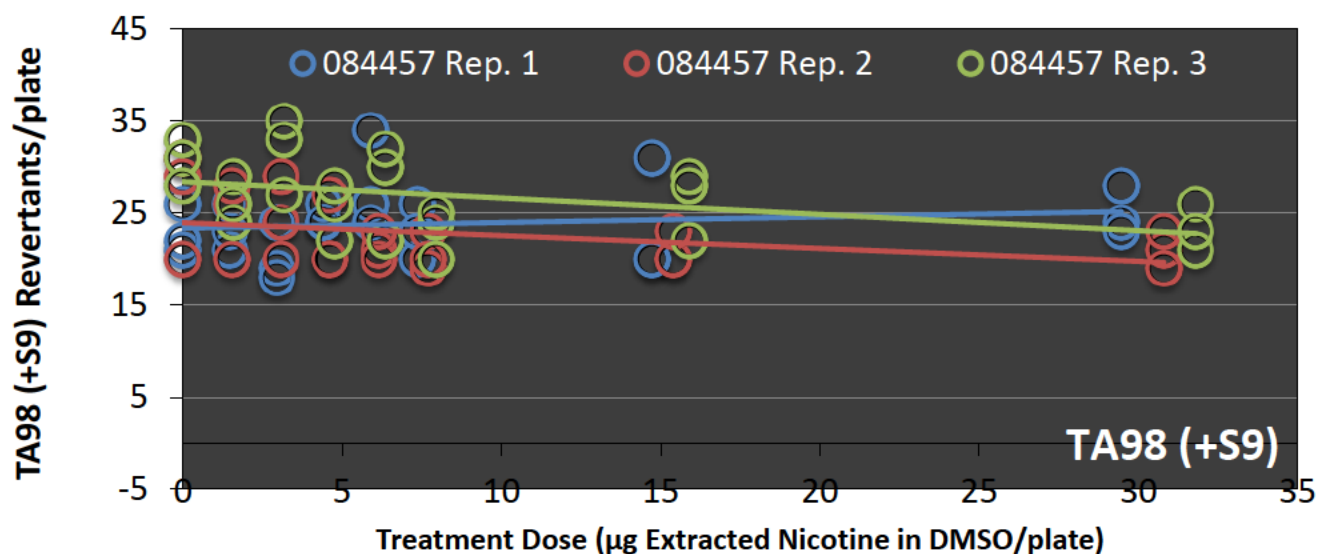


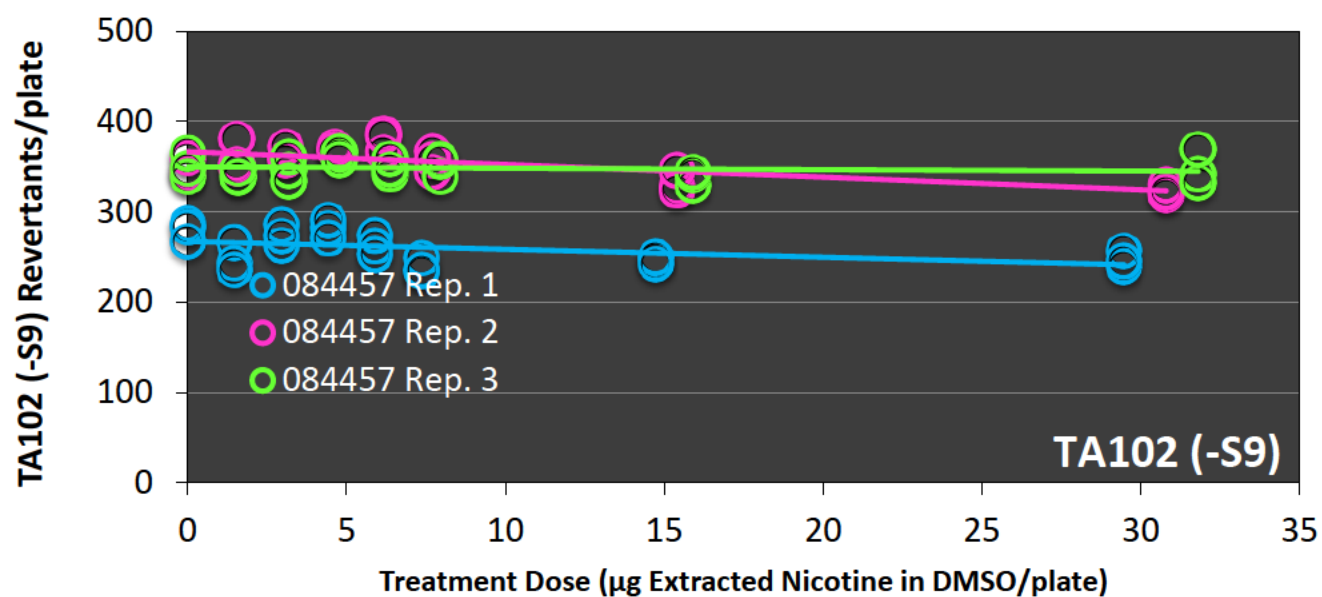
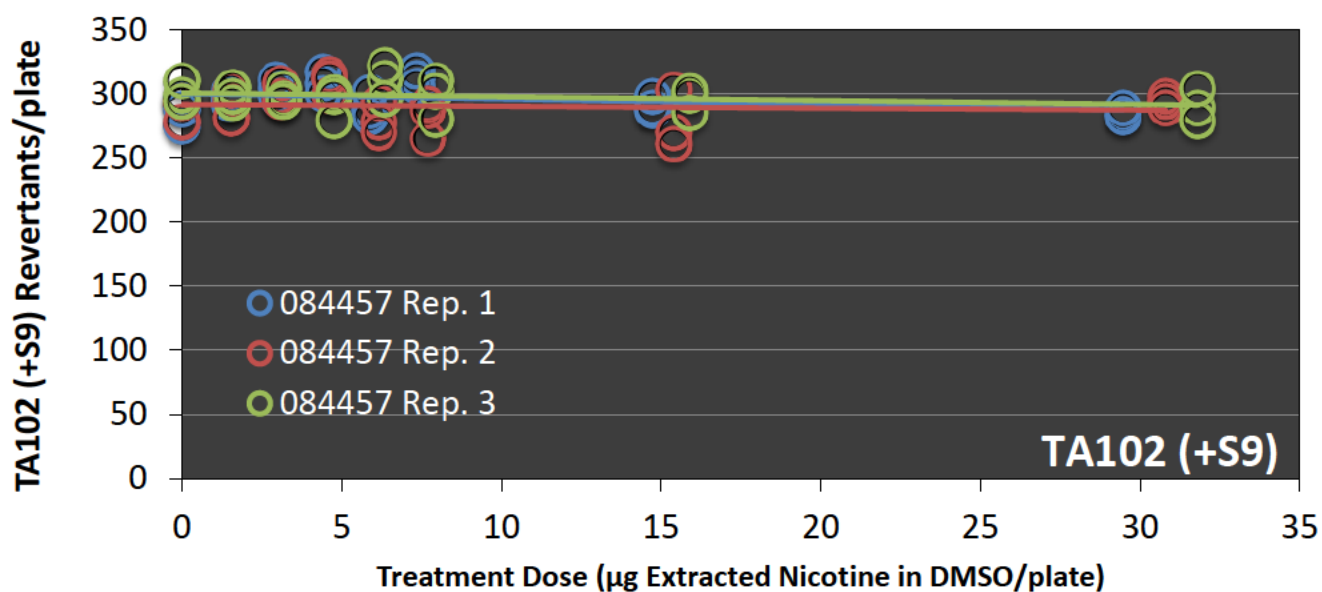
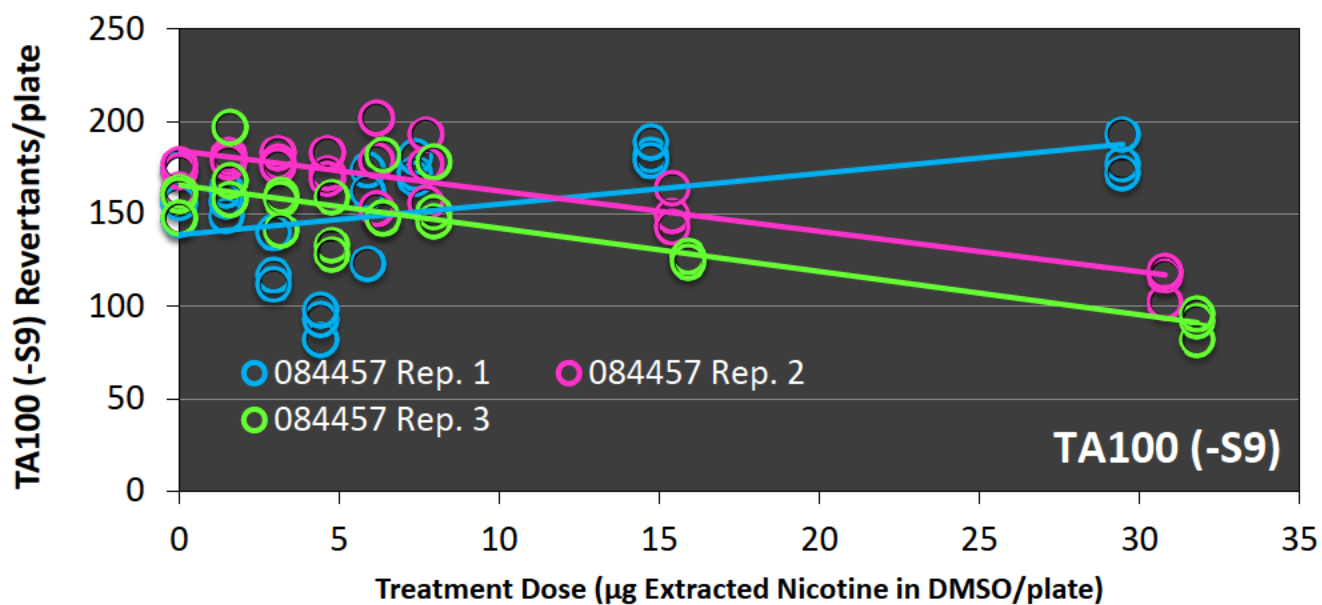


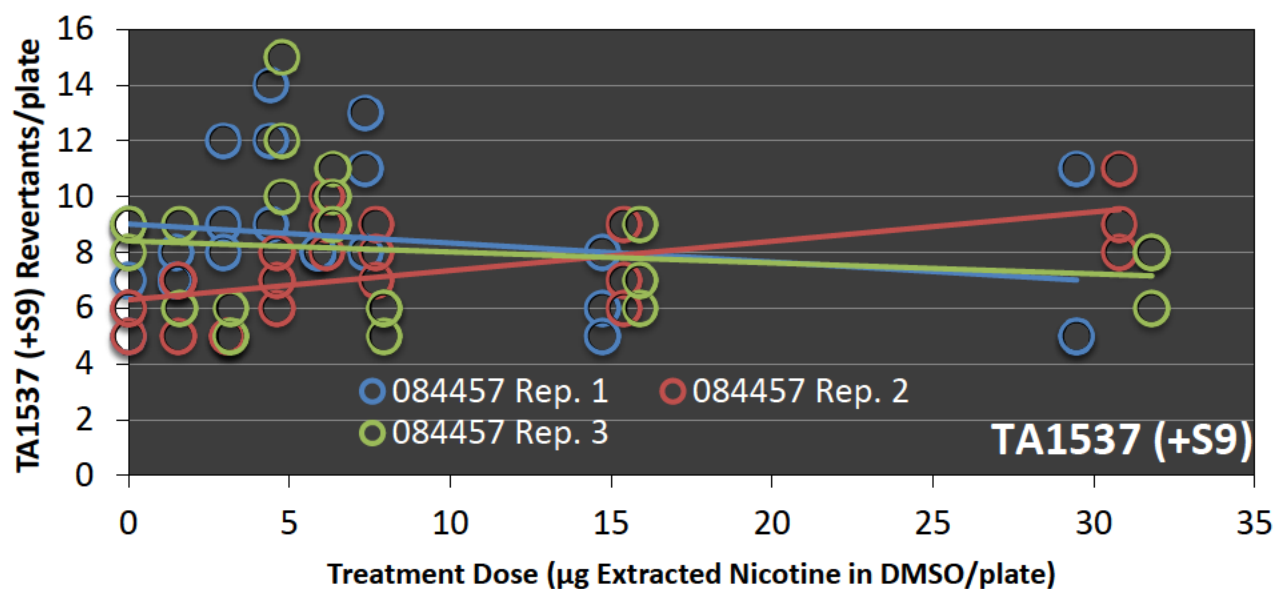
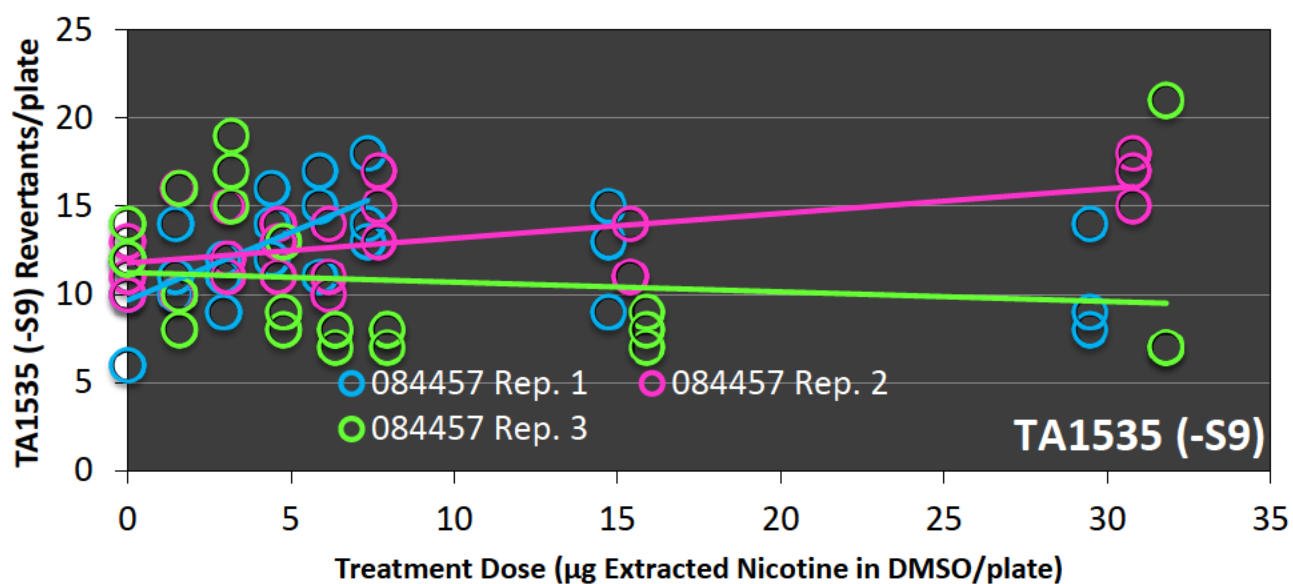
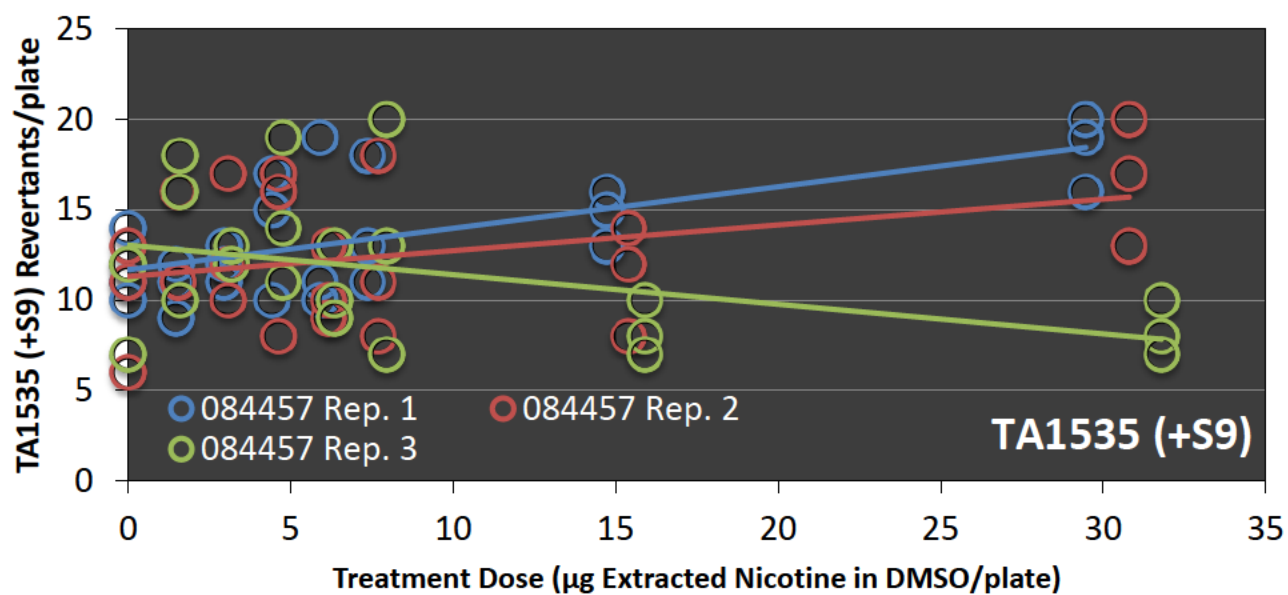


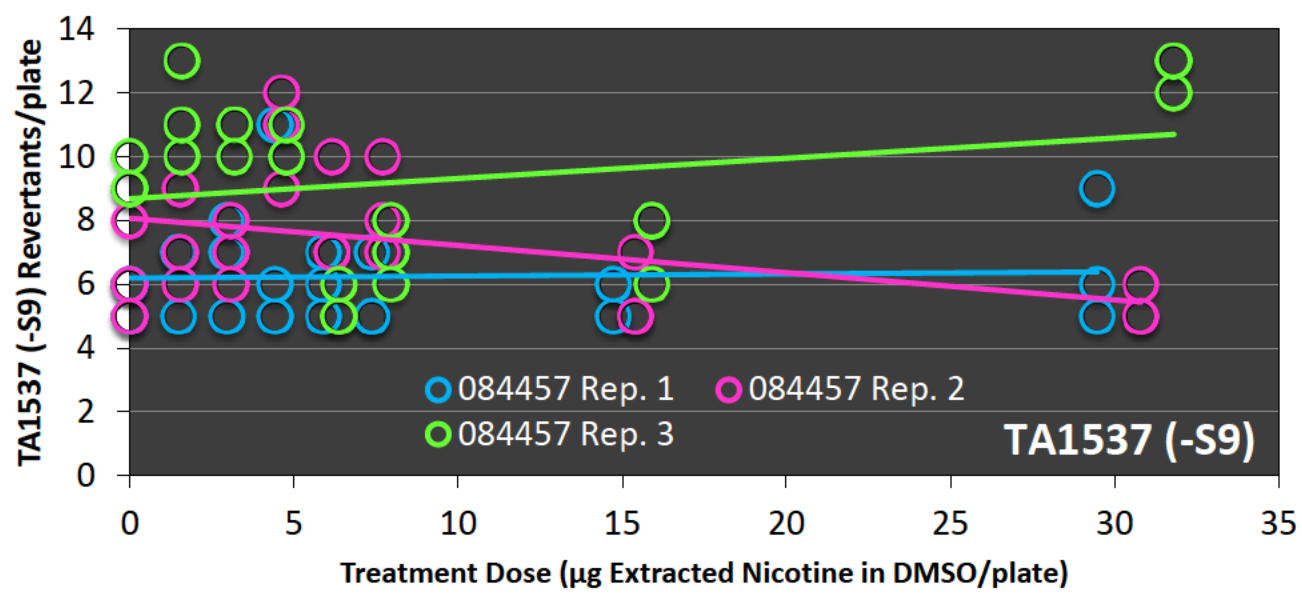




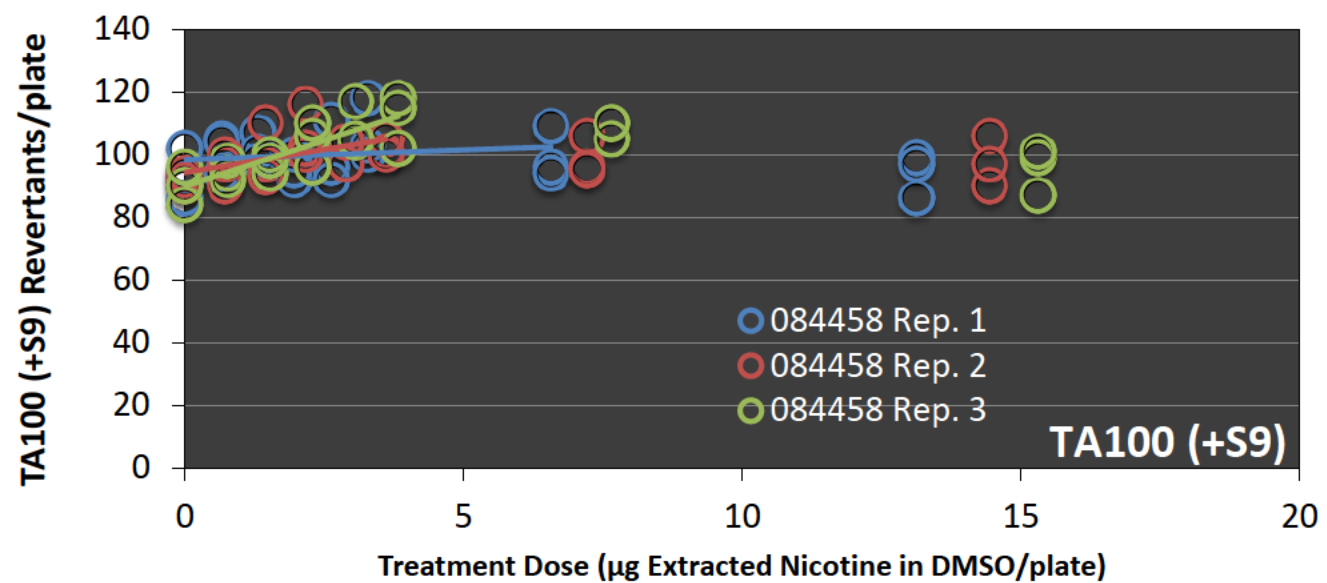
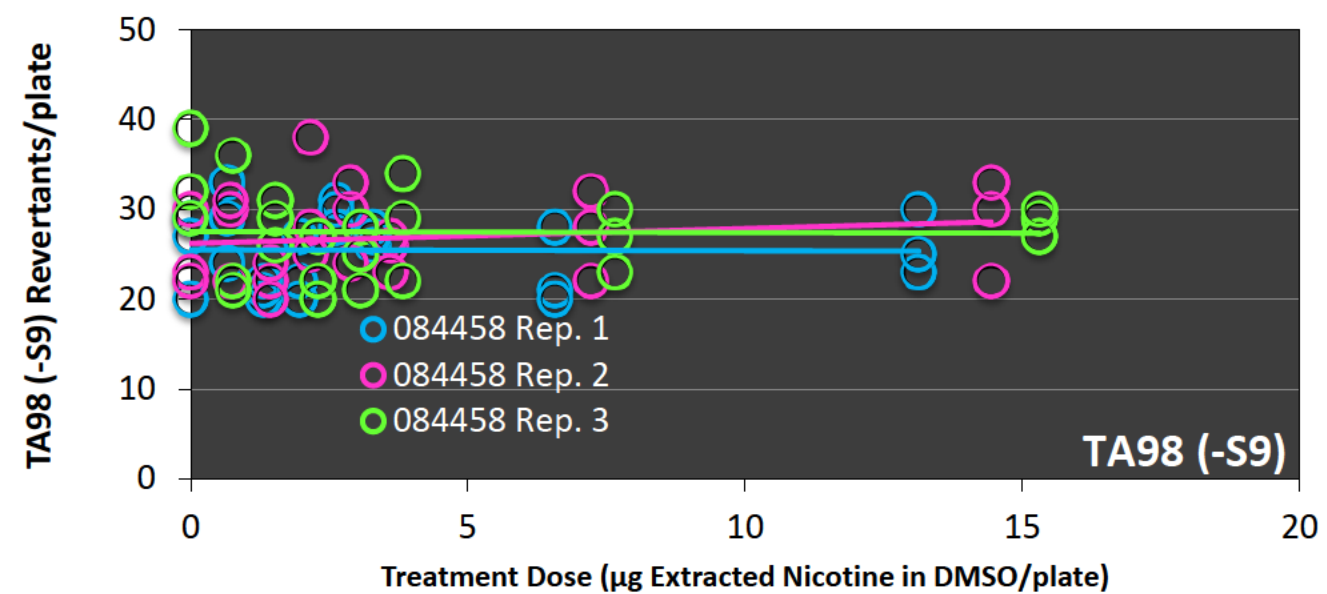
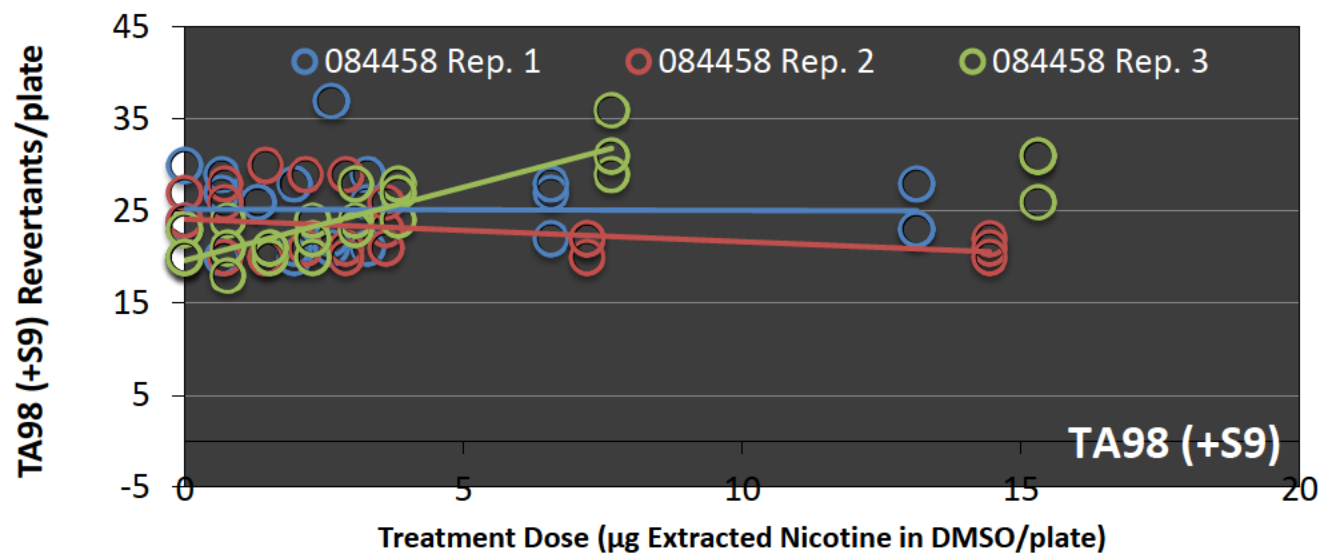




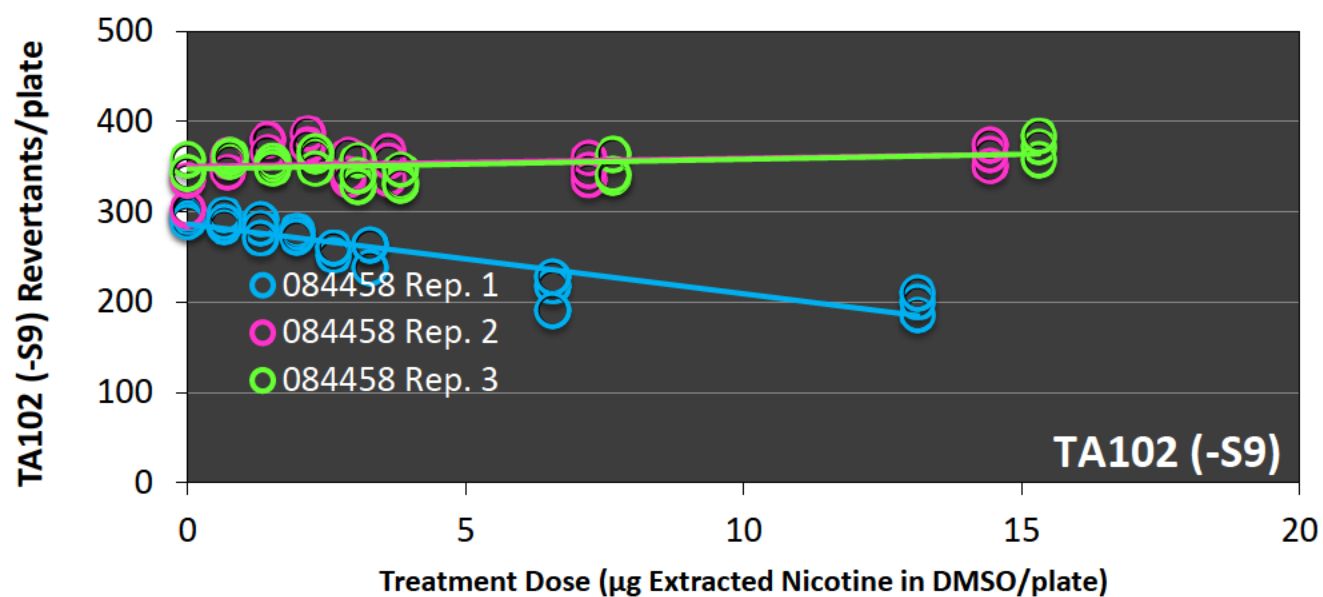
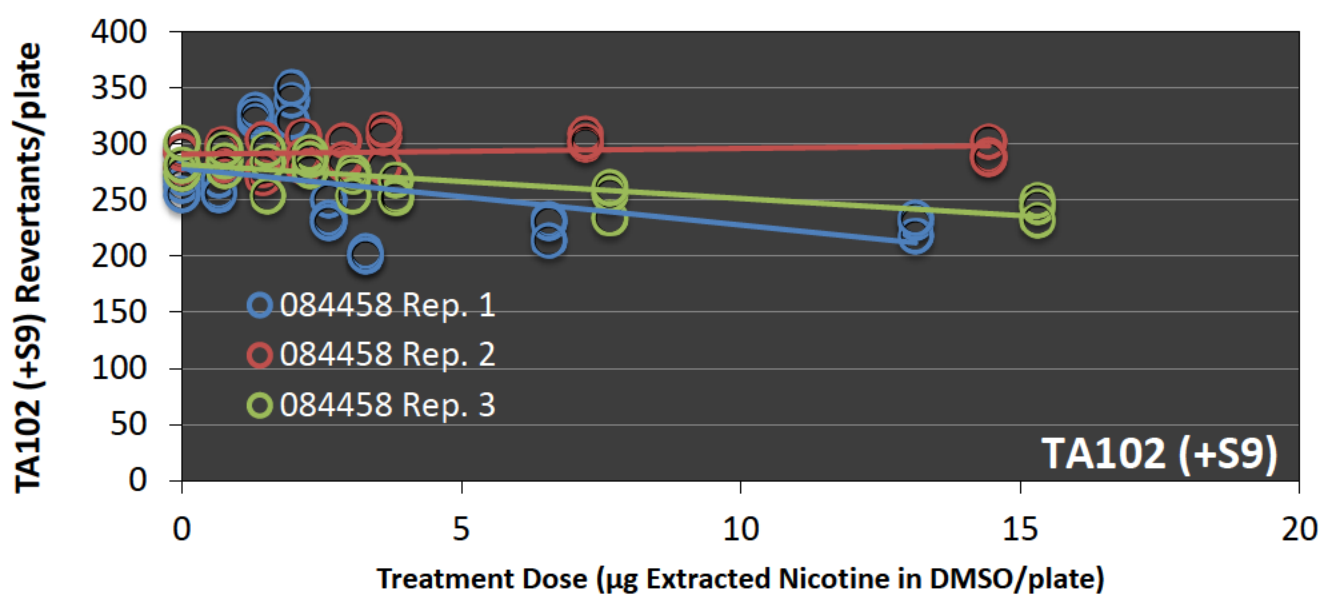
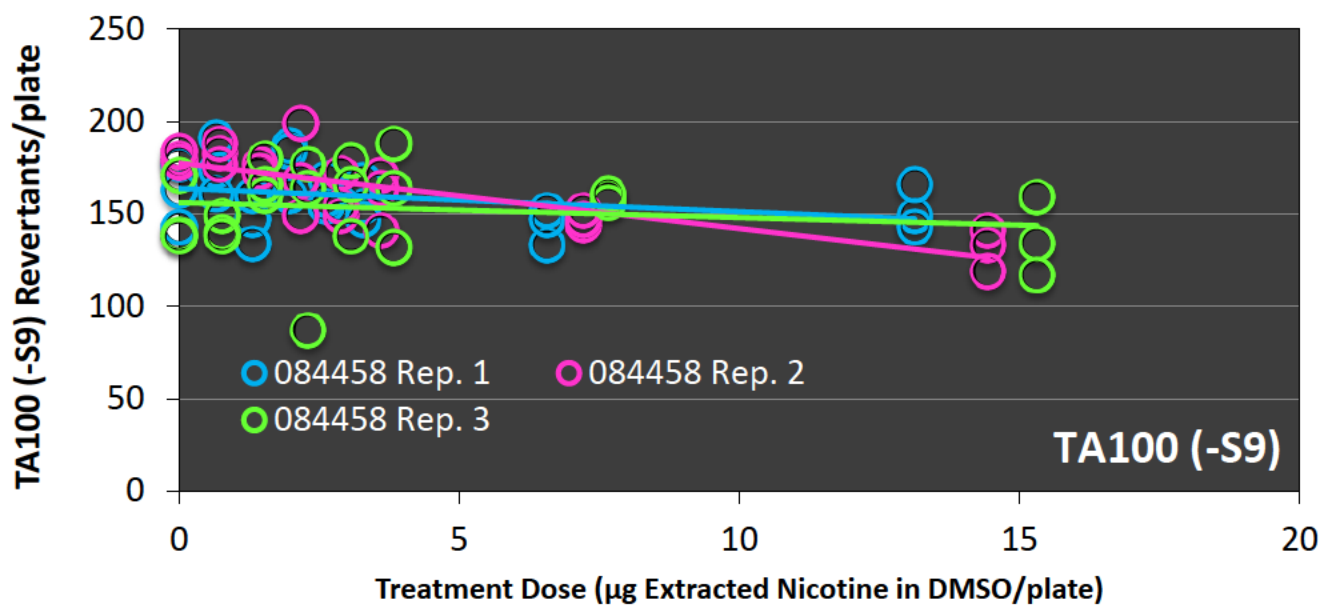


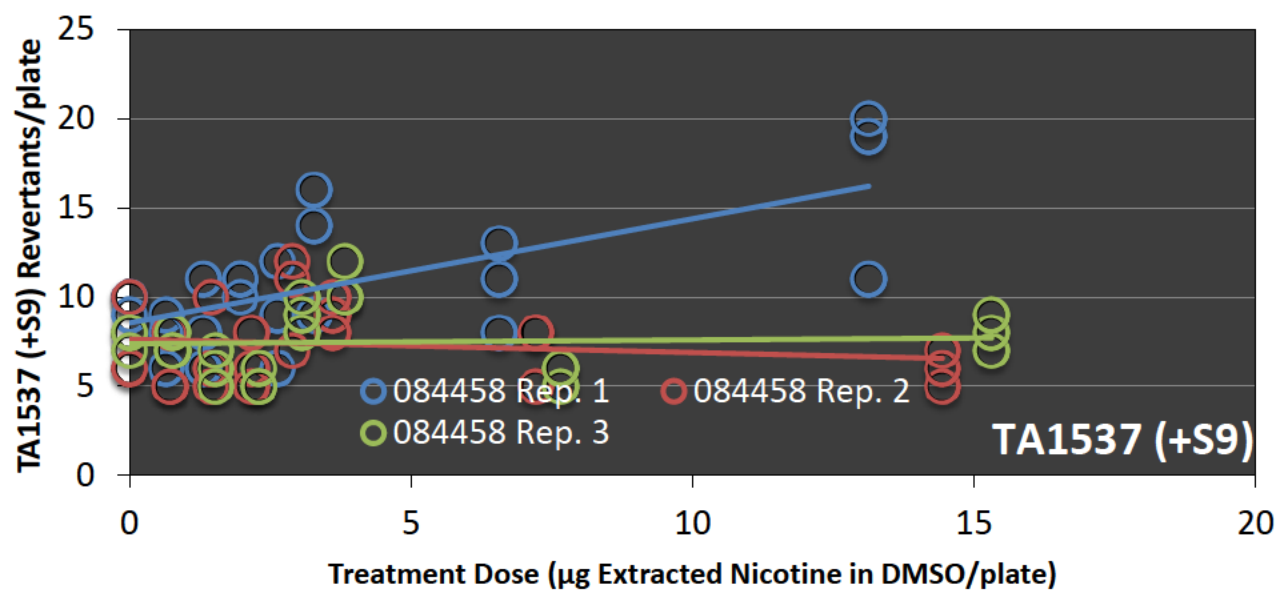
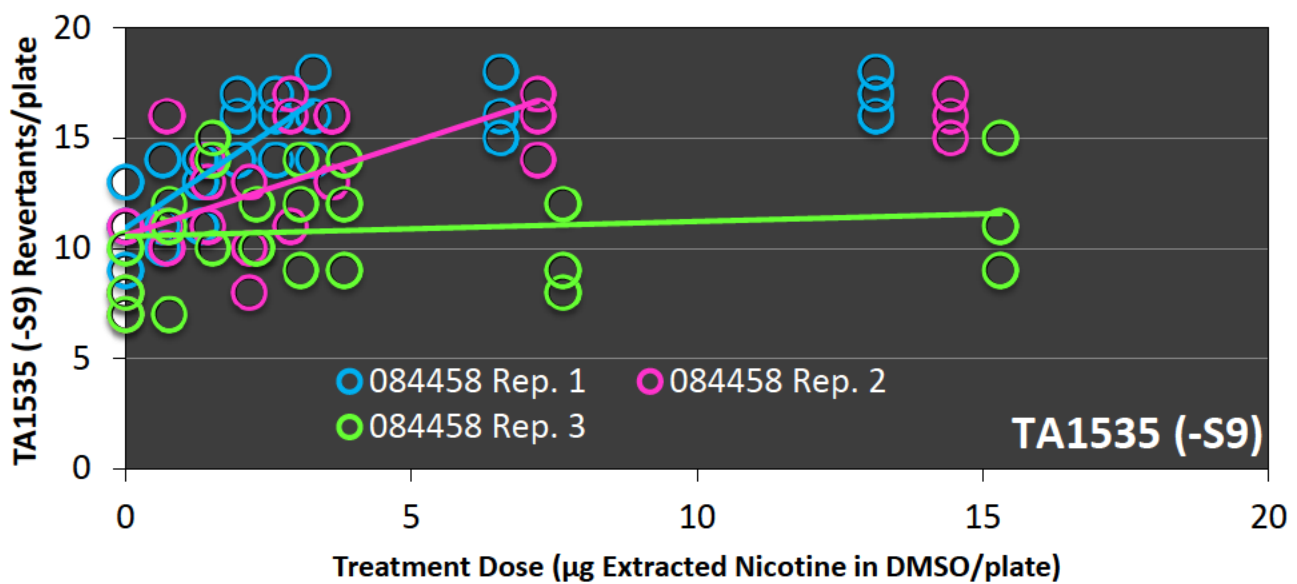
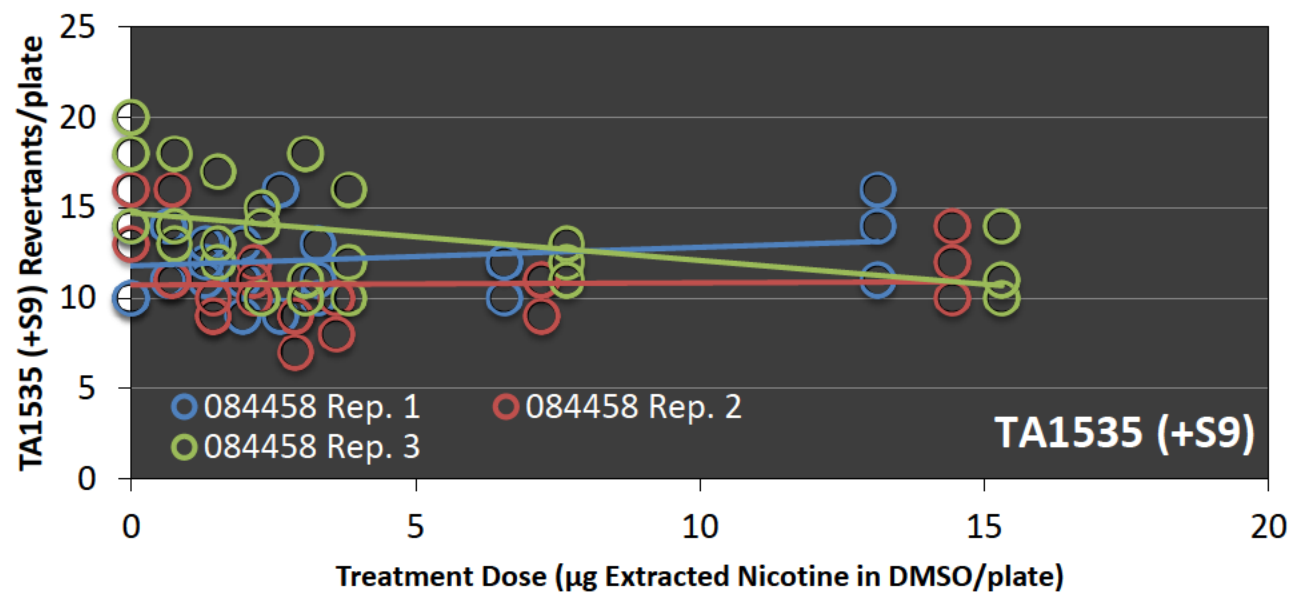


