
**Toxicology of Smokeless Tobacco Products:
In Vitro Micronucleus Assay**

***Labstat International ULC
Supplemental Analysis Report***



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

Project Code: M100

Original Date: January 20, 2011
Revision 1 Date: January 2, 2012

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1 Use of Labstat's¹ Analytical Reports²

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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³ *Unless superseded by a specific contractual obligation or other written agreement.*

2 Administrative Information⁴

2.1 Quotation Reference

Quotation Number: T2671 & T2672

Date of Quotation: October 6, 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

The samples to be tested for M100 were received on September 16, 2008 and October 21, 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. Additional product of one brand was received on October 21, 2008 and consisted of 90 tins. There was no physical damage to the containers, bag or tins. Individual pouches, 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

Sample ID	Sample Description
084455	Mellow Sticks
084456	Copenhagen Long Cut
084457	Ariva Wintergreen
084458	Fresh Orbs

2.6 Special Instructions

Some of the products required for testing were removed from inventory remaining from Projects M97, M78L and M78M. Labstat International ULC supplied the "Kentucky Reference 2R4F" (Sample ID 084396).

2.7 Date of Supplemental Report

Original: January 20, 2011

Revision 1: January 2, 2012

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

2.8 Revision History

2.8.1 Revision 1

This revision was required due to an inquiry from the client (client CRO # 2011-016-M100 Supplemental MN).

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.



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

See the 'Methods' section of the micronucleus assay test report for the M100 project.

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 *M100 Supplemental_mn_tpm_dataCF.xls* (micronucleus assay results for TPM of tobacco brand 084396) and *M100 Supplemental_mn_wt_dataCF.xls* (micronucleus assay results for smokeless tobacco products).

5.1.1 'Unit of Use' Doses

Using the unit of use and 'per unit' as received weight of each smokeless tobacco product, as supplied by the client in the table below, the doses of smokeless tobacco reported in the *M100*

Supplemental_mn_wt_dataCF.xls data file were expressed 'per unit' and the calculated doses are part of the raw data and summary data sheets in the column labelled "Unit of Use Dose ('units'/mL)". The unit of use for sample 084396 was defined as one cigarette and hence the 'unit of use' doses for this brand are 'cigarettes/mL'.

Sample ID	Sample Description	Unit of Use	Weight 'as rec'd' (grams)
084394	Camel SNUS Frost	1 pouch	0.6
084395	2S3	2.5 grams	2.5
084454	Fresh Strips	1	0.125
084455	Mellow Sticks	1 stick	0.516
084456	Copenhagen Long Cut	2.5 grams	2.5
084457	Ariva Wintergreen	1	0.28
084458	Fresh Orbs	1	0.225

6 'Unit of Use' Genotoxicity 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 *M100 Supplemental_mn_wt_stats_Unit.xls* (dose-response curve analysis results for smokeless tobacco products on a 'unit of use/mL' dose basis) and *M100 Supplemental_mn_tpm+wt_stats_Unit.xls* (dose-response curve analysis results for smoked and smokeless tobacco products on a 'unit of use' dose basis).

6.2 Methodology

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2.

3.

4.

(b) (4)

5.

6.3 Specific Activity Determinations

(b) (4)

6.4 Comparisons among Smokeless Tobacco Products

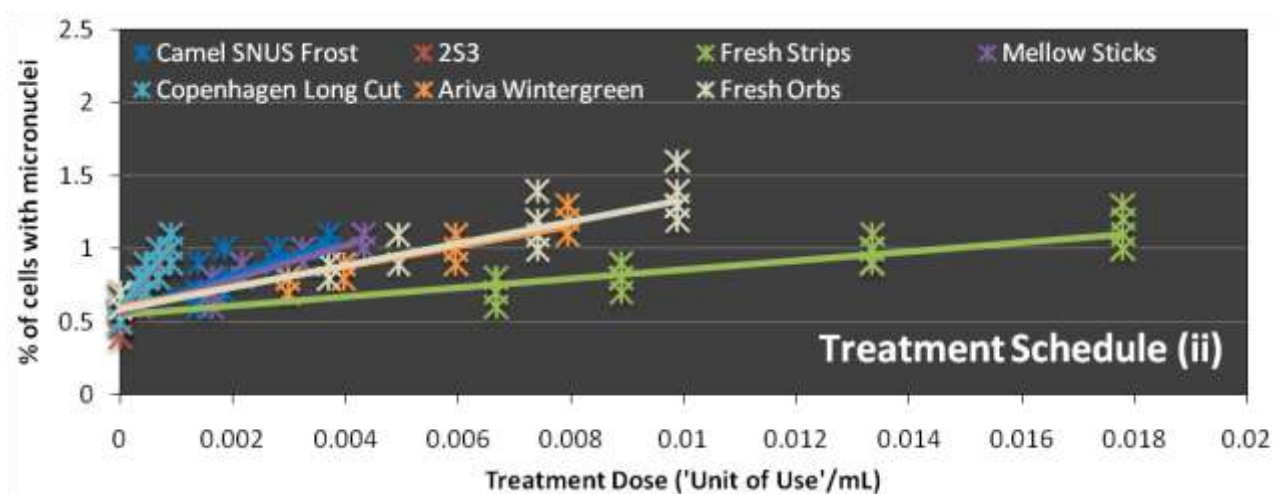
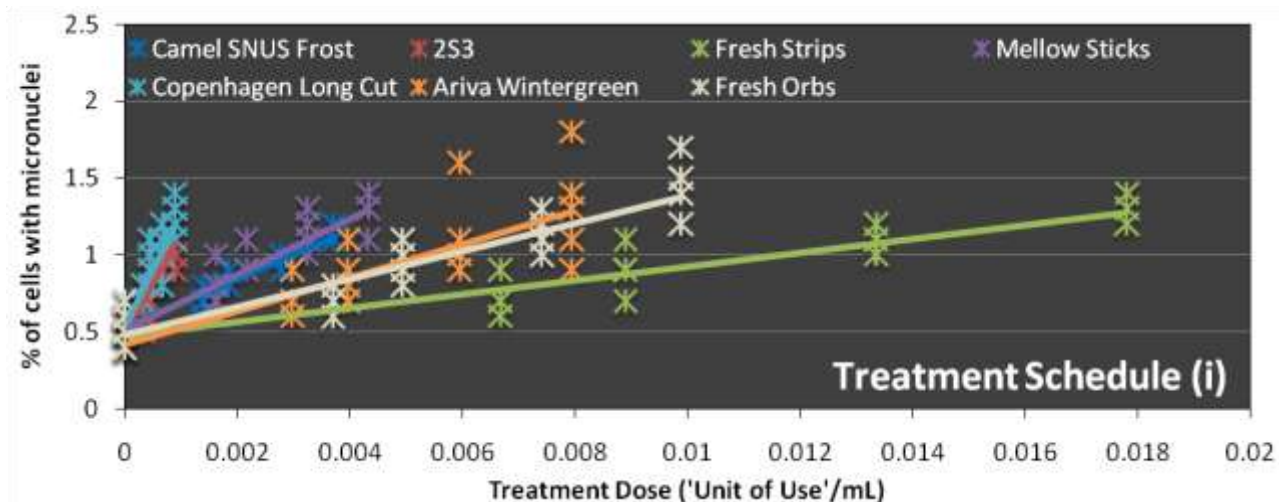
6.4.1 Individual Replicate Slopes and Slope Statistics