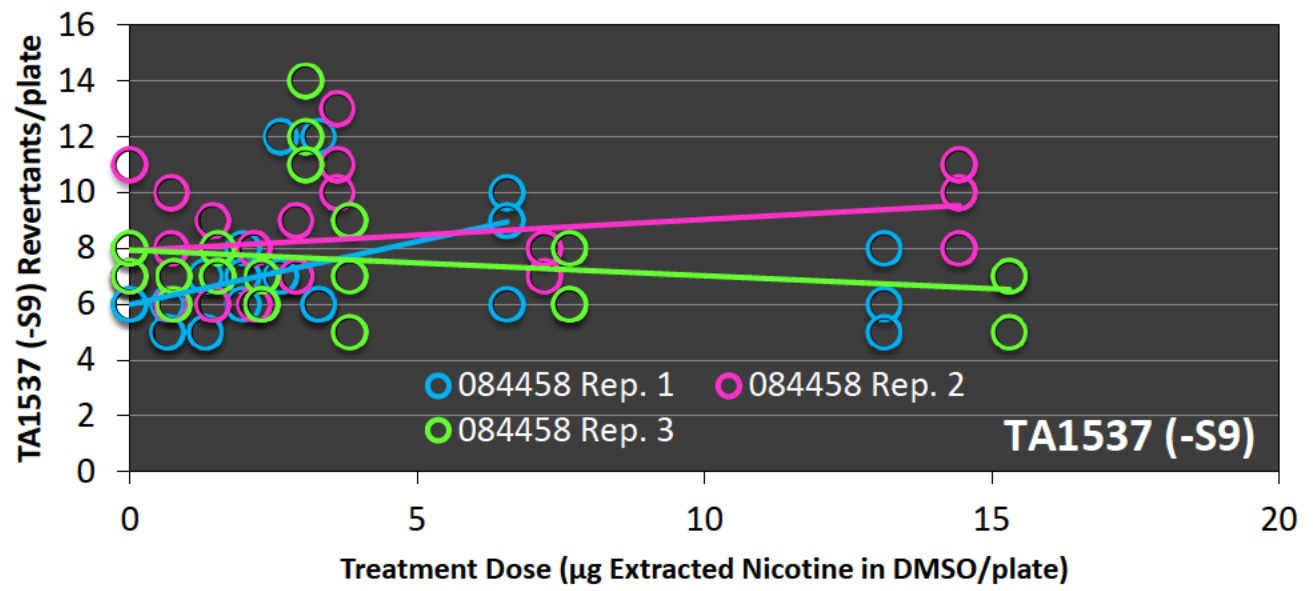












**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/mg 'Extracted Smokeless Tobacco in DMSO' (ST))**

|                          |           |                     | Number of Revertant Colonies/mg 'Extracted Smokeless Tobacco in DMSO' |        |               |        |               |        |   |       |              |  |                 |
|--------------------------|-----------|---------------------|---|--------|---------------|--------|---------------|--------|---|-------|--------------|--|-----------------|
| Strain and S9 Activation | Sample ID | Sample Description  | Replicate 1   |        | Replicate 2   |        | Replicate 3   |        | Statistics for Replicate 'ST' Slope Estimates |       |              |  |                 |
|                          |           |                     | Dose Range  |        | Dose Range    |        | Dose Range    |        | Standard                                      |       |              | t-test p-value (H <sub>0</sub> : mean = 0) |                 |
|                          |           |                     | (mg ST/plate)   | slope  | (mg ST/plate) | slope  | (mg ST/plate) | slope  | Mean  | Error | 95% C.I.     | p-value                                    | significance    |
| TA98 (+S9)               | 084394    | Camel SNUS Frost    | 0 - 5.556   | 0.725  | 0 - 5.558     | 1.63   | 0 - 5.557     | -1.45  | 0.303   | 0.915 | 0* - 4.24    | 0.772                                      | not significant |
| TA98 (+S9)               | 084395    | 2S3                 | 0 - 5.558   | 2.79   | 0 - 5.558     | 0.241  | 0 - 5.557     | 2.17   | 1.73  | 0.767 | 0* - 5.04    | 0.152                                      | not significant |
| TA98 (+S9)               | 084454    | Fresh Strips        | 0 - 5.558   | -0.380 | 0 - 5.557     | 0.484  | 0 - 2.779     | -2.47  | 0*  | 0.877 | 0* - 2.99    | 0.463                                      | not significant |
| TA98 (+S9)               | 084455    | Mellow Sticks       | 0 - 5.558   | -1.04  | 0 - 5.559     | 0.010  | 0 - 5.556     | 1.07   | 0.014   | 0.612 | 0* - 2.65    | 0.984                                      | not significant |
| TA98 (+S9)               | 084456    | Copenhagen Long Cut | 0 - 5.559   | 2.74   | 0 - 5.558     | 2.70   | 0 - 5.559     | 1.75   | 2.39  | 0.323 | 1 - 3.78     | 0.018                                      | significant     |
| TA98 (+S9)               | 084457    | Ariva Wintergreen   | 0 - 5.556   | 0.325  | 0 - 5.556     | -0.772 | 0 - 5.556     | -1.01  | 0*  | 0.412 | 0* - 1.28    | 0.359                                      | not significant |
| TA98 (+S9)               | 084458    | Fresh Orbs          | 0 - 5.558   | -0.034 | 0 - 5.557     | -0.638 | 0 - 2.778     | 4.38   | 1.24  | 1.58  | 0* - 8.05    | 0.516                                      | not significant |
| TA98 (-S9)               | 084394    | Camel SNUS Frost    | 0 - 5.556   | -0.275 | 0 - 5.558     | 1.09   | 0 - 2.778     | 0      | 0.272   | 0.417 | 0* - 2.07    | 0.581                                      | not significant |
| TA98 (-S9)               | 084395    | 2S3                 | 0 - 5.558   | 0.490  | 0 - 5.558     | -0.574 | 0 - 2.779     | -0.289 | 0*  | 0.318 | 0* - 1.24    | 0.733                                      | not significant |
| TA98 (-S9)               | 084454    | Fresh Strips        | 0 - 5.558   | 0.881  | 0 - 5.557     | -0.080 | 0 - 5.558     | 0.915  | 0.572   | 0.326 | 0* - 1.98    | 0.222                                      | not significant |
| TA98 (-S9)               | 084455    | Mellow Sticks       | 0 - 5.558   | 1.49   | 0 - 5.559     | 1.11   | 0 - 5.556     | 1.09   | 1.23  | 0.131 | 0.664 - 1.79 | 0.011                                      | significant     |
| TA98 (-S9)               | 084456    | Copenhagen Long Cut | 0 - 5.559   | 0.160  | 0 - 5.558     | 0.198  | 0 - 5.559     | 0.534  | 0.297   | 0.119 | 0* - 0.808   | 0.129                                      | not significant |
| TA98 (-S9)               | 084457    | Ariva Wintergreen   | 0 - 5.556   | -0.357 | 0 - 2.778     | 1.33   | 0 - 5.556     | 0.632  | 0.534   | 0.489 | 0* - 2.64    | 0.389                                      | not significant |
| TA98 (-S9)               | 084458    | Fresh Orbs          | 0 - 5.558   | -0.027 | 0 - 5.557     | 0.429  | 0 - 5.556     | -0.031 | 0.123   | 0.153 | 0* - 0.78    | 0.504                                      | not significant |
| TA100 (+S9)              | 084394    | Camel SNUS Frost    | 0 - 1.389   | 1.34   | 0 - 1.389     | 13.5   | 0 - 1.389     | 18.5   | 11.1  | 5.09  | 0* - 33      | 0.161                                      | not significant |
| TA100 (+S9)              | 084395    | 2S3                 | 0 - 1.112   | 12.4   | 0 - 1.112     | 28.4   | 0 - 1.111     | 11.4   | 17.4  | 5.52  | 0* - 41.2    | 0.088                                      | not significant |
| TA100 (+S9)              | 084454    | Fresh Strips        | 0 - 1.389   | 18.9   | 0 - 2.779     | 10.8   | 0 - 1.389     | 13.2   | 14.3  | 2.40  | 3.96 - 24.6  | 0.027                                      | significant     |
| TA100 (+S9)              | 084455    | Mellow Sticks       | 0 - 2.779   | 12.6   | 0 - 1.39      | 18.6   | 0 - 2.778     | 8.29   | 13.2  | 2.99  | 0.298 - 26   | 0.048                                      | significant     |
| TA100 (+S9)              | 084456    | Copenhagen Long Cut | 0 - 2.779   | 13.6   | 0 - 1.39      | 25.6   | 0 - 1.39      | 19.1   | 19.4  | 3.45  | 4.56 - 34.3  | 0.030                                      | significant     |
| TA100 (+S9)              | 084457    | Ariva Wintergreen   | 0 - 1.111   | 30.4   | 0 - 5.556     | 2.76   | 0 - 1.389     | 11.8   | 15.0  | 8.12  | 0* - 49.9    | 0.206                                      | not significant |
| TA100 (+S9)              | 084458    | Fresh Orbs          | 0 - 2.779   | 1.48   | 0 - 1.389     | 7.61   | 0 - 1.389     | 16.1   | 8.41  | 4.25  | 0* - 26.7    | 0.186                                      | not significant |
| TA100 (-S9)              | 084394    | Camel SNUS Frost    | 0 - 5.556   | 2.41   | 0 - 5.558     | 4.56   | 0 - 5.557     | 6.62   | 4.53  | 1.21  | 0* - 9.76    | 0.065                                      | not significant |
| TA100 (-S9)              | 084395    | 2S3                 | 0 - 2.779   | 4.07   | 0 - 5.558     | 4.29   | 0 - 5.557     | 5.52   | 4.63  | 0.453 | 2.68 - 6.58  | 0.009                                      | significant     |
| TA100 (-S9)              | 084454    | Fresh Strips        | 0 - 5.558   | -4.00  | 0 - 5.557     | 1.13   | 0 - 2.779     | 2.67   | 0*  | 2.02  | 0* - 8.61    | 0.977                                      | not significant |
| TA100 (-S9)              | 084455    | Mellow Sticks       | 0 - 2.779   | 10.6   | 0 - 5.559     | -0.418 | 0 - 5.556     | -6.98  | 1.06  | 5.12  | 0* - 23.1    | 0.855                                      | not significant |
| TA100 (-S9)              | 084456    | Copenhagen Long Cut | 0 - 2.779   | 19.0   | 0 - 2.779     | 0.031  | 0 - 2.78      | 5.45   | 8.16  | 5.64  | 0* - 32.4    | 0.285                                      | not significant |
| TA100 (-S9)              | 084457    | Ariva Wintergreen   | 0 - 5.556   | 8.82   | 0 - 5.556     | -12.1  | 0 - 5.556     | -13.4  | 0*  | 7.20  | 0* - 25.4    | 0.521                                      | not significant |
| TA100 (-S9)              | 084458    | Fresh Orbs          | 0 - 5.558   | -2.95  | 0 - 5.557     | -9.19  | 0 - 5.556     | -2.24  | 0*  | 2.21  | 0* - 4.7     | 0.162                                      | not significant |
| TA102 (+S9)              | 084394    | Camel SNUS Frost    | 0 - 1.111   | 41.8   | 0 - 1.389     | 57.1   | 0 - 1.389     | 41.6   | 46.8  | 5.13  | 24.8 - 68.9  | 0.012                                      | significant     |
| TA102 (+S9)              | 084395    | 2S3                 | 0 - 1.112   | 47.0   | 0 - 5.558     | 4.38   | 0 - 1.389     | 16.5   | 22.6  | 12.7  | 0* - 77.2    | 0.217                                      | not significant |
| TA102 (+S9)              | 084454    | Fresh Strips        | 0 - 5.558   | 1.11   | 0 - 5.557     | -3.37  | 0 - 5.558     | 0.670  | 0*  | 1.42  | 0* - 5.6     | 0.746                                      | not significant |
| TA102 (+S9)              | 084455    | Mellow Sticks       | 0 - 5.558   | 3.46   | 0 - 5.559     | 1.53   | 0 - 5.556     | 2.68   | 2.56  | 0.562 | 0.141 - 4.97 | 0.045                                      | significant     |
| TA102 (+S9)              | 084456    | Copenhagen Long Cut | 0 - 5.559   | 8.03   | 0 - 5.558     | 2.00   | 0 - 5.559     | 4.17   | 4.74  | 1.76  | 0* - 12.3    | 0.115                                      | not significant |
| TA102 (+S9)              | 084457    | Ariva Wintergreen   | 0 - 5.556   | -2.24  | 0 - 5.556     | -0.834 | 0 - 5.556     | -1.69  | 0*  | 0.410 | 0* - 0.174   | 0.061                                      | not significant |
| TA102 (+S9)              | 084458    | Fresh Orbs          | 0 - 5.558   | -11.9  | 0 - 5.557     | 1.35   | 0 - 5.556     | -8.35  | 0*  | 3.96  | 0* - 10.7    | 0.252                                      | not significant |
| TA102 (-S9)              | 084394    | Camel SNUS Frost    | 0 - 5.556   | -2.44  | 0 - 2.779     | 5.49   | 0 - 5.557     | -1.42  | 0.546   | 2.49  | 0* - 11.3    | 0.847                                      | not significant |
| TA102 (-S9)              | 084395    | 2S3                 | 0 - 5.558   | 1.78   | 0 - 5.558     | 5.40   | 0 - 5.557     | 12.3   | 6.51  | 3.10  | 0* - 19.9    | 0.171                                      | not significant |

**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/mg 'Extracted Smokeless Tobacco in DMSO' (ST))**

|                             |              |                       | Number of Revertant Colonies/mg 'Extracted Smokeless Tobacco in DMSO' |        |               |        |               |        |   |       |              |  |                 |
|-----------------------------|--------------|-----------------------|---|--------|---------------|--------|---------------|--------|---|-------|--------------|--|-----------------|
| Strain and<br>S9 Activation | Sample<br>ID | Sample<br>Description | Replicate 1   |        | Replicate 2   |        | Replicate 3   |        | Statistics for Replicate 'ST' Slope Estimates |       |              |  |                 |
|                             |              |                       | Dose Range  |        | Dose Range    |        | Dose Range    |        | Standard                                      |       |              | t-test p-value (H <sub>0</sub> : mean = 0) |                 |
|                             |              |                       | (mg ST/plate)   | slope  | (mg ST/plate) | slope  | (mg ST/plate) | slope  | Mean  | Error | 95% C.I.     | p-value                                    | significance    |
| TA102 (-S9)                 | 084454       | Fresh Strips          | 0 - 5.558   | -0.802 | 0 - 5.557     | 5.84   | 0 - 1.389     | 47.3   | 17.5  | 15.1  | 0* - 82.3    | 0.366                                      | not significant |
| TA102 (-S9)                 | 084455       | Mellow Sticks         | 0 - 2.779   | 3.79   | 0 - 5.559     | 3.11   | 0 - 5.556     | 0.227  | 2.38  | 1.09  | 0* - 7.07    | 0.162                                      | not significant |
| TA102 (-S9)                 | 084456       | Copenhagen Long Cut   | 0 - 5.559   | -0.022 | 0 - 5.558     | 4.87   | 0 - 2.78      | 31.5   | 12.1  | 9.79  | 0* - 54.2    | 0.342                                      | not significant |
| TA102 (-S9)                 | 084457       | Ariva Wintergreen     | 0 - 5.556   | -4.62  | 0 - 5.556     | -7.76  | 0 - 5.556     | -0.872 | 0*  | 1.99  | 0* - 4.15    | 0.157                                      | not significant |
| TA102 (-S9)                 | 084458       | Fresh Orbs            | 0 - 5.558   | -18.2  | 0 - 5.557     | 2.41   | 0 - 5.556     | 3.03   | 0*  | 6.99  | 0* - 25.8    | 0.604                                      | not significant |
| TA1535 (+S9)                | 084394       | Camel SNUS Frost      | 0 - 5.556   | 0.085  | 0 - 5.558     | 0.521  | 0 - 5.557     | -1.04  | 0*  | 0.465 | 0* - 1.86    | 0.785                                      | not significant |
| TA1535 (+S9)                | 084395       | 2S3                   | 0 - 5.558   | 0.370  | 0 - 5.558     | 0.150  | 0 - 5.557     | -0.052 | 0.156   | 0.122 | 0* - 0.679   | 0.328                                      | not significant |
| TA1535 (+S9)                | 084454       | Fresh Strips          | 0 - 5.558   | 0.364  | 0 - 5.557     | 0.333  | 0 - 5.558     | -0.362 | 0.112   | 0.237 | 0* - 1.13    | 0.684                                      | not significant |
| TA1535 (+S9)                | 084455       | Mellow Sticks         | 0 - 5.558   | -0.066 | 0 - 5.559     | -0.793 | 0 - 2.778     | 1.51   | 0.216   | 0.678 | 0* - 3.13    | 0.781                                      | not significant |
| TA1535 (+S9)                | 084456       | Copenhagen Long Cut   | 0 - 5.559   | 0.171  | 0 - 5.558     | 0.216  | 0 - 5.559     | -0.233 | 0.051   | 0.143 | 0* - 0.666   | 0.753                                      | not significant |
| TA1535 (+S9)                | 084457       | Ariva Wintergreen     | 0 - 5.556   | 1.22   | 0 - 5.556     | 0.791  | 0 - 5.556     | -0.937 | 0.357   | 0.659 | 0* - 3.19    | 0.642                                      | not significant |
| TA1535 (+S9)                | 084458       | Fresh Orbs            | 0 - 5.558   | 0.244  | 0 - 5.557     | 0.030  | 0 - 5.556     | -0.722 | 0*  | 0.293 | 0* - 1.11    | 0.661                                      | not significant |
| TA1535 (-S9)                | 084394       | Camel SNUS Frost      | 0 - 5.556   | 0.069  | 0 - 5.558     | 0.958  | 0 - 5.557     | -0.561 | 0.155   | 0.440 | 0* - 2.05    | 0.758                                      | not significant |
| TA1535 (-S9)                | 084395       | 2S3                   | 0 - 5.558   | -0.270 | 0 - 5.558     | 0.294  | 0 - 5.557     | 0.933  | 0.319   | 0.347 | 0* - 1.81    | 0.455                                      | not significant |
| TA1535 (-S9)                | 084454       | Fresh Strips          | 0 - 2.779   | 0.670  | 0 - 2.779     | 1.64   | 0 - 2.779     | 1.10   | 1.14  | 0.282 | 0* - 2.35    | 0.056                                      | not significant |
| TA1535 (-S9)                | 084455       | Mellow Sticks         | 0 - 5.558   | -0.794 | 0 - 5.559     | 0.066  | 0 - 5.556     | -0.063 | 0*  | 0.268 | 0* - 0.888   | 0.429                                      | not significant |
| TA1535 (-S9)                | 084456       | Copenhagen Long Cut   | 0 - 5.559   | 0.392  | 0 - 5.558     | 0.917  | 0 - 2.78      | 1.78   | 1.03  | 0.404 | 0* - 2.77    | 0.126                                      | not significant |
| TA1535 (-S9)                | 084457       | Ariva Wintergreen     | 0 - 1.389   | 4.08   | 0 - 5.556     | 0.779  | 0 - 5.556     | -0.311 | 1.52  | 1.32  | 0* - 7.19    | 0.370                                      | not significant |
| TA1535 (-S9)                | 084458       | Fresh Orbs            | 0 - 1.389   | 4.11   | 0 - 2.778     | 2.19   | 0 - 5.556     | 0.185  | 2.16  | 1.13  | 0* - 7.04    | 0.197                                      | not significant |
| TA1537 (+S9)                | 084394       | Camel SNUS Frost      | 0 - 2.778   | 2.92   | 0 - 5.558     | 1.26   | 0 - 5.557     | 1.32   | 1.83  | 0.544 | 0* - 4.17    | 0.078                                      | not significant |
| TA1537 (+S9)                | 084395       | 2S3                   | 0 - 1.39  | 7.81   | 0 - 5.558     | 1.07   | 0 - 5.557     | 0.976  | 3.29  | 2.26  | 0* - 13      | 0.284                                      | not significant |
| TA1537 (+S9)                | 084454       | Fresh Strips          | 0 - 5.558   | 0.187  | 0 - 5.557     | -0.076 | 0 - 5.558     | -0.307 | 0*  | 0.143 | 0* - 0.549   | 0.690                                      | not significant |
| TA1537 (+S9)                | 084455       | Mellow Sticks         | 0 - 5.558   | -0.366 | 0 - 5.559     | 0.237  | 0 - 5.556     | 0.563  | 0.145   | 0.272 | 0* - 1.31    | 0.648                                      | not significant |
| TA1537 (+S9)                | 084456       | Copenhagen Long Cut   | 0 - 2.779   | 2.42   | 0 - 2.779     | 1.85   | 0 - 5.559     | 1.02   | 1.76  | 0.406 | 0.018 - 3.51 | 0.049                                      | significant     |
| TA1537 (+S9)                | 084457       | Ariva Wintergreen     | 0 - 5.556   | -0.361 | 0 - 5.556     | 0.584  | 0 - 5.556     | -0.223 | 0*  | 0.295 | 0* - 1.27    | 0.999                                      | not significant |
| TA1537 (+S9)                | 084458       | Fresh Orbs            | 0 - 5.558   | 1.38   | 0 - 5.557     | -0.191 | 0 - 5.556     | 0.061  | 0.415   | 0.486 | 0* - 2.51    | 0.483                                      | not significant |
| TA1537 (-S9)                | 084394       | Camel SNUS Frost      | 0 - 1.389   | 4.15   | 0 - 5.558     | 0.873  | 0 - 2.778     | 2.20   | 2.41  | 0.951 | 0* - 6.5     | 0.127                                      | not significant |
| TA1537 (-S9)                | 084395       | 2S3                   | 0 - 5.558   | 1.86   | 0 - 2.779     | 1.89   | 0 - 2.779     | 0.608  | 1.45  | 0.423 | 0* - 3.27    | 0.075                                      | not significant |
| TA1537 (-S9)                | 084454       | Fresh Strips          | 0 - 5.558   | -0.085 | 0 - 5.557     | 0.269  | 0 - 5.558     | 0.111  | 0.098   | 0.102 | 0* - 0.538   | 0.438                                      | not significant |
| TA1537 (-S9)                | 084455       | Mellow Sticks         | 0 - 5.558   | 0.069  | 0 - 5.559     | -0.276 | 0 - 5.556     | -0.244 | 0*  | 0.110 | 0* - 0.323   | 0.305                                      | not significant |
| TA1537 (-S9)                | 084456       | Copenhagen Long Cut   | 0 - 5.559   | 0.127  | 0 - 5.558     | -0.370 | 0 - 5.559     | 0.384  | 0.047   | 0.221 | 0* - 0.999   | 0.850                                      | not significant |
| TA1537 (-S9)                | 084457       | Ariva Wintergreen     | 0 - 5.556   | 0.033  | 0 - 5.556     | -0.473 | 0 - 5.556     | 0.363  | 0*  | 0.243 | 0* - 1.02    | 0.925                                      | not significant |
| TA1537 (-S9)                | 084458       | Fresh Orbs            | 0 - 2.779   | 1.07   | 0 - 5.557     | 0.292  | 0 - 5.556     | -0.255 | 0.368   | 0.383 | 0* - 2.02    | 0.439                                      | not significant |

0\*: Mean or lower bound of the 95% confidence interval has been truncated at 0.

### One-Way ANOVA of Mean 'Extracted Smokeless Tobacco' Slope Estimates Among Test Samples

TA98 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 25.34344663    | 6  | 4.223907772 | 1.843   | 0.162   |
| Within Samples | 32.0863542     | 14 | 2.291882443 |         |         |
| Total (Corr.)  | 57.42980084    | 20 |             |         |         |

TA100 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 246.4331607    | 6  | 41.07219345 | 0.574   | 0.745   |
| Within Samples | 1002.588573    | 14 | 71.6134695  |         |         |
| Total (Corr.)  | 1249.021734    | 20 |             |         |         |

TA102 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 6329.977012    | 6  | 1054.996169 | 11.796  | <b>0.000</b> |
| Within Samples | 1252.09159     | 14 | 89.43511359 |         |              |
| Total (Corr.)  | 7582.068602    | 20 |             |         |              |

TA1535 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.616518762    | 6  | 0.102753127 | 0.186   | 0.976   |
| Within Samples | 7.721113541    | 14 | 0.55150811  |         |         |
| Total (Corr.)  | 8.337632303    | 20 |             |         |         |

TA1537 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 29.06242817    | 6  | 4.843738028 | 1.882   | 0.154   |
| Within Samples | 36.02530581    | 14 | 2.573236129 |         |         |
| Total (Corr.)  | 65.08773398    | 20 |             |         |         |

### One-Way ANOVA of Mean 'Extracted Smokeless Tobacco' Slope Estimates Among Test Samples

TA98 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 3.336241037    | 6  | 0.556040173 | 1.922   | 0.147   |
| Within Samples | 4.050267975    | 14 | 0.289304855 |         |         |
| Total (Corr.)  | 7.386509012    | 20 |             |         |         |

TA100 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 463.375301     | 6  | 77.22921683 | 1.496   | 0.250   |
| Within Samples | 722.732757     | 14 | 51.62376835 |         |         |
| Total (Corr.)  | 1186.108058    | 20 |             |         |         |

TA102 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 1218.56803     | 6  | 203.0946717 | 1.207   | 0.359   |
| Within Samples | 2355.101109    | 14 | 168.2215078 |         |         |
| Total (Corr.)  | 3573.669139    | 20 |             |         |         |

TA1535 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 12.84511755    | 6  | 2.140852925 | 1.366   | 0.294   |
| Within Samples | 21.93974156    | 14 | 1.567124397 |         |         |
| Total (Corr.)  | 34.78485911    | 20 |             |         |         |

TA1537 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 16.6869585     | 6  | 2.78115975  | 4.767   | <b>0.008</b> |
| Within Samples | 8.167497821    | 14 | 0.583392701 |         |              |
| Total (Corr.)  | 24.85445632    | 20 |             |         |              |

One-way ANOVA analysis indicates significant differences (at  $\alpha = 0.05$ ) among mean 'Extracted Smokeless Tobacco' specific activity slope estimates for test samples with TA102 (+S9) and TA1537 (-S9).

**Evaluation of Ratio (Max ÷ Min) of Standard Deviations of  
'Extracted Smokeless Tobacco' Slope Estimates and  
Corresponding Method of Comparison**

| <b>Strain and<br/>S9 Activation</b> | <b>Std. Dev. Ratio<br/>(Max ÷ Min)</b> | <b>Method of<br/>Comparison</b>    |
|-------------------------------------|--|------------------------------------|
| TA98 (+S9)                          | 4.9                                    | ANOVA (equal variance)             |
| TA98 (-S9)                          | 4.1                                    | ANOVA (equal variance)             |
| TA100 (+S9)                         | 3.4                                    | ANOVA (equal variance)             |
| TA100 (-S9)                         | 15.9                                   | Pairwise T-test (unequal variance) |
| TA102 (+S9)                         | 30.9                                   | Pairwise T-test (unequal variance) |
| TA102 (-S9)                         | 13.8                                   | ANOVA (equal variance)             |
| TA1535 (+S9)                        | 5.6                                    | ANOVA (equal variance)             |
| TA1535 (-S9)                        | 4.9                                    | ANOVA (equal variance)             |
| TA1537 (+S9)                        | 15.9                                   | Pairwise T-test (unequal variance) |
| TA1537 (-S9)                        | 9.3                                    | ANOVA (equal variance)             |



**Evaluation of Ratio (Max ÷ Min) of Standard Deviations of  
'Extracted Smokeless Tobacco' Slope Estimates and  
Corresponding Method of Comparison**

**ANOVA-Based Comparison Tests of Mean 'Extracted Smokeless Tobacco' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| ANOVA-Based<br>Comparison | TA98 (+S9) |         |                                    | TA100 (+S9) |         |                                    | TA102 (+S9) |         |                                    | TA1535 (+S9) |         |                                    | TA1537 (+S9) |         |                                    |
|---------------------------|------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                           | f-ratio    | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395         | 1.3404     | 0.2663  | not significant                    | 0.83        | 0.3783  | not significant                    | 9.8385      | 0.0073  | not significant                    | 0.2459       | 0.6276  | not significant                    | 1.2307       | 0.2860  | not significant                    |
| <b>084394 vs. 084454</b>  | 0.7810     | 0.3918  | not significant                    | 0.2121      | 0.6522  | not significant                    | 37.627      | 0.0000  | <b>significant</b>                 | 0.1785       | 0.6791  | not significant                    | 2.0999       | 0.1693  | not significant                    |
| <b>084394 vs. 084455</b>  | 0.0548     | 0.8184  | not significant                    | 0.0889      | 0.7700  | not significant                    | 32.883      | 0.0001  | <b>significant</b>                 | 0.3531       | 0.5618  | not significant                    | 1.6600       | 0.2185  | not significant                    |
| <b>084394 vs. 084456</b>  | 2.86       | 0.1128  | not significant                    | 1.45        | 0.2487  | not significant                    | 29.727      | 0.0001  | <b>significant</b>                 | 0.1046       | 0.7512  | not significant                    | 0.0028       | 0.9589  | not significant                    |
| <b>084394 vs. 084457</b>  | 0.4074     | 0.5336  | not significant                    | 0.3144      | 0.5838  | not significant                    | 39.333      | 0.0000  | <b>significant</b>                 | 0.6841       | 0.4221  | not significant                    | 1.9575       | 0.1835  | not significant                    |
| <b>084394 vs. 084458</b>  | 0.5711     | 0.4623  | not significant                    | 0.1518      | 0.7027  | not significant                    | 47.373      | 0.0000  | <b>significant</b>                 | 0.0001       | 0.9940  | not significant                    | 1.1701       | 0.2977  | not significant                    |
| 084395 vs. 084454         | 4.17       | 0.0605  | not significant                    | 0.20        | 0.6601  | not significant                    | 8.9845      | 0.0096  | not significant                    | 0.0054       | 0.9425  | not significant                    | 6.5458       | 0.0227  | not significant                    |
| 084395 vs. 084455         | 1.9371     | 0.1857  | not significant                    | 0.37        | 0.5505  | not significant                    | 6.7481      | 0.0211  | not significant                    | 0.0097       | 0.9231  | not significant                    | 5.7493       | 0.0310  | not significant                    |
| 084395 vs. 084456         | 0.2854     | 0.6016  | not significant                    | 0.0863      | 0.7733  | not significant                    | 5.3622      | 0.0363  | not significant                    | 0.0298       | 0.8655  | not significant                    | 1.3499       | 0.2647  | not significant                    |
| 084395 vs. 084457         | 3.23       | 0.0941  | not significant                    | 0.12        | 0.7322  | not significant                    | 9.8282      | 0.0073  | not significant                    | 0.1097       | 0.7454  | not significant                    | 6.2925       | 0.0251  | not significant                    |
| <b>084395 vs. 084458</b>  | 0.1616     | 0.6937  | not significant                    | 1.69        | 0.2148  | not significant                    | 14.034      | 0.0022  | <b>significant</b>                 | 0.2536       | 0.6224  | not significant                    | 4.8009       | 0.0459  | not significant                    |
| 084454 vs. 084455         | 0.4222     | 0.5264  | not significant                    | 0.0264      | 0.8733  | not significant                    | 0.1598      | 0.6954  | not significant                    | 0.0295       | 0.8661  | not significant                    | 0.0258       | 0.8746  | not significant                    |
| 084454 vs. 084456         | 6.63       | 0.0220  | not significant                    | 0.55        | 0.4698  | not significant                    | 0.4648      | 0.5065  | not significant                    | 0.0098       | 0.9224  | not significant                    | 1.9506       | 0.1843  | not significant                    |
| 084454 vs. 084457         | 0.0603     | 0.8096  | not significant                    | 0.0100      | 0.9216  | not significant                    | 0.0189      | 0.8925  | not significant                    | 0.1637       | 0.6919  | not significant                    | 0.0025       | 0.9608  | not significant                    |
| 084454 vs. 084458         | 2.6880     | 0.1234  | not significant                    | 0.7228      | 0.4095  | not significant                    | 0.5606      | 0.4664  | not significant                    | 0.1851       | 0.6736  | not significant                    | 0.1350       | 0.7188  | not significant                    |
| 084455 vs. 084456         | 3.71       | 0.0747  | not significant                    | 0.82        | 0.3805  | not significant                    | 0.0796      | 0.7820  | not significant                    | 0.0734       | 0.7905  | not significant                    | 1 5275       | 0.2368  | not significant                    |
| 084455 vs. 084457         | 0.1634     | 0.6922  | not significant                    | 0.0690      | 0.7967  | not significant                    | 0.2887      | 0.5995  | not significant                    | 0.0542       | 0.8192  | not significant                    | 0 0123       | 0.9134  | not significant                    |
| 084455 vs. 084458         | 0.9796     | 0.3391  | not significant                    | 0.4729      | 0.5029  | not significant                    | 1.3189      | 0.2700  | not significant                    | 0.3623       | 0.5568  | not significant                    | 0.0427       | 0.8392  | not significant                    |
| 084456 vs. 084457         | 5.43       | 0.0353  | not significant                    | 0.41        | 0.5307  | not significant                    | 0.6713      | 0.4263  | not significant                    | 0.2537       | 0.6223  | not significant                    | 1.8135       | 0.1995  | not significant                    |
| 084456 vs. 084458         | 0.88       | 0.3650  | not significant                    | 2.54        | 0.1334  | not significant                    | 2.0463      | 0.1745  | not significant                    | 0.1096       | 0.7455  | not significant                    | 1.0593       | 0.3208  | not significant                    |
| 084457 vs. 084458         | 1.9432     | 0.1851  | not significant                    | 0.9031      | 0.3581  | not significant                    | 0.3735      | 0.5509  | not significant                    | 0.6969       | 0.4179  | not significant                    | 0.1007       | 0.7556  | not significant                    |

**ANOVA-Based Comparison Tests of Mean 'Extracted Smokeless Tobacco' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| ANOVA-Based<br>Comparison | TA98 (-S9) |         |                                    | TA100 (-S9) |         |                                    | TA102 (-S9) |         |                                    | TA1535 (-S9) |         |                                    | TA1537 (-S9) |         |                                    |
|---------------------------|------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                           | f-ratio    | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395         | 0.8143     | 0.3821  | not significant                    | 0.0003      | 0.9867  | not significant                    | 0.3172      | 0.5822  | not significant                    | 0.0257       | 0.8749  | not significant                    | 2.3399       | 0.1484  | not significant                    |
| <b>084394 vs. 084454</b>  | 0.4662     | 0.5059  | not significant                    | 0.6132      | 0.4466  | not significant                    | 2.5495      | 0.1326  | not significant                    | 0.9211       | 0.3535  | not significant                    | 13.714       | 0.0024  | <b>significant</b>                 |
| <b>084394 vs. 084455</b>  | 4.7519     | 0.0468  | not significant                    | 0.3491      | 0.5640  | not significant                    | 0.0298      | 0.8653  | not significant                    | 0.1678       | 0.6883  | not significant                    | 16.822       | 0.0011  | <b>significant</b>                 |
| <b>084394 vs. 084456</b>  | 0.0034     | 0.9546  | not significant                    | 0.3823      | 0.5463  | not significant                    | 1.1929      | 0.2932  | not significant                    | 0.7310       | 0.4070  | not significant                    | 14.325       | 0.0020  | <b>significant</b>                 |
| <b>084394 vs. 084457</b>  | 0.3569     | 0.5598  | not significant                    | 2.9581      | 0.1075  | not significant                    | 0.2198      | 0.6464  | not significant                    | 1.7722       | 0.2044  | not significant                    | 15.227       | 0.0016  | <b>significant</b>                 |
| 084394 vs. 084458         | 0.1143     | 0.7403  | not significant                    | 2.5256      | 0.1343  | not significant                    | 0.2066      | 0.6564  | not significant                    | 3.8548       | 0.0698  | not significant                    | 10.700       | 0.0056  | not significant                    |
| 084395 vs. 084454         | 2.5128     | 0.1352  | not significant                    | 0.6400      | 0.4371  | not significant                    | 1.0682      | 0.3189  | not significant                    | 0.6390       | 0.4374  | not significant                    | 4.72         | 0.0474  | not significant                    |
| 084395 vs. 084455         | 9.5006     | 0.0081  | not significant                    | 0.3694      | 0.5531  | not significant                    | 0.1524      | 0.7021  | not significant                    | 0.3250       | 0.5777  | not significant                    | 6.61         | 0.0222  | not significant                    |
| 084395 vs. 084456         | 0.9223     | 0.3532  | not significant                    | 0.3617      | 0.5572  | not significant                    | 0.2799      | 0.6051  | not significant                    | 0.4824       | 0.4987  | not significant                    | 5.09         | 0.0407  | not significant                    |
| 084395 vs. 084457         | 2.2494     | 0.1559  | not significant                    | 3.0166      | 0.1044  | not significant                    | 1.0650      | 0.3196  | not significant                    | 1.3709       | 0.2612  | not significant                    | 5.63         | 0.0325  | not significant                    |
| 084395 vs. 084458         | 0.3185     | 0.5815  | not significant                    | 2.5797      | 0.1306  | not significant                    | 1.0357      | 0.3261  | not significant                    | 3.2507       | 0.0930  | not significant                    | 3.03         | 0.1035  | not significant                    |
| 084454 vs. 084455         | 2.2413     | 0.1566  | not significant                    | 0.0370      | 0.8503  | not significant                    | 2.0277      | 0.1764  | not significant                    | 1.8752       | 0.1924  | not significant                    | 0.1586       | 0.6965  | not significant                    |
| 084454 vs. 084456         | 0.3904     | 0.5421  | not significant                    | 1.9640      | 0.1829  | not significant                    | 0.2545      | 0.6217  | not significant                    | 0.0110       | 0.9180  | not significant                    | 0.0067       | 0.9361  | not significant                    |
| 084454 vs. 084457         | 0.0073     | 0.9332  | not significant                    | 0.8776      | 0.3647  | not significant                    | 4.2665      | 0.0579  | not significant                    | 0.1380       | 0.7158  | not significant                    | 0.0396       | 0.8452  | not significant                    |
| 084454 vs. 084458         | 1.0421     | 0.3246  | not significant                    | 0.6498      | 0.4337  | not significant                    | 4.2077      | 0.0594  | not significant                    | 1.0073       | 0.3326  | not significant                    | 0.1868       | 0.6721  | not significant                    |
| 084455 vs. 084456         | 4.5026     | 0.0522  | not significant                    | 1.4622      | 0.2466  | not significant                    | 0.8454      | 0.3734  | not significant                    | 1.5993       | 0.2267  | not significant                    | 0.1003       | 0.7562  | not significant                    |
| 084455 vs. 084457         | 2.5043     | 0.1359  | not significant                    | 1.2748      | 0.2779  | not significant                    | 0.4116      | 0.5315  | not significant                    | 3.0307       | 0.1036  | not significant                    | 0.0397       | 0.8449  | not significant                    |
| 084455 vs. 084458         | 6.3401     | 0.0246  | not significant                    | 0.9967      | 0.3351  | not significant                    | 0.3935      | 0.5406  | not significant                    | 5.6312       | 0.0325  | not significant                    | 0.6897       | 0.4202  | not significant                    |
| 084456 vs. 084457         | 0.2910     | 0.5981  | not significant                    | 5.4674      | 0.0347  | not significant                    | 2.4368      | 0.1408  | not significant                    | 0.2268       | 0.6412  | not significant                    | 0.0138       | 0.9083  | not significant                    |
| 084456 vs. 084458         | 0.1568     | 0.6981  | not significant                    | 4.8733      | 0.0445  | not significant                    | 2.3924      | 0.1442  | not significant                    | 1.2285       | 0.2864  | not significant                    | 0.2640       | 0.6154  | not significant                    |
| 084457 vs. 084458         | 0.8751     | 0.3654  | not significant                    | 0.0171      | 0.8979  | not significant                    | 0.0002      | 0.9888  | not significant                    | 0.3996       | 0.5375  | not significant                    | 0.3984       | 0.5381  | not significant                    |

Some ANOVA-based comparison p-values for tester strains TA102 (+S9) and TA1537 (-S9) were significant at  $\alpha = 0.05$ .

Significant differences in mean 'Extracted Smokeless Tobacco' specific activity slope were detected in TA102 (+S9) between Camel SNUS Frost (084394) and each of {Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456), Ariva Wintergreen (084457), Fresh Orbs (084458)} and between 2S3 Research Moist Snuff (084395) and Fresh Orbs (084458).