The following table of results was obtained for the individual replicate slope estimates and the summary statistics over the three replicate slopes for each smokeless tobacco test sample under both treatment schedules.

		Replicate Slope Analysis [%MNC/('Unit'/mL)]								
Treatment	Sample	Replicate 1		Replicate 2		Replicate 3		Slope Statistics		
Schedule	ID	'Unit' Dose (units/mL)	slope	'Unit' Dose (units/mL)	slope	'Unit' Dose (units/mL)	slope	mean	S.E.	95% C.I.
Schedule (i)	084394	0 - 0.0037	158	0 - 0.0037	161	0 - 0.0037	152	157	2	147 - 168
Schedule (i)	084395	0 - 0.0009	692	0 - 0.0009	577	0 - 0.0009	636	635	33	492 - 777
Schedule (i)	084454	0 - 0.0178	44.5	0 - 0.0178	48.9	0 - 0.0178	40.7	44.7	2.4	34.5 - 54.8
Schedule (i)	084455	0 - 0.0043	203	0 - 0.0043	176	0 - 0.0043	161	180	12	127 - 233
Schedule (i)	084456	0 - 0.0009	814	0 - 0.0009	858	0 - 0.0009	552	742	95	331 - 1152
Schedule (i)	084457	0 - 0.0079	144	0 - 0.0079	101	0 - 0.0079	79.7	108	19	27 - 189
Schedule (i)	084458	0 - 0.0099	112	0 - 0.0099	79.2	0 - 0.0099	81.2	90.9	10.8	44.6 - 137
Schedule (ii)	084394	0 - 0.0037	96.2	0 - 0.0037	143	0 - 0.0037	134	124	14	63 - 185
Schedule (ii)	084395	0 - 0.0009	469	0 - 0.0009	389	0 - 0.0009	530	463	41	286 - 639
Schedule (ii)	084454	0 - 0.0178	31.4	0 - 0.0178	30.8	0 - 0.0178	30.4	30.9	0.3	29.7 - 32.1
Schedule (ii)	084455	0 - 0.0043	93.3	0 - 0.0043	119	0 - 0.0043	138	117	13	61.3 - 172
Schedule (ii)	084456	0 - 0.0009	486	0 - 0.0009	460	0 - 0.0009	445	464	12	411 - 516
Schedule (ii)	084457	0 - 0.0079	49.8	0 - 0.0079	76.4	0 - 0.0079	81.1	69.1	9.7	27.3 - 111
Schedule (ii)	084458	0 - 0.0099	85.4	0 - 0.0099	67.7	0 - 0.0099	71.7	75.0	5.3	51.9 - 98

6.4.2 Data Plots

Plots of all replicate smokeless tobacco test samples can be found in the file *M100 Supplemental_mn_wt_stats_Unit.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 'unit of use' slope estimates among smokeless tobacco test samples yielded the following:

Treatment Schedule	Variation Source	Sum of Squares	d.f.	Mean Square	F Ratio	P value
Treatment Schedule (i)	Among Samples	1454272	6	242379	52.15	< 0.001
	Within Samples	65064	14	4647		
	Total	1519336	20			
Treatment Schedule (ii)	Among Samples	636679	6	106113	106.64	< 0.001
	Within Samples	13931	14	995		
	Total	650610	20			

One-way ANOVA analysis indicates significant differences, at $\alpha = 0.05$, among mean '% micronucleated cells/('Unit of Use'/mL)' slope estimates for smokeless tobacco test samples assayed under both treatment schedules (i) and (ii).

6.4.4 Contrasts of Interest

(b) (4)

Method Applied for Contrasts

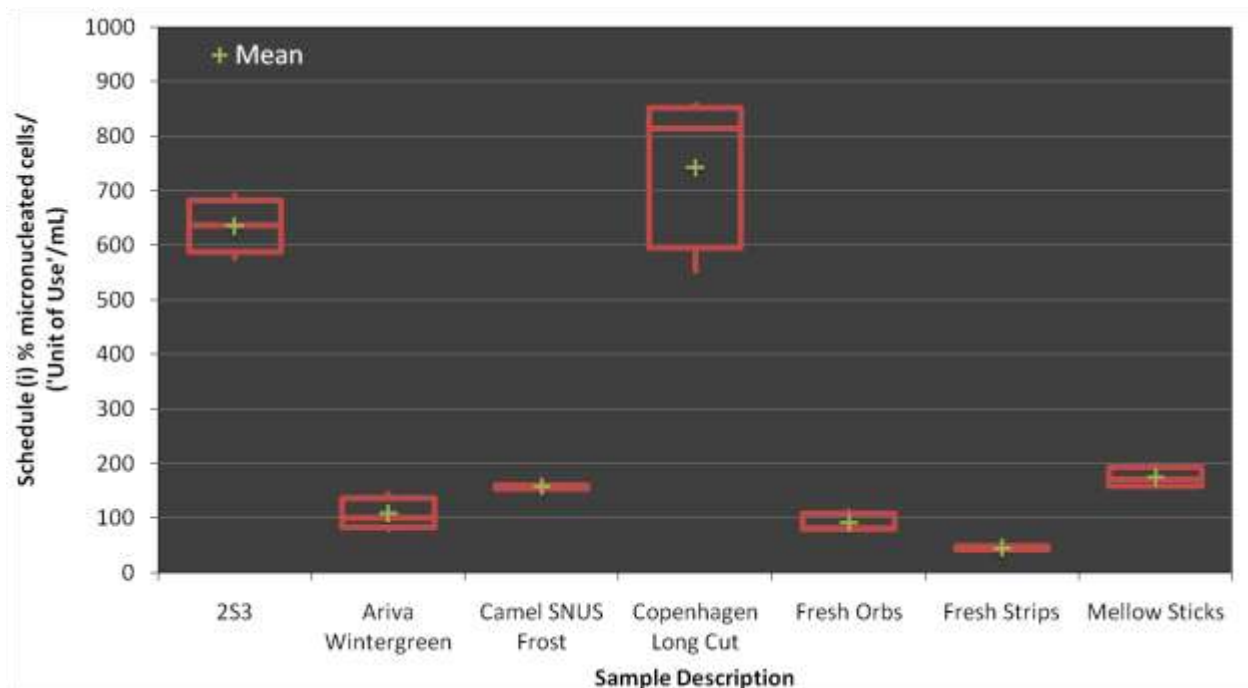
(b) (4)