Significant differences in mean 'Extracted Smokeless Tobacco' specific activity slope were detected in TA1537 (-S9) between Camel SNUS Frost (084394) and each of {Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456), Ariva Wintergreen (084457)}

**Pairwise T-Test Comparisons of Mean 'Extracted Smokeless Tobacco' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| Pairwise T-test<br>Comparison | TA98 (+S9)  |         |                                    | TA100 (+S9) |         |                                    | TA102 (+S9) |         |                                    | TA1535 (+S9) |         |                                    | TA1537 (+S9) |         |                                    |
|-------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                               | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395             |             |         |                                    |             |         |                                    | 1.76954     | 0.1515  | not significant                    |              |         |                                    | 0.623998     | 0.5665  | not significant                    |
| <b>084394 vs. 084454</b>      |             |         |                                    |             |         |                                    | 8.893338    | 0.0009  | <b>significant</b>                 |              |         |                                    | 3.376765     | 0.0279  | not significant                    |
| <b>084394 vs. 084455</b>      |             |         |                                    |             |         |                                    | 8.577096    | 0.0010  | <b>significant</b>                 |              |         |                                    | 2.776061     | 0.0500  | not significant                    |
| <b>084394 vs. 084456</b>      |             |         |                                    |             |         |                                    | 7.75824     | 0.0015  | <b>significant</b>                 |              |         |                                    | 0.101308     | 0.9242  | not significant                    |
| <b>084394 vs. 084457</b>      |             |         |                                    |             |         |                                    | 9.406724    | 0.0007  | <b>significant</b>                 |              |         |                                    | 2.963306     | 0.0414  | not significant                    |
| <b>084394 vs. 084458</b>      |             |         |                                    |             |         |                                    | 8.195479    | 0.0012  | <b>significant</b>                 |              |         |                                    | 1.943068     | 0.1239  | not significant                    |
| 084395 vs. 084454             |             |         |                                    |             |         |                                    | 1.81267     | 0.1441  | not significant                    |              |         |                                    | 1.477058     | 0.2137  | not significant                    |
| 084395 vs. 084455             |             |         |                                    |             |         |                                    | 1.579276    | 0.1894  | not significant                    |              |         |                                    | 1.377127     | 0.2405  | not significant                    |
| 084395 vs. 084456             |             |         |                                    |             |         |                                    | 1.395745    | 0.2353  | not significant                    |              |         |                                    | 0.661546     | 0.5444  | not significant                    |
| 084395 vs. 084457             |             |         |                                    |             |         |                                    | 1.906783    | 0.1292  | not significant                    |              |         |                                    | 1.43893      | 0.2236  | not significant                    |
| 084395 vs. 084458             |             |         |                                    |             |         |                                    | 2.17595     | 0.0952  | not significant                    |              |         |                                    | 1.239249     | 0.2830  | not significant                    |
| 084454 vs. 084455             |             |         |                                    |             |         |                                    | 2.015307    | 0.1141  | not significant                    |              |         |                                    | 0.685274     | 0.5308  | not significant                    |
| 084454 vs. 084456             |             |         |                                    |             |         |                                    | 2.321495    | 0.0810  | not significant                    |              |         |                                    | 4.25263      | 0.0131  | not significant                    |
| 084454 vs. 084457             |             |         |                                    |             |         |                                    | 0.71646     | 0.5133  | not significant                    |              |         |                                    | 0.199945     | 0.8513  | not significant                    |
| 084454 vs. 084458             |             |         |                                    |             |         |                                    | 1.372319    | 0.2419  | not significant                    |              |         |                                    | 0.950134     | 0.3958  | not significant                    |
| 084455 vs. 084456             |             |         |                                    |             |         |                                    | 1.176392    | 0.3047  | not significant                    |              |         |                                    | 3.313893     | 0.0295  | not significant                    |
| 084455 vs. 084457             |             |         |                                    |             |         |                                    | 5.964829    | 0.0040  | not significant                    |              |         |                                    | 0.361574     | 0.7360  | not significant                    |
| 084455 vs. 084458             |             |         |                                    |             |         |                                    | 2.214629    | 0.0912  | not significant                    |              |         |                                    | 0.486144     | 0.6523  | not significant                    |
| 084456 vs. 084457             |             |         |                                    |             |         |                                    | 3.492948    | 0.0251  | not significant                    |              |         |                                    | 3.516891     | 0.0245  | not significant                    |
| 084456 vs. 084458             |             |         |                                    |             |         |                                    | 2.545463    | 0.0636  | not significant                    |              |         |                                    | 2.12945      | 0.1003  | not significant                    |
| 084457 vs. 084458             |             |         |                                    |             |         |                                    | 1.183984    | 0.3020  | not significant                    |              |         |                                    | 0.731486     | 0.5050  | not significant                    |

**Pairwise T-Test Comparisons of Mean 'Extracted Smokeless Tobacco' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| Pairwise T-test<br>Comparison | TA98 (-S9)  |         |                                    | TA100 (-S9) |         |                                    | TA102 (-S9) |         |                                    | TA1535 (-S9) |         |                                    | TA1537 (-S9) |         |                                    |
|-------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                               | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395             |             |         |                                    | 0.076598    | 0.9426  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084454             |             |         |                                    | 1.952138    | 0.1227  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084455             |             |         |                                    | 0.65827     | 0.5463  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084456             |             |         |                                    | 0.629179    | 0.5634  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084457             |             |         |                                    | 1.381999    | 0.2391  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084458             |             |         |                                    | 3.701244    | 0.0208  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084454             |             |         |                                    | 2.272052    | 0.0855  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084455             |             |         |                                    | 0.693206    | 0.5263  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084456             |             |         |                                    | 0.624001    | 0.5665  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084457             |             |         |                                    | 1.412546    | 0.2307  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084458             |             |         |                                    | 4.183074    | 0.0139  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084455             |             |         |                                    | 0.204827    | 0.8477  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084456             |             |         |                                    | 1.373578    | 0.2415  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084457             |             |         |                                    | 0.735138    | 0.5030  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084458             |             |         |                                    | 1.582456    | 0.1887  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084456             |             |         |                                    | 0.93133     | 0.4044  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084457             |             |         |                                    | 0.74959     | 0.4952  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084458             |             |         |                                    | 1.049874    | 0.3530  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084456 vs. 084457             |             |         |                                    | 1.500341    | 0.2079  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084456 vs. 084458             |             |         |                                    | 2.139718    | 0.0991  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |
| 084457 vs. 084458             |             |         |                                    | 0.101828    | 0.9238  | not significant                    |             |         |                                    |              |         |                                    |              |         |                                    |

Pairwise t-test comparison p-values less than the Bonferroni-adjusted  $\alpha = 0.05$  indicate that significant differences in mean 'Extracted Smokeless Tobacco' specific activity slope were as follows for strain TA102 (+S9):

TA102 (+S9): Camel SNUS Frost (084394) was significantly different from each of {Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456), Ariva Wintergreen (084457), Fresh Orbs (084458)}

**Number of Mean 'Extracted Smokeless Tobacco' Slope Estimates Significantly Greater than Zero (0), the Corresponding Number of Paired Comparisons and Comparison Method**

| Strain and S9 Activation | # of Significant Mean Slopes | Number of Comparisons | Std. Dev. Ratio (Max ÷ Min) | Method of Comparison   |
|--------------------------|------------------------------|-----------------------|-----------------------------|------------------------|
| TA98 (+S9)               | 1                            | 0                     | 1.4                         | ANOVA (equal variance) |
| TA98 (-S9)               | 1                            | 0                     |                             |                        |
| TA100 (+S9)              | 3                            | 3                     |                             |                        |
| TA100 (-S9)              | 1                            | 0                     |                             |                        |
| TA102 (+S9)              | 2                            | 1                     | 9.1                         | ANOVA (equal variance) |
| TA102 (-S9)              | 0                            | 0                     |                             |                        |
| TA1535 (+S9)             | 0                            | 0                     |                             |                        |
| TA1535 (-S9)             | 0                            | 0                     |                             |                        |
| TA1537 (+S9)             | 1                            | 0                     |                             |                        |
| TA1537 (-S9)             | 0                            | 0                     |                             |                        |

**One-Way ANOVA and ANOVA-Based Comparisons Among Test Samples of Mean 'Extracted Smokeless Tobacco' Slope Estimates that are Significantly Greater than Zero (0)**

TA100 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 66.758         | 2  | 33.379      | 1.253   | 0.351   |
| Within Samples | 159.794        | 6  | 26.632      |         |         |
| Total (Corr.)  | 226.552        | 8  |             |         |         |

| TA100 (+S9)            |         |         |                                 |
|------------------------|---------|---------|---------------------------------|
| ANOVA-Based Comparison | f-ratio | p-value | significance at $\alpha = 0.05$ |
| 084454 vs. 084455      | 0.07    | 0.7989  | not significant                 |
| 084454 vs. 084456      | 1.48    | 0.2688  | not significant                 |
| 084455 vs. 084456      | 2.20    | 0.1881  | not significant                 |

TA102 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 2940.879       | 1  | 2940.88     | 73.57   | 0.001   |
| Within Samples | 159.903        | 4  | 39.976      |         |         |
| Total (Corr.)  | 3100.782       | 5  |             |         |         |

| TA102 (+S9)            |         |         |                                 |
|------------------------|---------|---------|---------------------------------|
| ANOVA-Based Comparison | f-ratio | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084455      | 73.57   | 0.0010  | significant                     |

Both TA100 (+S9) and TA102 (+S9) strains have more than one test sample for which the mean 'extracted smokeless tobacco' specific activity slope estimate is greater than zero (0) .

**TA100 (+S9):**

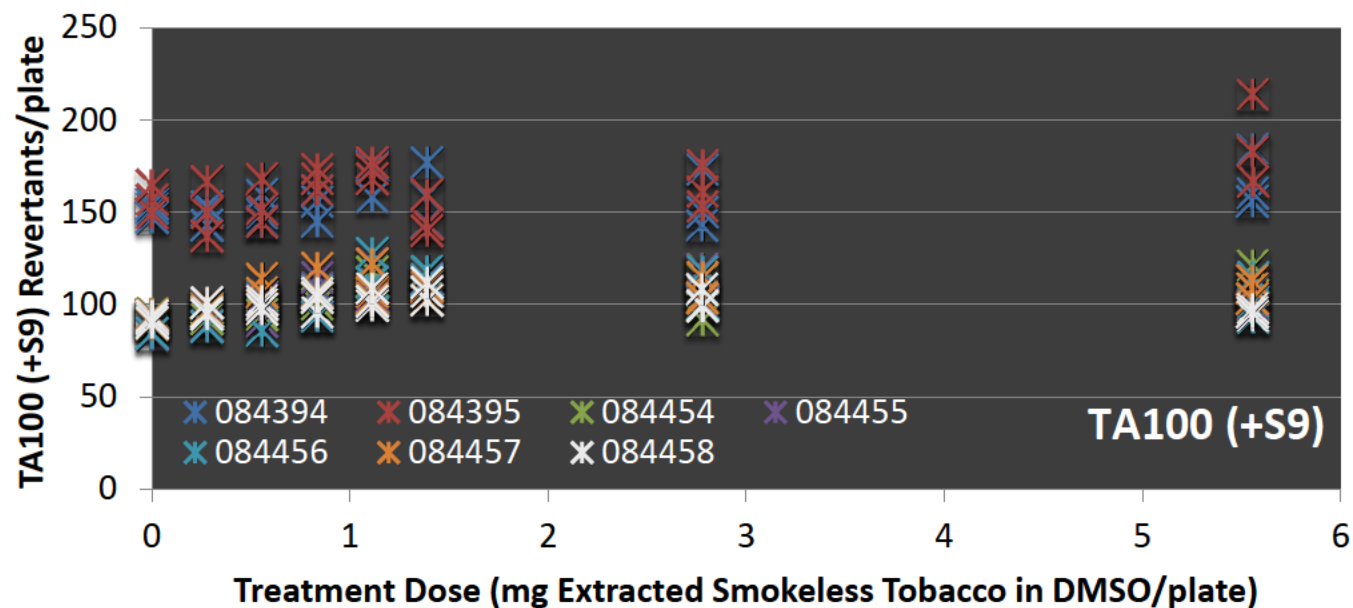
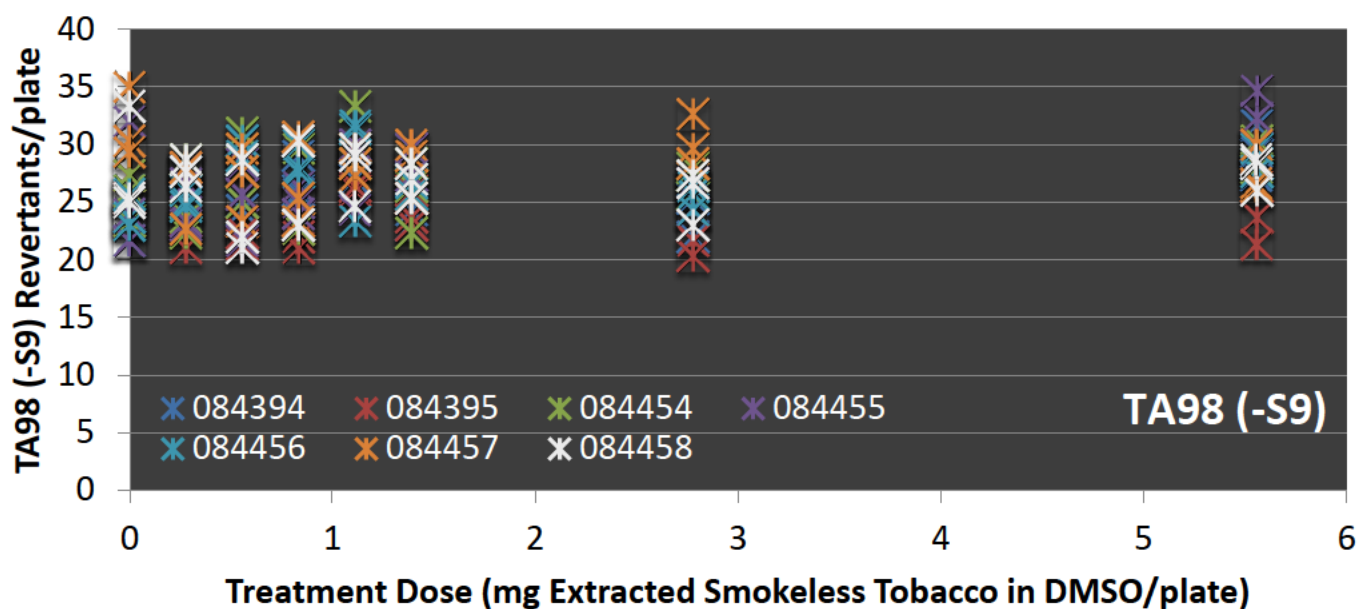
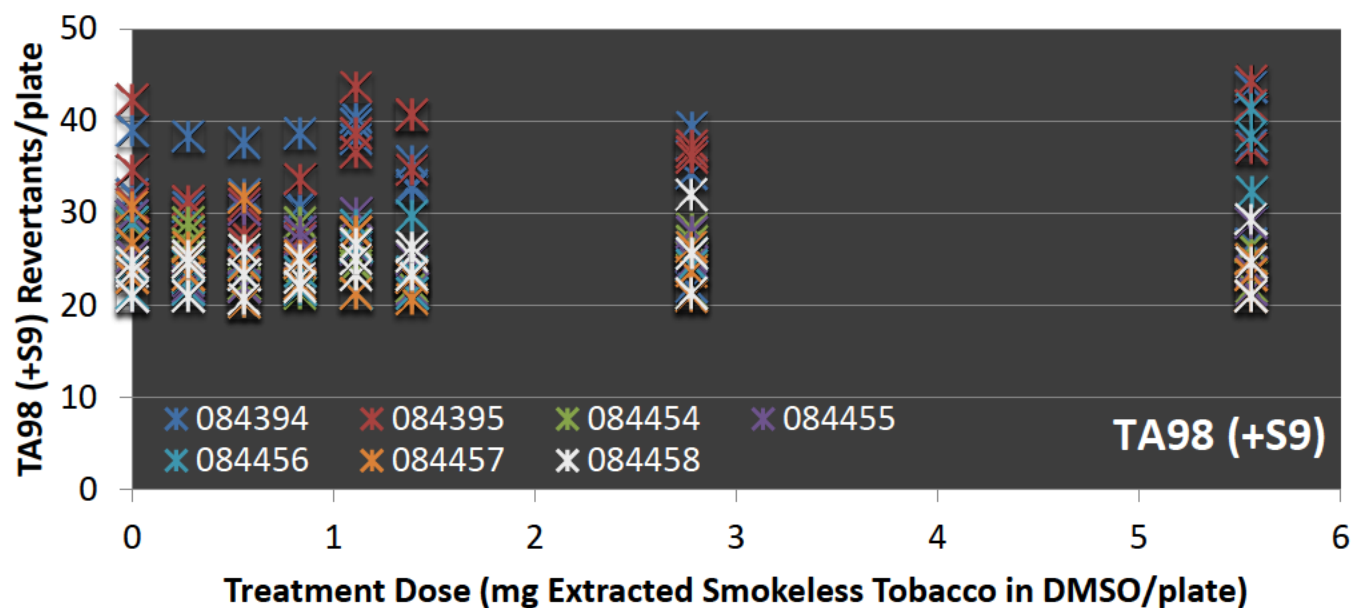
No significant differences among mean 'Extracted Smokeless Tobacco' specific activity slope estimates were detected in TA100 (+S9) among test samples 084454 (Fresh Strips), 084455 (Mellow Sticks) and 084456 (Copenhagen Long Cut).

**TA102 (+S9):**

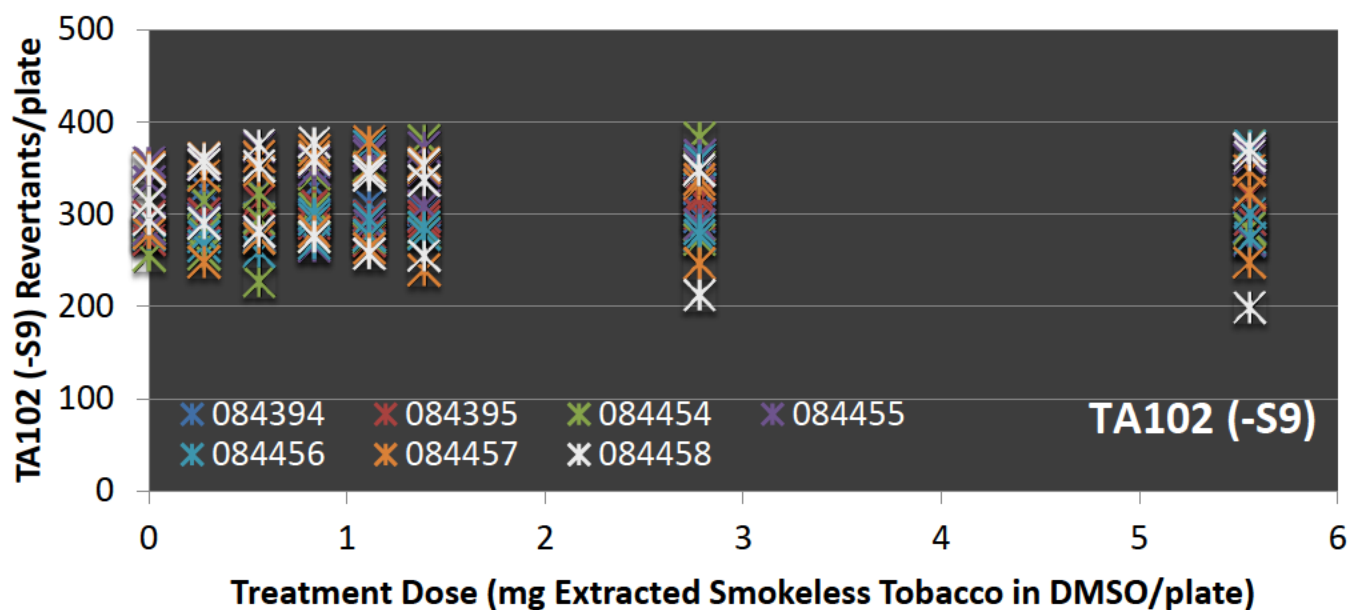
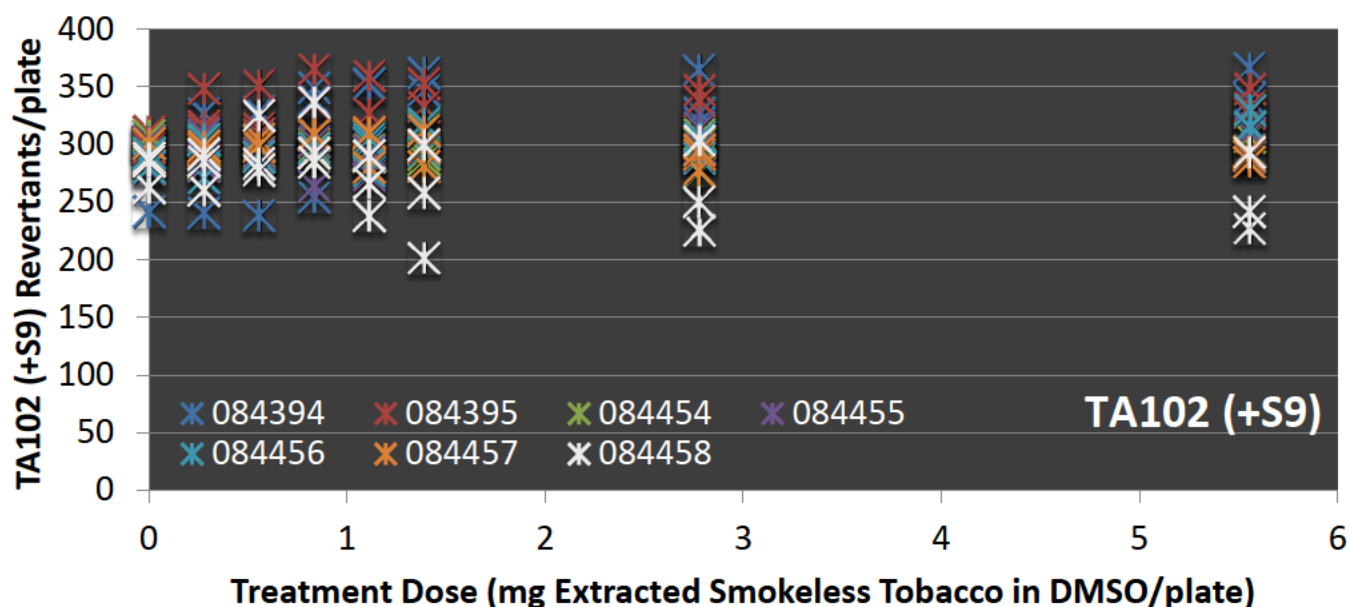
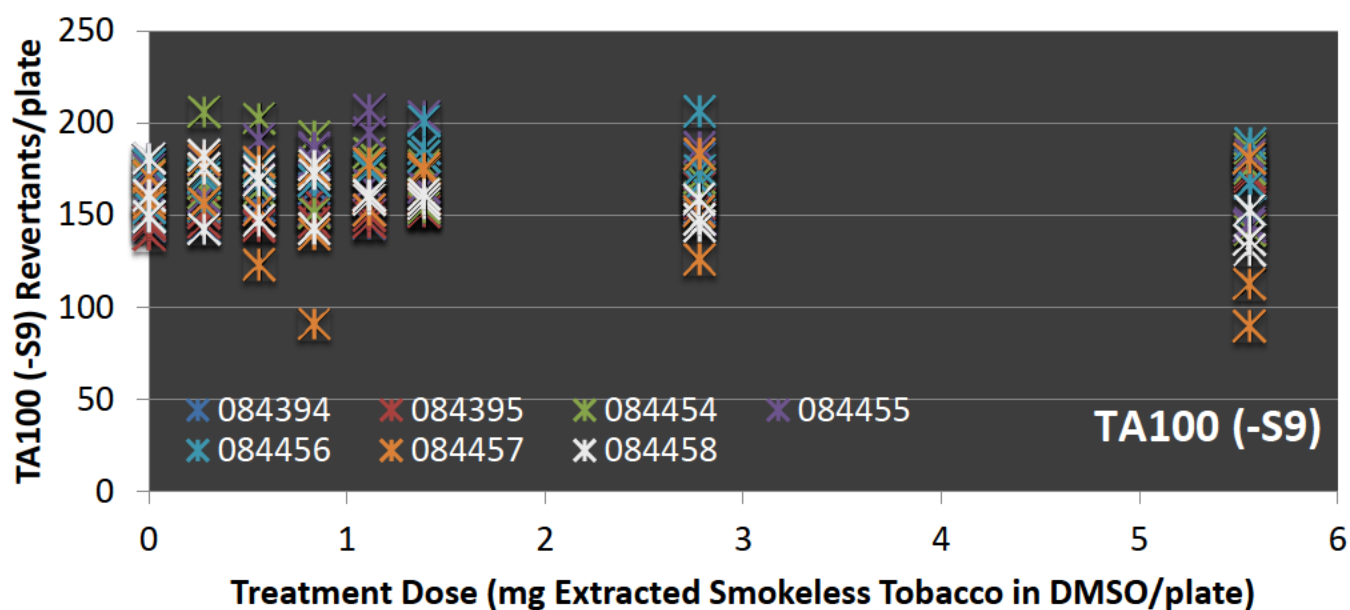
Significant differences among mean 'Extracted Smokeless Tobacco' specific activity slope estimates were detected in TA102 (+S9) between test samples 084394 (Camel SNUS Frost) and 084455 (Mellow Sticks) .

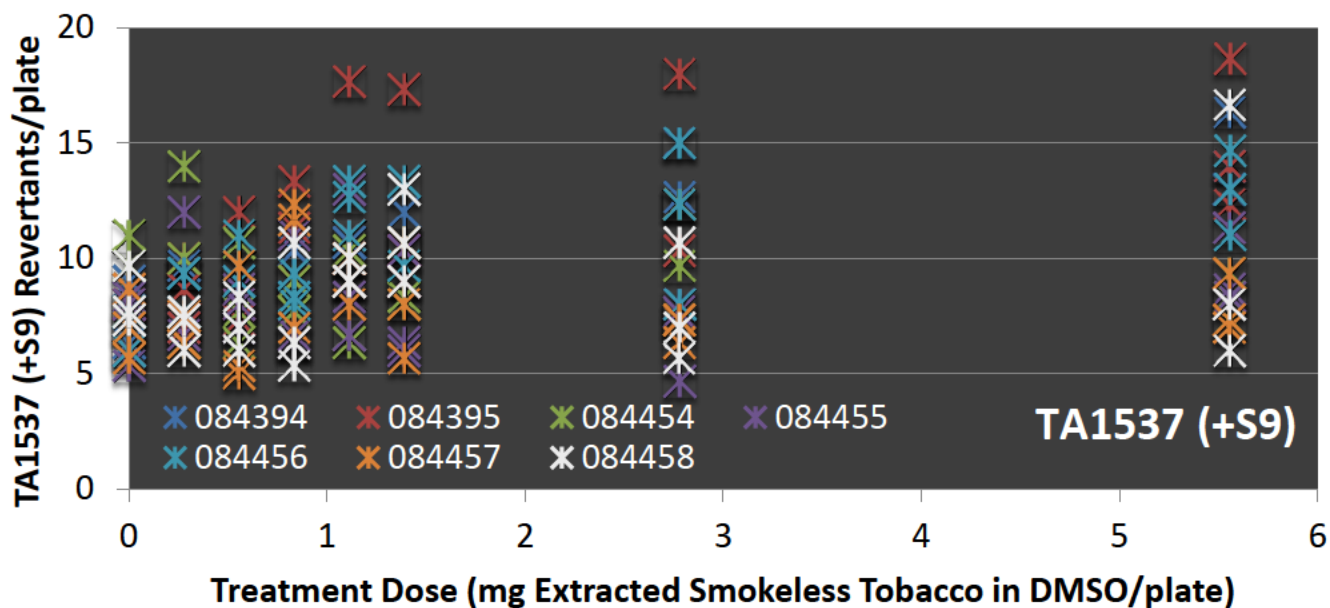
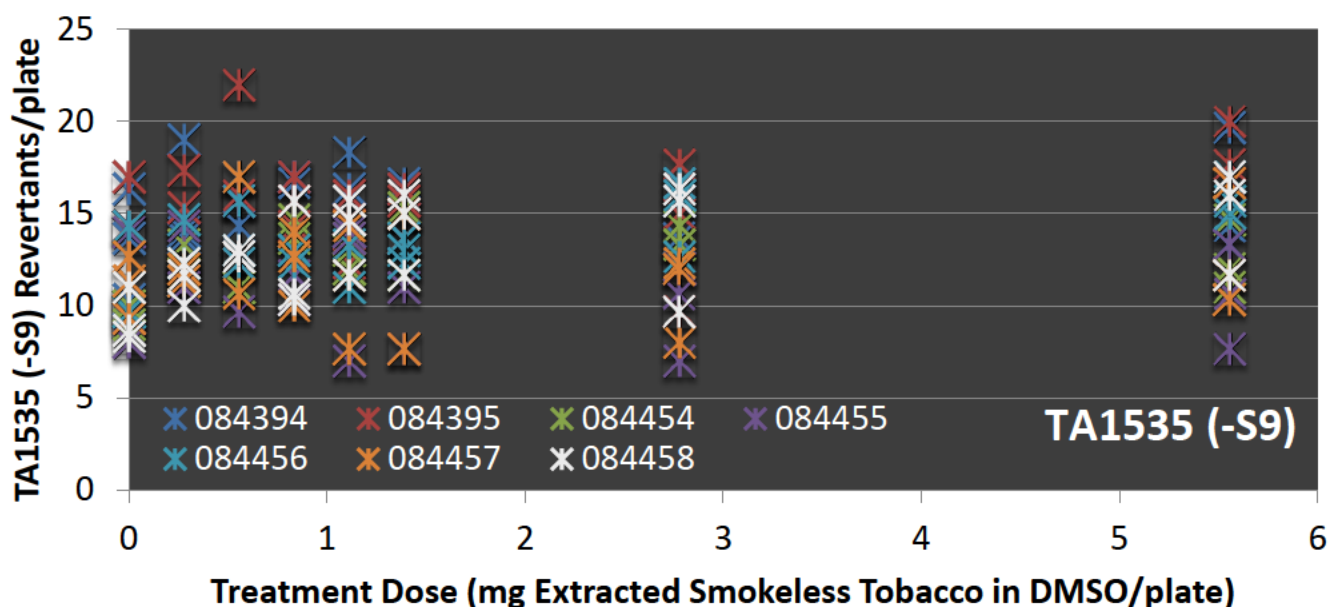
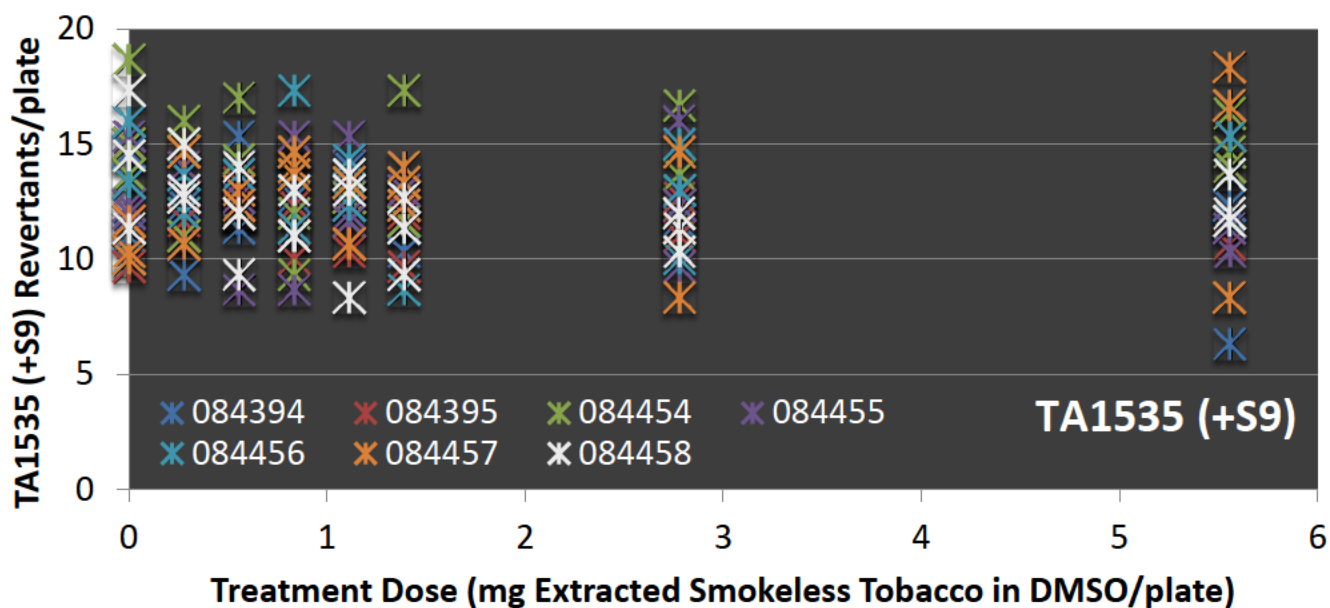
**Number of Mean 'Extracted Smokeless Tobacco' Slope Estimates Significantly Greater than Zero (0), the Corresponding Number of Paired Comparisons and Comparison Method**

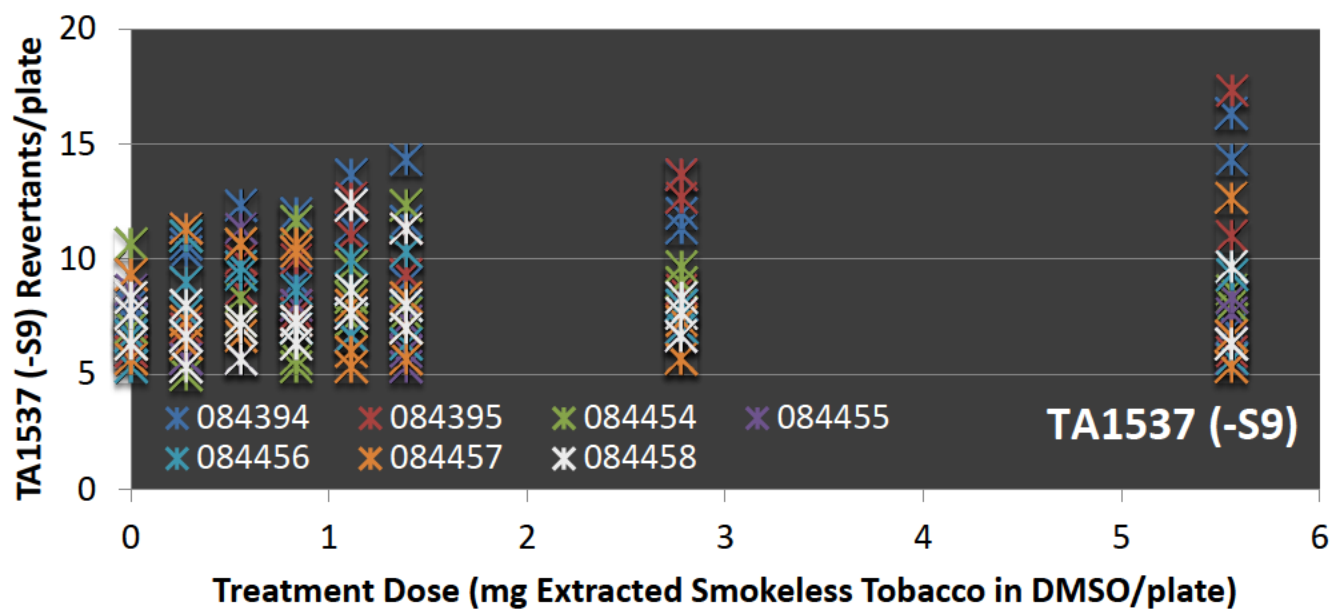
**One-Way ANOVA and ANOVA-Based Comparisons Among Test Samples of Mean 'Extracted Smokeless Tobacco' Slope Estimates that are Significantly Greater than Zero (0)**

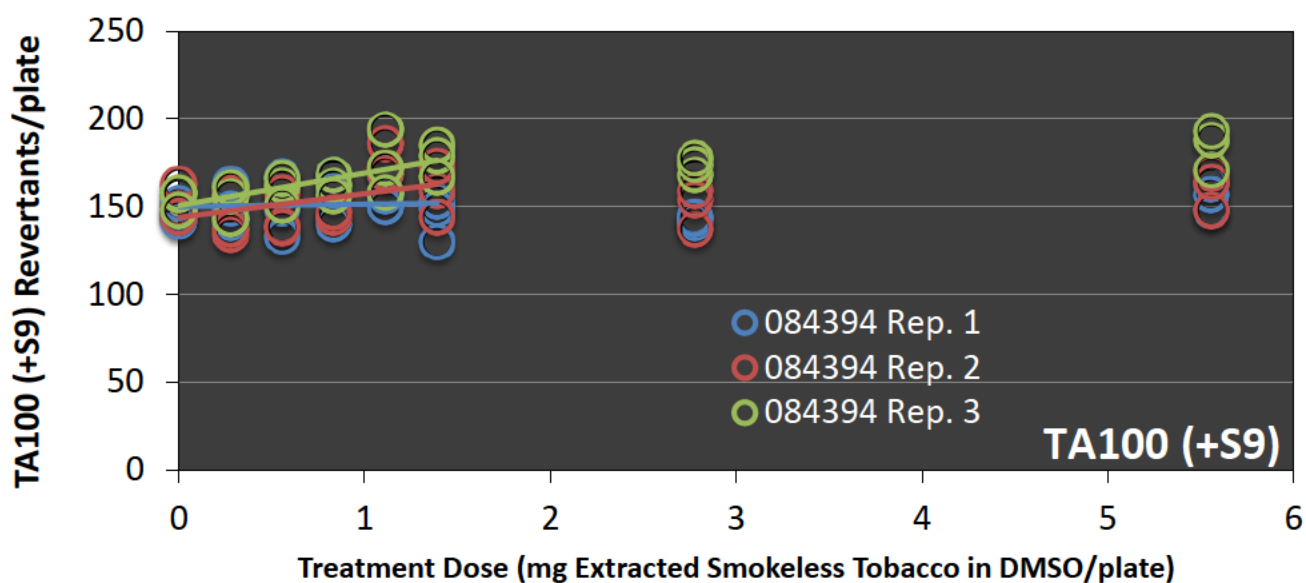
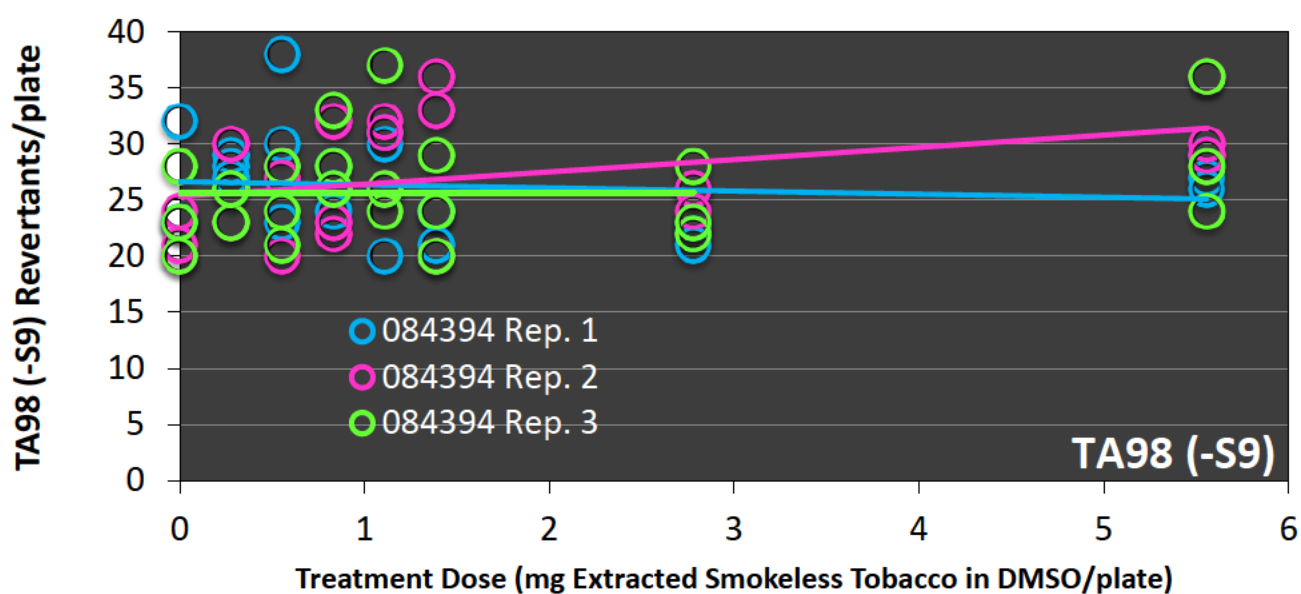
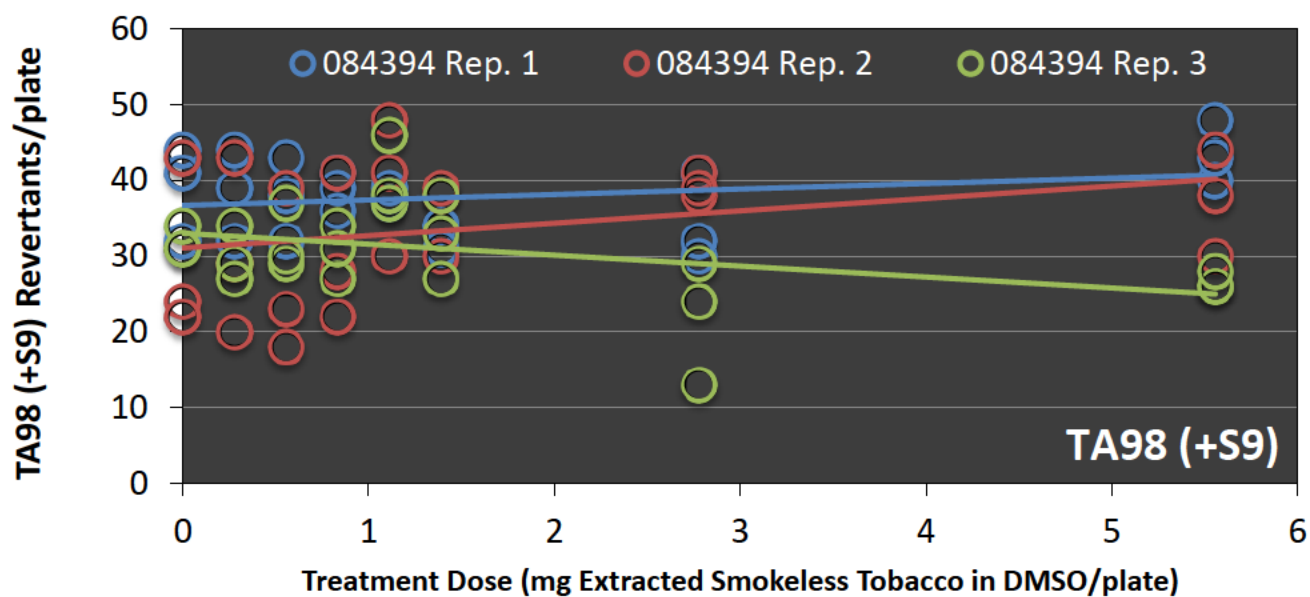