Contrasts of Interest

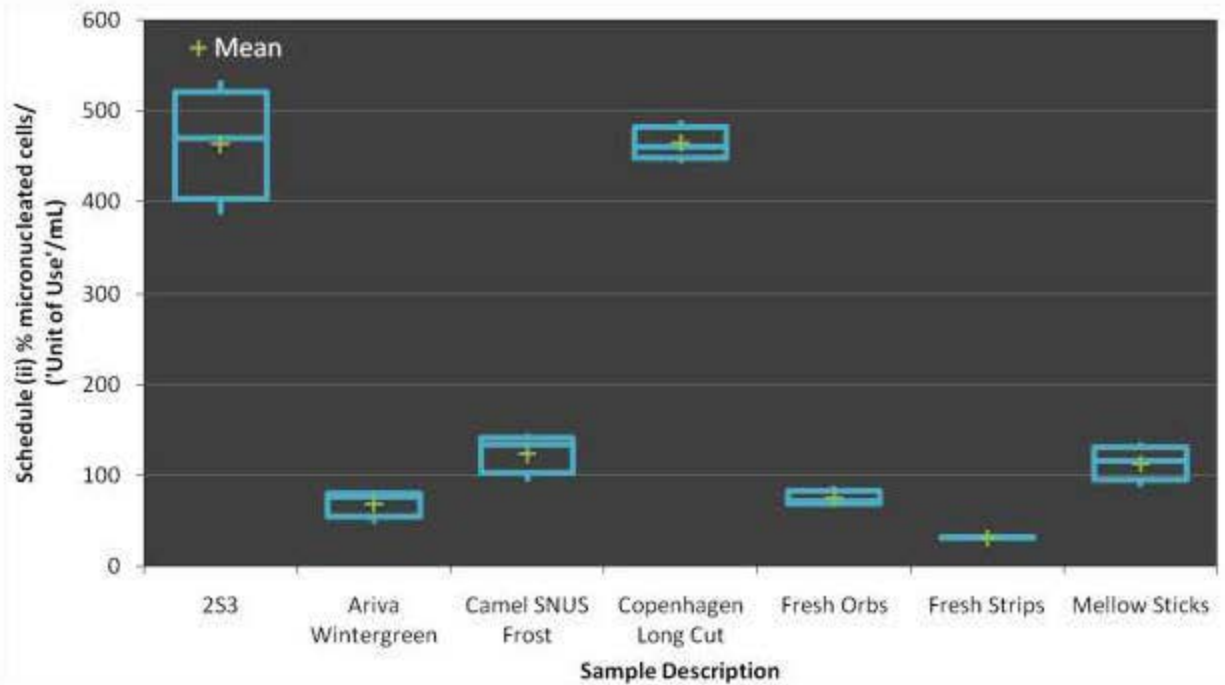
Contrast of Interest	Treatment Schedule (i)			Treatment Schedule (ii)		
	t-statistic	p-value	significance at $\alpha = 0.05$	t-statistic	p-value	significance at $\alpha = 0.05$
084394 vs. 084395	14.3657	0.0001	significant	7.8018	0.0015	significant
084394 vs. 084454	32.9417	0.0000	significant	6.5598	0.0028	not significant
084394 vs. 084455	1.8226	0.1424	not significant	0.3889	0.7172	not significant
084394 vs. 084456	6.1201	0.0036	not significant	18.1445	0.0001	significant
084394 vs. 084457	2.5845	0.0610	not significant	3.1968	0.0330	not significant
084394 vs. 084458	5.9935	0.0039	not significant	3.2403	0.0317	not significant
084395 vs. 084454	17.7552	0.0001	significant	10.5321	0.0005	significant
084395 vs. 084455	12.8742	0.0002	significant	8.0512	0.0013	significant
084395 vs. 084456	1.0571	0.3501	not significant	0.0198	0.9851	not significant

Contrast of Interest	Treatment Schedule (i)			Treatment Schedule (ii)		
	t-statistic	p-value	significance at $\alpha = 0.05$	t-statistic	p-value	significance at $\alpha = 0.05$
084395 vs. 084457	13.8106	0.0002	significant	9.3413	0.0007	significant
084395 vs. 084458	15.6008	0.0001	significant	9.3784	0.0007	significant
084454 vs. 084455	10.8712	0.0004	significant	6.6582	0.0026	not significant
084454 vs. 084456	7.2989	0.0019	significant	35.5799	0.0000	significant
084454 vs. 084457	3.3363	0.0289	not significant	3.9290	0.0171	not significant
084454 vs. 084458	4.1906	0.0138	not significant	8.2282	0.0012	significant
084455 vs. 084456	5.8366	0.0043	not significant	19.5802	0.0000	significant
084455 vs. 084457	3.1986	0.0329	not significant	2.9487	0.0420	not significant
084455 vs. 084458	5.4628	0.0055	not significant	2.9930	0.0402	not significant
084456 vs. 084457	6.5112	0.0029	not significant	25.3401	0.0000	significant
084456 vs. 084458	6.7735	0.0025	not significant	29.2606	0.0000	significant
084457 vs. 084458	0.7894	0.4740	not significant	0.5266	0.6263	not significant

Pairwise t-test comparison p-values less than the Bonferroni-adjusted $\alpha = 0.05$ indicate that significant differences in mean 'unit of use' slope were detected between **Fresh Strips (084454)** and each of {**Camel SNUS Frost (084394)**, **Mellow Sticks (084455)**, **2S3 (084395)**, **Copenhagen Long Cut (084456)**} as well as **2S3 Research Moist Snuff (084395)** and each of {**Fresh Orbs (084458)**, **Ariva Wintergreen (084457)**, **Camel SNUS Frost (084394)**, **Mellow Sticks (084455)**} under treatment schedule (i).



Pairwise t-test comparison p-values less than the Bonferroni-adjusted $\alpha = 0.05$ indicate that significant differences in mean 'unit of use' slope were detected between **2S3 Research Moist Snuff (084395)** as well as **Copenhagen Long Cut (084456)** and each of {**Camel SNUS Frost (084394)**, **Mellow Sticks (084455)**, **Fresh Orbs (084458)**, **Ariva Wintergreen (084457)**, **Fresh Strips (084454)**} plus **Fresh Strips (084454)** and **Fresh Orbs (084458)** under treatment schedule (ii).



6.5 Comparisons between Smoked and Smokeless Tobacco Products

6.5.1 Individual Replicate Slopes and Slope Statistics

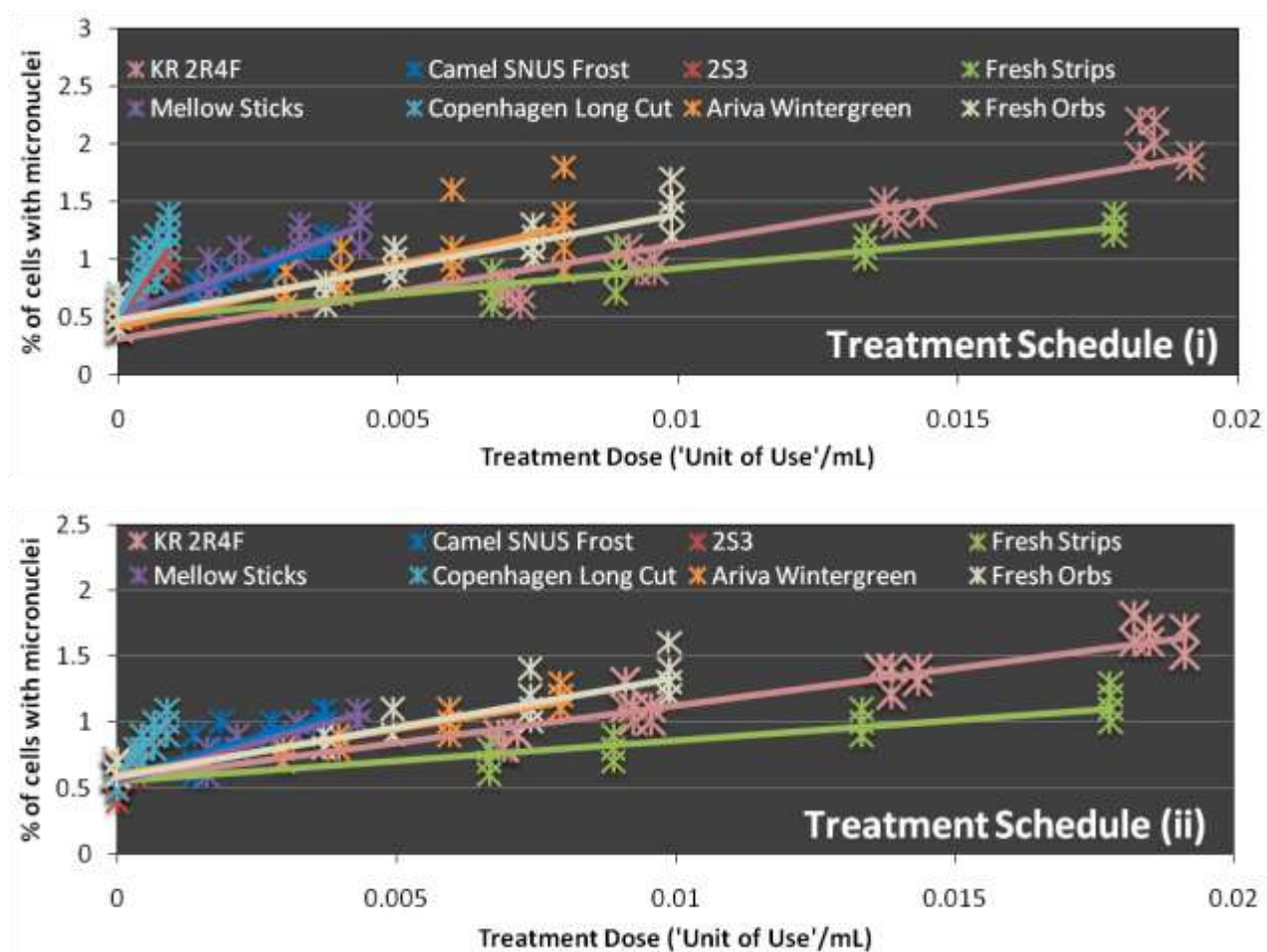
The following table of results was obtained for the individual replicate slope estimates, and the summary statistics, on a 'Unit of Use' dose basis over the three replicate slopes for each smoked and smokeless tobacco test sample under both treatment schedules. The file *M100*

Supplemental_mn_tpm+wt_stats_Unit.xls gives tables of results for all the smokeless tobacco samples plus the tobacco smoke CSC of the KR 2R4F (084396) samples on a 'unit of use' dose basis (see table in section 5.1.1 for defined units).