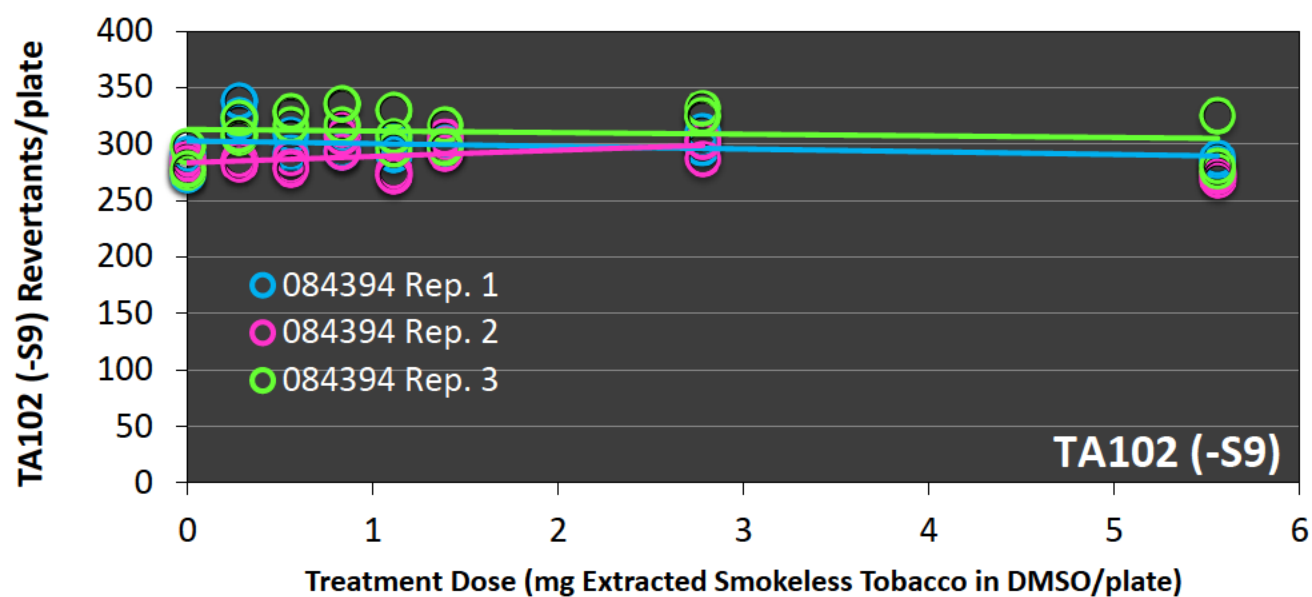
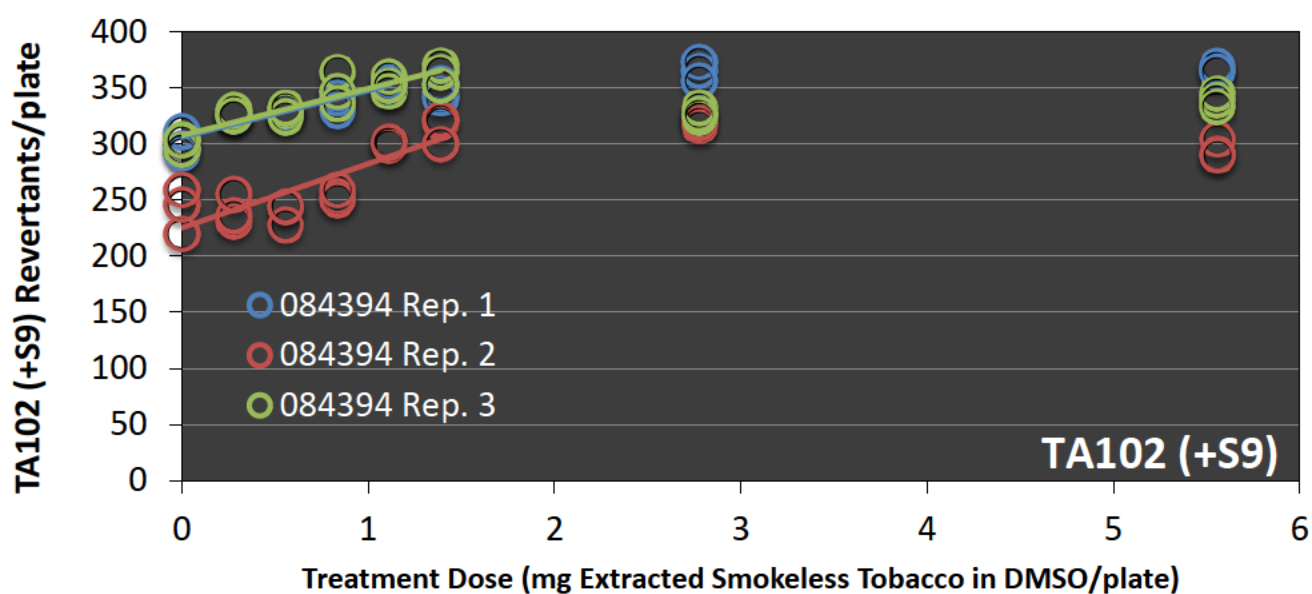
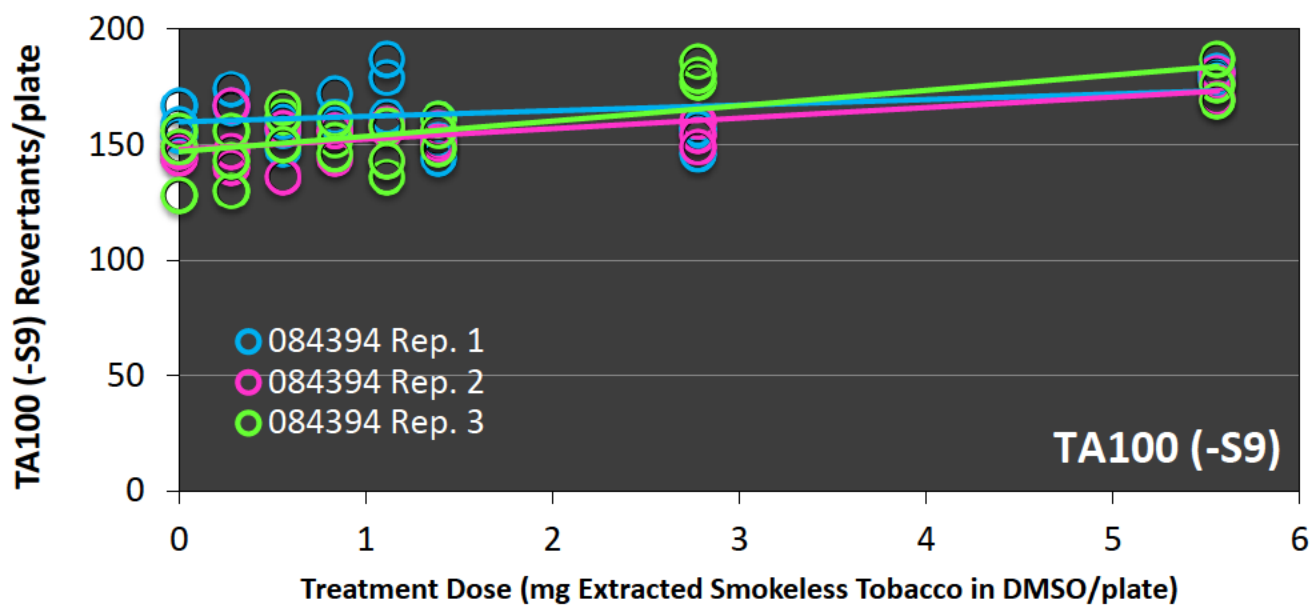


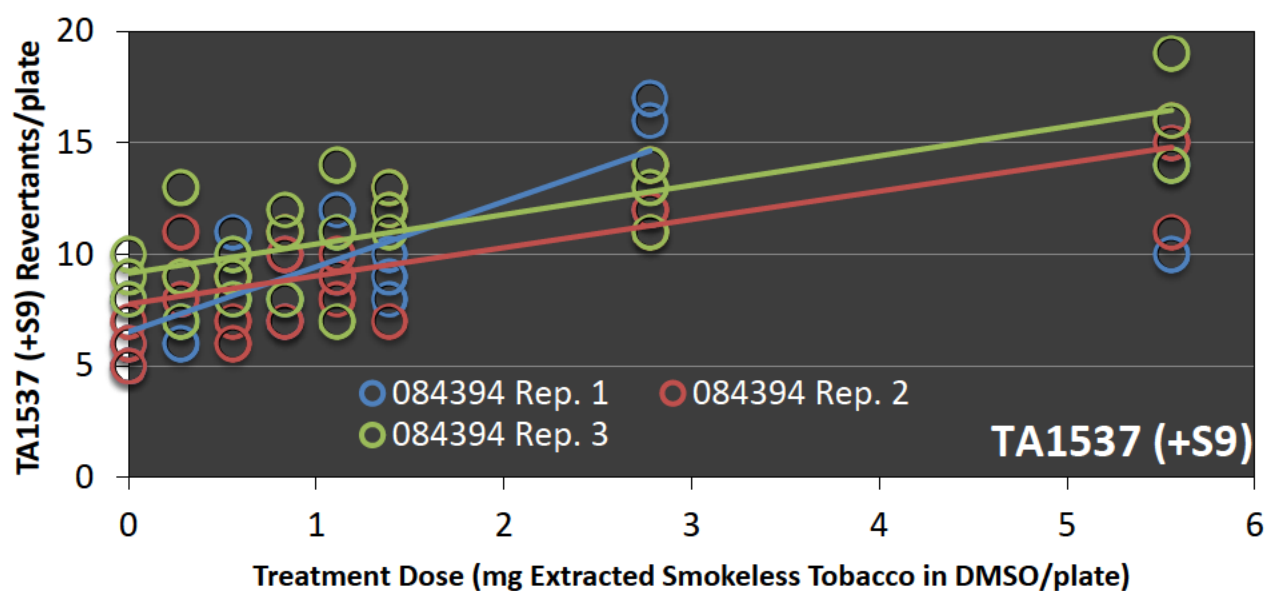
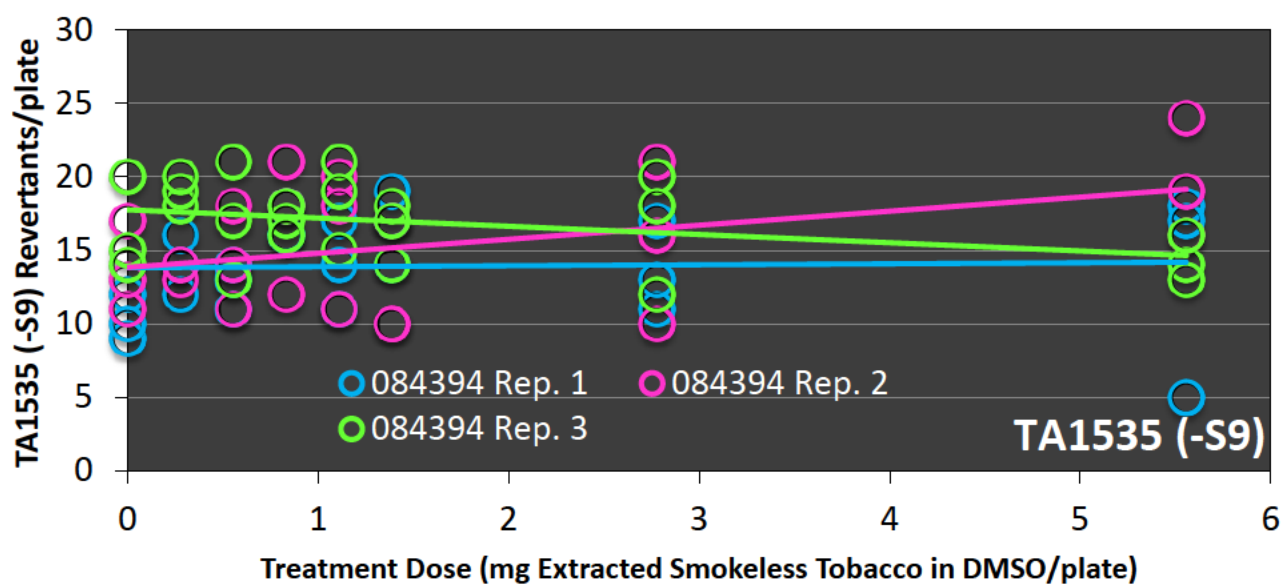
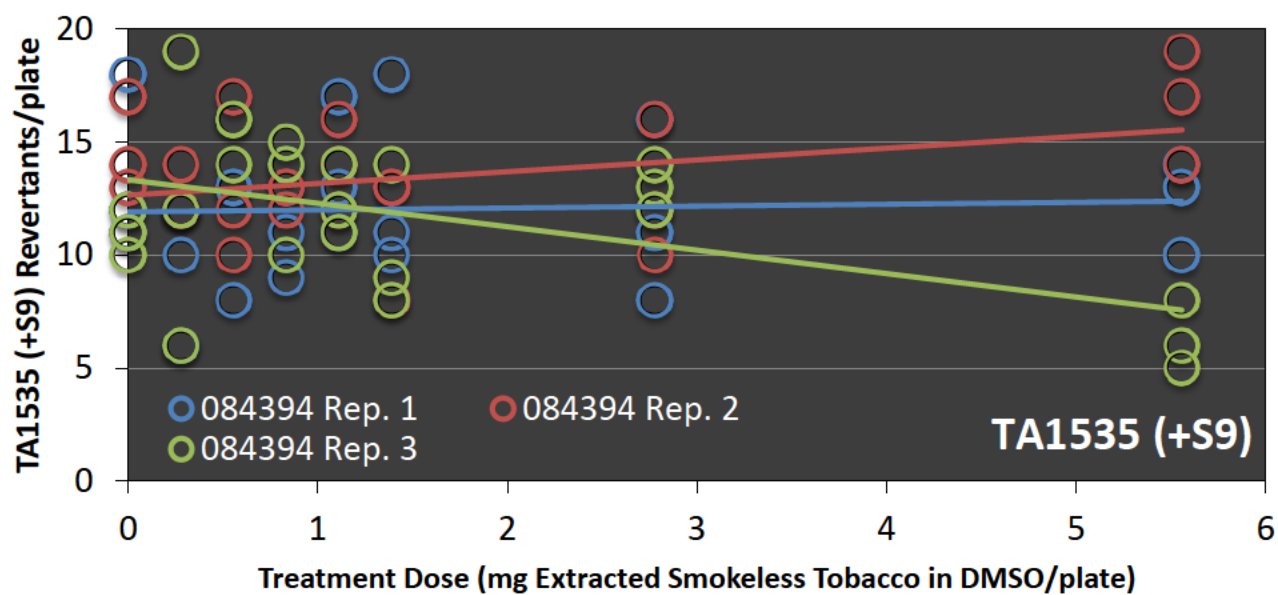


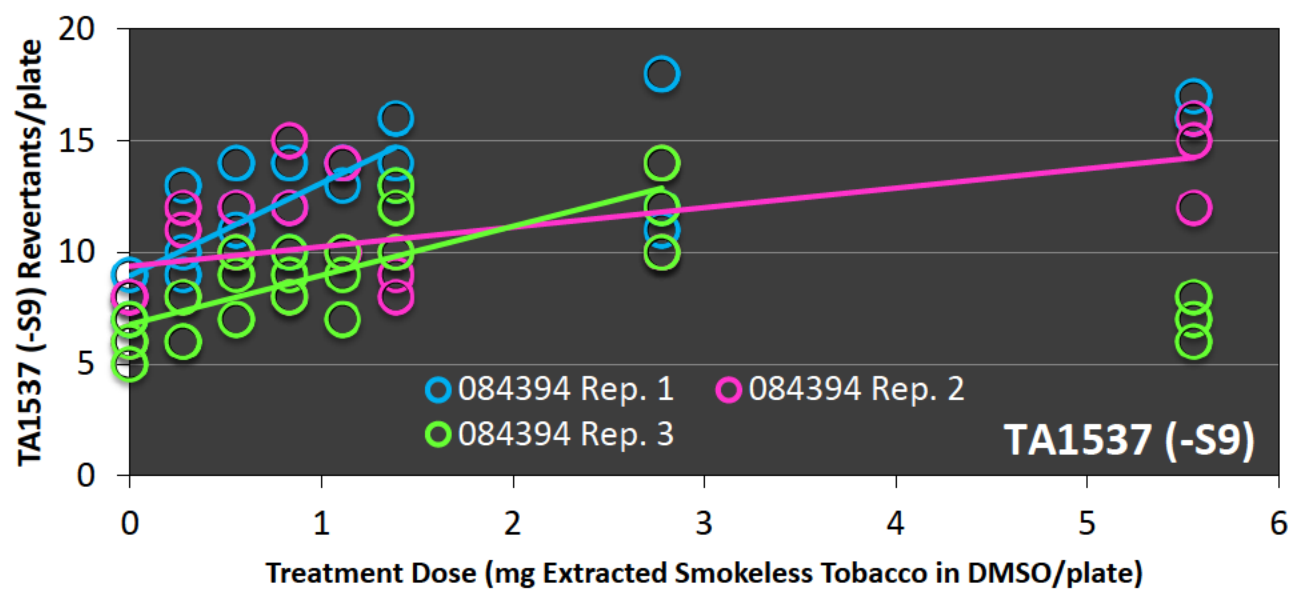




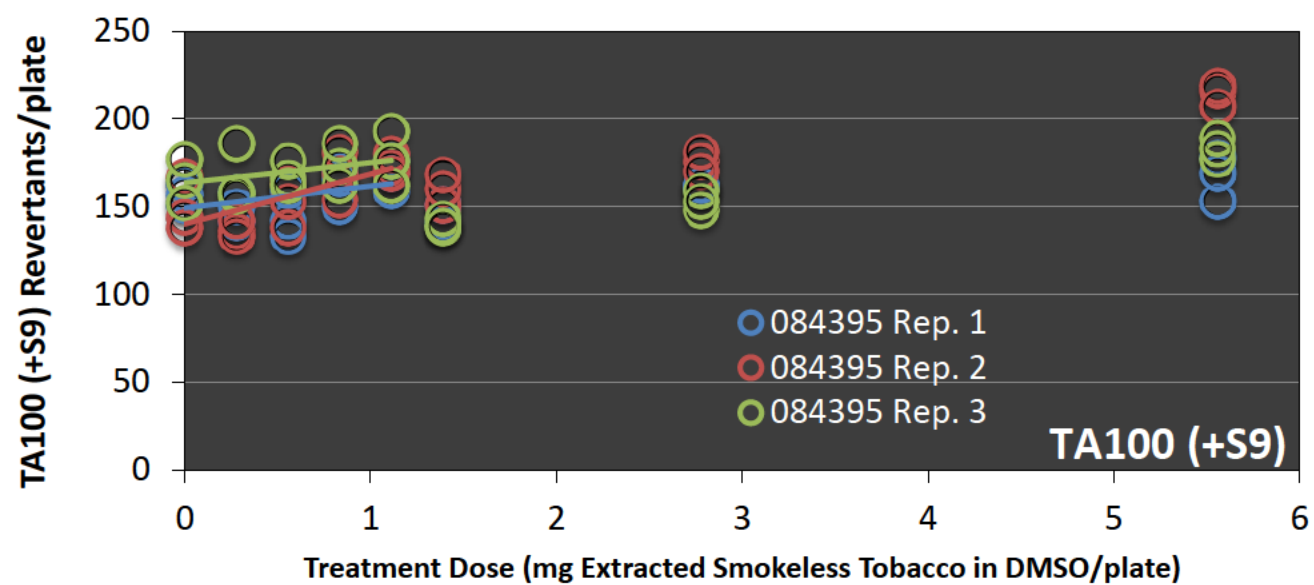
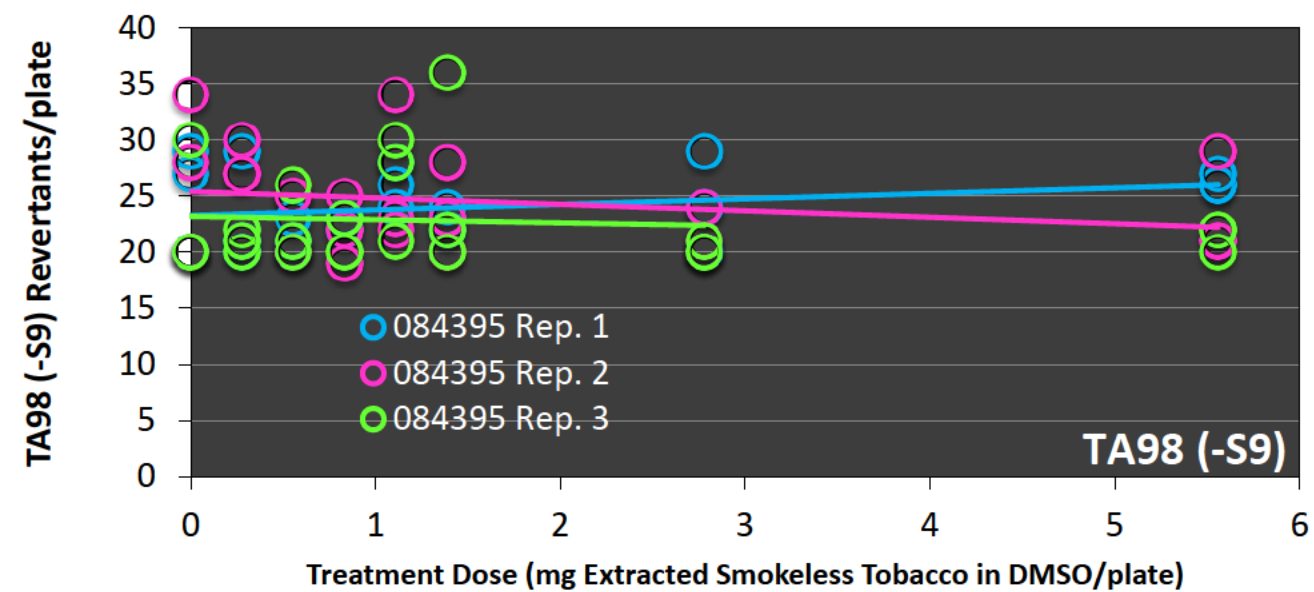
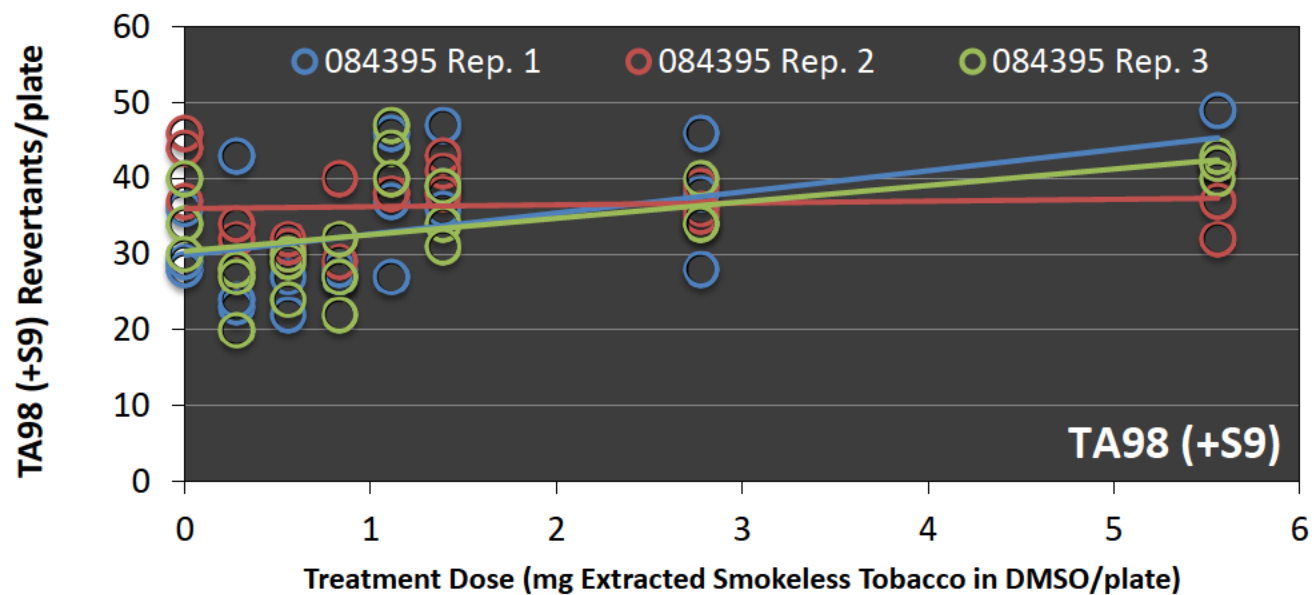




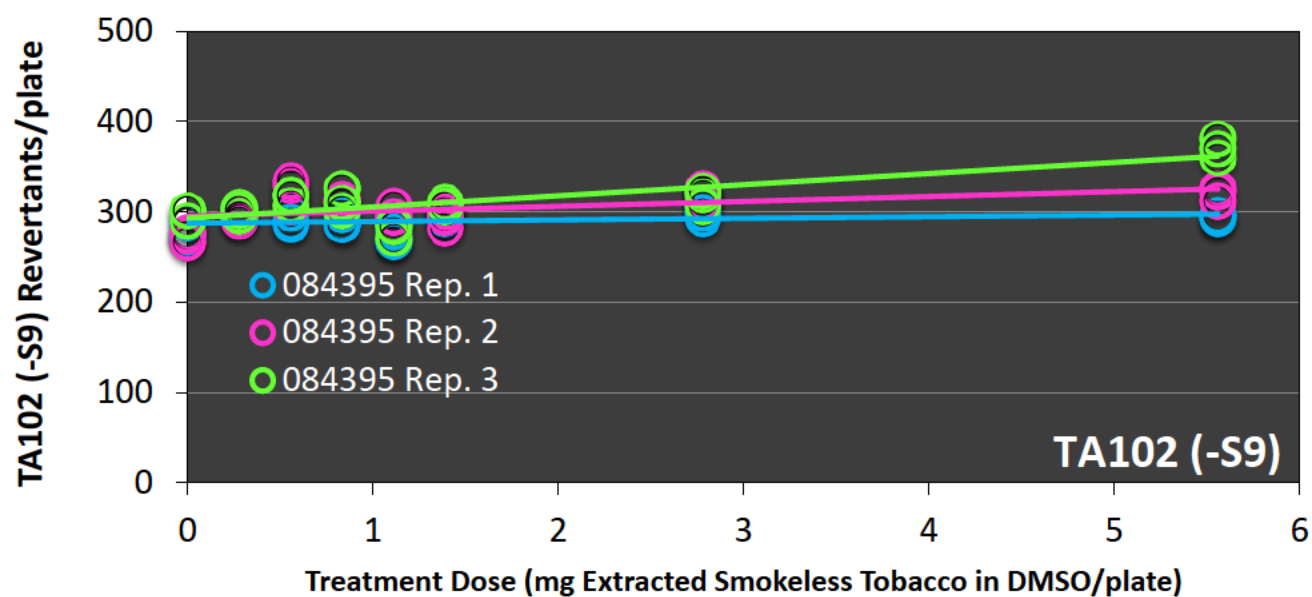
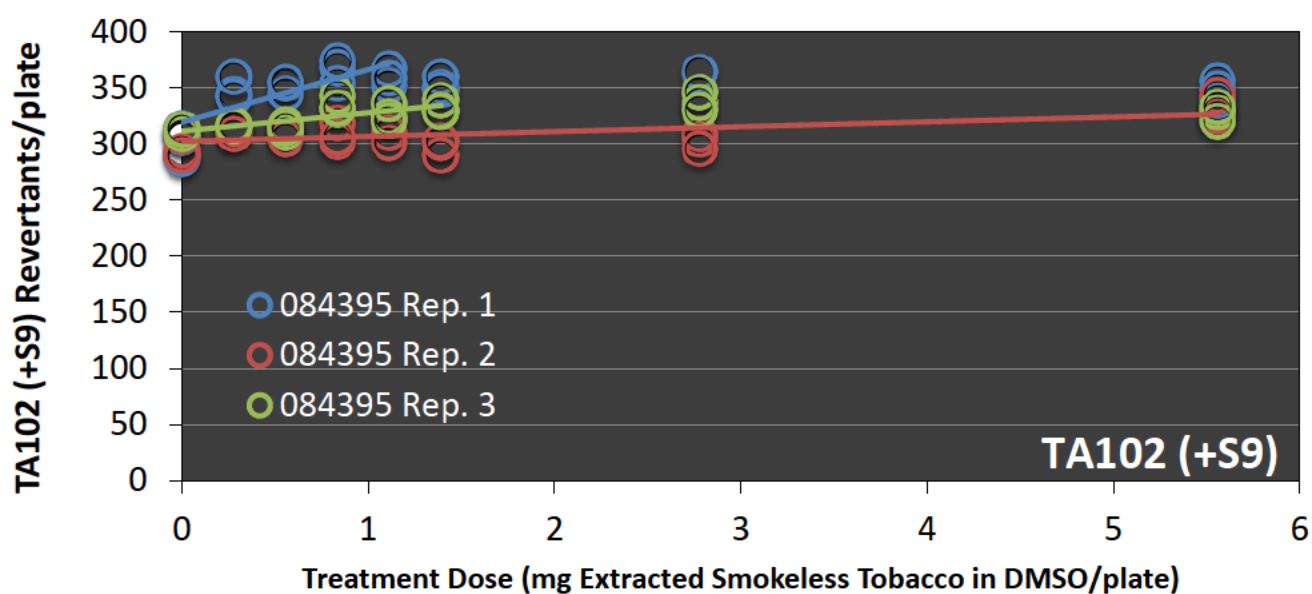
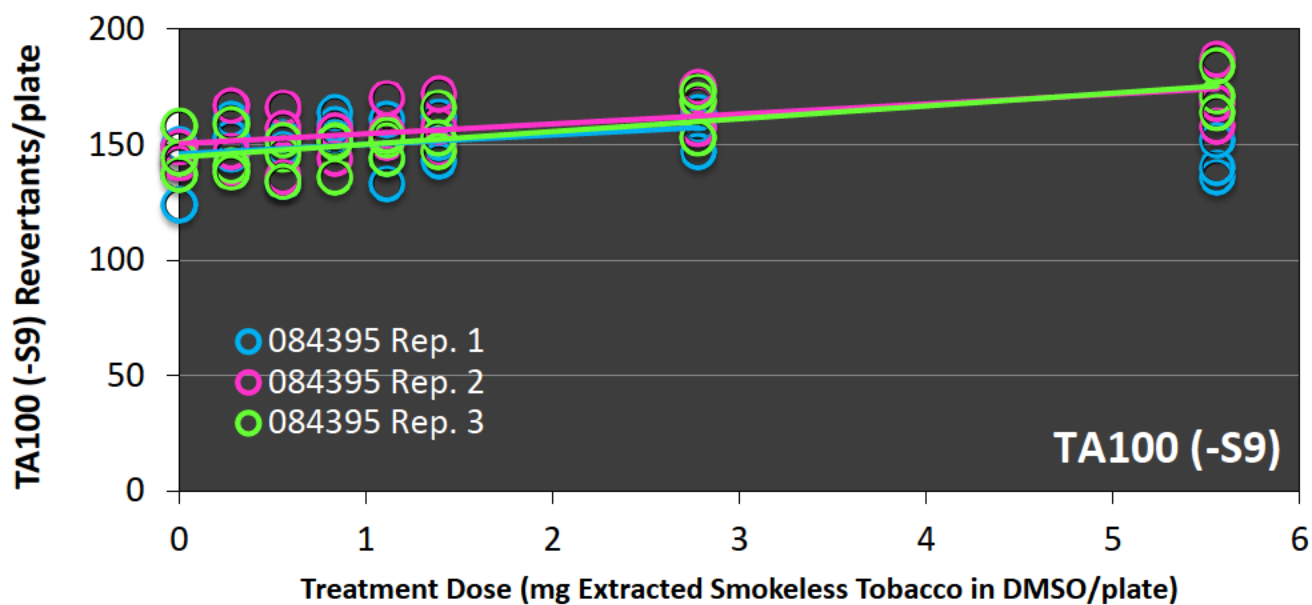


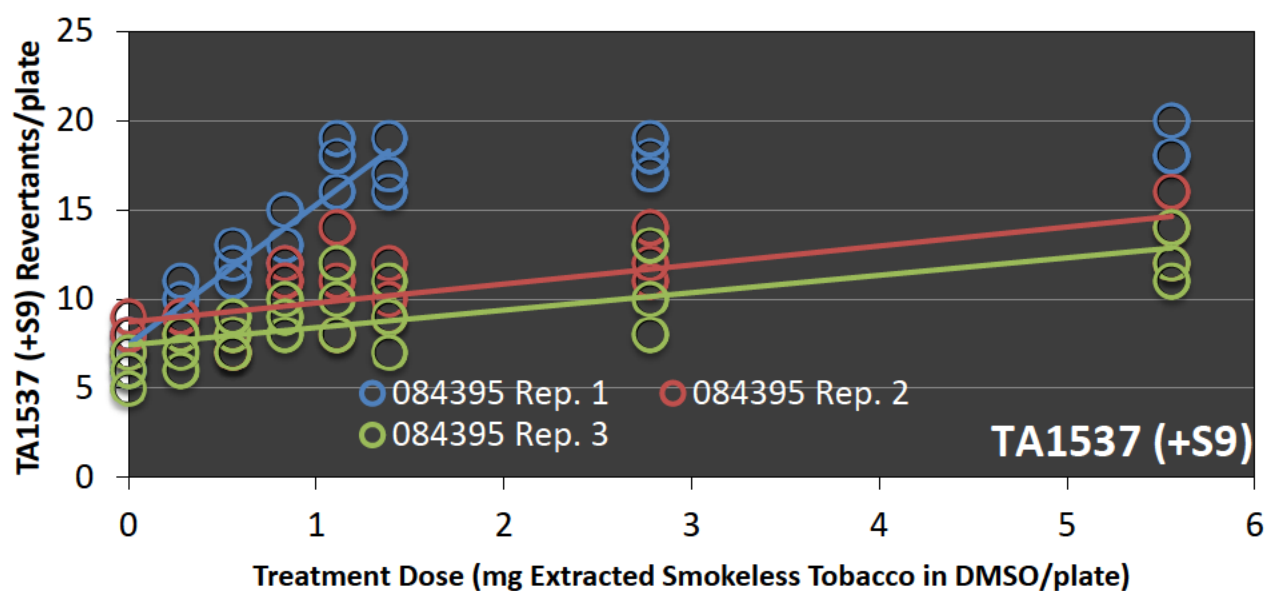
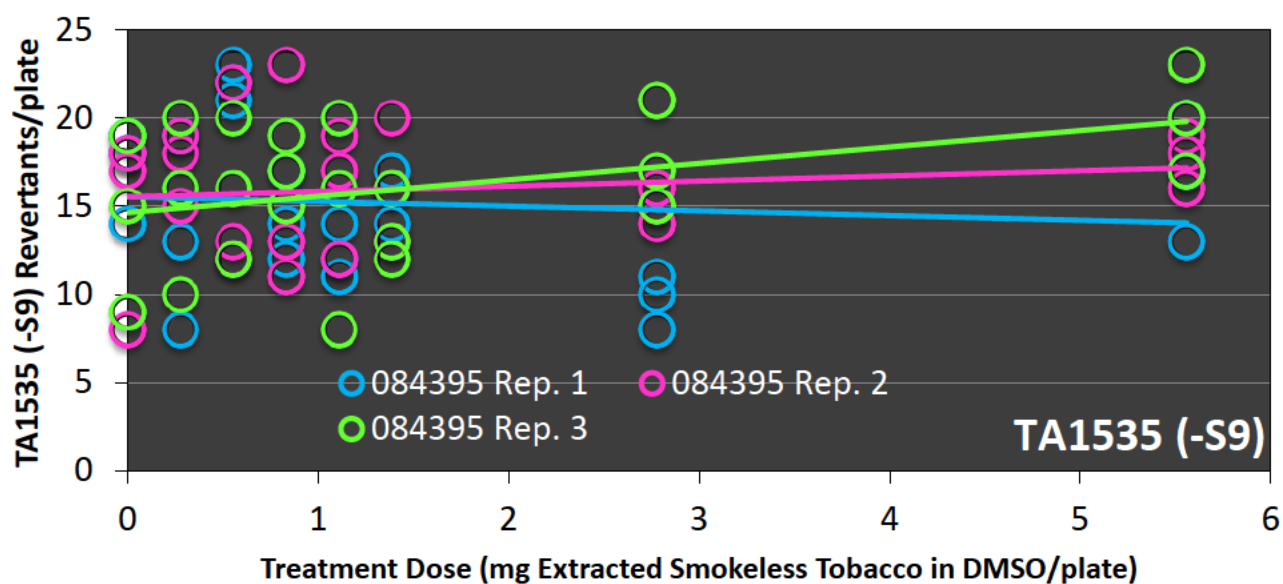
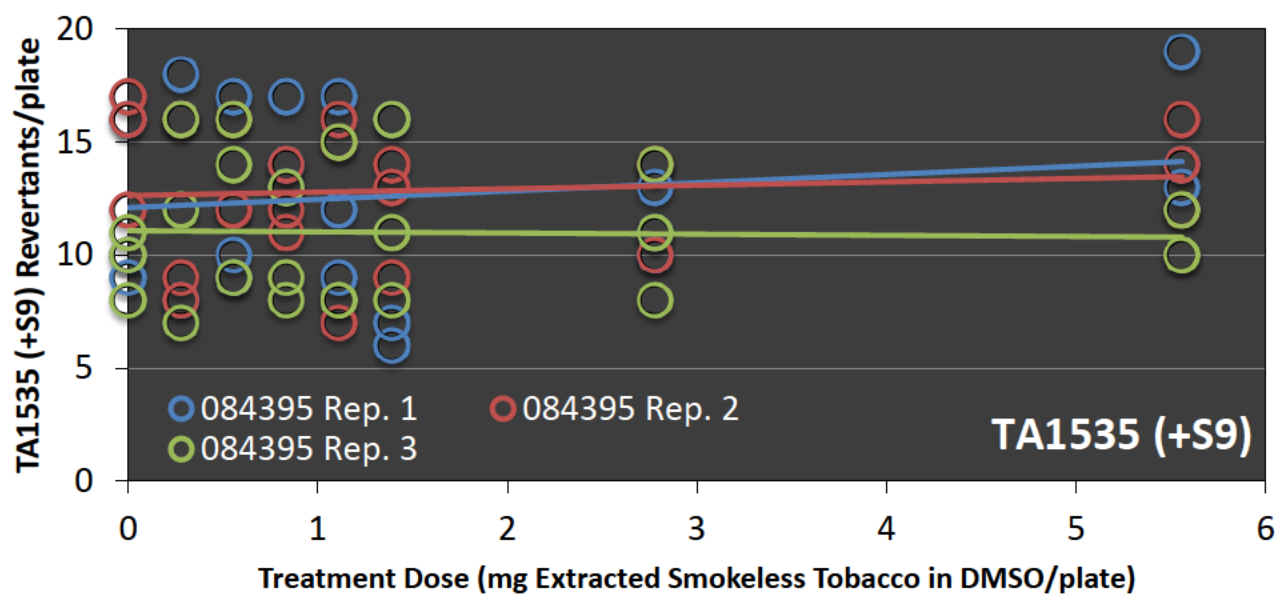


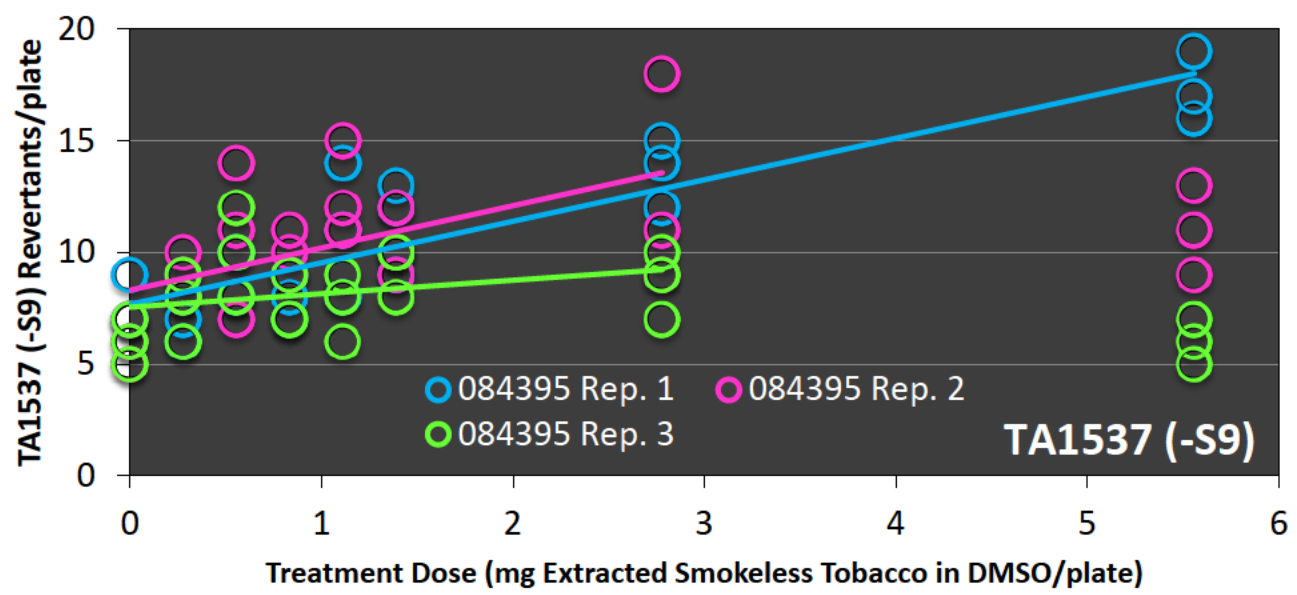


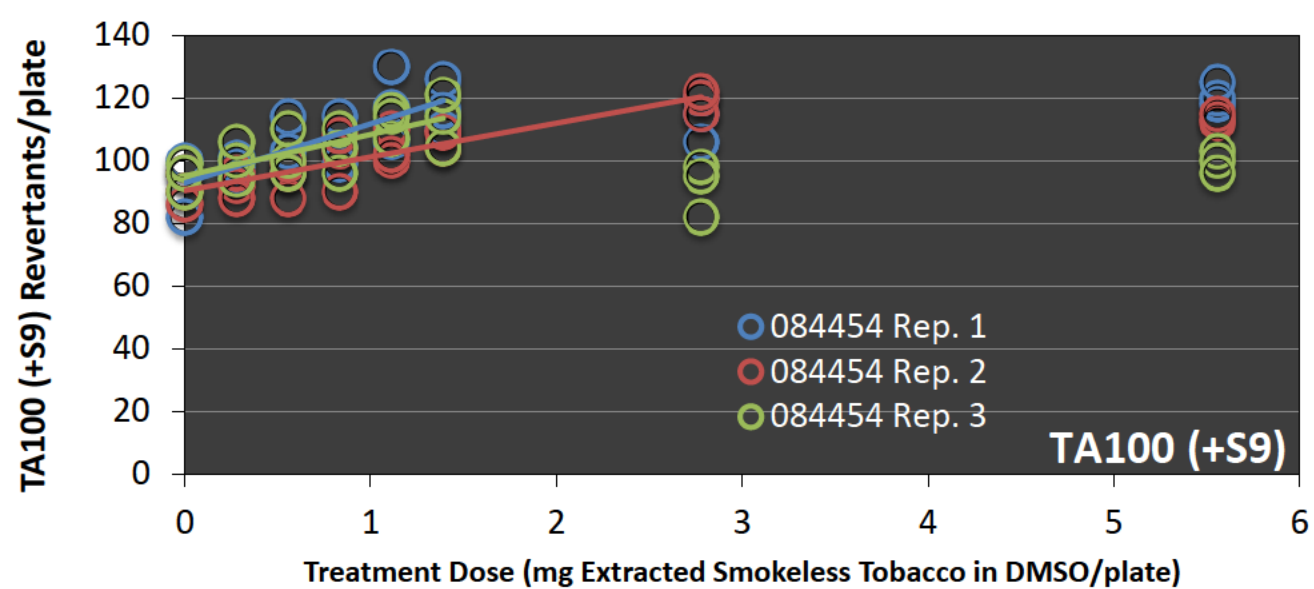
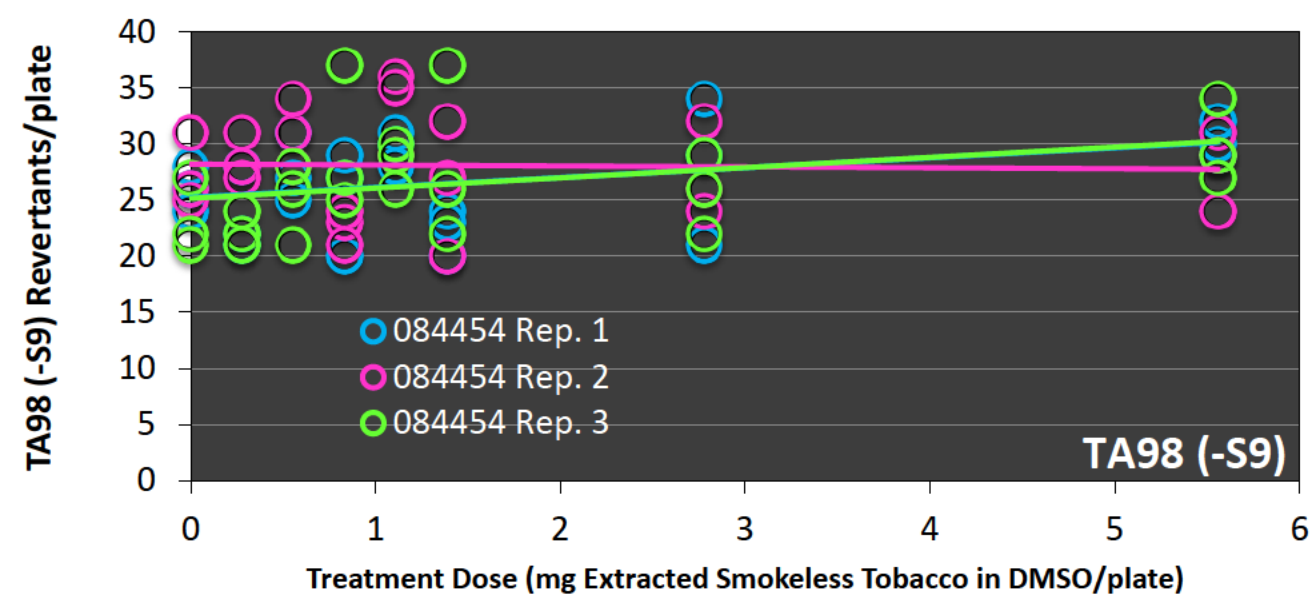
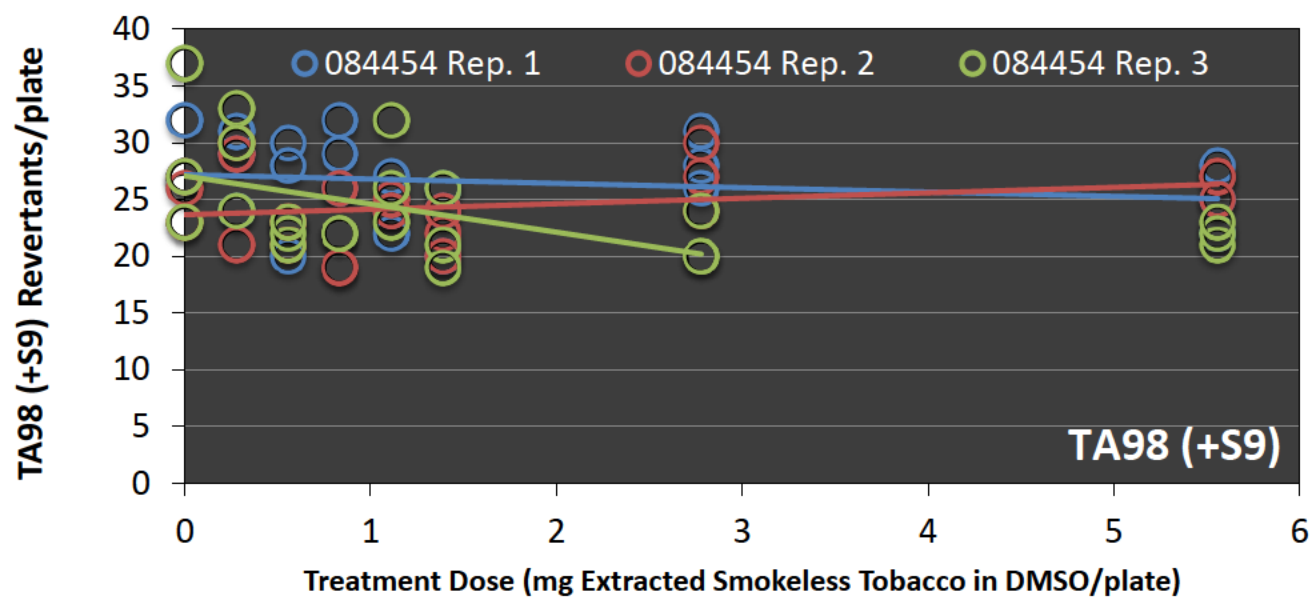