		Replicate Slope Analysis [%MNC/('Unit'/mL)]								
Treatment	Sample	Replicate 1		Replicate 2		Replicate 3		Slope Statistics		
Schedule	ID	Unit Dose (unit/mL)	slope	Unit Dose (unit/mL)	slope	Unit Dose (unit/mL)	slope	mean	S.E.	95% C.I.
Schedule (i)	084394	0 - 0.0037	158	0 - 0.0037	161	0 - 0.0037	152	157	2	147 - 168
Schedule (i)	084395	0 - 0.0009	692	0 - 0.0009	577	0 - 0.0009	636	635	33	492 - 777
Schedule (i)	084396	0 - 0.0182	88.3	0 - 0.0185	82.5	0 - 0.0191	76.0	82.3	3.5	67 - 97.5
Schedule (i)	084454	0 - 0.0178	44.5	0 - 0.0178	48.9	0 - 0.0178	40.7	44.7	2.4	34.5 - 54.8
Schedule (i)	084455	0 - 0.0043	203	0 - 0.0043	176	0 - 0.0043	161	180	12	127 - 233
Schedule (i)	084456	0 - 0.0009	814	0 - 0.0009	858	0 - 0.0009	552	742	95	331 - 1152
Schedule (i)	084457	0 - 0.0079	144	0 - 0.0079	101	0 - 0.0079	79.7	108	19	27 - 189
Schedule (i)	084458	0 - 0.0099	112	0 - 0.0099	79.2	0 - 0.0099	81.2	90.9	10.8	44.6 - 137
Schedule (ii)	084394	0 - 0.0037	96.2	0 - 0.0037	143	0 - 0.0037	134	124	14	63 - 185
Schedule (ii)	084395	0 - 0.0009	469	0 - 0.0009	389	0 - 0.0009	530	463	41	286 - 639
Schedule (ii)	084396	0 - 0.0182	59.5	0 - 0.0185	57.8	0 - 0.0191	53.4	56.9	1.8	49.1 - 64.8
Schedule (ii)	084454	0 - 0.0178	31.4	0 - 0.0178	30.8	0 - 0.0178	30.4	30.9	0.3	29.7 - 32.1
Schedule (ii)	084455	0 - 0.0043	93.3	0 - 0.0043	119	0 - 0.0043	138	117	13	61.3 - 172
Schedule (ii)	084456	0 - 0.0009	486	0 - 0.0009	460	0 - 0.0009	445	464	12	411 - 516
Schedule (ii)	084457	0 - 0.0079	49.8	0 - 0.0079	76.4	0 - 0.0079	81.1	69.1	9.7	27.3 - 111
Schedule (ii)	084458	0 - 0.0099	85.4	0 - 0.0099	67.7	0 - 0.0099	71.7	75.0	5.3	51.9 - 98

6.5.2 Data Plots

Plots of all replicate smoked and smokeless tobacco test samples expressed on a 'Unit of Use' dose basis can be found in the file *M100 Supplemental_mn_tpm+wt_stats_Unit.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.



6.5.3 One-Way ANOVA Results

One-way ANOVA comparisons of mean 'unit of use' and 'cigarette' slope estimates among all 7 smokeless and one smoked tobacco test sample yielded the following:

Treatment Schedule	Variation Source	Sum of Squares	d.f.	Mean Square	F Ratio	P value
Treatment Schedule (i)	Among Samples	1556508	7	222358	54.62	< 0.001
	Within Samples	65139	16	4071		
	Total	1621646	23			
Treatment Schedule (ii)	Among Samples	684414	7	97773	112.13	< 0.001
	Within Samples	13951	16	872		
	Total	698365	23			

One-way ANOVA analysis indicates significant differences, at $\alpha = 0.05$, among mean 'Unit of Use' slope estimates for smoked and smokeless tobacco samples assayed under both treatment schedules (i) and (ii).

6.5.4 Contrasts of Interest

(b) (4)

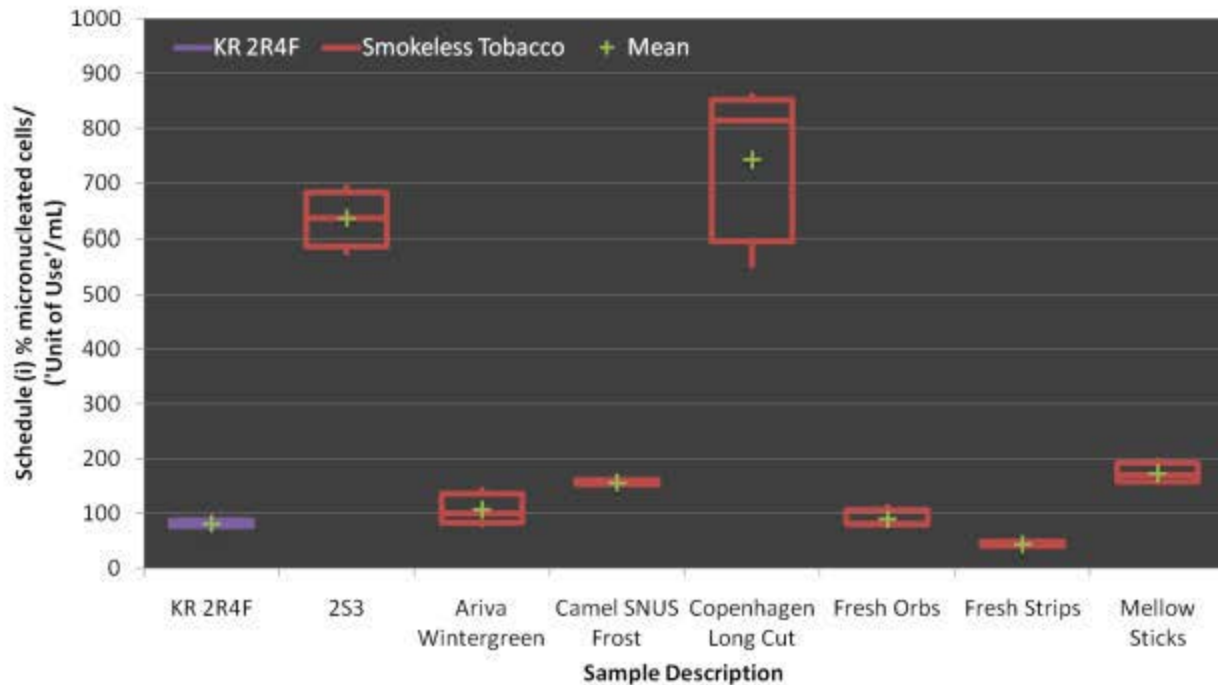
Method Applied for Contrasts

(b) (4)

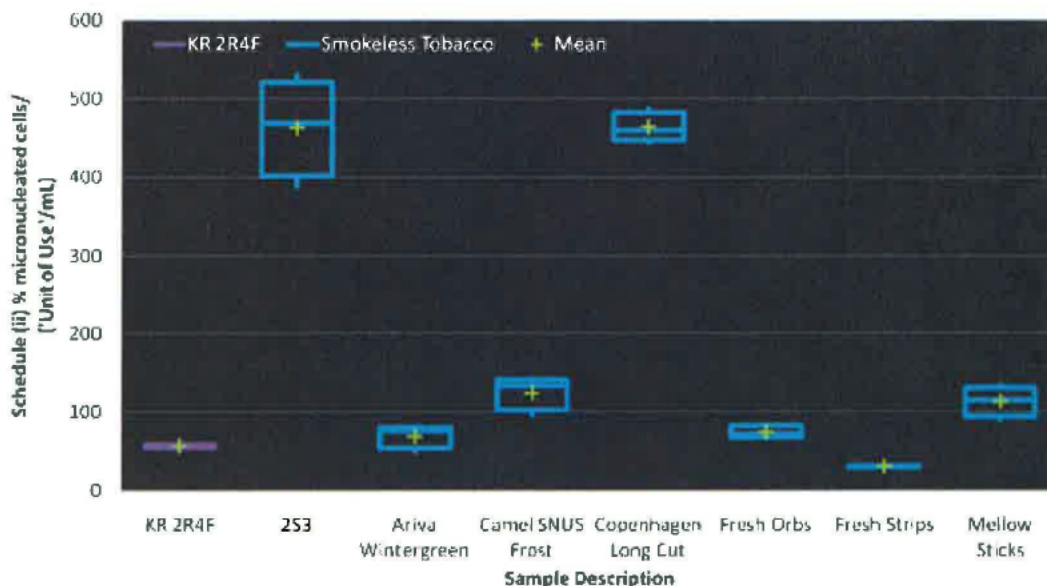
Contrasts of Interest

Contrast of Interest	Treatment Schedule (i)			Treatment Schedule (ii)		
	t-statistic	p-value	significance at $\alpha = 0.05$	t-statistic	p-value	significance at $\alpha = 0.05$
084394 vs. 084396	17.37	0.0001	significant	4.691	0.0094	not significant
084395 vs. 084396	16.57	0.0001	significant	9.888	0.0006	significant
084454 vs. 084396	8.835	0.0009	significant	14.12	1.5E-04	significant
084455 vs. 084396	7.680	0.0015	significant	4.593	0.0101	not significant
084456 vs. 084396	6.903	0.0023	significant	33.08	5.0E-06	significant
084457 vs. 084396	1.346	0.2497	not significant	1.231	0.2857	not significant
084458 vs. 084396	0.7638	0.4875	not significant	3.190	0.0332	not significant

Pairwise t-test comparison p-values less than the Bonferroni-adjusted $\alpha = 0.05$ indicate that under treatment schedule (i), significant differences in mean 'unit of use' specific activity slope were detected between KR 2R4F (084396) and the following smokeless tobacco extracts on a 'unit of use' dose basis: {Camel SNUS Frost (084394), 2S3 Research Moist Snuff (084395), Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456)}.



Pairwise t-test comparison p-values less than the Bonferroni-adjusted $\alpha = 0.05$ indicate that under treatment schedule (ii), significant differences in mean 'unit of use' specific activity slope were detected between KR 2R4F (084396) and the following smokeless tobacco extracts on a 'unit of use' dose basis: {2S3 Research Moist Snuff (084395), Fresh Strips (084454), Copenhagen Long Cut (084456)}.



7 Attribution

7.1 Original

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

Dated: January 20, 2011

Wendy Wagstaff

Wendy Wagstaff
Senior Statistician
Labstat International ULC

7.2 Revision 1

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

Dated: January 2, 2012

Wendy Wagstaff

Wendy Wagstaff
Senior Statistician
Labstat International ULC

Report prepared by Labstat International ULC

Appendix A

Scope of Accreditation



Standards Council of Canada
Conseil canadien des normes

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K1P 8N7

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

SCOPE OF ACCREDITATION

LABSTAT INTERNATIONAL ULC
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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

CLIENTS SERVED: All interested parties

FIELDS OF TESTING: Biological, Chemical/Physical

ISSUED ON: 2008-10-06

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 – Part 1:

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

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Standards Council of Canada, Accredited Laboratory No. 368

	Gas-Chromatographic Method
ISO 15592-2	Fine-cut Tobacco and smoking articles made from it – Methods of sampling, conditioning and analysis – Part 2: Atmosphere for conditioning and testing
ISO 15592-3	Fine-cut Tobacco and smoking articles made from it – Methods of sampling, conditioning and analysis – Part 3: Determination of total particulate matter of smoking articles using a routine analytical smoking machine, preparation for the determination of water and nicotine, and calculation of nicotine-free dry particulate matter
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-124	Determination of Vinyl Chloride, 1,3-Butadiene, Isoprene, Acrylonitrile, Benzene, Toluene, Styrene and Acetamide in Mainstream Tobacco Smoke (Expanded List)
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 Tobacco Smoke
TMS-133	Determination of Selected Heterocyclic Aromatic Amines (HAAs) in Mainstream Tobacco Smoke
TMS-135	Determination of Tobacco Specific Nitrosamines in Mainstream Tobacco Smoke by Liquid Chromatography–Tandem Mass Spectrometry
TMS-137	Determination of Acetamide and Acrylamide in Mainstream Tobacco Smoke
TSS-219	Determination of Selected Polynuclear Aromatic Hydrocarbons (PAHs) in Sidestream Tobacco Smoke
TSS-222	Determination of Sidestream Tobacco Smoke pH
TWT-303	Determination of Carbonyls in Tobacco Samples
TWT-320	Determination of 1- and 2- Aminonaphthalene and 3- and 4-Aminobiphenyl in Tobacco Samples
TWT-321	

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	Determination Of Nicotine Alkaloids And Reducing Sugars In Tobacco Samples
TWT-324	Determination of Nicotine in Tobacco Samples (CDC method)
TWT-332	Determination of Volatile Nitrosamines in Tobacco Samples
TWT-333	Determination of Tobacco Specific Nitrosamines in Tobacco Samples by Liquid Chromatography–Tandem Mass Spectrometry
TWT-334	Determination of Chloride in Tobacco Samples
TWT-335	Determination of Selected Polycyclic Aromatic Hydrocarbons (PAHs) in Tobacco Samples
TWT-336	Determination of Acrylamide in Tobacco Samples by Liquid Chromatography – Tandem Mass Spectrometry
TWT-337	Determination of 1,3–Butadiene and Benzene in Tobacco Samples

(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
T-207	Determination of Toxic Trace Metals in Sidestream Smoke