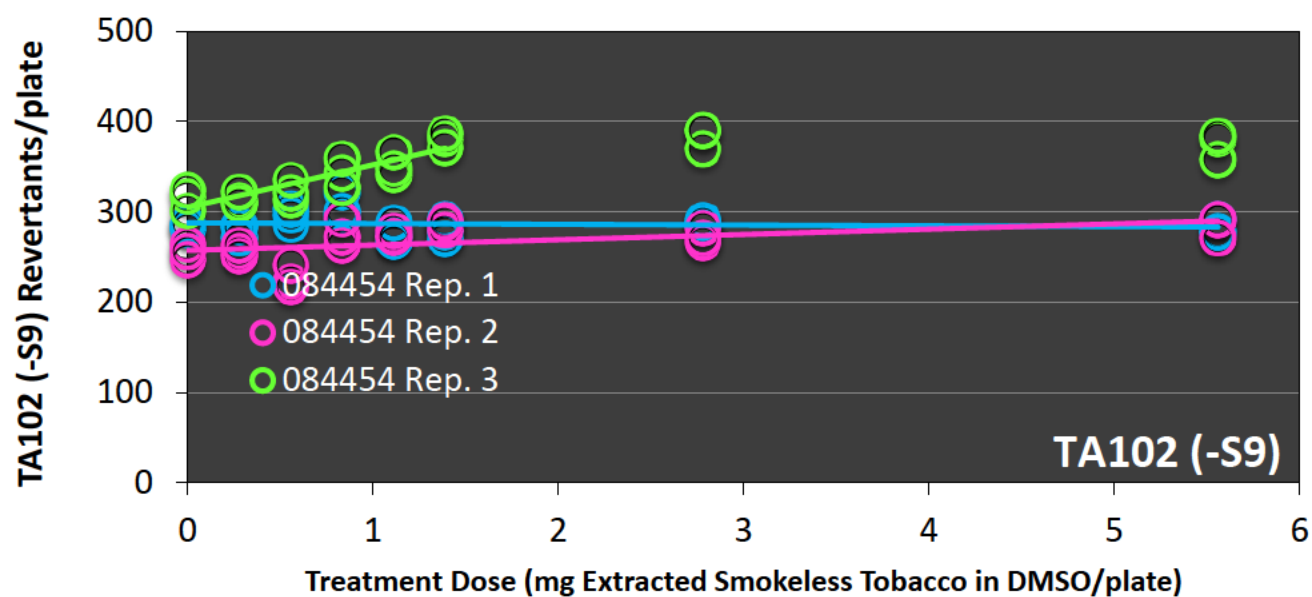
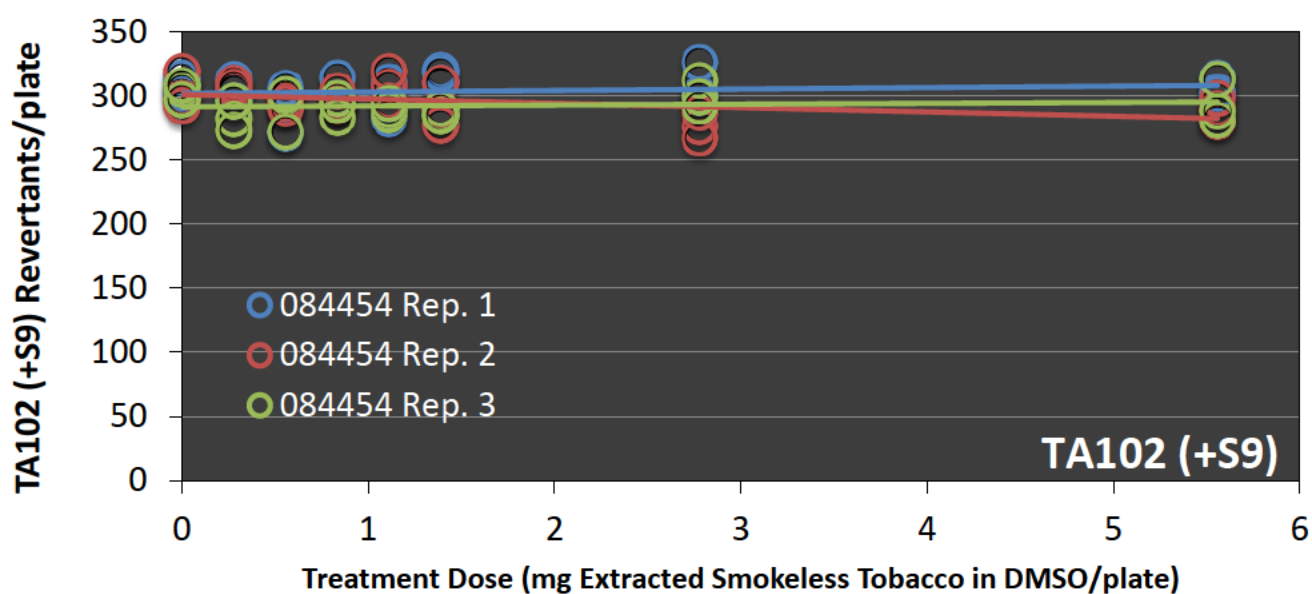
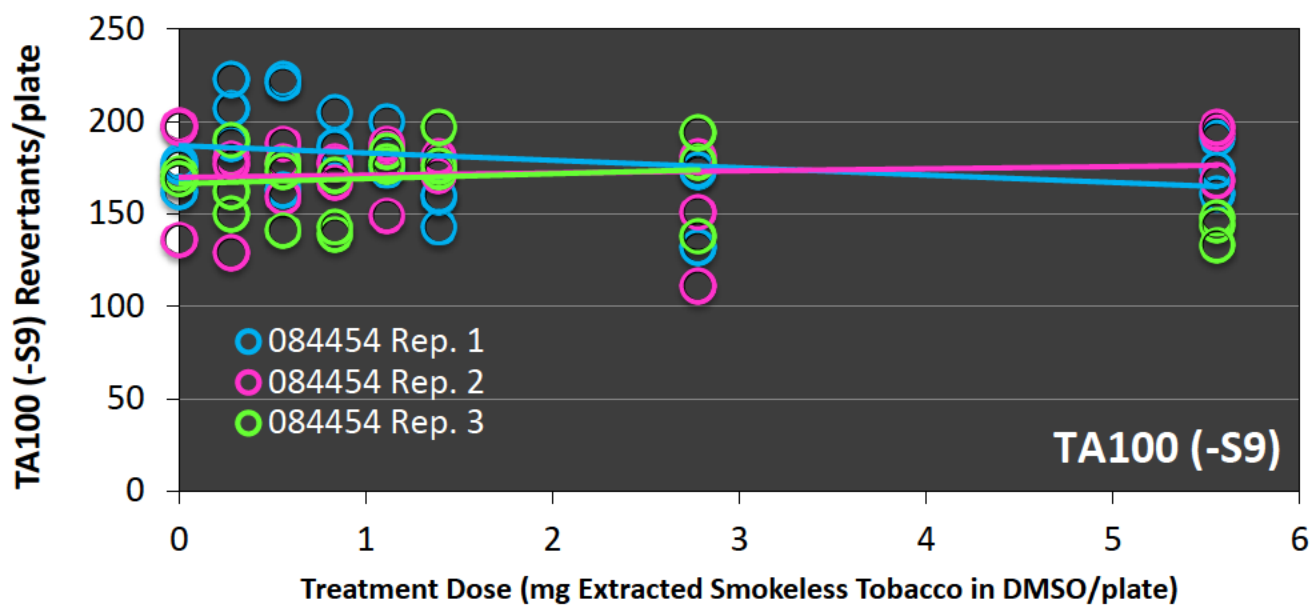


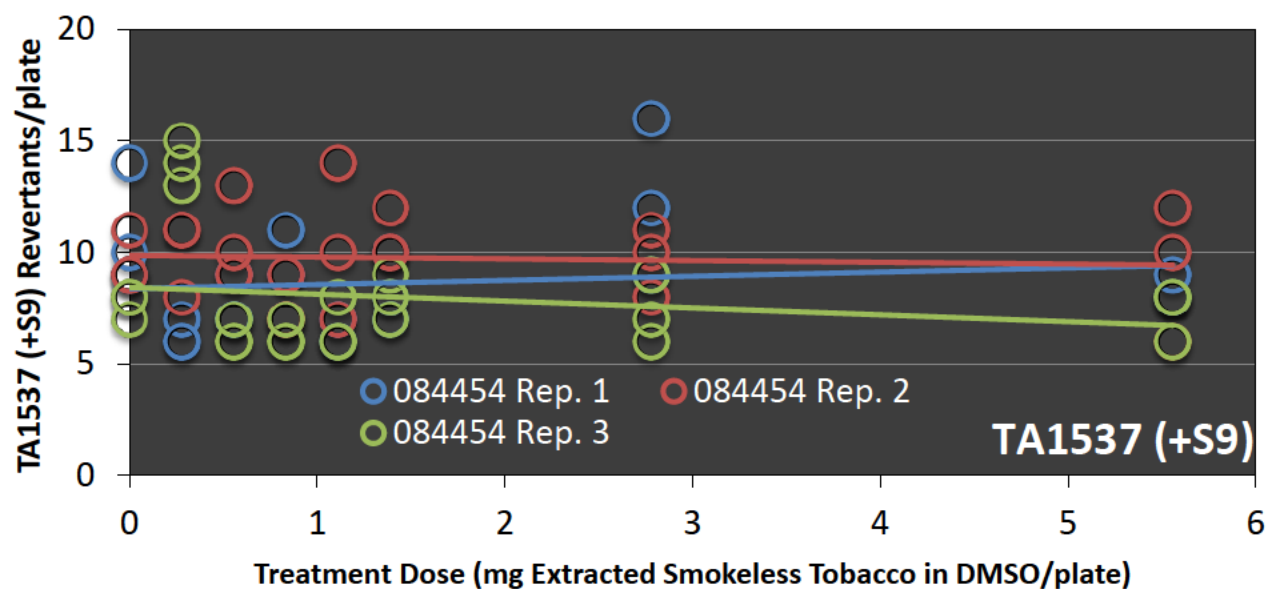
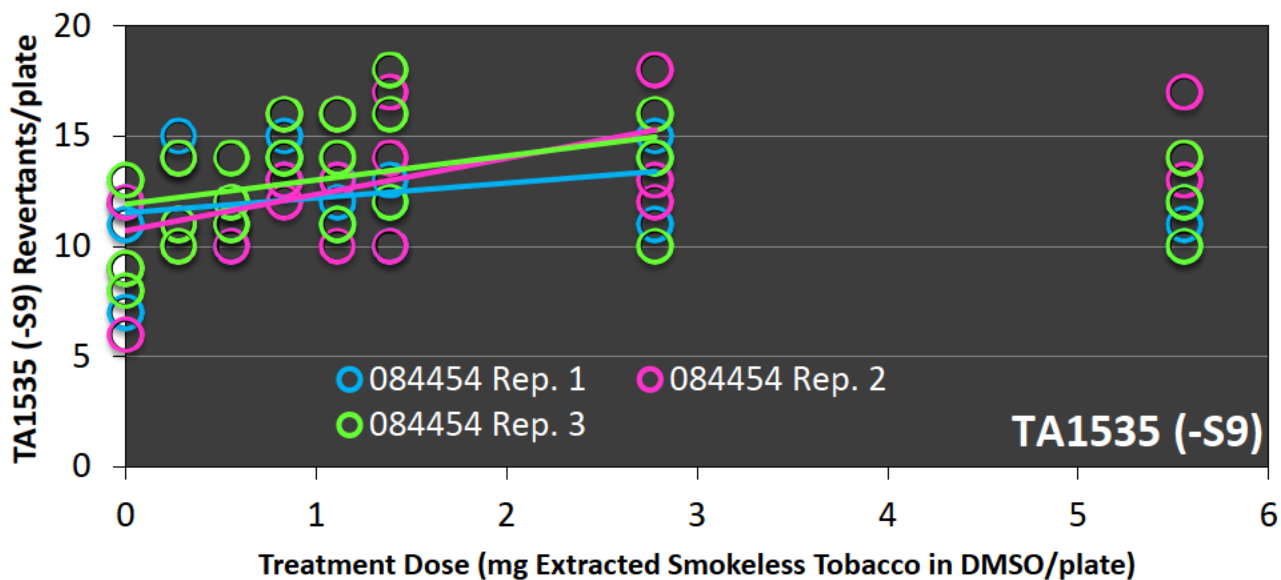
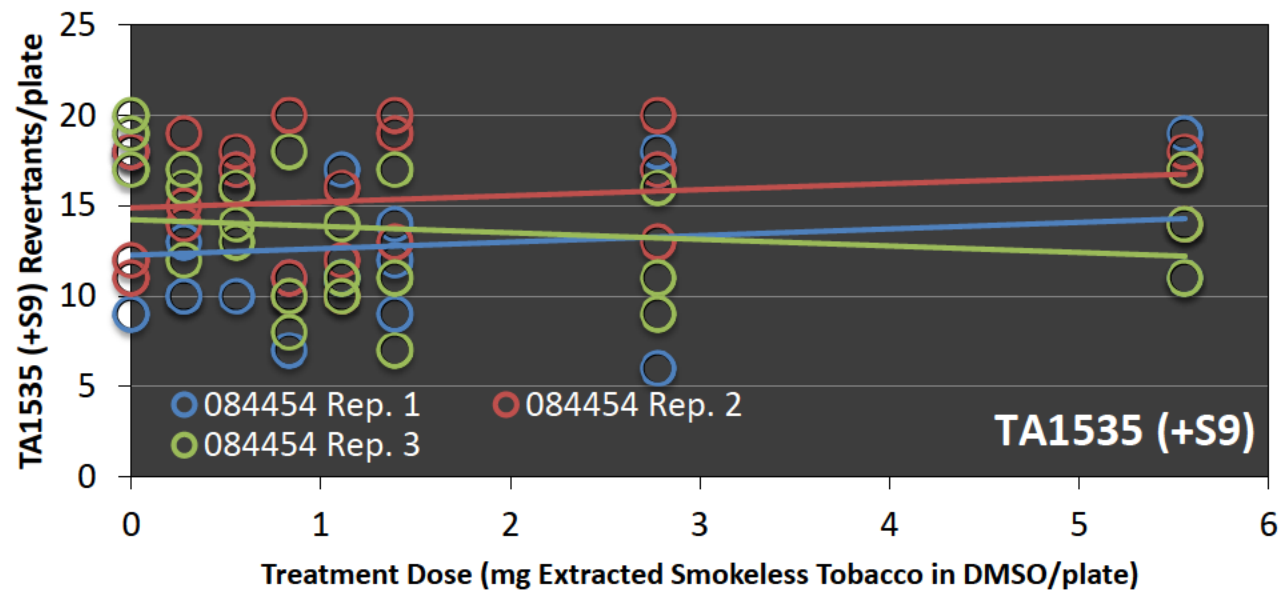


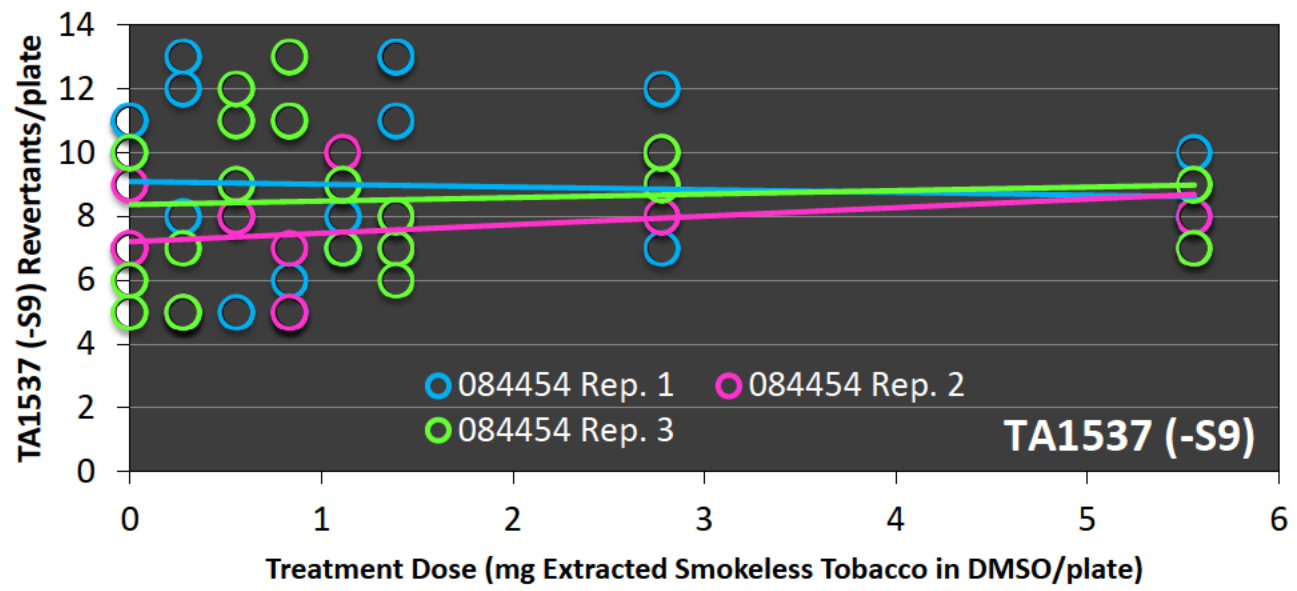




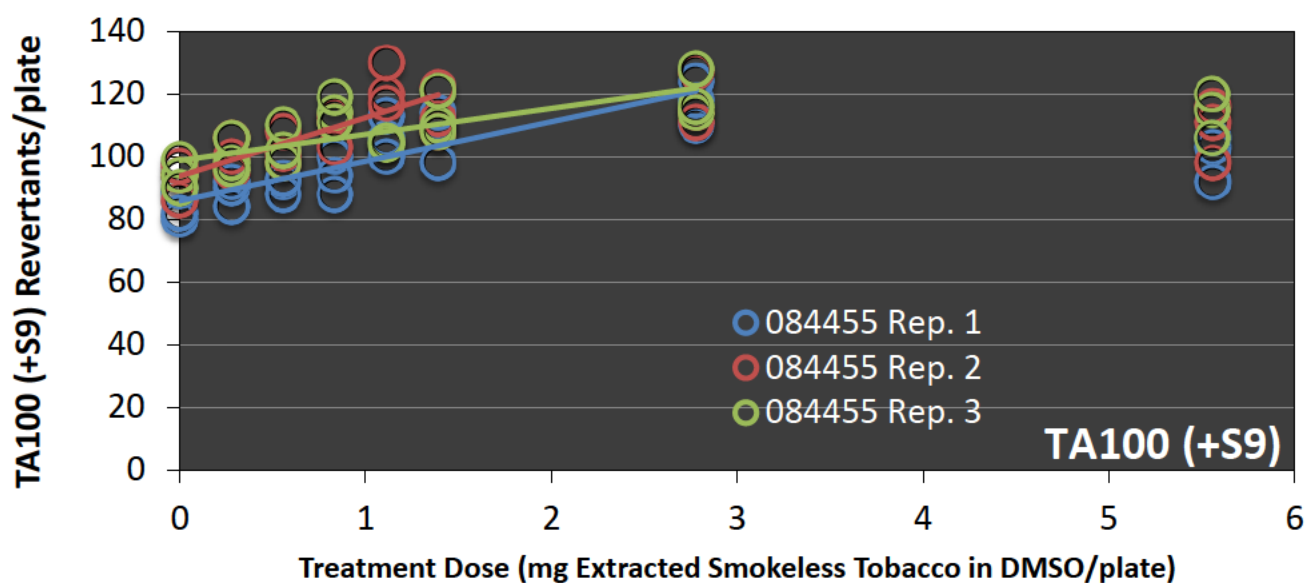
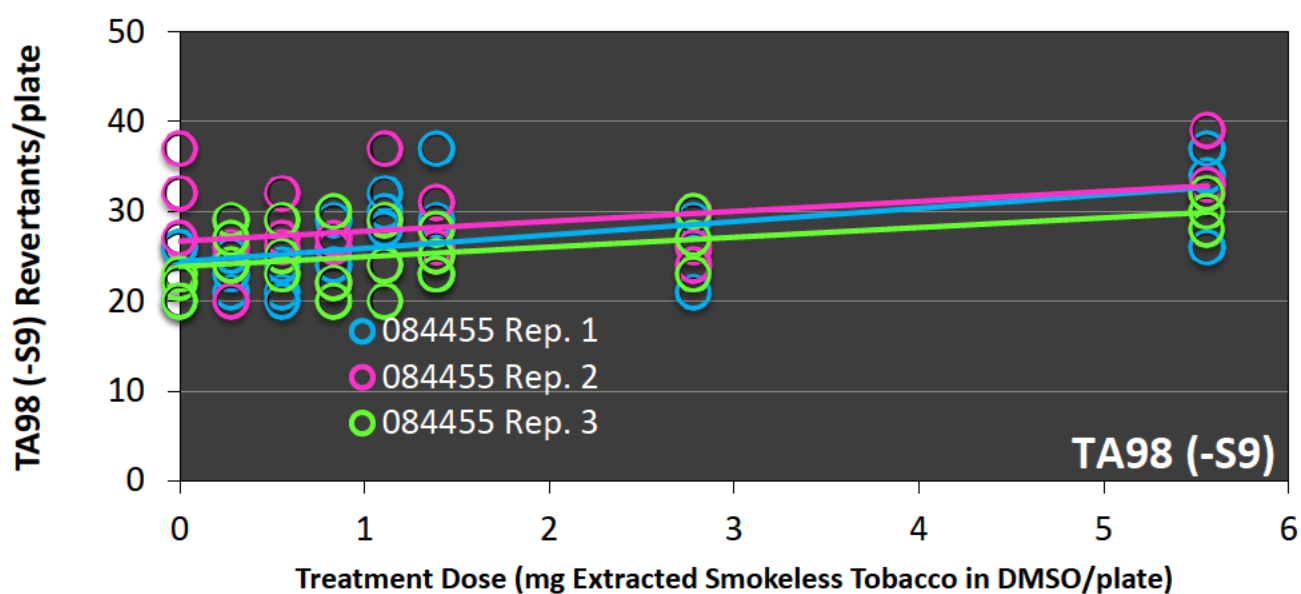
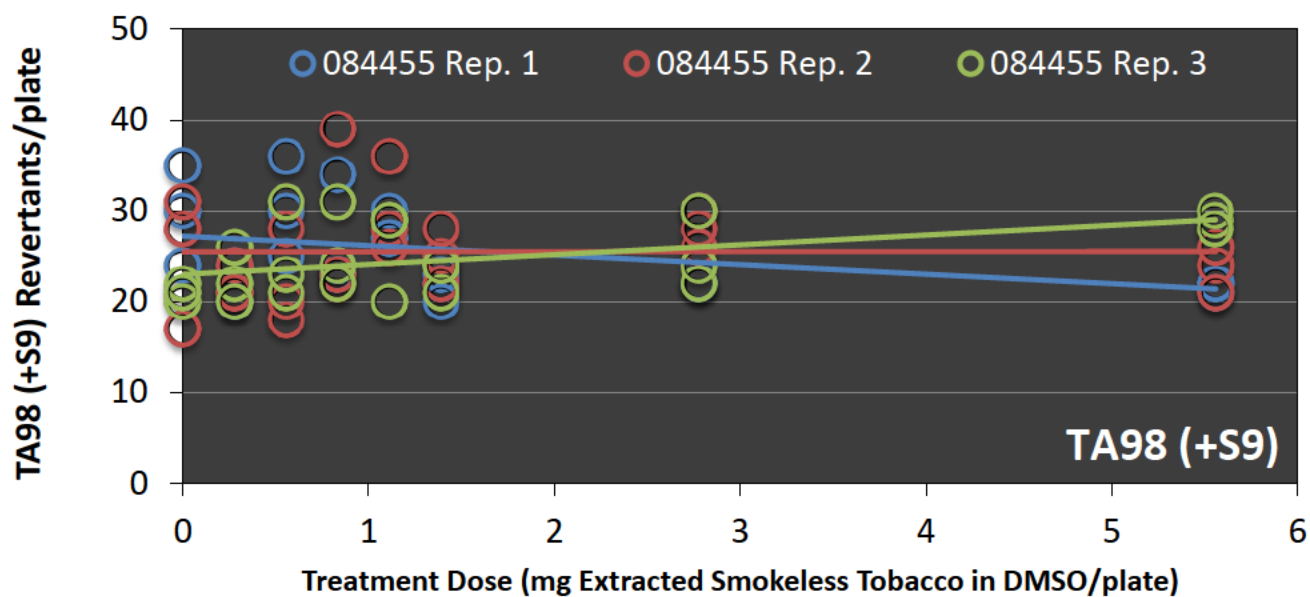




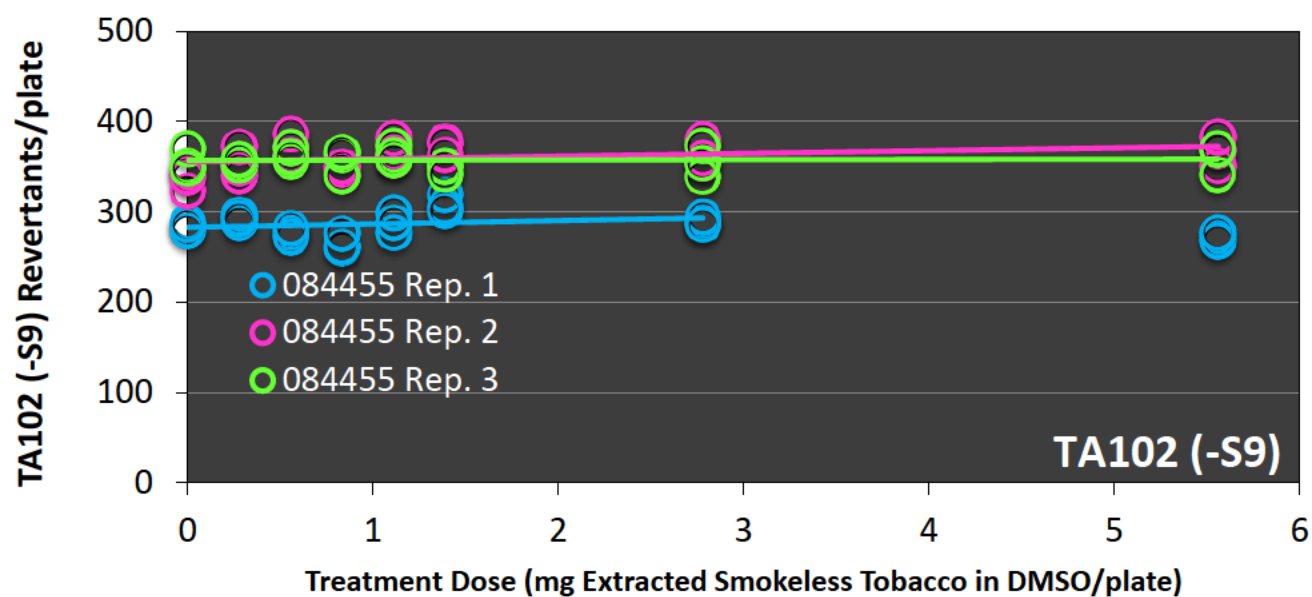
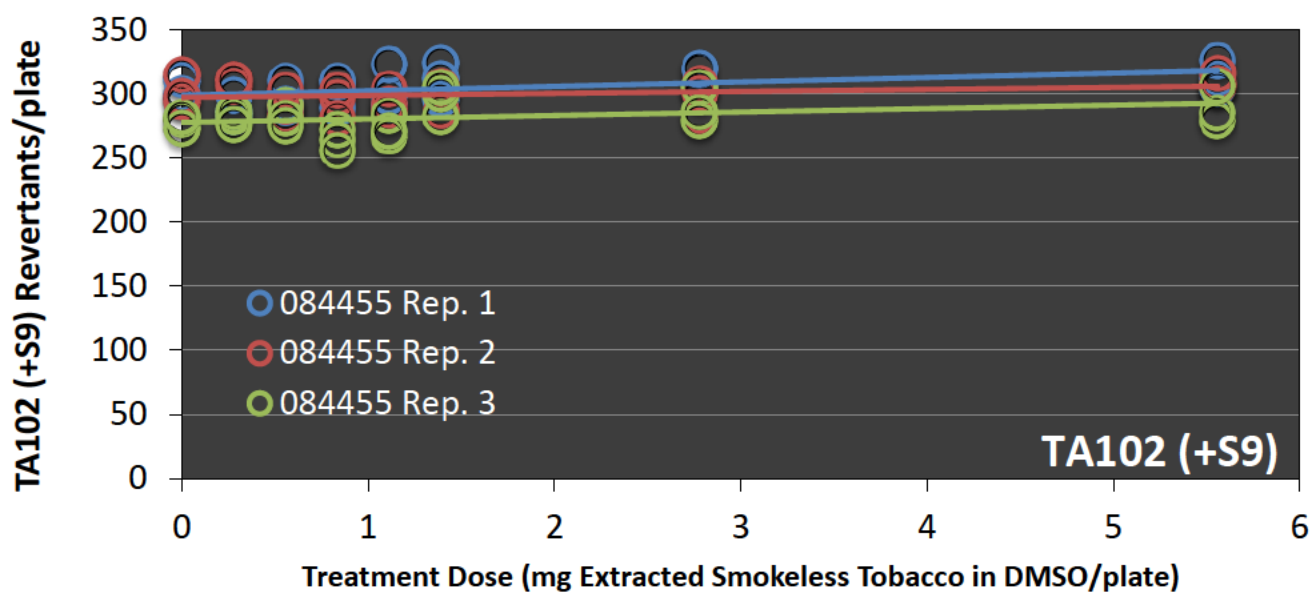
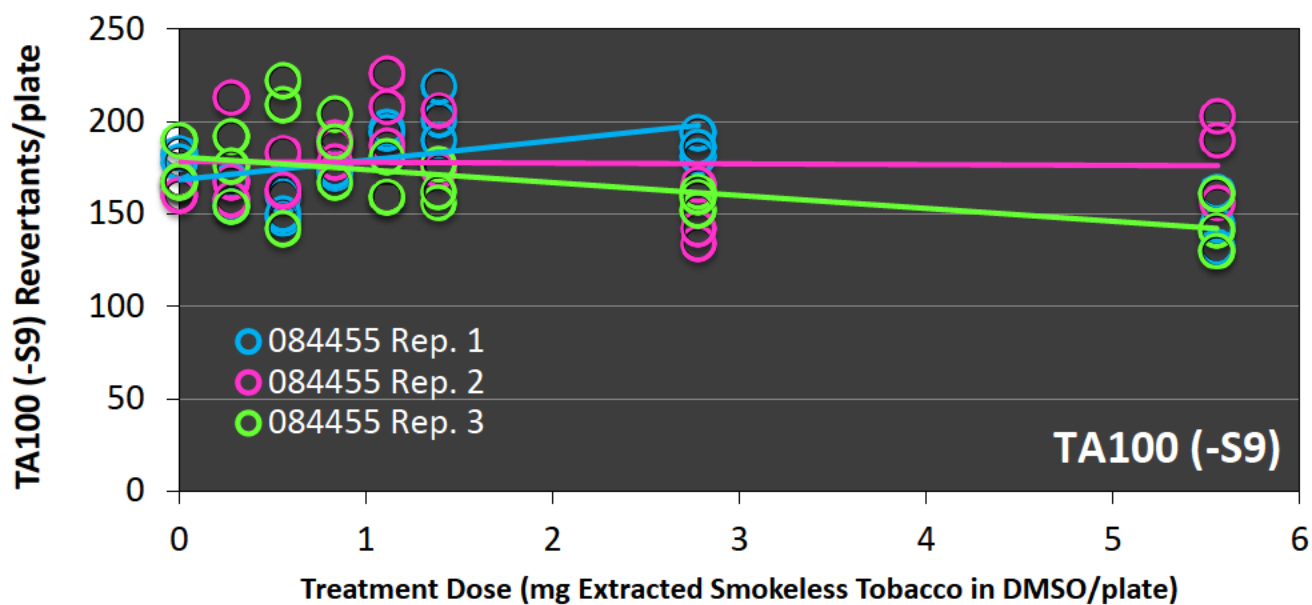


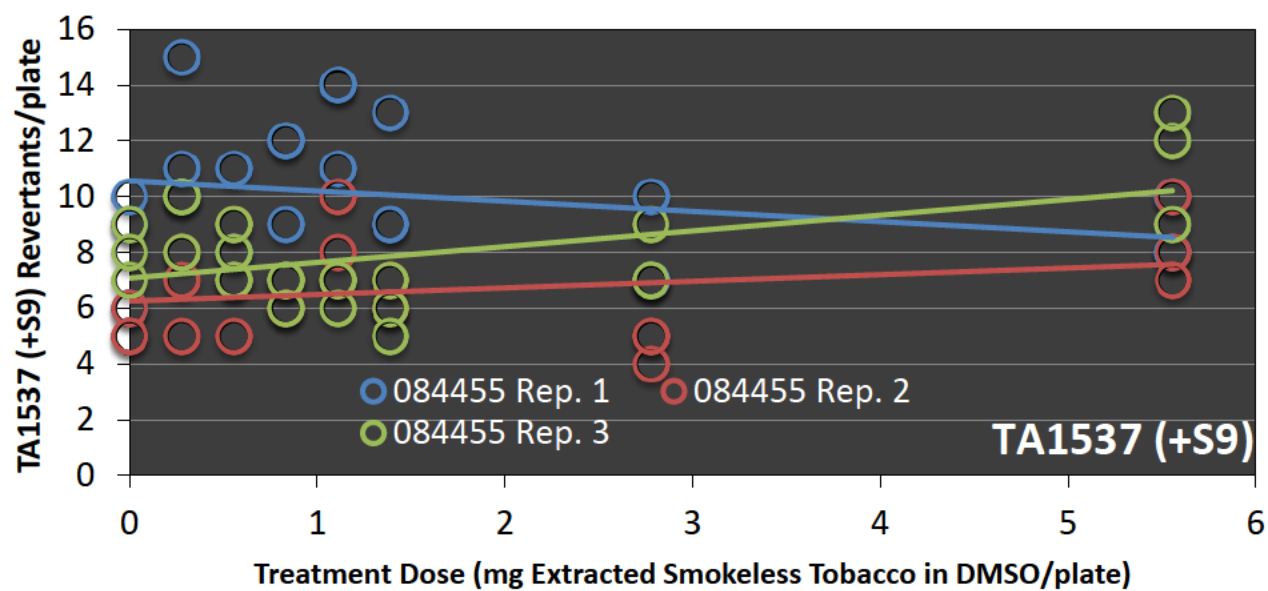
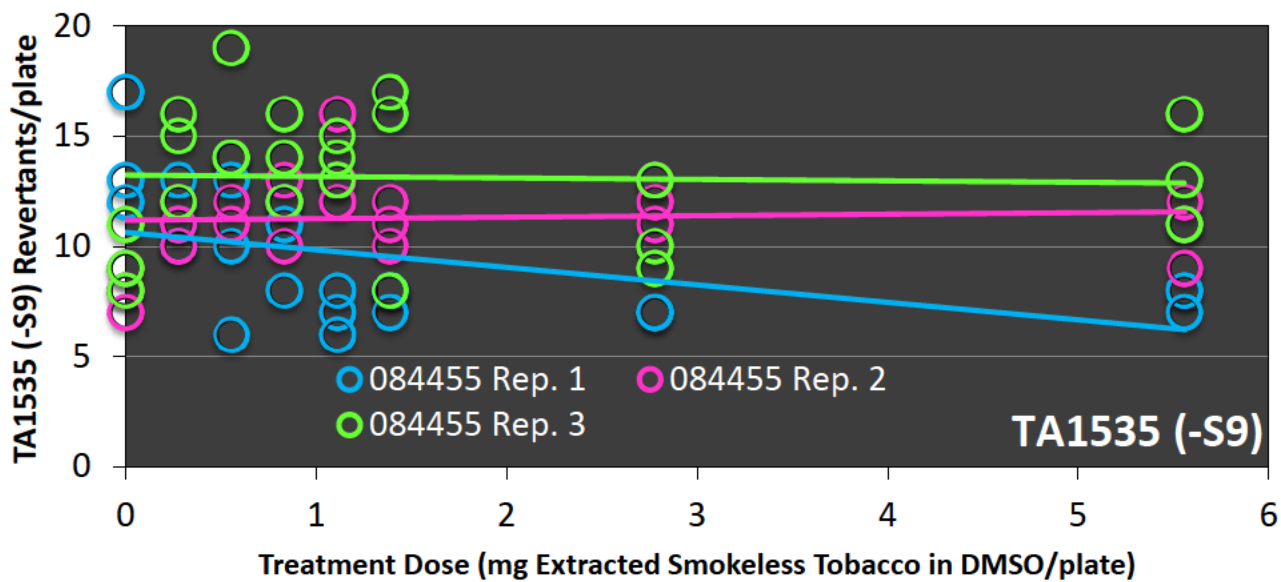
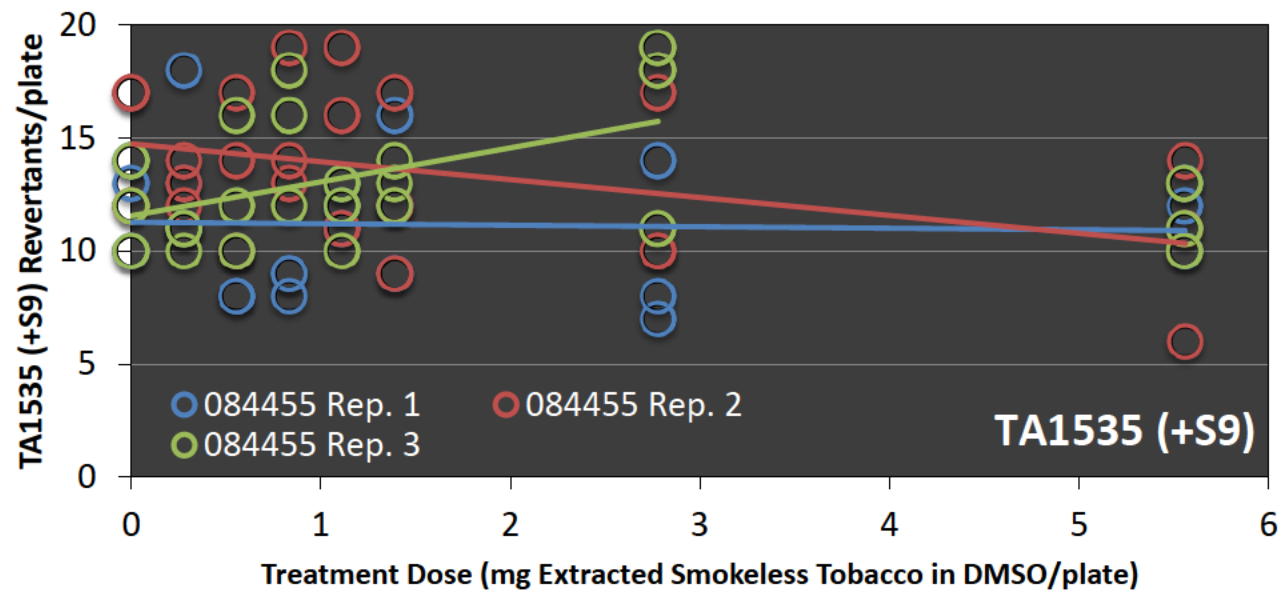