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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 from 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 Physiological Fluid Samples
TME-002	Determination of Creatinine in Urine
TME-003	Determination of 3-Hydroxycotinine in Physiological Fluid Samples
TME-004	<i>Salmonella Typhimurium</i> Reverse Mutation Assay: Microsuspension Method For Testing Urine Mutagenicity
TME-005	Determination of Nicotine and its Major Metabolites in Urine by Liquid Chromatography – Tandem Mass Spectrometry

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TME-006	Determination of S-Phenylmercapturic Acid (S-PMA) in Urine by Liquid Chromatography – Tandem Mass Spectrometry
TME-007	Determination of 8-Hydroxy-2'-Deoxyguanosine (8-OHdG) in Urine by Liquid Chromatography – Tandem Mass Spectrometry
TME-008	Determination of 1-Hydroxypyrene (1-HOP) in Urine by Liquid Chromatography – Tandem Mass Spectrometry
TME-009	Determination of 4-(Methyl-Nitrosamino)-1-(3-Pyridyl)-1-Butanol (NNAL) and its Glucuronides in Urine by Liquid Chromatography – Tandem Mass Spectrometry
TME-010	Determination of 1,3-Butadiene Urinary Metabolites by Liquid Chromatography – Tandem Mass Spectrometry
TME-011	Determination of 3-Hydroxypropylmercapturic Acid (3-HPMA) in Urine by Liquid Chromatography – Tandem Mass Spectrometry
TME-012	Determination of Selected Arylamines in Urine by Gas Chromatography – Mass Spectrometry (GC-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)

CDC: Centers for Disease Control and Prevention

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: 2008-10-06

Number of Scope Listings: 93
SCC 1003-15/420

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Standards Council of Canada Accredited Laboratory No. 985

Partner File #0

Partner: None

Appendix B

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

Use of Labstat's¹ Analytical Reports²

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Sample ID	Sample Description
084396	Kentucky Reference 2R4F

LABSTAT INTERNATIONAL ULC

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Project: M100

Period: November 6, 2008

Smoking Data[†] for *In Vitro* Micronucleus Assay analysis**TPM and 'Unit of Use' Dose Data for *In Vitro* MN Assay**

Set Number	Run Number	Sample ID	Replicate Number	Smoking Date	Cigarettes Smoked	Puff Count (per cig)	MS TPM (mg/cig) ¹	Nicotine (mg/cig)	Smoking Machine	TPM Dose (mg/mL media)					'Unit of Use' Dose (cigs/mL media)				
										1	2	3	4	5	1	2	3	4	5
1	2	084396	1	6-Nov-08	20	8.8	11.0	0.734	Borgwaldt Rotary	0	0.075	0.100	0.150	0.200	0	0.007	0.009	0.014	0.018
1	3	084396	2	6-Nov-08	20	9.1	10.8	0.767	Borgwaldt Rotary	0	0.075	0.100	0.150	0.200	0	0.007	0.009	0.014	0.018
1	4	084396	3	6-Nov-08	20	8.7	10.5	0.731	Borgwaldt Rotary	0	0.075	0.100	0.150	0.200	0	0.007	0.010	0.014	0.019

[†] Samples generated under 'ISO' smoking conditions:

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

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

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation**
(% Micronuclei and % Cytotoxicity as determined by Relative Increase in Cell Counts (RICC))

Set Number	Run Number	Sample ID	Replicate Number	Treatment Schedule	TPM (mg/mL)	Unit of Use (cigs/mL)	Treatment Time (h)	Metabolic Activation	% Cytotoxicity (by RICC)			% Micronuclei		
									Flask 1	Flask 2	Average	Flask 1	Flask 2	Average
1	2	084396	1	Schedule (i)	0	0	3	-S9	0	0	0	0.50	0.50	0.50
1	2	084396	1	Schedule (i)	0.075	0.007	3	-S9	19.0	12.7	15.8	0.80	0.80	0.80
1	2	084396	1	Schedule (i)	0.100	0.009	3	-S9	27.7	26.1	26.9	1.20	1.10	1.15
1	2	084396	1	Schedule (i)	0.150	0.014	3	-S9	48.9	51.5	50.2	1.50	1.50	1.50
1	2	084396	1	Schedule (i)	0.200	0.018	3	-S9	81.8	77.6	79.7	2.20	2.40	2.30
1	3	084396	2	Schedule (i)	0	0	3	-S9	0	0	0	0.70	0.50	0.60
1	3	084396	2	Schedule (i)	0.075	0.007	3	-S9	19.8	20.7	20.3	0.80	0.70	0.75
1	3	084396	2	Schedule (i)	0.100	0.009	3	-S9	31.5	42.2	36.9	1.00	0.90	0.95
1	3	084396	2	Schedule (i)	0.150	0.014	3	-S9	62.2	57.8	60.0	1.40	1.50	1.45
1	3	084396	2	Schedule (i)	0.200	0.018	3	-S9	83.8	89.7	86.7	2.10	2.30	2.20
1	4	084396	3	Schedule (i)	0	0	3	-S9	0	0	0	0.40	0.50	0.45
1	4	084396	3	Schedule (i)	0.075	0.007	3	-S9	10.4	12.0	11.2	0.60	0.80	0.70
1	4	084396	3	Schedule (i)	0.100	0.010	3	-S9	31.2	30.7	30.9	1.00	1.10	1.05
1	4	084396	3	Schedule (i)	0.150	0.014	3	-S9	50.6	53.3	52.0	1.40	1.50	1.45
1	4	084396	3	Schedule (i)	0.200	0.019	3	-S9	81.8	86.0	83.9	1.80	2.00	1.90
1	2	084396	1	Schedule (ii)	0	0	3	+S9	0	0	0	0.70	0.70	0.70
1	2	084396	1	Schedule (ii)	0.075	0.007	3	+S9	5.3	5.4	5.4	0.90	0.90	0.90
1	2	084396	1	Schedule (ii)	0.100	0.009	3	+S9	12.9	10.1	11.5	1.30	1.20	1.25
1	2	084396	1	Schedule (ii)	0.150	0.014	3	+S9	25.0	24.0	24.5	1.60	1.40	1.50
1	2	084396	1	Schedule (ii)	0.200	0.018	3	+S9	35.6	38.8	37.2	1.90	1.70	1.80
1	3	084396	2	Schedule (ii)	0	0	3	+S9	0	0	0	0.60	0.60	0.60
1	3	084396	2	Schedule (ii)	0.075	0.007	3	+S9	15.8	10.1	12.9	0.90	0.80	0.85
1	3	084396	2	Schedule (ii)	0.100	0.009	3	+S9	22.6	17.3	19.9	1.10	1.10	1.10
1	3	084396	2	Schedule (ii)	0.150	0.014	3	+S9	32.9	32.4	32.6	1.30	1.40	1.35
1	3	084396	2	Schedule (ii)	0.200	0.018	3	+S9	41.8	41.0	41.4	1.60	1.70	1.65
1	4	084396	3	Schedule (ii)	0	0	3	+S9	0	0	0	0.60	0.60	0.60
1	4	084396	3	Schedule (ii)	0.075	0.007	3	+S9	16.9	17.2	17.1	1.00	0.90	0.95
1	4	084396	3	Schedule (ii)	0.100	0.010	3	+S9	29.2	25.0	27.1	1.10	1.10	1.10
1	4	084396	3	Schedule (ii)	0.150	0.014	3	+S9	36.2	35.9	36.0	1.50	1.30	1.40
1	4	084396	3	Schedule (ii)	0.200	0.019	3	+S9	43.8	41.4	42.6	1.70	1.50	1.60