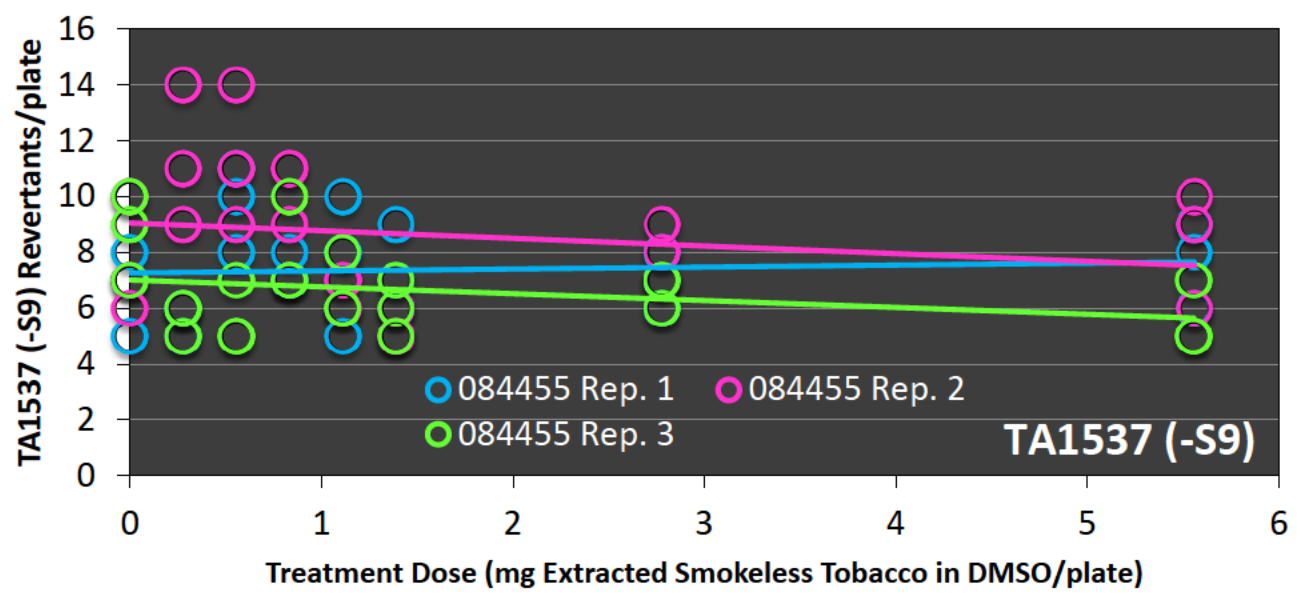


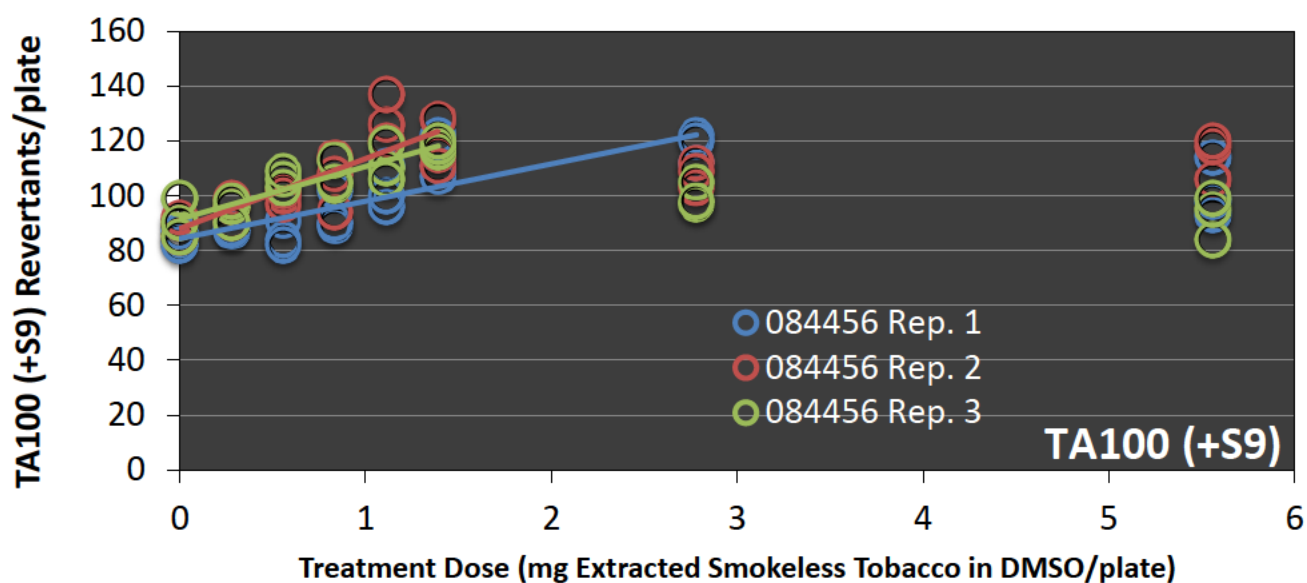
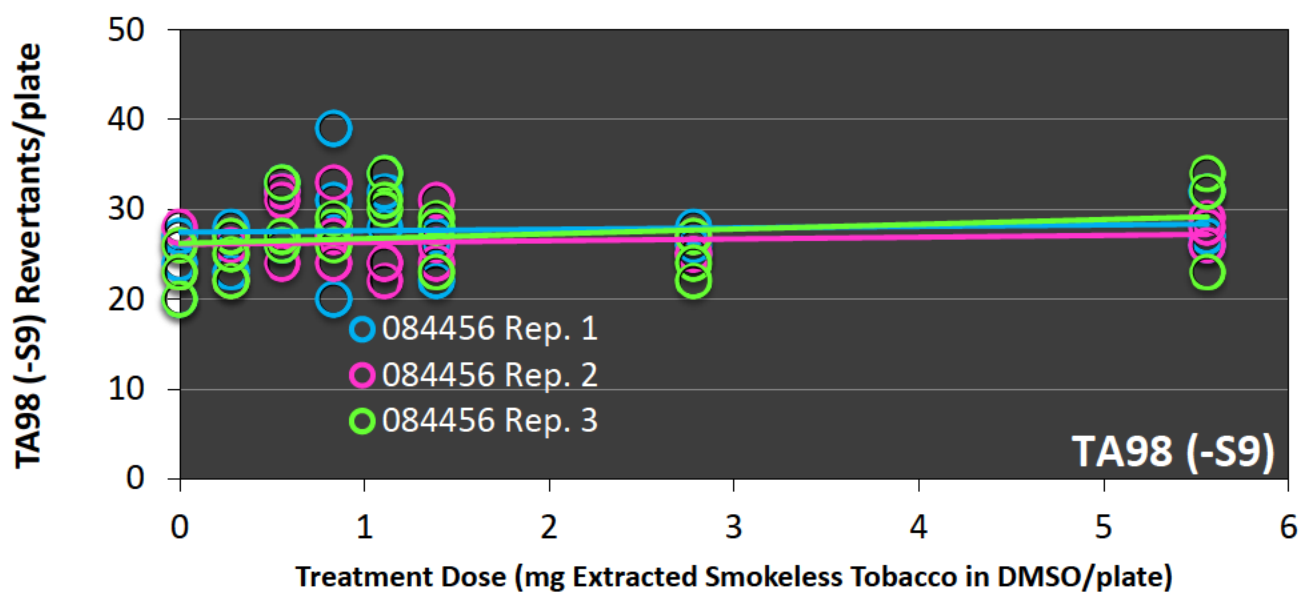
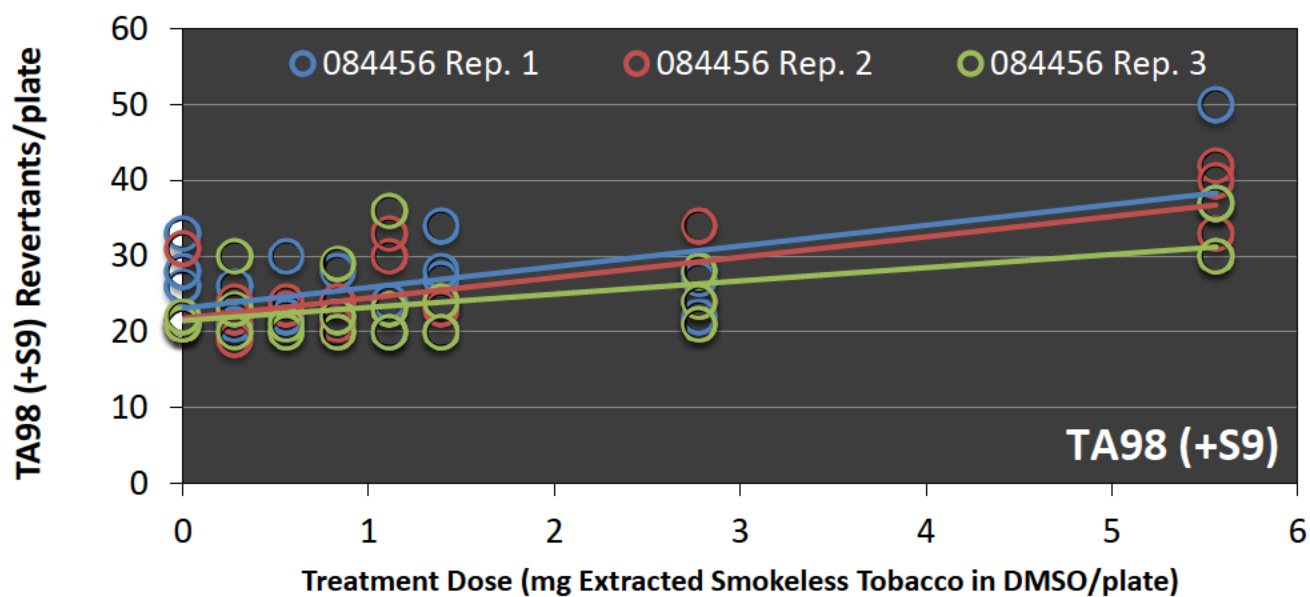


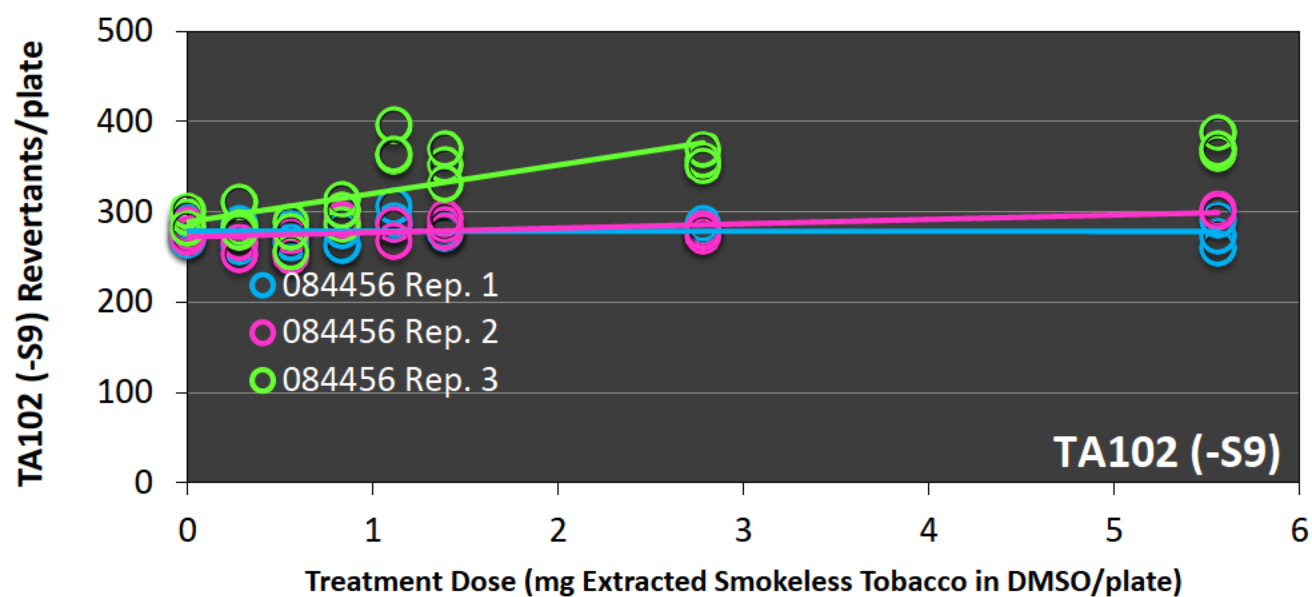
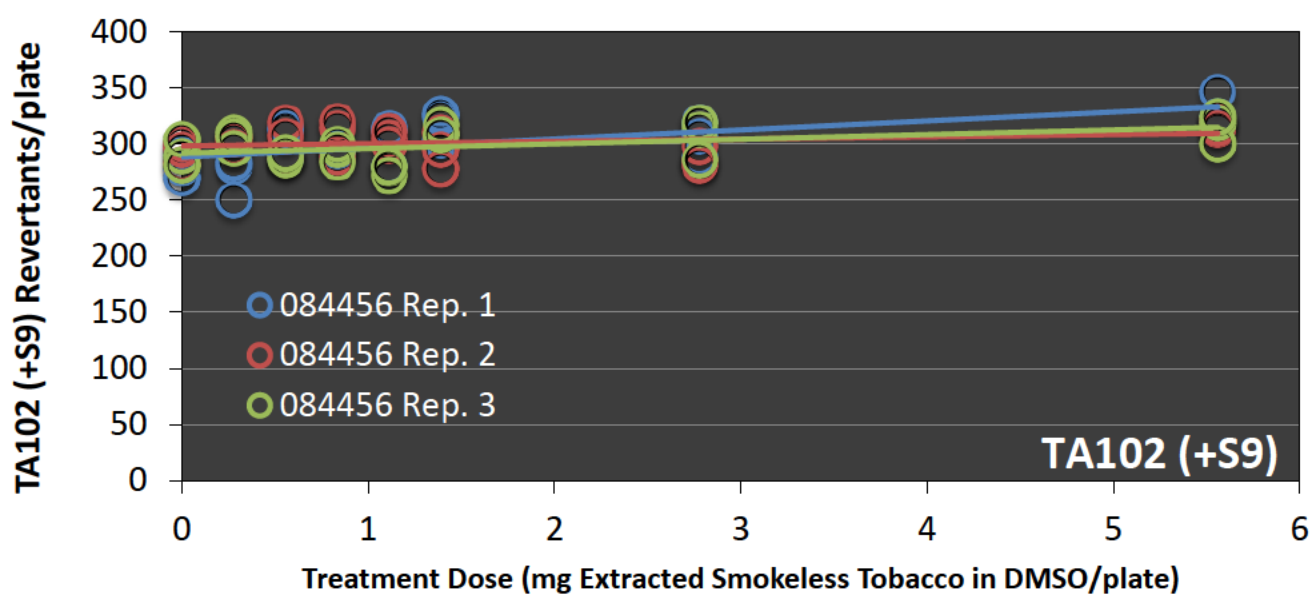
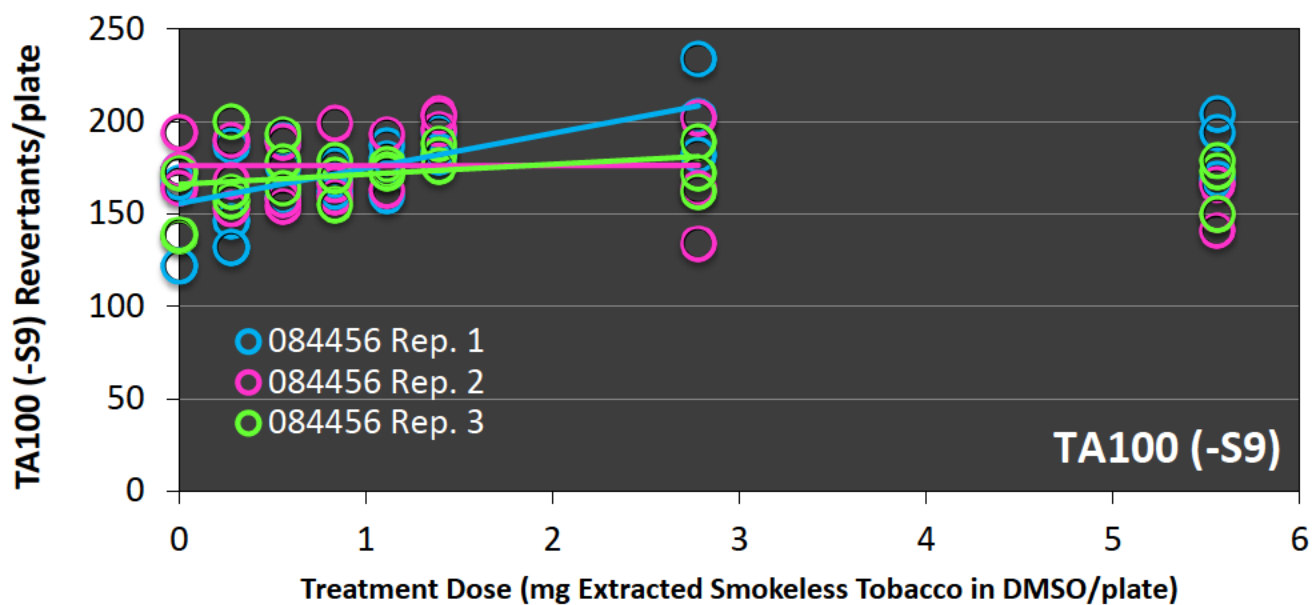


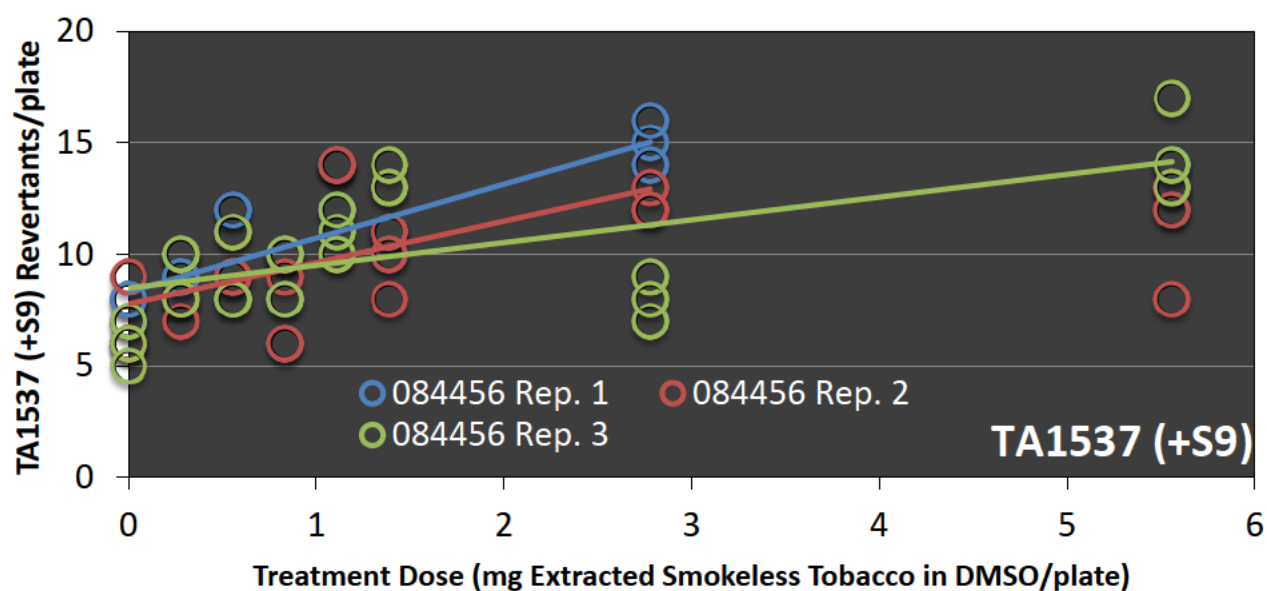
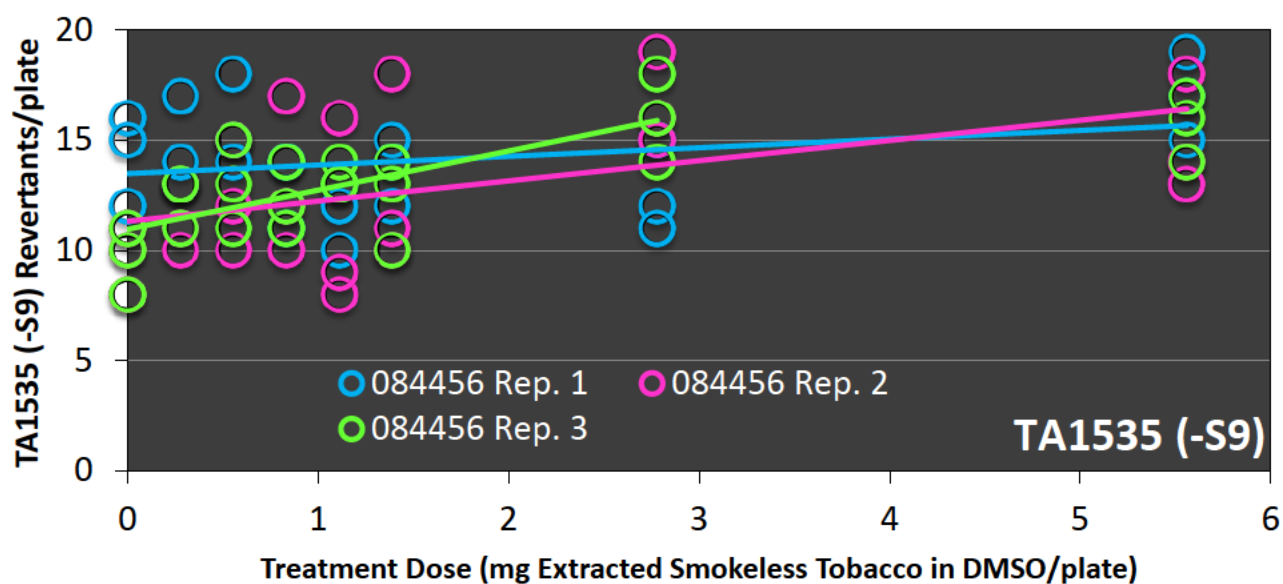
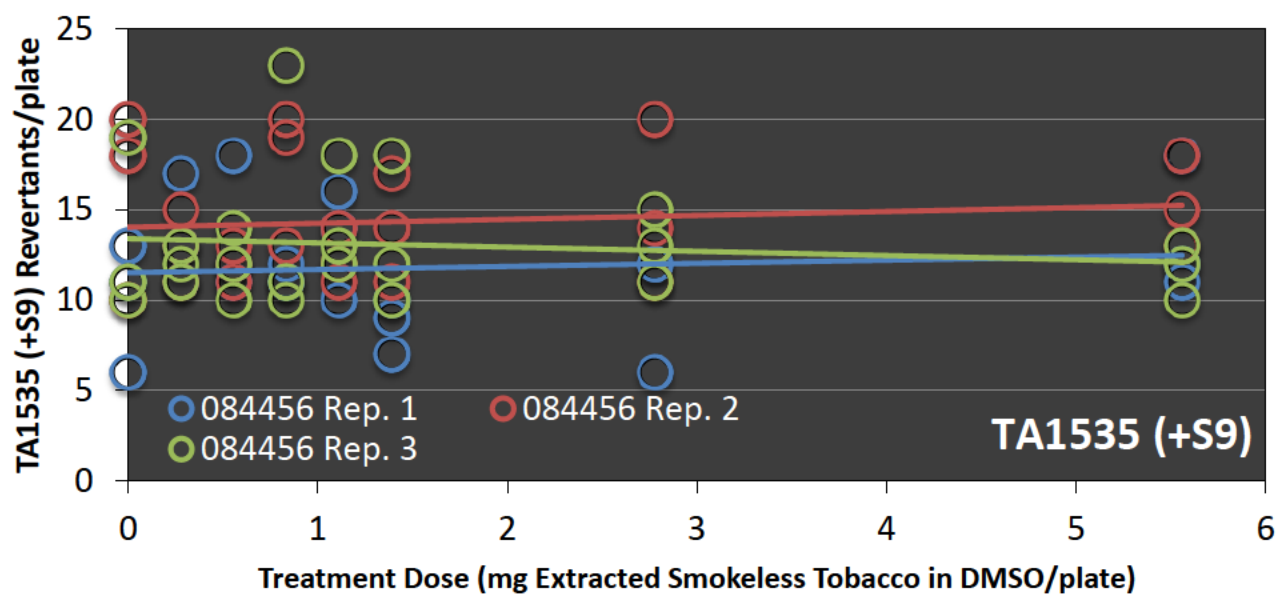


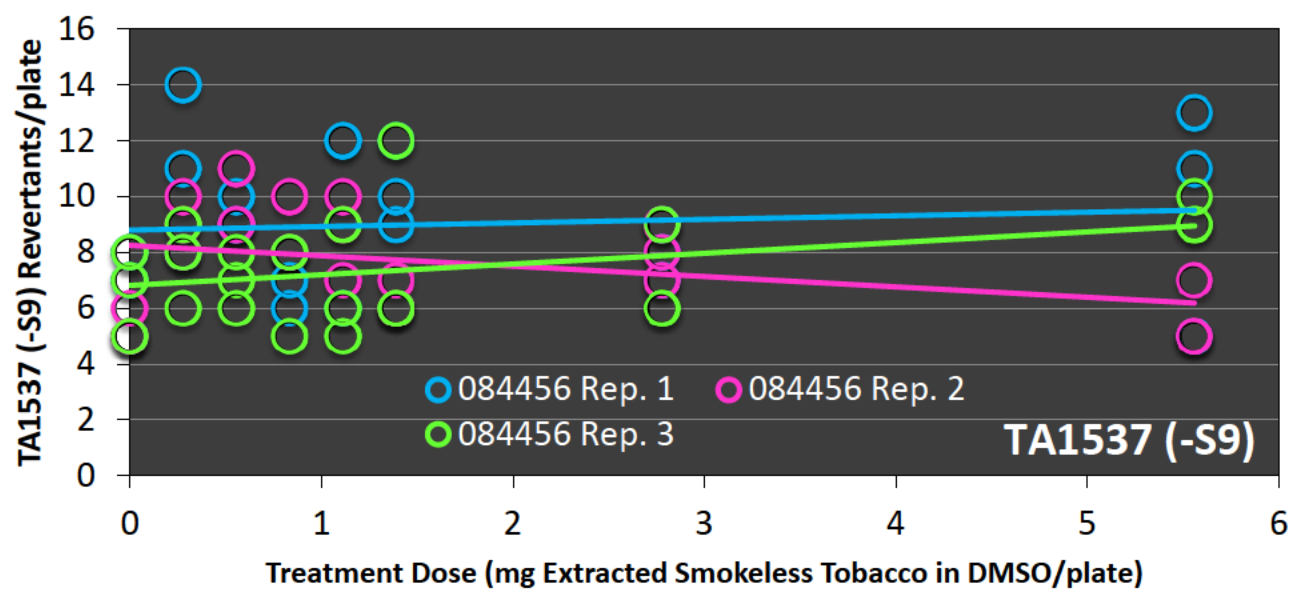




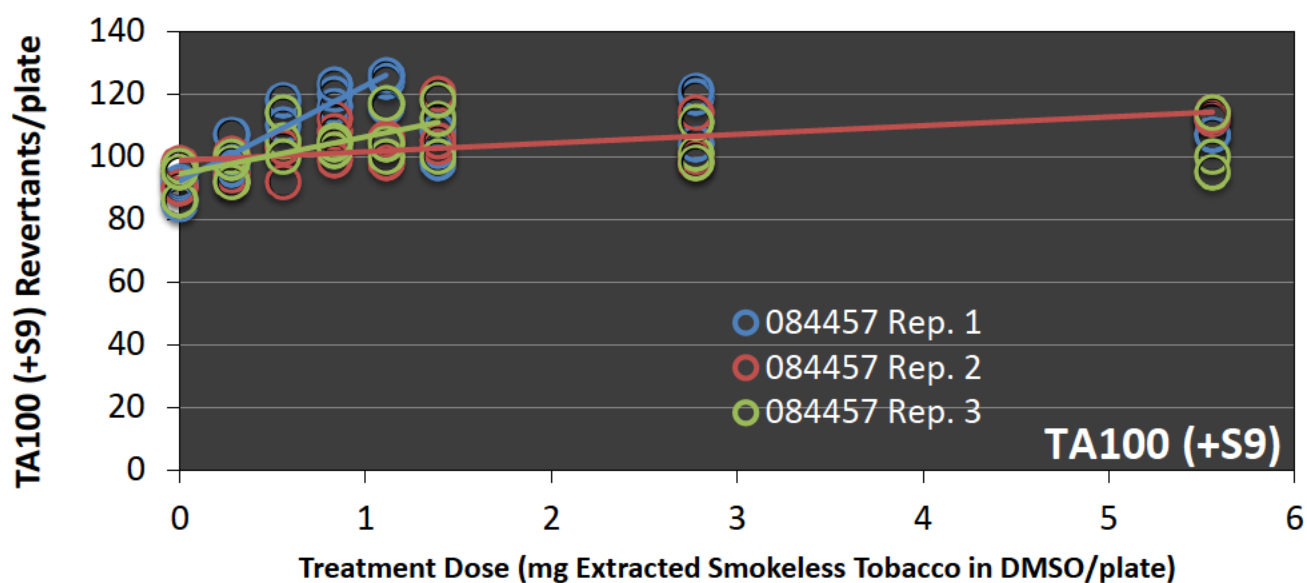
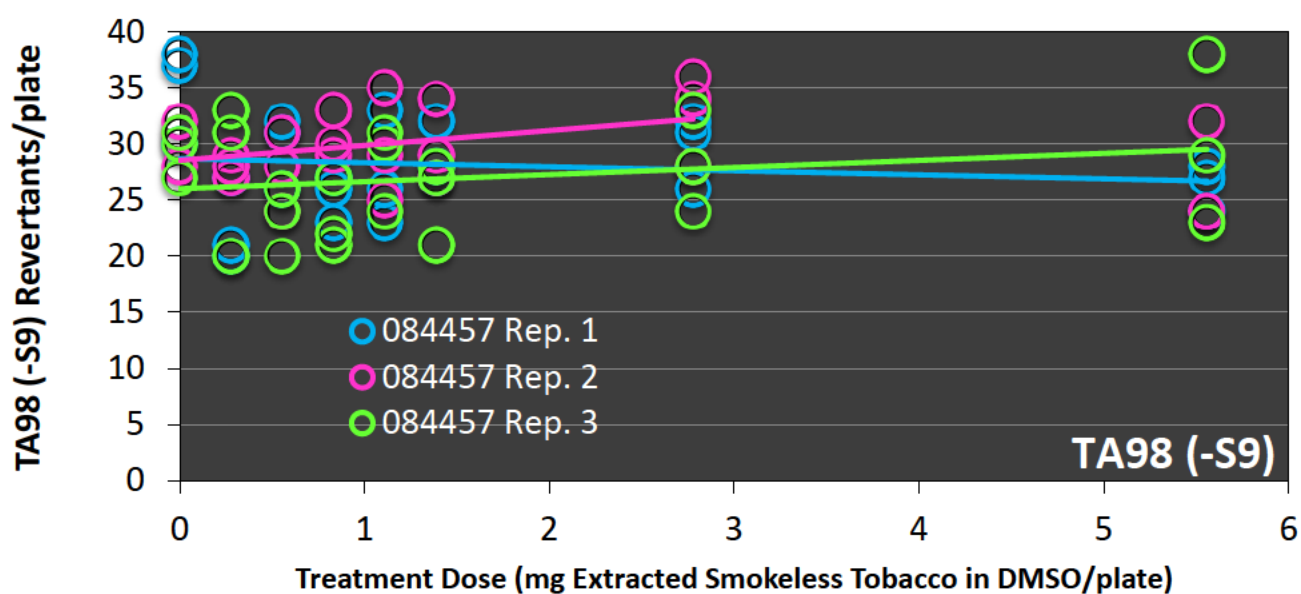
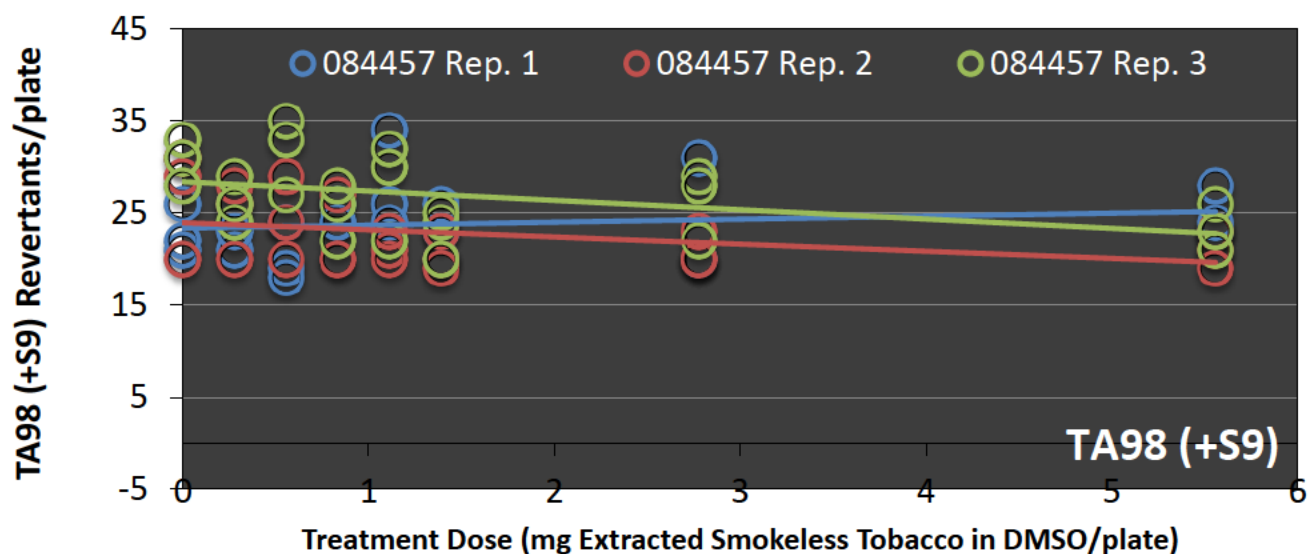




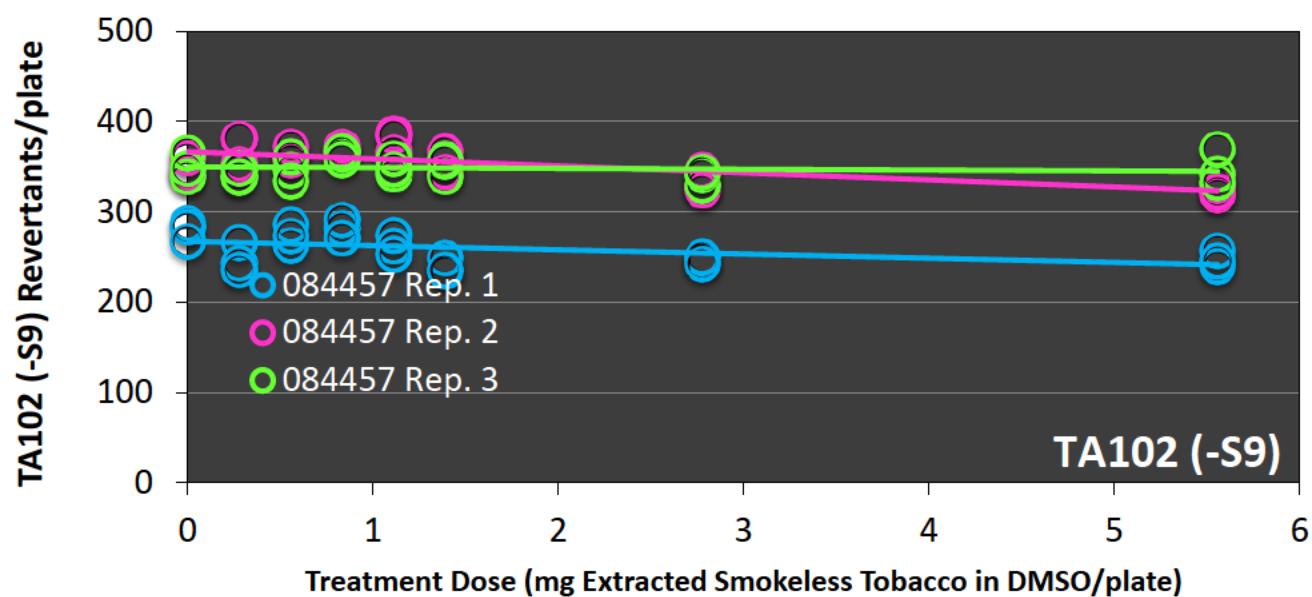
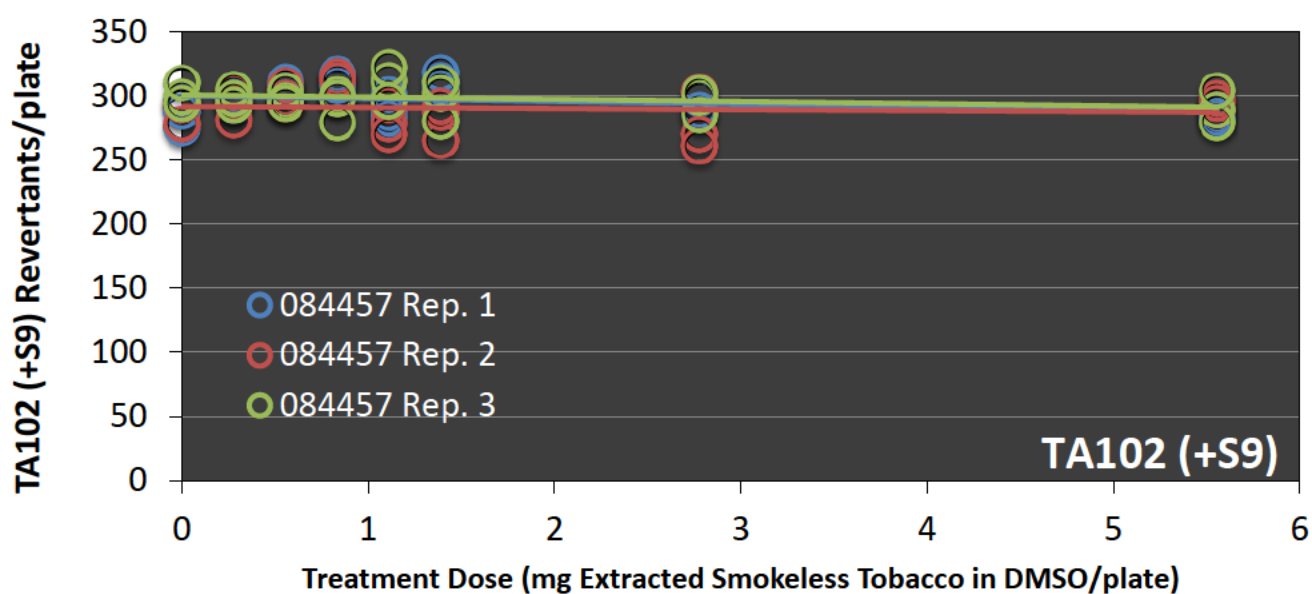
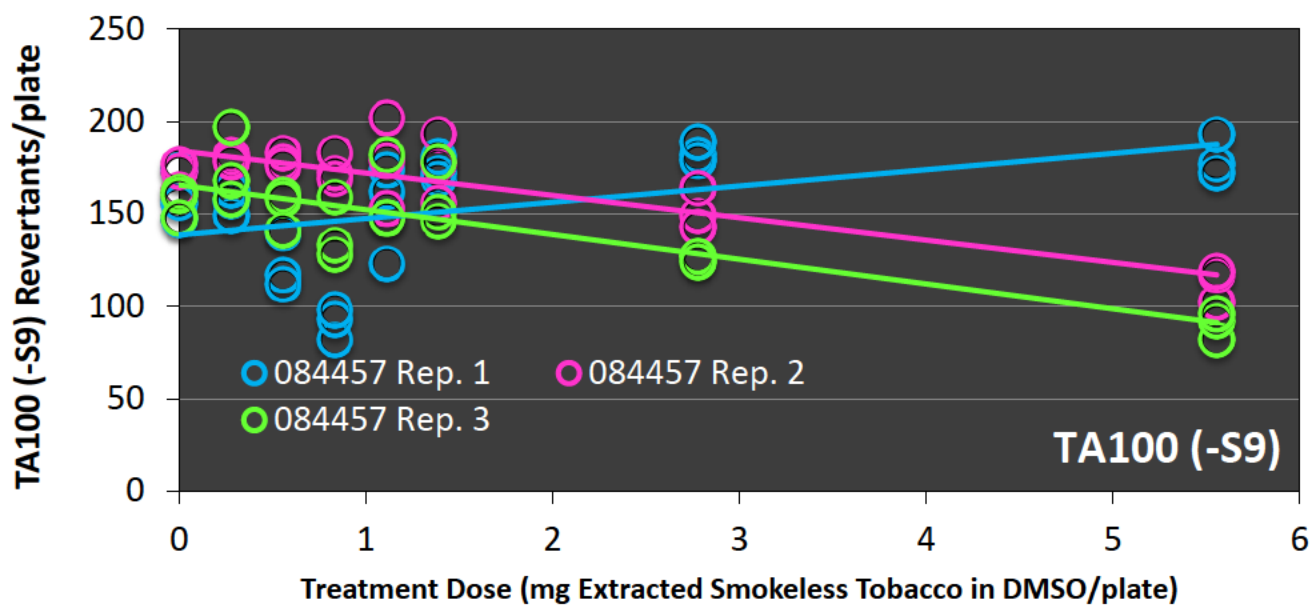


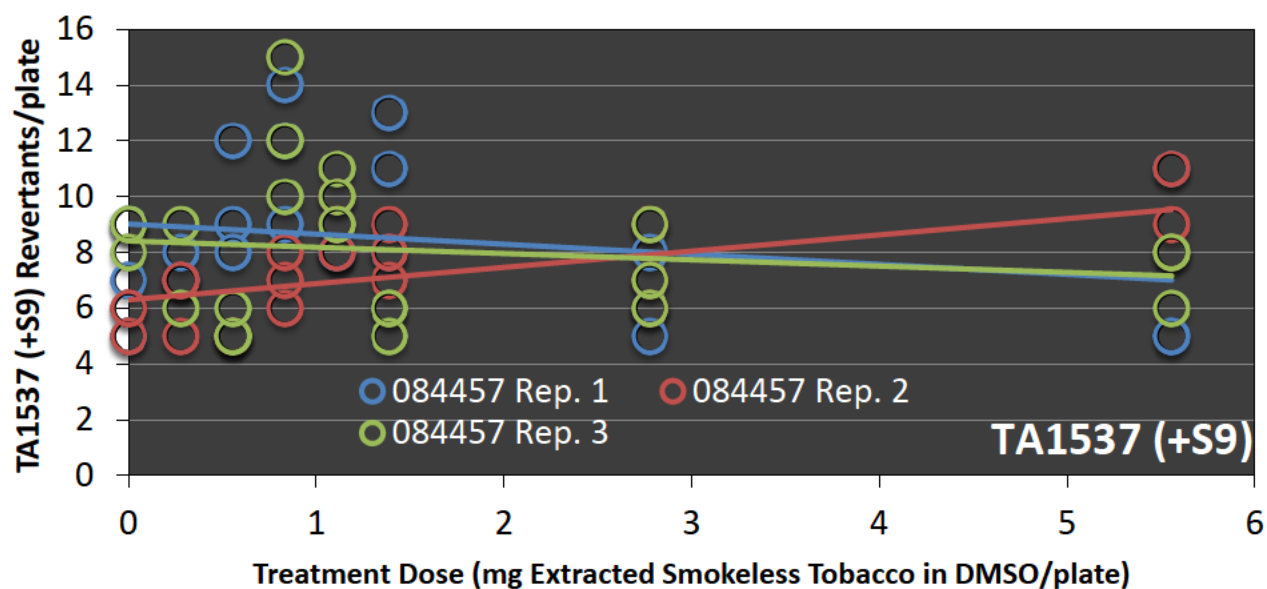
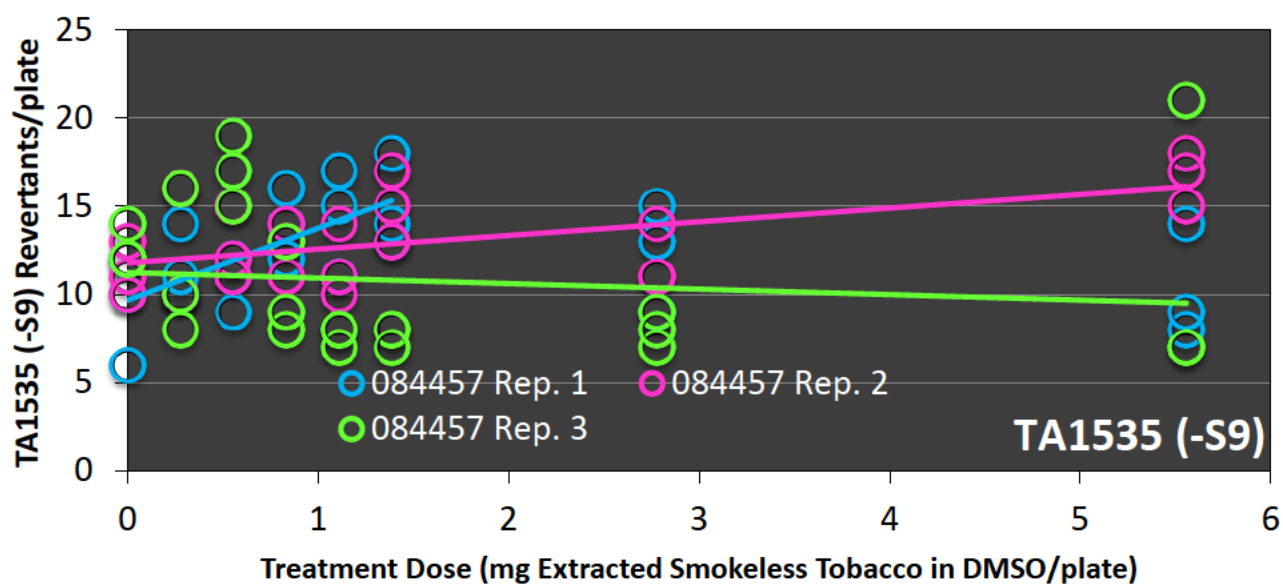
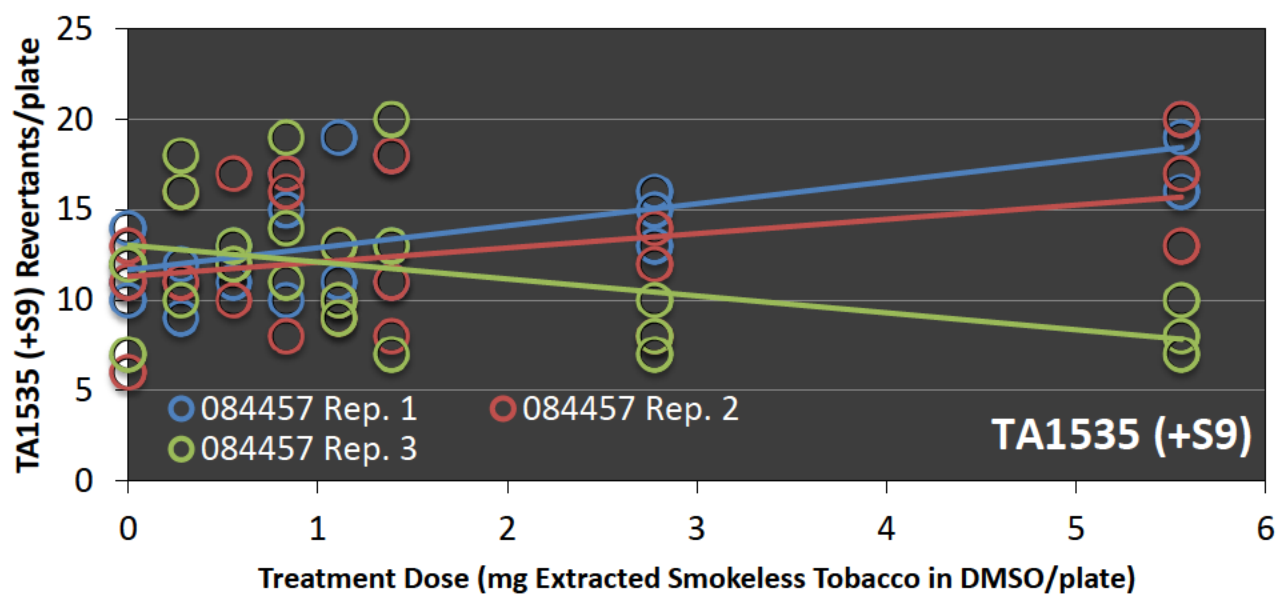


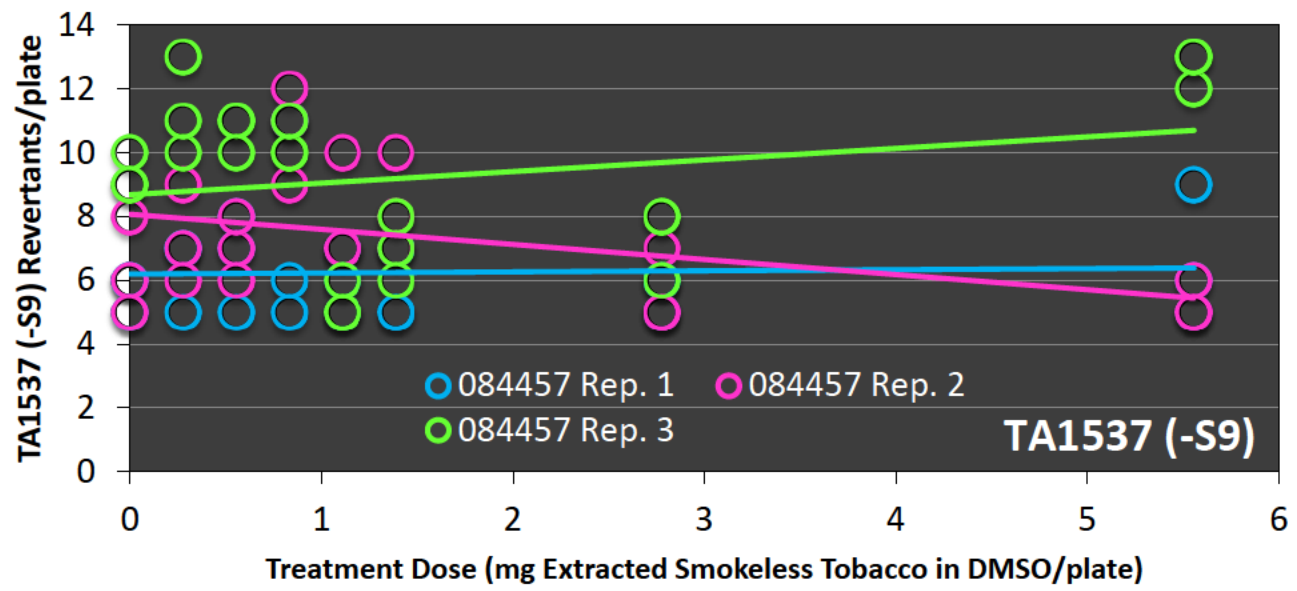


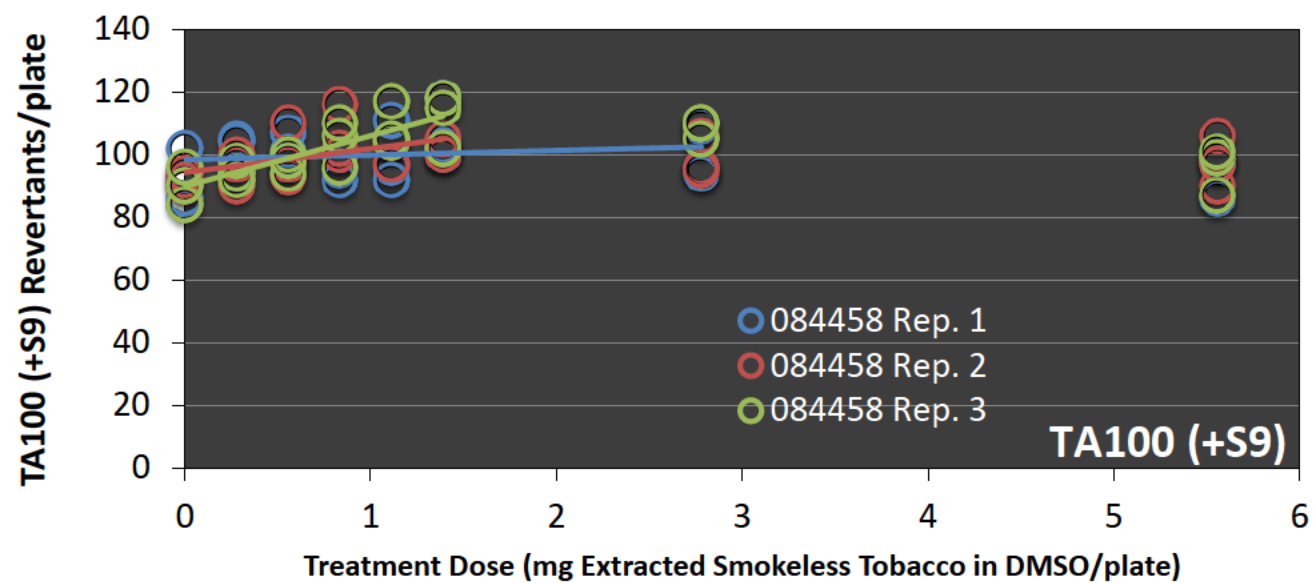
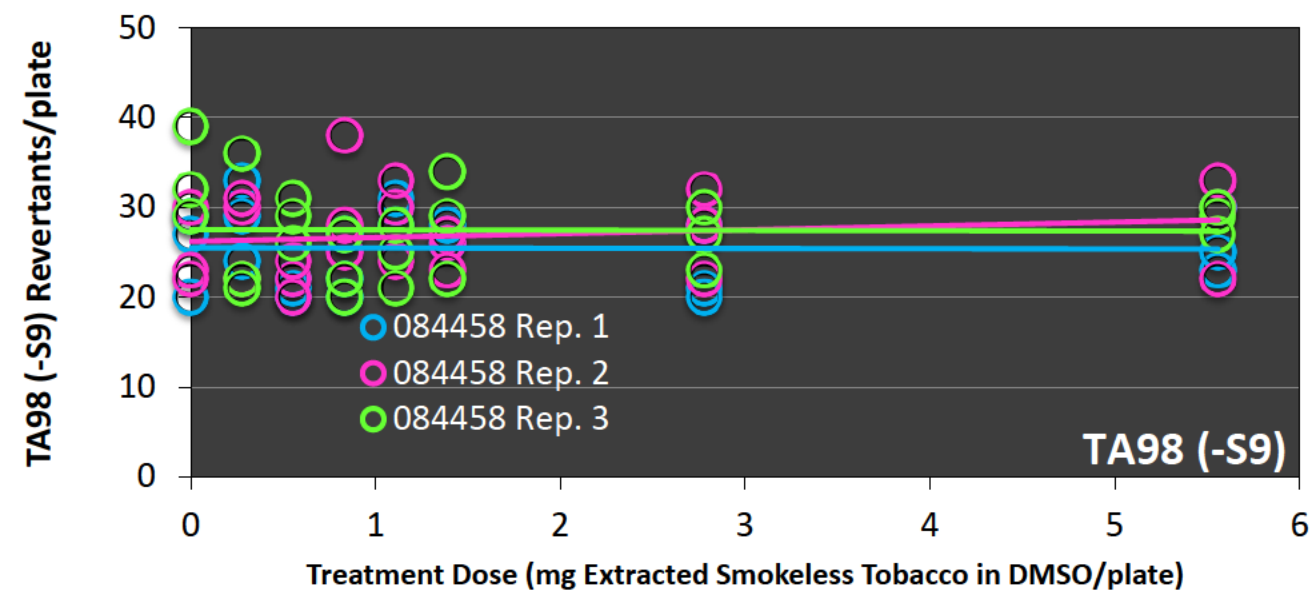
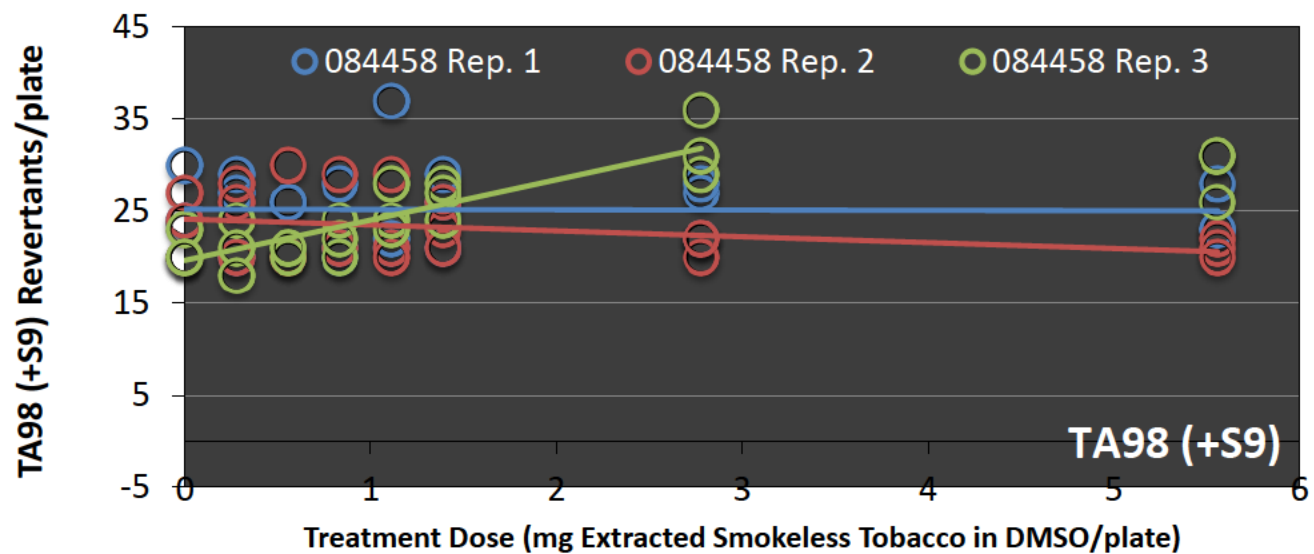


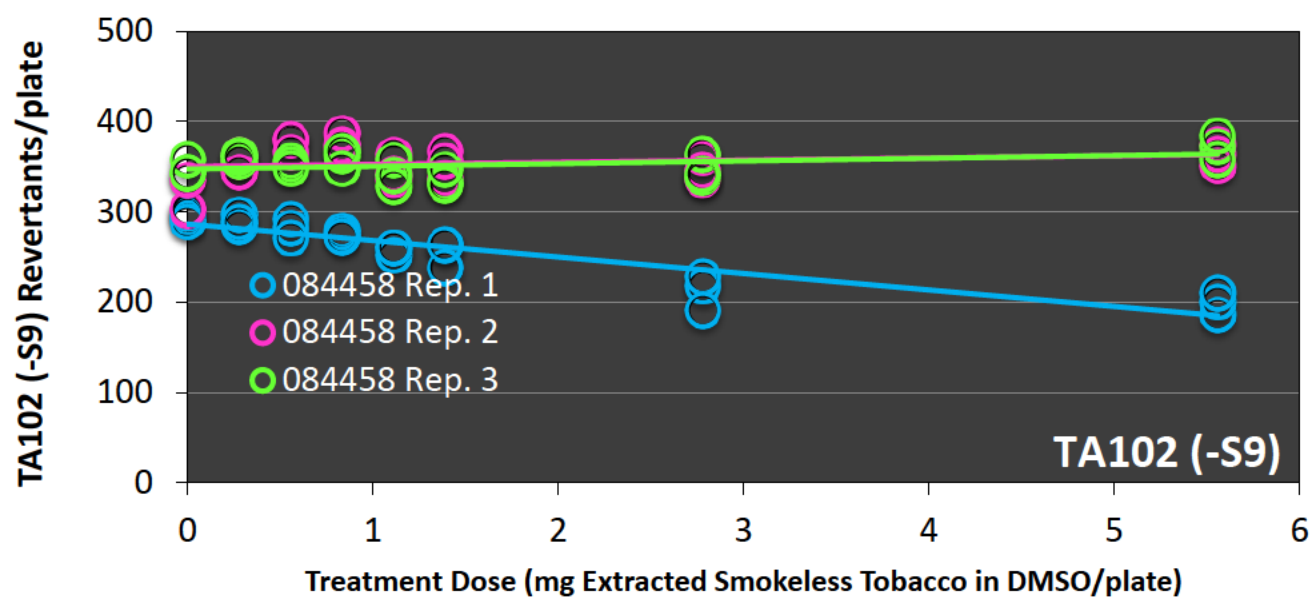
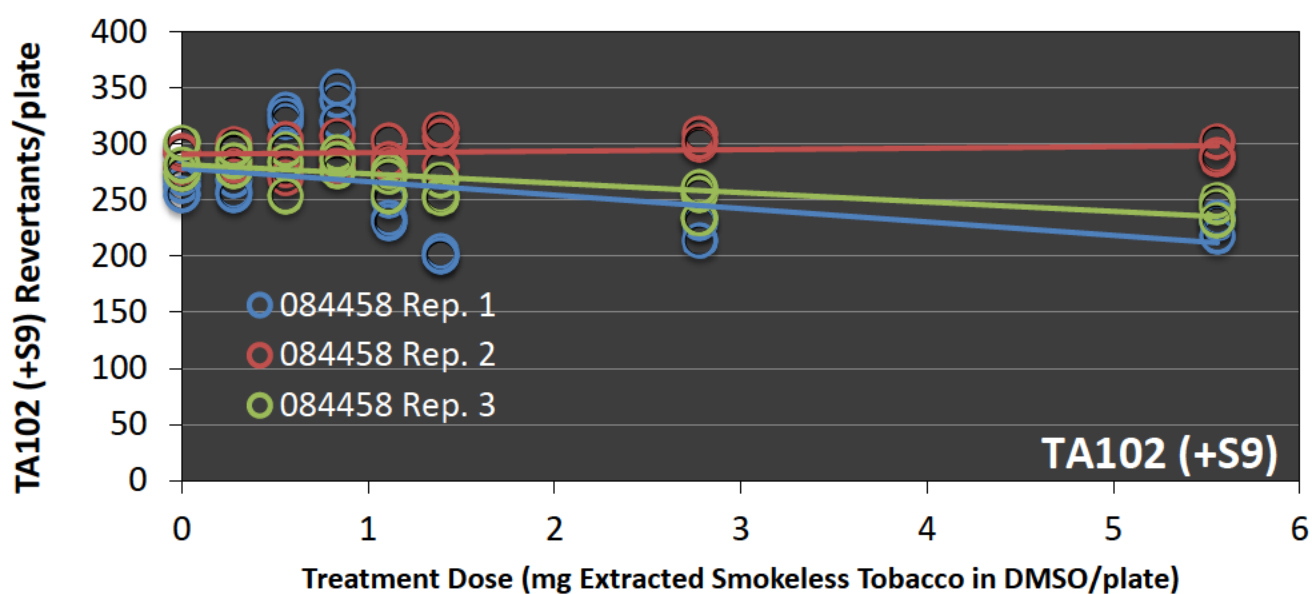
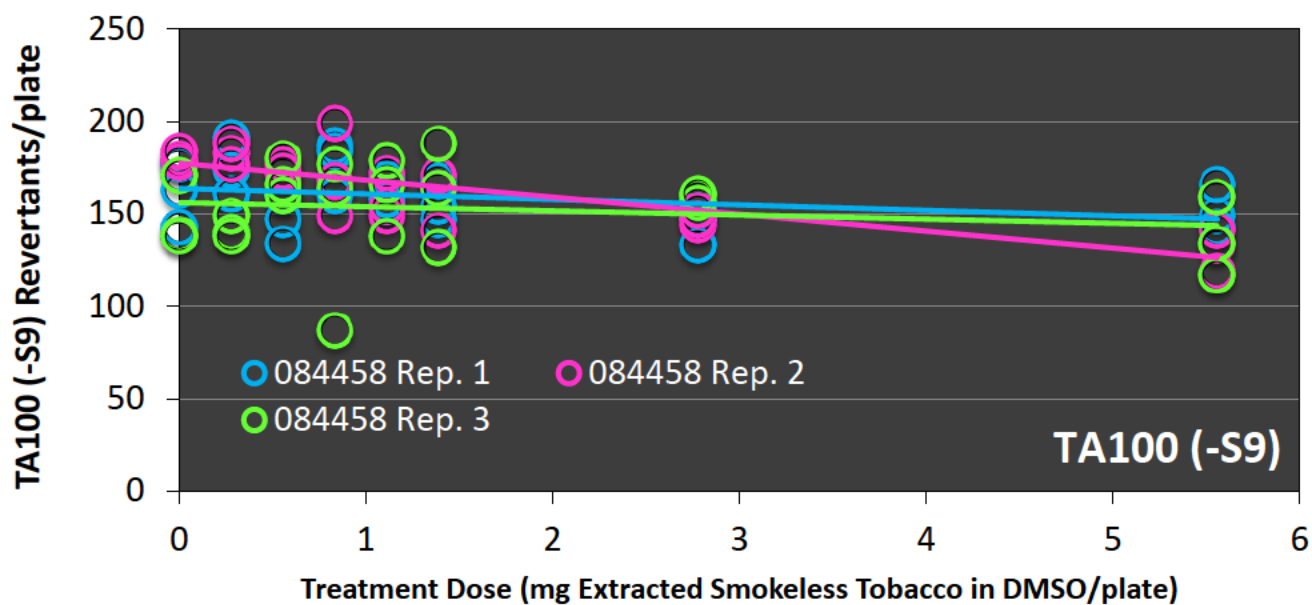


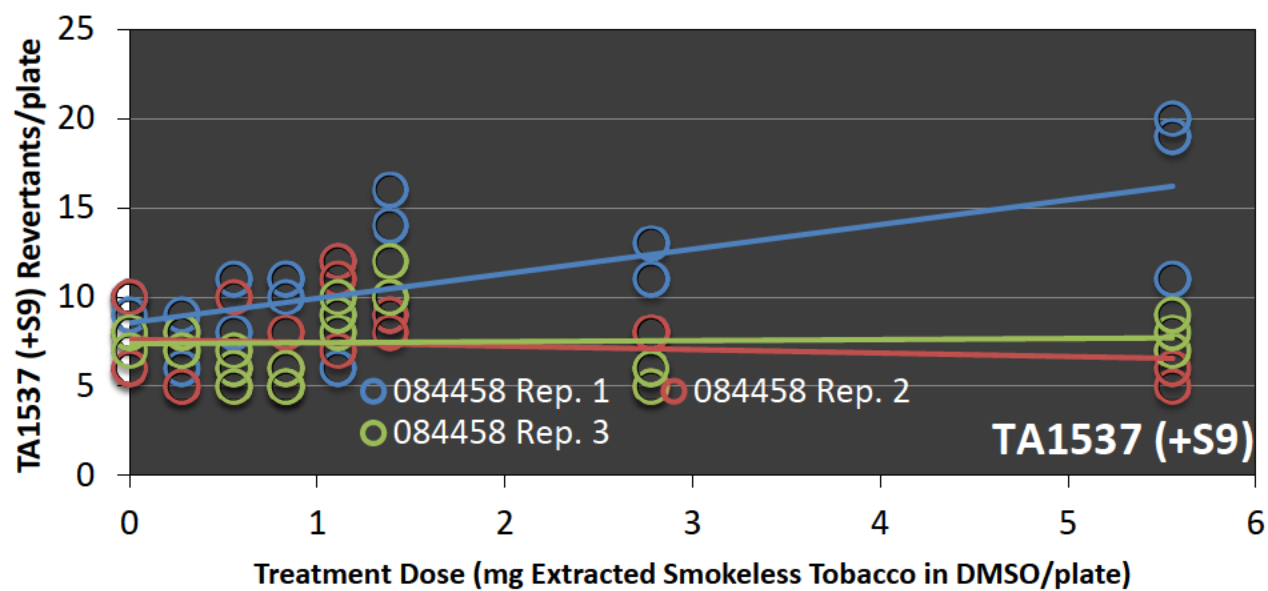
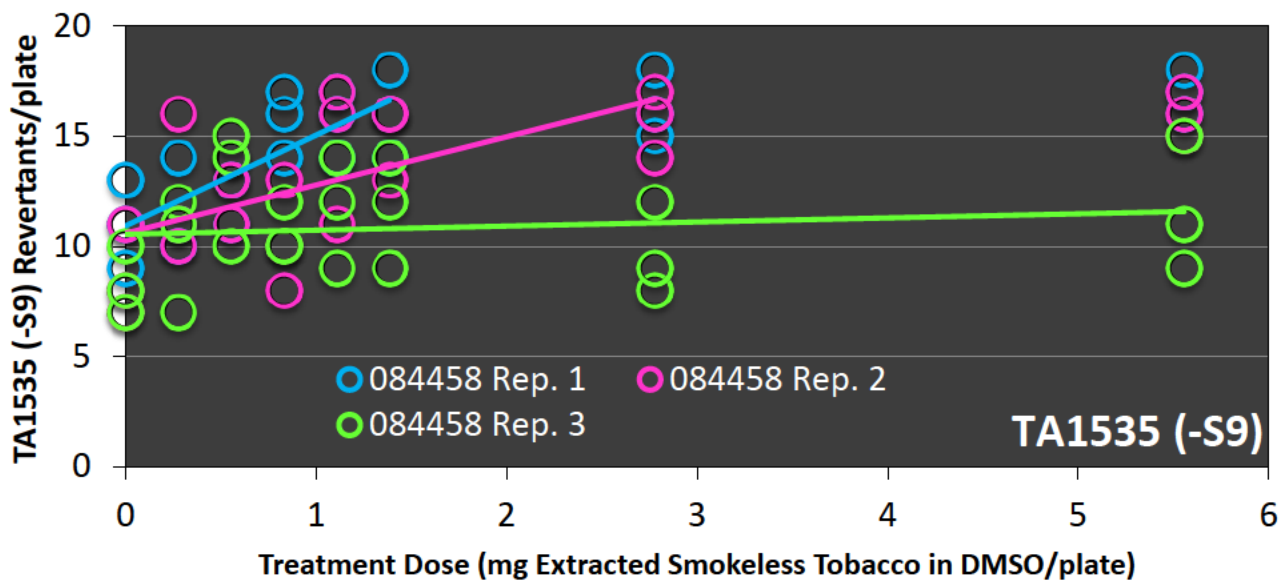
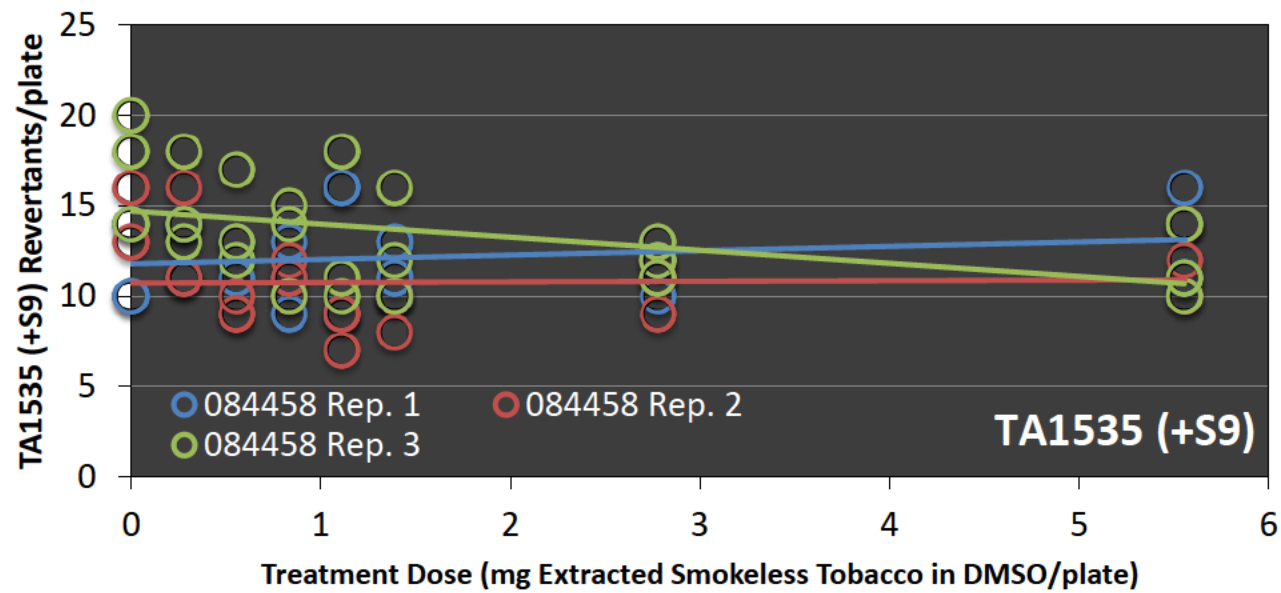


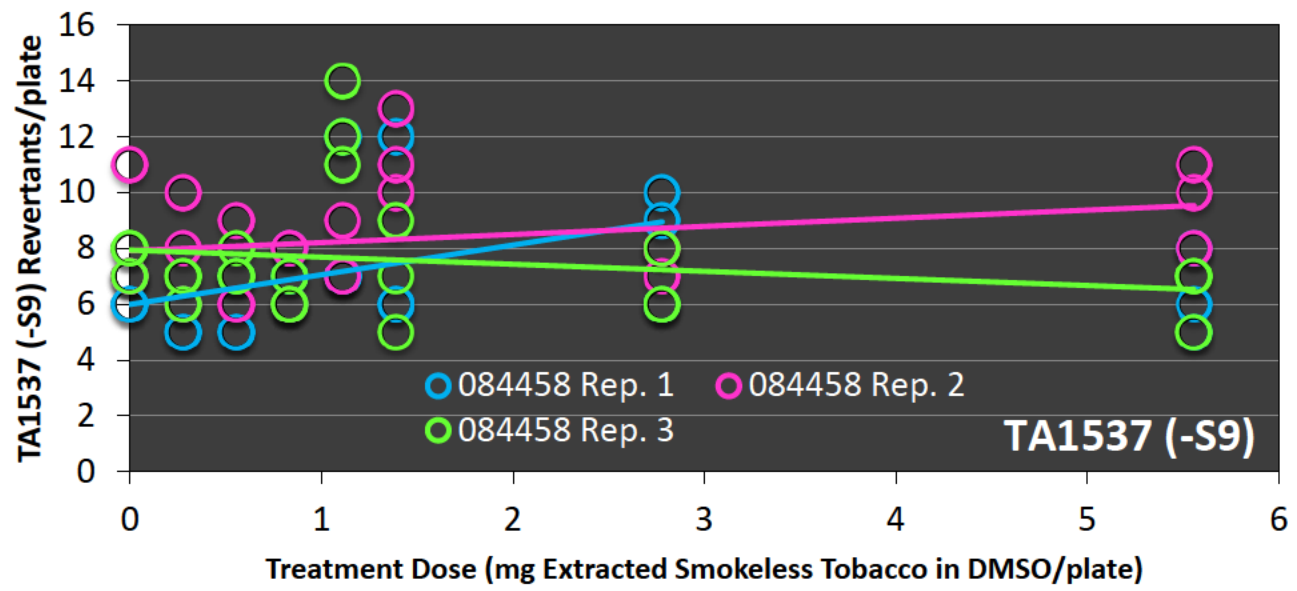












**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' (ST-H<sub>2</sub>O))**

| Strain and<br>S9 Activation | Sample<br>ID | Sample<br>Description | Number of Revertant Colonies/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' |        |                                |        |                                |        |  |       |              |  |                    |
|-----------------------------|--------------|-----------------------|--|--------|--------------------------------|--------|--------------------------------|--------|--|-------|--------------|--|--------------------|
|                             |              |                       | Replicate 1  |        | Replicate 2                    |        | Replicate 3                    |        | Statistics for Replicate 'ST-H <sub>2</sub> O' Slope Estimates |       |              |  |                    |
|                             |              |                       | Dose Range   |        | Dose Range                     |        | Dose Range                     |        | Standard   |       |              | t-test p-value (H <sub>0</sub> : mean = 0) |                    |
|                             |              |                       | (mg ST-H <sub>2</sub> O/plate)   | slope  | (mg ST-H <sub>2</sub> O/plate) | slope  | (mg ST-H <sub>2</sub> O/plate) | slope  | Mean   | Error | 95% C.I.     | p-value                                    | significance       |
| TA98 (+S9)                  | 084394       | Camel SNUS Frost      | 0 - 3.793  | 1.06   | 0 - 3.794                      | 2.39   | 0 - 3.794                      | -2.12  | 0.444  | 1.340 | 0* - 6.21    | 0.772                                      | not significant    |
| TA98 (+S9)                  | 084395       | 2S3                   | 0 - 2.556  | 6.07   | 0 - 2.556                      | 0.525  | 0 - 2.555                      | 4.72   | 3.77   | 1.669 | 0* - 11      | 0.152                                      | not significant    |
| TA98 (+S9)                  | 084454       | Fresh Strips          | 0 - 4.941  | -0.428 | 0 - 4.94                       | 0.544  | 0 - 2.47                       | -2.78  | 0*   | 0.987 | 0* - 3.36    | 0.463                                      | not significant    |
| TA98 (+S9)                  | 084455       | Mellow Sticks         | 0 - 5.22   | -1.11  | 0 - 5.222                      | 0.011  | 0 - 5.218                      | 1.14   | 0.014  | 0.651 | 0* - 2.82    | 0.984                                      | not significant    |
| TA98 (+S9)                  | 084456       | Copenhagen Long Cut   | 0 - 2.481  | 6.13   | 0 - 2.481                      | 6.04   | 0 - 2.481                      | 3.92   | 5.36   | 0.723 | 2.25 - 8.48  | 0.018                                      | <b>significant</b> |
| TA98 (+S9)                  | 084457       | Ariva Wintergreen     | 0 - 5.352  | 0.338  | 0 - 5.351                      | -0.802 | 0 - 5.352                      | -1.05  | 0*   | 0.427 | 0* - 1.33    | 0.359                                      | not significant    |
| TA98 (+S9)                  | 084458       | Fresh Orbs            | 0 - 5.272  | -0.036 | 0 - 5.271                      | -0.672 | 0 - 2.635                      | 4.62   | 1.30   | 1.67  | 0* - 8.48    | 0.516                                      | not significant    |
| TA98 (-S9)                  | 084394       | Camel SNUS Frost      | 0 - 3.793  | -0.402 | 0 - 3.794                      | 1.60   | 0 - 1.897                      | 0.000  | 0.398  | 0.611 | 0* - 3.03    | 0.581                                      | not significant    |
| TA98 (-S9)                  | 084395       | 2S3                   | 0 - 2.556  | 1.07   | 0 - 2.556                      | -1.25  | 0 - 1.278                      | -0.630 | 0*   | 0.692 | 0* - 2.71    | 0.733                                      | not significant    |
| TA98 (-S9)                  | 084454       | Fresh Strips          | 0 - 4.941  | 0.991  | 0 - 4.94                       | -0.091 | 0 - 4.941                      | 1.03   | 0.643  | 0.367 | 0* - 2.22    | 0.222                                      | not significant    |
| TA98 (-S9)                  | 084455       | Mellow Sticks         | 0 - 5.22   | 1.59   | 0 - 5.222                      | 1.18   | 0 - 5.218                      | 1.16   | 1.31   | 0.140 | 0.707 - 1.91 | 0.011                                      | <b>significant</b> |
| TA98 (-S9)                  | 084456       | Copenhagen Long Cut   | 0 - 2.481  | 0.359  | 0 - 2.481                      | 0.443  | 0 - 2.481                      | 1.20   | 0.666  | 0.266 | 0* - 1.81    | 0.129                                      | not significant    |
| TA98 (-S9)                  | 084457       | Ariva Wintergreen     | 0 - 5.352  | -0.371 | 0 - 2.676                      | 1.38   | 0 - 5.352                      | 0.656  | 0.555  | 0.508 | 0* - 2.74    | 0.389                                      | not significant    |
| TA98 (-S9)                  | 084458       | Fresh Orbs            | 0 - 5.272  | -0.029 | 0 - 5.271                      | 0.452  | 0 - 5.27                       | -0.033 | 0.130  | 0.161 | 0* - 0.823   | 0.504                                      | not significant    |
| TA100 (+S9)                 | 084394       | Camel SNUS Frost      | 0 - 0.948  | 1.96   | 0 - 0.949                      | 19.8   | 0 - 0.948                      | 27.1   | 16.3   | 7.46  | 0* - 48.3    | 0.161                                      | not significant    |
| TA100 (+S9)                 | 084395       | 2S3                   | 0 - 0.511  | 26.9   | 0 - 0.511                      | 61.8   | 0 - 0.511                      | 24.8   | 37.8   | 12.01 | 0* - 89.5    | 0.088                                      | not significant    |
| TA100 (+S9)                 | 084454       | Fresh Strips          | 0 - 1.235  | 21.2   | 0 - 2.47                       | 12.1   | 0 - 1.235                      | 14.8   | 16.1   | 2.70  | 4.45 - 27.7  | 0.027                                      | <b>significant</b> |
| TA100 (+S9)                 | 084455       | Mellow Sticks         | 0 - 2.61   | 13.4   | 0 - 1.305                      | 19.8   | 0 - 2.609                      | 8.83   | 14.0   | 3.18  | 0.317 - 27.7 | 0.048                                      | <b>significant</b> |
| TA100 (+S9)                 | 084456       | Copenhagen Long Cut   | 0 - 1.241  | 30.5   | 0 - 0.62                       | 57.3   | 0 - 0.62                       | 42.8   | 43.5   | 7.74  | 10.2 - 76.8  | 0.030                                      | <b>significant</b> |
| TA100 (+S9)                 | 084457       | Ariva Wintergreen     | 0 - 1.07   | 31.5   | 0 - 5.351                      | 2.86   | 0 - 1.338                      | 12.3   | 15.6   | 8.43  | 0* - 51.8    | 0.206                                      | not significant    |
| TA100 (+S9)                 | 084458       | Fresh Orbs            | 0 - 2.636  | 1.56   | 0 - 1.318                      | 8.02   | 0 - 1.317                      | 17.0   | 8.87   | 4.48  | 0* - 28.2    | 0.186                                      | not significant    |
| TA100 (-S9)                 | 084394       | Camel SNUS Frost      | 0 - 3.793  | 3.53   | 0 - 3.794                      | 6.68   | 0 - 3.794                      | 9.69   | 6.63   | 1.78  | 0* - 14.3    | 0.065                                      | not significant    |
| TA100 (-S9)                 | 084395       | 2S3                   | 0 - 1.278  | 8.85   | 0 - 2.556                      | 9.34   | 0 - 2.555                      | 12.0   | 10.1   | 0.985 | 5.83 - 14.3  | 0.009                                      | <b>significant</b> |
| TA100 (-S9)                 | 084454       | Fresh Strips          | 0 - 4.941  | -4.50  | 0 - 4.94                       | 1.27   | 0 - 2.47                       | 3.01   | 0*   | 2.27  | 0* - 9.68    | 0.977                                      | not significant    |
| TA100 (-S9)                 | 084455       | Mellow Sticks         | 0 - 2.61   | 11.3   | 0 - 5.222                      | -0.445 | 0 - 5.218                      | -7.43  | 1.13   | 5.45  | 0* - 24.6    | 0.855                                      | not significant    |
| TA100 (-S9)                 | 084456       | Copenhagen Long Cut   | 0 - 1.241  | 42.5   | 0 - 1.24                       | 0.070  | 0 - 1.241                      | 12.2   | 18.3   | 12.63 | 0* - 72.6    | 0.285                                      | not significant    |
| TA100 (-S9)                 | 084457       | Ariva Wintergreen     | 0 - 5.352  | 9.16   | 0 - 5.351                      | -12.6  | 0 - 5.352                      | -13.9  | 0*   | 7.47  | 0* - 26.4    | 0.521                                      | not significant    |
| TA100 (-S9)                 | 084458       | Fresh Orbs            | 0 - 5.272  | -3.11  | 0 - 5.271                      | -9.69  | 0 - 5.27                       | -2.36  | 0*   | 2.33  | 0* - 4.95    | 0.162                                      | not significant    |
| TA102 (+S9)                 | 084394       | Camel SNUS Frost      | 0 - 0.759  | 61.2   | 0 - 0.949                      | 83.6   | 0 - 0.948                      | 61.0   | 68.6   | 7.52  | 36.3 - 101   | 0.012                                      | <b>significant</b> |
| TA102 (+S9)                 | 084395       | 2S3                   | 0 - 0.511  | 102    | 0 - 2.556                      | 9.52   | 0 - 0.639                      | 35.8   | 49.2   | 27.6  | 0* - 168     | 0.217                                      | not significant    |
| TA102 (+S9)                 | 084454       | Fresh Strips          | 0 - 4.941  | 1.25   | 0 - 4.94                       | -3.79  | 0 - 4.941                      | 0.753  | 0*   | 1.60  | 0* - 6.3     | 0.746                                      | not significant    |
| TA102 (+S9)                 | 084455       | Mellow Sticks         | 0 - 5.22   | 3.69   | 0 - 5.222                      | 1.63   | 0 - 5.218                      | 2.85   | 2.72   | 0.598 | 0.15 - 5.3   | 0.045                                      | <b>significant</b> |
| TA102 (+S9)                 | 084456       | Copenhagen Long Cut   | 0 - 2.481  | 18.0   | 0 - 2.481                      | 4.48   | 0 - 2.481                      | 9.35   | 10.6   | 3.95  | 0* - 27.6    | 0.115                                      | not significant    |
| TA102 (+S9)                 | 084457       | Ariva Wintergreen     | 0 - 5.352  | -2.33  | 0 - 5.351                      | -0.866 | 0 - 5.352                      | -1.76  | 0*   | 0.426 | 0* - 0.181   | 0.061                                      | not significant    |
| TA102 (+S9)                 | 084458       | Fresh Orbs            | 0 - 5.272  | -12.6  | 0 - 5.271                      | 1.42   | 0 - 5.27                       | -8.81  | 0*   | 4.18  | 0* - 11.3    | 0.252                                      | not significant    |
| TA102 (-S9)                 | 084394       | Camel SNUS Frost      | 0 - 3.793  | -3.57  | 0 - 1.897                      | 8.05   | 0 - 3.794                      | -2.08  | 0.799  | 3.65  | 0* - 16.5    | 0.847                                      | not significant    |
| TA102 (-S9)                 | 084395       | 2S3                   | 0 - 2.556  | 3.87   | 0 - 2.556                      | 11.7   | 0 - 2.555                      | 26.9   | 14.2   | 6.74  | 0* - 43.2    | 0.171                                      | not significant    |



**Slope Analysis of the Linear Portion of the Dose-Response Curve  
(Revertant Colonies/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' (ST-H<sub>2</sub>O))**

| Strain and S9 Activation | Sample ID | Sample Description  | Number of Revertant Colonies/mg 'Extracted Moisture-Corrected Smokeless Tobacco in DMSO' |        |                                |        |                                |        |  |       |             |  |                 |  |
|--------------------------|-----------|---------------------|--|--------|--------------------------------|--------|--------------------------------|--------|--|-------|-------------|--|-----------------|--|
|                          |           |                     | Replicate 1  |        | Replicate 2                    |        | Replicate 3                    |        | Statistics for Replicate 'ST-H <sub>2</sub> O' Slope Estimates |       |             |  |                 |  |
|                          |           |                     | Dose Range   |        | Dose Range                     |        | Dose Range                     |        | Standard   |       |             | t-test p-value (H <sub>0</sub> : mean = 0) |                 |  |
|                          |           |                     | (mg ST-H <sub>2</sub> O/plate)   | slope  | (mg ST-H <sub>2</sub> O/plate) | slope  | (mg ST-H <sub>2</sub> O/plate) | slope  | Mean   | Error | 95% C.I.    | p-value                                    | significance    |  |
| TA102 (-S9)              | 084454    | Fresh Strips        | 0 - 4.941  | -0.902 | 0 - 4.94                       | 6.57   | 0 - 1.235                      | 53.2   | 19.6   | 16.9  | 0* - 92.5   | 0.366                                      | not significant |  |
| TA102 (-S9)              | 084455    | Mellow Sticks       | 0 - 2.61   | 4.04   | 0 - 5.222                      | 3.31   | 0 - 5.218                      | 0.241  | 2.53   | 1.16  | 0* - 7.53   | 0.162                                      | not significant |  |
| TA102 (-S9)              | 084456    | Copenhagen Long Cut | 0 - 2.481  | -0.049 | 0 - 2.481                      | 10.9   | 0 - 1.241                      | 70.6   | 27.1   | 21.94 | 0* - 122    | 0.342                                      | not significant |  |
| TA102 (-S9)              | 084457    | Ariva Wintergreen   | 0 - 5.352  | -4.80  | 0 - 5.351                      | -8.06  | 0 - 5.352                      | -0.906 | 0*   | 2.07  | 0* - 4.31   | 0.157                                      | not significant |  |
| TA102 (-S9)              | 084458    | Fresh Orbs          | 0 - 5.272  | -19.2  | 0 - 5.271                      | 2.55   | 0 - 5.27                       | 3.19   | 0*   | 7.37  | 0* - 27.2   | 0.604                                      | not significant |  |
| TA1535 (+S9)             | 084394    | Camel SNUS Frost    | 0 - 3.793  | 0.124  | 0 - 3.794                      | 0.763  | 0 - 3.794                      | -1.52  | 0*   | 0.681 | 0* - 2.72   | 0.785                                      | not significant |  |
| TA1535 (+S9)             | 084395    | 2S3                 | 0 - 2.556  | 0.804  | 0 - 2.556                      | 0.327  | 0 - 2.555                      | -0.112 | 0.340  | 0.264 | 0* - 1.48   | 0.328                                      | not significant |  |
| TA1535 (+S9)             | 084454    | Fresh Strips        | 0 - 4.941  | 0.409  | 0 - 4.94                       | 0.374  | 0 - 4.941                      | -0.407 | 0.126  | 0.266 | 0* - 1.27   | 0.684                                      | not significant |  |
| TA1535 (+S9)             | 084455    | Mellow Sticks       | 0 - 5.22   | -0.070 | 0 - 5.222                      | -0.844 | 0 - 2.609                      | 1.60   | 0.230  | 0.722 | 0* - 3.34   | 0.781                                      | not significant |  |
| TA1535 (+S9)             | 084456    | Copenhagen Long Cut | 0 - 2.481  | 0.384  | 0 - 2.481                      | 0.484  | 0 - 2.481                      | -0.522 | 0.115  | 0.320 | 0* - 1.49   | 0.753                                      | not significant |  |
| TA1535 (+S9)             | 084457    | Ariva Wintergreen   | 0 - 5.352  | 1.26   | 0 - 5.351                      | 0.821  | 0 - 5.352                      | -0.973 | 0.371  | 0.684 | 0* - 3.31   | 0.642                                      | not significant |  |
| TA1535 (+S9)             | 084458    | Fresh Orbs          | 0 - 5.272  | 0.258  | 0 - 5.271                      | 0.032  | 0 - 5.27                       | -0.762 | 0*   | 0.309 | 0* - 1.17   | 0.661                                      | not significant |  |
| TA1535 (-S9)             | 084394    | Camel SNUS Frost    | 0 - 3.793  | 0.100  | 0 - 3.794                      | 1.40   | 0 - 3.794                      | -0.822 | 0.227  | 0.645 | 0* - 3      | 0.758                                      | not significant |  |
| TA1535 (-S9)             | 084395    | 2S3                 | 0 - 2.556  | -0.586 | 0 - 2.556                      | 0.639  | 0 - 2.555                      | 2.03   | 0.694  | 0.755 | 0* - 3.94   | 0.455                                      | not significant |  |
| TA1535 (-S9)             | 084454    | Fresh Strips        | 0 - 2.47   | 0.754  | 0 - 2.47                       | 1.85   | 0 - 2.47                       | 1.23   | 1.28   | 0.317 | 0* - 2.64   | 0.056                                      | not significant |  |
| TA1535 (-S9)             | 084455    | Mellow Sticks       | 0 - 5.22   | -0.845 | 0 - 5.222                      | 0.070  | 0 - 5.218                      | -0.067 | 0*   | 0.285 | 0* - 0.946  | 0.429                                      | not significant |  |
| TA1535 (-S9)             | 084456    | Copenhagen Long Cut | 0 - 2.481  | 0.879  | 0 - 2.481                      | 2.05   | 0 - 1.241                      | 3.98   | 2.31   | 0.905 | 0* - 6.2    | 0.126                                      | not significant |  |
| TA1535 (-S9)             | 084457    | Ariva Wintergreen   | 0 - 1.338  | 4.24   | 0 - 5.351                      | 0.809  | 0 - 5.352                      | -0.323 | 1.57   | 1.37  | 0* - 7.47   | 0.370                                      | not significant |  |
| TA1535 (-S9)             | 084458    | Fresh Orbs          | 0 - 1.318  | 4.34   | 0 - 2.636                      | 2.31   | 0 - 5.27                       | 0.195  | 2.28   | 1.20  | 0* - 7.42   | 0.197                                      | not significant |  |
| TA1537 (+S9)             | 084394    | Camel SNUS Frost    | 0 - 1.897  | 4.28   | 0 - 3.794                      | 1.85   | 0 - 3.794                      | 1.93   | 2.68   | 0.796 | 0* - 6.11   | 0.078                                      | not significant |  |
| TA1537 (+S9)             | 084395    | 2S3                 | 0 - 0.639  | 17.0   | 0 - 2.556                      | 2.32   | 0 - 2.555                      | 2.12   | 7.14   | 4.92  | 0* - 28.3   | 0.284                                      | not significant |  |
| TA1537 (+S9)             | 084454    | Fresh Strips        | 0 - 4.941  | 0.210  | 0 - 4.94                       | -0.086 | 0 - 4.941                      | -0.346 | 0*   | 0.161 | 0* - 0.617  | 0.690                                      | not significant |  |
| TA1537 (+S9)             | 084455    | Mellow Sticks       | 0 - 5.22   | -0.389 | 0 - 5.222                      | 0.252  | 0 - 5.218                      | 0.599  | 0.154  | 0.290 | 0* - 1.4    | 0.648                                      | not significant |  |
| TA1537 (+S9)             | 084456    | Copenhagen Long Cut | 0 - 1.241  | 5.41   | 0 - 1.24                       | 4.15   | 0 - 2.481                      | 2.29   | 3.95   | 0.909 | 0.04 - 7.86 | 0.049                                      | significant     |  |
| TA1537 (+S9)             | 084457    | Ariva Wintergreen   | 0 - 5.352  | -0.375 | 0 - 5.351                      | 0.606  | 0 - 5.352                      | -0.232 | 0*   | 0.306 | 0* - 1.32   | 0.999                                      | not significant |  |
| TA1537 (+S9)             | 084458    | Fresh Orbs          | 0 - 5.272  | 1.45   | 0 - 5.271                      | -0.201 | 0 - 5.27                       | 0.064  | 0.438  | 0.512 | 0* - 2.64   | 0.483                                      | not significant |  |
| TA1537 (-S9)             | 084394    | Camel SNUS Frost    | 0 - 0.948  | 6.08   | 0 - 3.794                      | 1.28   | 0 - 1.897                      | 3.22   | 3.53   | 1.393 | 0* - 9.52   | 0.127                                      | not significant |  |
| TA1537 (-S9)             | 084395    | 2S3                 | 0 - 2.556  | 4.05   | 0 - 1.278                      | 4.12   | 0 - 1.278                      | 1.32   | 3.16   | 0.920 | 0* - 7.12   | 0.075                                      | not significant |  |
| TA1537 (-S9)             | 084454    | Fresh Strips        | 0 - 4.941  | -0.096 | 0 - 4.94                       | 0.302  | 0 - 4.941                      | 0.125  | 0.110  | 0.115 | 0* - 0.606  | 0.438                                      | not significant |  |
| TA1537 (-S9)             | 084455    | Mellow Sticks       | 0 - 5.22   | 0.074  | 0 - 5.222                      | -0.293 | 0 - 5.218                      | -0.260 | 0*   | 0.117 | 0* - 0.344  | 0.305                                      | not significant |  |
| TA1537 (-S9)             | 084456    | Copenhagen Long Cut | 0 - 2.481  | 0.285  | 0 - 2.481                      | -0.828 | 0 - 2.481                      | 0.861  | 0.106  | 0.496 | 0* - 2.24   | 0.850                                      | not significant |  |
| TA1537 (-S9)             | 084457    | Ariva Wintergreen   | 0 - 5.352  | 0.034  | 0 - 5.351                      | -0.491 | 0 - 5.352                      | 0.377  | 0*   | 0.252 | 0* - 1.06   | 0.925                                      | not significant |  |
| TA1537 (-S9)             | 084458    | Fresh Orbs          | 0 - 2.636  | 1.12   | 0 - 5.271                      | 0.307  | 0 - 5.27                       | -0.269 | 0.388  | 0.404 | 0* - 2.13   | 0.439                                      | not significant |  |

0\*: Mean or lower bound of the 95% confidence interval has been truncated at 0.

### One-Way ANOVA of Mean 'Extracted Moisture-Corrected Smokeless Tobacco' Slope Estimates Among Test Samples

TA98 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 99.09717278    | 6  | 16.51619546 | 4.070   | <b>0.014</b> |
| Within Samples | 56.80848684    | 14 | 4.05774906  |         |              |
| Total (Corr.)  | 155.9056596    | 20 |             |         |              |

TA100 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 3175.483288    | 6  | 529.2472146 | 3.352   | <b>0.029</b> |
| Within Samples | 2210.375596    | 14 | 157.8839712 |         |              |
| Total (Corr.)  | 5385.858884    | 20 |             |         |              |

TA102 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 15475.1107     | 6  | 2579.185116 | 7.046   | <b>0.001</b> |
| Within Samples | 5124.873831    | 14 | 366.0624165 |         |              |
| Total (Corr.)  | 20599.98453    | 20 |             |         |              |

TA1535 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 0.929754219    | 6  | 0.154959036 | 0.202   | 0.971   |
| Within Samples | 10.74664367    | 14 | 0.767617405 |         |         |
| Total (Corr.)  | 11.67639789    | 20 |             |         |         |

TA1537 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 134.6347429    | 6  | 22.43912381 | 2.000   | 0.134   |
| Within Samples | 157.0346808    | 14 | 11.21676291 |         |         |
| Total (Corr.)  | 291.6694237    | 20 |             |         |         |

### One-Way ANOVA of Mean 'Extracted Moisture-Corrected Smokeless Tobacco' Slope Estimates Among Test Samples

TA98 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 4.336430708    | 6  | 0.722738451 | 1.240   | 0.344   |
| Within Samples | 8.159457846    | 14 | 0.582818418 |         |         |
| Total (Corr.)  | 12.49588855    | 20 |             |         |         |

TA100 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 1346.050894    | 6  | 224.3418157 | 2.015   | 0.131   |
| Within Samples | 1558.496222    | 14 | 111.3211587 |         |         |
| Total (Corr.)  | 2904.547116    | 20 |             |         |         |

TA102 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 2807.624332    | 6  | 467.9373887 | 1.231   | 0.348   |
| Within Samples | 5321.468772    | 14 | 380.1049123 |         |         |
| Total (Corr.)  | 8129.093104    | 20 |             |         |         |

TA1535 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value |
|----------------|----------------|----|-------------|---------|---------|
| Among Samples  | 17.73636021    | 6  | 2.956060035 | 1.303   | 0.318   |
| Within Samples | 31.76324971    | 14 | 2.268803551 |         |         |
| Total (Corr.)  | 49.49960993    | 20 |             |         |         |

TA1537 (-S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 46.25592548    | 6  | 7.709320914 | 5.472   | <b>0.004</b> |
| Within Samples | 19.72316585    | 14 | 1.408797561 |         |              |
| Total (Corr.)  | 65.97909134    | 20 |             |         |              |

One-way ANOVA analysis indicates significant differences (at  $\alpha = 0.05$ ) among mean 'Extracted Moisture-Corrected Smokeless Tobacco' specific activity slope estimates for test samples with TA98 (+S9), TA100 (+S9), TA102 (+S9) and TA1537 (-S9).

**Evaluation of Ratio (Max ÷ Min) of Standard Deviations of  
'Extracted Moisture-Corrected Smokeless Tobacco' Slope  
Estimates and Corresponding Method of Comparison**

| <b>Strain and<br/>S9 Activation</b> | <b>Std. Dev. Ratio<br/>(Max ÷ Min)</b> | <b>Method of<br/>Comparison</b>    |
|-------------------------------------|--|------------------------------------|
| TA98 (+S9)                          | 3.9                                    | ANOVA (equal variance)             |
| TA98 (-S9)                          | 5.0                                    | ANOVA (equal variance)             |
| TA100 (+S9)                         | 4.4                                    | ANOVA (equal variance)             |
| TA100 (-S9)                         | 12.8                                   | ANOVA (equal variance)             |
| TA102 (+S9)                         | 64.8                                   | Pairwise T-test (unequal variance) |
| TA102 (-S9)                         | 18.9                                   | Pairwise T-test (unequal variance) |
| TA1535 (+S9)                        | 2.7                                    | ANOVA (equal variance)             |
| TA1535 (-S9)                        | 4.8                                    | ANOVA (equal variance)             |
| TA1537 (+S9)                        | 30.7                                   | Pairwise T-test (unequal variance) |
| TA1537 (-S9)                        | 12.1                                   | ANOVA (equal variance)             |

**Evaluation of Ratio (Max ÷ Min) of Standard Deviations of  
'Extracted Moisture-Corrected Smokeless Tobacco' Slope  
Estimates and Corresponding Method of Comparison**

**ANOVA-Based Comparison Tests of Mean 'Extracted Moisture-Corrected Smokeless Tobacco' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| ANOVA-Based<br>Comparison | TA98 (+S9) |         |                                    | TA100 (+S9) |         |                                    | TA102 (+S9) |         |                                    | TA1535 (+S9) |         |                                    | TA1537 (+S9) |         |                                    |
|---------------------------|------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                           | f-ratio    | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395         | 4.093      | 0.0626  | not significant                    | 4.415       | 0.0542  | not significant                    | 1.545       | 0.2343  | not significant                    | 0.594        | 0.4537  | not significant                    | 2.661        | 0.1251  | not significant                    |
| <b>084394 vs. 084454</b>  | 0.656      | 0.4317  | not significant                    | 0.000       | 0.9852  | not significant                    | 19.619      | 0.0006  | <b>significant</b>                 | 0.222        | 0.6445  | not significant                    | 1.017        | 0.3304  | not significant                    |
| <b>084394 vs. 084455</b>  | 0.068      | 0.7980  | not significant                    | 0.048       | 0.8296  | not significant                    | 17.783      | 0.0009  | <b>significant</b>                 | 0.381        | 0.5471  | not significant                    | 0.856        | 0.3706  | not significant                    |
| <b>084394 vs. 084456</b>  | 8.951      | 0.0097  | not significant                    | 7.054       | 0.0188  | not significant                    | 13.779      | 0.0023  | <b>significant</b>                 | 0.209        | 0.6545  | not significant                    | 0.215        | 0.6501  | not significant                    |
| <b>084394 vs. 084457</b>  | 0.332      | 0.5734  | not significant                    | 0.005       | 0.9455  | not significant                    | 20.223      | 0.0005  | <b>significant</b>                 | 0.663        | 0.4293  | not significant                    | 0.963        | 0.3430  | not significant                    |
| <b>084394 vs. 084458</b>  | 0.274      | 0.6090  | not significant                    | 0.520       | 0.4828  | not significant                    | 23.204      | 0.0003  | <b>significant</b>                 | 0.006        | 0.9404  | not significant                    | 0.674        | 0.4253  | not significant                    |
| 084395 vs. 084454         | 8.024      | 0.0133  | not significant                    | 4.495       | 0.0523  | not significant                    | 10.154      | 0.0066  | not significant                    | 0.089        | 0.7693  | not significant                    | 6.968        | 0.0194  | not significant                    |
| 084395 vs. 084455         | 5.216      | 0.0385  | not significant                    | 5.385       | 0.0359  | not significant                    | 8.845       | 0.0101  | not significant                    | 0.024        | 0.8802  | not significant                    | 6.535        | 0.0228  | not significant                    |
| 084395 vs. 084456         | 0.939      | 0.3490  | not significant                    | 0.308       | 0.5879  | not significant                    | 6.097       | 0.0270  | not significant                    | 0.098        | 0.7587  | not significant                    | 1.364        | 0.2624  | not significant                    |
| 084395 vs. 084457         | 6.757      | 0.0210  | not significant                    | 4.713       | 0.0476  | not significant                    | 10.589      | 0.0058  | not significant                    | 0.002        | 0.9660  | not significant                    | 6.827        | 0.0205  | not significant                    |
| 084395 vs. 084458         | 2.249      | 0.1559  | not significant                    | 7.965       | 0.0136  | not significant                    | 12.775      | 0.0031  | not significant                    | 0.482        | 0.4987  | not significant                    | 6.015        | 0.0279  | not significant                    |
| 084454 vs. 084455         | 0.301      | 0.5918  | not significant                    | 0.040       | 0.8441  | not significant                    | 0.045       | 0.8349  | not significant                    | 0.021        | 0.8863  | not significant                    | 0.007        | 0.9347  | not significant                    |
| <b>084454 vs. 084456</b>  | 14.452     | 0.0019  | <b>significant</b>                 | 7.155       | 0.0181  | not significant                    | 0.514       | 0.4850  | not significant                    | 0.000        | 0.9889  | not significant                    | 2.167        | 0.1632  | not significant                    |
| 084454 vs. 084457         | 0.054      | 0.8190  | not significant                    | 0.003       | 0.9602  | not significant                    | 0.005       | 0.9470  | not significant                    | 0.117        | 0.7371  | not significant                    | 0.001        | 0.9789  | not significant                    |
| 084454 vs. 084458         | 1.777      | 0.2039  | not significant                    | 0.493       | 0.4941  | not significant                    | 0.150       | 0.7040  | not significant                    | 0.156        | 0.6985  | not significant                    | 0.035        | 0.8542  | not significant                    |
| 084455 vs. 084456         | 10.581     | 0.0058  | not significant                    | 8.267       | 0.0122  | not significant                    | 0.255       | 0.6215  | not significant                    | 0.026        | 0.8753  | not significant                    | 1.928        | 0.1867  | not significant                    |
| 084455 vs. 084457         | 0.100      | 0.7570  | not significant                    | 0.022       | 0.8832  | not significant                    | 0.078       | 0.7835  | not significant                    | 0.039        | 0.8467  | not significant                    | 0.003        | 0.9558  | not significant                    |
| 084455 vs. 084458         | 0.615      | 0.4461  | not significant                    | 0.252       | 0.6237  | not significant                    | 0.360       | 0.5580  | not significant                    | 0.293        | 0.5970  | not significant                    | 0.011        | 0.9188  | not significant                    |
| 084456 vs. 084457         | 12.733     | 0.0031  | not significant                    | 7.429       | 0.0164  | not significant                    | 0.616       | 0.4456  | not significant                    | 0.127        | 0.7266  | not significant                    | 2.088        | 0.1705  | not significant                    |
| 084456 vs. 084458         | 6.095      | 0.0271  | not significant                    | 11.403      | 0.0045  | not significant                    | 1.221       | 0.2878  | not significant                    | 0.145        | 0.7087  | not significant                    | 1.651        | 0.2197  | not significant                    |
| 084457 vs. 084458         | 1.209      | 0.2900  | not significant                    | 0.424       | 0.5254  | not significant                    | 0.102       | 0.7536  | not significant                    | 0.545        | 0.4727  | not significant                    | 0.026        | 0.8750  | not significant                    |

**ANOVA-Based Comparison Tests of Mean 'Extracted Moisture-Corrected Smokeless Tobacco' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| ANOVA-Based<br>Comparison | TA98 (-S9) |         |                                    | TA100 (-S9) |         |                                    | TA102 (-S9) |         |                                    | TA1535 (-S9) |         |                                    | TA1537 (-S9) |         |                                    |
|---------------------------|------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                           | f-ratio    | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio     | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ | f-ratio      | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395         | 1.151      | 0.3014  | not significant                    | 0.159       | 0.6964  | not significant                    | 0.704       | 0.4155  | not significant                    | 0.144        | 0.7100  | not significant                    | 0.142        | 0.7121  | not significant                    |
| 084394 vs. 084454         | 0.154      | 0.7003  | not significant                    | 0.606       | 0.4492  | not significant                    | 1.400       | 0.2564  | not significant                    | 0.730        | 0.4073  | not significant                    | 12.425       | 0.0034  | not significant                    |
| <b>084394 vs. 084455</b>  | 2.134      | 0.1662  | not significant                    | 0.408       | 0.5333  | not significant                    | 0.012       | 0.9150  | not significant                    | 0.171        | 0.6859  | not significant                    | 14.469       | 0.0019  | <b>significant</b>                 |
| 084394 vs. 084456         | 0.185      | 0.6739  | not significant                    | 1.826       | 0.1980  | not significant                    | 2.737       | 0.1203  | not significant                    | 2.856        | 0.1132  | not significant                    | 12.457       | 0.0033  | not significant                    |
| 084394 vs. 084457         | 0.063      | 0.8055  | not significant                    | 2.074       | 0.1718  | not significant                    | 0.115       | 0.7401  | not significant                    | 1.199        | 0.2921  | not significant                    | 13.444       | 0.0025  | not significant                    |
| 084394 vs. 084458         | 0.185      | 0.6737  | not significant                    | 1.841       | 0.1964  | not significant                    | 0.111       | 0.7442  | not significant                    | 2.784        | 0.1174  | not significant                    | 10.490       | 0.0059  | not significant                    |
| 084395 vs. 084454         | 2.149      | 0.1648  | not significant                    | 1.385       | 0.2589  | not significant                    | 0.118       | 0.7359  | not significant                    | 0.226        | 0.6421  | not significant                    | 9.911        | 0.0071  | not significant                    |
| 084395 vs. 084455         | 6.420      | 0.0239  | not significant                    | 1.076       | 0.3173  | not significant                    | 0.534       | 0.4771  | not significant                    | 0.628        | 0.4414  | not significant                    | 11.746       | 0.0041  | not significant                    |
| 084395 vs. 084456         | 2.259      | 0.1551  | not significant                    | 0.908       | 0.3568  | not significant                    | 0.665       | 0.4285  | not significant                    | 1.717        | 0.2111  | not significant                    | 9.940        | 0.0071  | not significant                    |
| 084395 vs. 084457         | 1.753      | 0.2067  | not significant                    | 3.380       | 0.0873  | not significant                    | 1.387       | 0.2586  | not significant                    | 0.512        | 0.4862  | not significant                    | 10.823       | 0.0054  | not significant                    |
| 084395 vs. 084458         | 0.413      | 0.5307  | not significant                    | 3.080       | 0.1011  | not significant                    | 1.373       | 0.2608  | not significant                    | 1.661        | 0.2183  | not significant                    | 8.192        | 0.0125  | not significant                    |
| 084454 vs. 084455         | 1.140      | 0.3037  | not significant                    | 0.020       | 0.8908  | not significant                    | 1.155       | 0.3007  | not significant                    | 1.606        | 0.2257  | not significant                    | 0.078        | 0.7844  | not significant                    |
| 084454 vs. 084456         | 0.001      | 0.9711  | not significant                    | 4.536       | 0.0514  | not significant                    | 0.222       | 0.6447  | not significant                    | 0.698        | 0.4175  | not significant                    | 0.000        | 0.9964  | not significant                    |
| 084454 vs. 084457         | 0.020      | 0.8891  | not significant                    | 0.438       | 0.5189  | not significant                    | 2.315       | 0.1504  | not significant                    | 0.058        | 0.8135  | not significant                    | 0.020        | 0.8894  | not significant                    |
| 084454 vs. 084458         | 0.677      | 0.4243  | not significant                    | 0.334       | 0.5723  | not significant                    | 2.299       | 0.1517  | not significant                    | 0.663        | 0.4293  | not significant                    | 0.082        | 0.7790  | not significant                    |
| 084455 vs. 084456         | 1.063      | 0.3201  | not significant                    | 3.960       | 0.0665  | not significant                    | 2.390       | 0.1444  | not significant                    | 4.422        | 0.0541  | not significant                    | 0.075        | 0.7878  | not significant                    |
| 084455 vs. 084457         | 1.464      | 0.2464  | not significant                    | 0.642       | 0.4363  | not significant                    | 0.200       | 0.6617  | not significant                    | 2.273        | 0.1539  | not significant                    | 0.019        | 0.8928  | not significant                    |
| 084455 vs. 084458         | 3.575      | 0.0795  | not significant                    | 0.516       | 0.4846  | not significant                    | 0.195       | 0.6656  | not significant                    | 4.332        | 0.0562  | not significant                    | 0.319        | 0.5810  | not significant                    |
| 084456 vs. 084457         | 0.032      | 0.8606  | not significant                    | 7.792       | 0.0144  | not significant                    | 3.972       | 0.0661  | not significant                    | 0.354        | 0.5613  | not significant                    | 0.019        | 0.8929  | not significant                    |
| 084456 vs. 084458         | 0.739      | 0.4043  | not significant                    | 7.333       | 0.0170  | not significant                    | 3.950       | 0.0668  | not significant                    | 0.000        | 0.9832  | not significant                    | 0.084        | 0.7756  | not significant                    |
| 084457 vs. 084458         | 0.464      | 0.5069  | not significant                    | 0.007       | 0.9347  | not significant                    | 0.000       | 0.9956  | not significant                    | 0.329        | 0.5753  | not significant                    | 0.183        | 0.6753  | not significant                    |

Some ANOVA-based comparison p-values for tester strains TA98 (+S9), TA102 (+S9) and TA1537 (-S9) were significant at  $\alpha = 0.05$ .

Significant differences in mean 'Extracted Moisture-Corrected Smokeless Tobacco' specific activity slope were detected in TA102 (+S9) between Camel SNUS Frost (084394) and each of {Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456), Ariva Wintergreen (084457), Fresh Orbs (084458)}

Significant difference in mean 'Extracted Moisture-Corrected Smokeless Tobacco' specific activity slope were detected in TA98 (+S9) between Fresh Strips (084454) and Copenhagen Long Cut (084456).

Significant differences in mean 'Extracted Moisture-Corrected Smokeless Tobacco' specific activity slope were detected in TA1537 (-S9) between Camel SNUS Frost (084394) and Mellow Sticks (084455).

**Pairwise T-Test Comparisons of Mean 'Extracted Moisture-Corrected Smokeless Tobacco' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| Pairwise T-test<br>Comparison | TA98 (+S9)  |         |                                    | TA100 (+S9) |         |                                    | TA102 (+S9) |         |                                    | TA1535 (+S9) |         |                                    | TA1537 (+S9) |         |                                    |
|-------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                               | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395             |             |         |                                    |             |         |                                    | 0.679       | 0.5345  | not significant                    |              |         |                                    | 0.894        | 0.4217  | not significant                    |
| <b>084394 vs. 084454</b>      |             |         |                                    |             |         |                                    | 9.003       | 0.0008  | <b>significant</b>                 |              |         |                                    | 3.395        | 0.0274  | not significant                    |
| <b>084394 vs. 084455</b>      |             |         |                                    |             |         |                                    | 8.737       | 0.0009  | <b>significant</b>                 |              |         |                                    | 2.986        | 0.0405  | not significant                    |
| 084394 vs. 084456             |             |         |                                    |             |         |                                    | 6.828       | 0.0024  | not significant                    |              |         |                                    | 1.049        | 0.3534  | not significant                    |
| <b>084394 vs. 084457</b>      |             |         |                                    |             |         |                                    | 9.331       | 0.0007  | <b>significant</b>                 |              |         |                                    | 3.146        | 0.0346  | not significant                    |
| <b>084394 vs. 084458</b>      |             |         |                                    |             |         |                                    | 8.750       | 0.0009  | <b>significant</b>                 |              |         |                                    | 2.372        | 0.0767  | not significant                    |
| 084395 vs. 084454             |             |         |                                    |             |         |                                    | 1.801       | 0.1461  | not significant                    |              |         |                                    | 1.465        | 0.2167  | not significant                    |
| 084395 vs. 084455             |             |         |                                    |             |         |                                    | 1.683       | 0.1676  | not significant                    |              |         |                                    | 1.417        | 0.2294  | not significant                    |
| 084395 vs. 084456             |             |         |                                    |             |         |                                    | 1.384       | 0.2386  | not significant                    |              |         |                                    | 0.638        | 0.5583  | not significant                    |
| 084395 vs. 084457             |             |         |                                    |             |         |                                    | 1.842       | 0.1393  | not significant                    |              |         |                                    | 1.448        | 0.2211  | not significant                    |
| 084395 vs. 084458             |             |         |                                    |             |         |                                    | 2.001       | 0.1160  | not significant                    |              |         |                                    | 1.355        | 0.2470  | not significant                    |
| 084454 vs. 084455             |             |         |                                    |             |         |                                    | 1.940       | 0.1244  | not significant                    |              |         |                                    | 0.689        | 0.5288  | not significant                    |
| 084454 vs. 084456             |             |         |                                    |             |         |                                    | 2.627       | 0.0584  | not significant                    |              |         |                                    | 4.360        | 0.0121  | not significant                    |
| 084454 vs. 084457             |             |         |                                    |             |         |                                    | 0.637       | 0.5586  | not significant                    |              |         |                                    | 0.213        | 0.8416  | not significant                    |
| 084454 vs. 084458             |             |         |                                    |             |         |                                    | 1.353       | 0.2474  | not significant                    |              |         |                                    | 0.954        | 0.3943  | not significant                    |
| 084455 vs. 084456             |             |         |                                    |             |         |                                    | 1.973       | 0.1198  | not significant                    |              |         |                                    | 3.980        | 0.0164  | not significant                    |
| 084455 vs. 084457             |             |         |                                    |             |         |                                    | 5.959       | 0.0040  | not significant                    |              |         |                                    | 0.366        | 0.7326  | not significant                    |
| 084455 vs. 084458             |             |         |                                    |             |         |                                    | 2.221       | 0.0906  | not significant                    |              |         |                                    | 0.482        | 0.6547  | not significant                    |
| 084456 vs. 084457             |             |         |                                    |             |         |                                    | 3.084       | 0.0368  | not significant                    |              |         |                                    | 4.119        | 0.0146  | not significant                    |
| 084456 vs. 084458             |             |         |                                    |             |         |                                    | 3.001       | 0.0399  | not significant                    |              |         |                                    | 3.367        | 0.0281  | not significant                    |
| 084457 vs. 084458             |             |         |                                    |             |         |                                    | 1.190       | 0.2998  | not significant                    |              |         |                                    | 0.734        | 0.5034  | not significant                    |



**Pairwise T-Test Comparisons of Mean 'Extracted Moisture-Corrected Smokeless Tobacco' Slope  
for Contrasts of Interest using Bonferroni-adjusted p-values**

| Pairwise T-test<br>Comparison | TA98 (-S9)  |         |                                    | TA100 (-S9) |         |                                    | TA102 (-S9) |         |                                    | TA1535 (-S9) |         |                                    | TA1537 (-S9) |         |                                    |
|-------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|-------------|---------|------------------------------------|--------------|---------|------------------------------------|--------------|---------|------------------------------------|
|                               | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ | t-statistic  | p-value | significance<br>at $\alpha = 0.05$ |
| 084394 vs. 084395             |             |         |                                    |             |         |                                    | 1.742       | 0.1564  | not significant                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084454             |             |         |                                    |             |         |                                    | 1.087       | 0.3382  | not significant                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084455             |             |         |                                    |             |         |                                    | 0.451       | 0.6750  | not significant                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084456             |             |         |                                    |             |         |                                    | 1.184       | 0.3018  | not significant                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084457             |             |         |                                    |             |         |                                    | 1.284       | 0.2685  | not significant                    |              |         |                                    |              |         |                                    |
| 084394 vs. 084458             |             |         |                                    |             |         |                                    | 0.644       | 0.5545  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084454             |             |         |                                    |             |         |                                    | 0.300       | 0.7788  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084455             |             |         |                                    |             |         |                                    | 1.699       | 0.1645  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084456             |             |         |                                    |             |         |                                    | 0.566       | 0.6019  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084457             |             |         |                                    |             |         |                                    | 2.658       | 0.0565  | not significant                    |              |         |                                    |              |         |                                    |
| 084395 vs. 084458             |             |         |                                    |             |         |                                    | 1.868       | 0.1352  | not significant                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084455             |             |         |                                    |             |         |                                    | 1.007       | 0.3707  | not significant                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084456             |             |         |                                    |             |         |                                    | 0.271       | 0.8000  | not significant                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084457             |             |         |                                    |             |         |                                    | 1.419       | 0.2288  | not significant                    |              |         |                                    |              |         |                                    |
| 084454 vs. 084458             |             |         |                                    |             |         |                                    | 1.306       | 0.2615  | not significant                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084456             |             |         |                                    |             |         |                                    | 1.120       | 0.3253  | not significant                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084457             |             |         |                                    |             |         |                                    | 2.999       | 0.0400  | not significant                    |              |         |                                    |              |         |                                    |
| 084455 vs. 084458             |             |         |                                    |             |         |                                    | 0.942       | 0.3996  | not significant                    |              |         |                                    |              |         |                                    |
| 084456 vs. 084457             |             |         |                                    |             |         |                                    | 1.440       | 0.2233  | not significant                    |              |         |                                    |              |         |                                    |
| 084456 vs. 084458             |             |         |                                    |             |         |                                    | 1.367       | 0.2434  | not significant                    |              |         |                                    |              |         |                                    |
| 084457 vs. 084458             |             |         |                                    |             |         |                                    | 0.012       | 0.9913  | not significant                    |              |         |                                    |              |         |                                    |

Pairwise t-test comparison p-values less than the Bonferroni-adjusted  $\alpha = 0.05$  indicate that significant differences in mean 'Extracted Moisture-Corrected Smokeless Tobacco' specific activity slope were as follows for strain TA102 (+S9):

TA102 (+S9): Camel SNUS Frost (084394) was significantly different from each of {Fresh Strips (084454), Mellow Sticks (084455), Ariva Wintergreen (084457), Fresh Orbs (084458)}

**Number of Mean 'Extracted Moisture-Corrected Smokeless Tobacco' Slope Estimates Significantly Greater than Zero (0), the Corresponding Number of Paired Comparisons and Comparison Method**

| Strain and S9 Activation | # of Significant Mean Slopes | Number of Comparisons | Std. Dev. Ratio (Max ÷ Min) | Method of Comparison   |
|--------------------------|------------------------------|-----------------------|-----------------------------|------------------------|
| TA98 (+S9)               | 1                            | 0                     |                             |                        |
| TA98 (-S9)               | 1                            | 0                     |                             |                        |
| TA100 (+S9)              | 3                            | 3                     | 2.9                         | ANOVA (equal variance) |
| TA100 (-S9)              | 1                            | 0                     |                             |                        |
| TA102 (+S9)              | 2                            | 1                     | 12.6                        | ANOVA (equal variance) |
| TA102 (-S9)              | 0                            | 0                     |                             |                        |
| TA1535 (+S9)             | 0                            | 0                     |                             |                        |
| TA1535 (-S9)             | 0                            | 0                     |                             |                        |
| TA1537 (+S9)             | 1                            | 0                     |                             |                        |
| TA1537 (-S9)             | 0                            | 0                     |                             |                        |

**One-Way ANOVA and ANOVA-Based Comparisons Among Test Samples of Mean 'Extracted Smokeless Tobacco' Slope Estimates that are Significantly Greater than Zero (0)**

TA100 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 1627.401       | 2  | 813.701     | 10.528  | <b>0.011</b> |
| Within Samples | 463.743        | 6  | 77.290      |         |              |
| Total (Corr.)  | 2091.144       | 8  |             |         |              |

| TA100 (+S9)            |         |         |                                 |
|------------------------|---------|---------|---------------------------------|
| ANOVA-Based Comparison | f-ratio | p-value | significance at $\alpha = 0.05$ |
| 084454 vs. 084455      | 0.08    | 0.7842  | not significant                 |
| 084454 vs. 084456      | 14.61   | 0.0087  | <b>significant</b>              |
| 084455 vs. 084456      | 16.89   | 0.0063  | <b>significant</b>              |

TA102 (+S9)

| Source         | Sum of Squares | Df | Mean Square | F-Ratio | P-Value      |
|----------------|----------------|----|-------------|---------|--------------|
| Among Samples  | 6509.537       | 1  | 6509.54     | 76.33   | <b>0.001</b> |
| Within Samples | 341.117        | 4  | 85.279      |         |              |
| Total (Corr.)  | 6850.654       | 5  |             |         |              |

| TA102 (+S9)            |         |         |                                 |
|------------------------|---------|---------|---------------------------------|
| ANOVA-Based Comparison | f-ratio | p-value | significance at $\alpha = 0.05$ |
| 084394 vs. 084455      | 76.33   | 0.0009  | <b>significant</b>              |

Both TA100 (+S9) and TA102 (+S9) strains have more than one test sample for which the mean 'extracted moisture-corrected smokeless tobacco' specific activity slope estimate is greater than zero (0) .

**TA100 (+S9):**

Significant differences among mean 'Extracted Moisture-Corrected Smokeless Tobacco' specific activity slope estimates were detected in TA100 (+S9) between test sample 084456 (Copenhagen Long Cut) and each of {084454 (Fresh Strips), 084455 (Mellow Sticks)}.

**TA102 (+S9):**

Significant differences among mean 'Extracted Smokeless Tobacco' specific activity slope estimates were detected in TA102 (+S9) between test samples 084394 (Camel SNUS Frost) and 084455 (Mellow Sticks) .

**Number of Mean 'Extracted Moisture-Corrected Smokeless Tobacco'  
Slope Estimates Significantly Greater than Zero (0), the Corresponding  
Number of Paired Comparisons and Comparison Method**

**One-Way ANOVA and ANOVA-Based Comparisons Among  
Test Samples of Mean 'Extracted Smokeless Tobacco'  
Slope Estimates that are Significantly Greater than Zero (0)**