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Project: M100

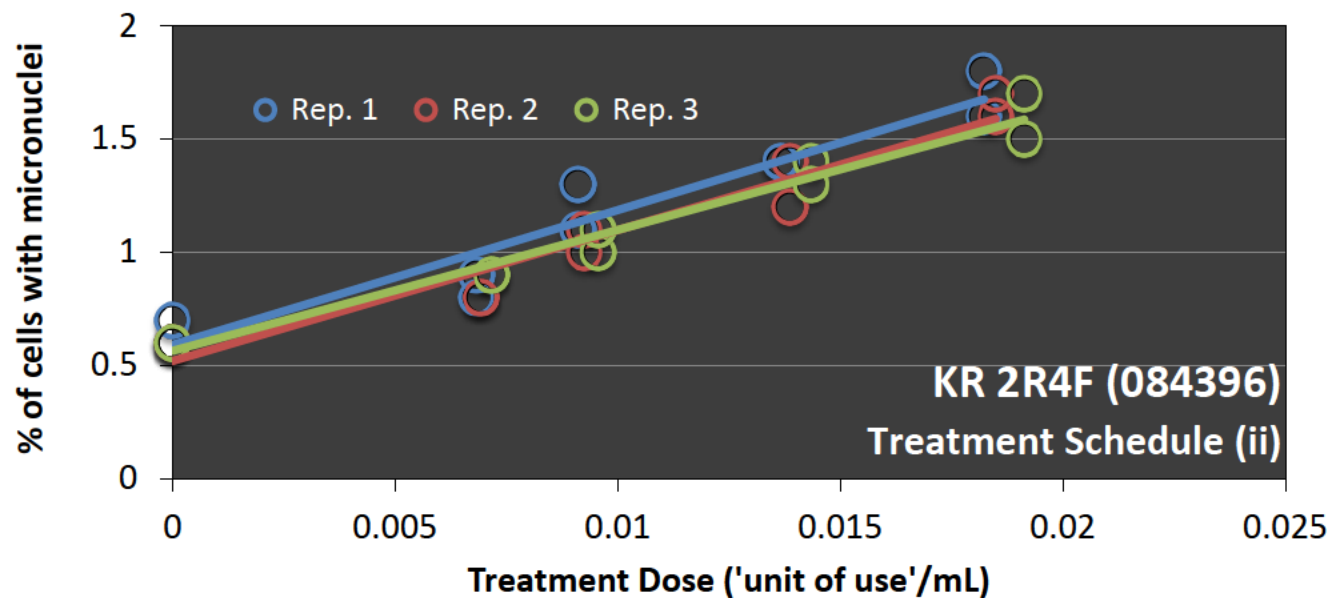
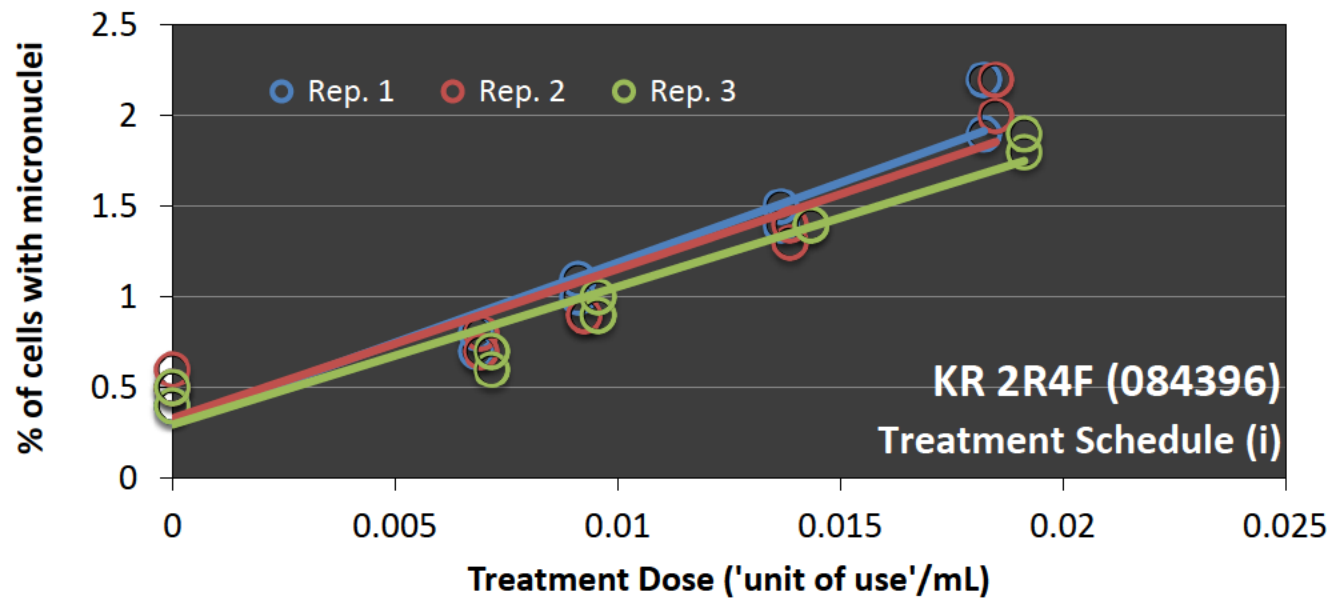
Period: November 28 - December 17, 2008

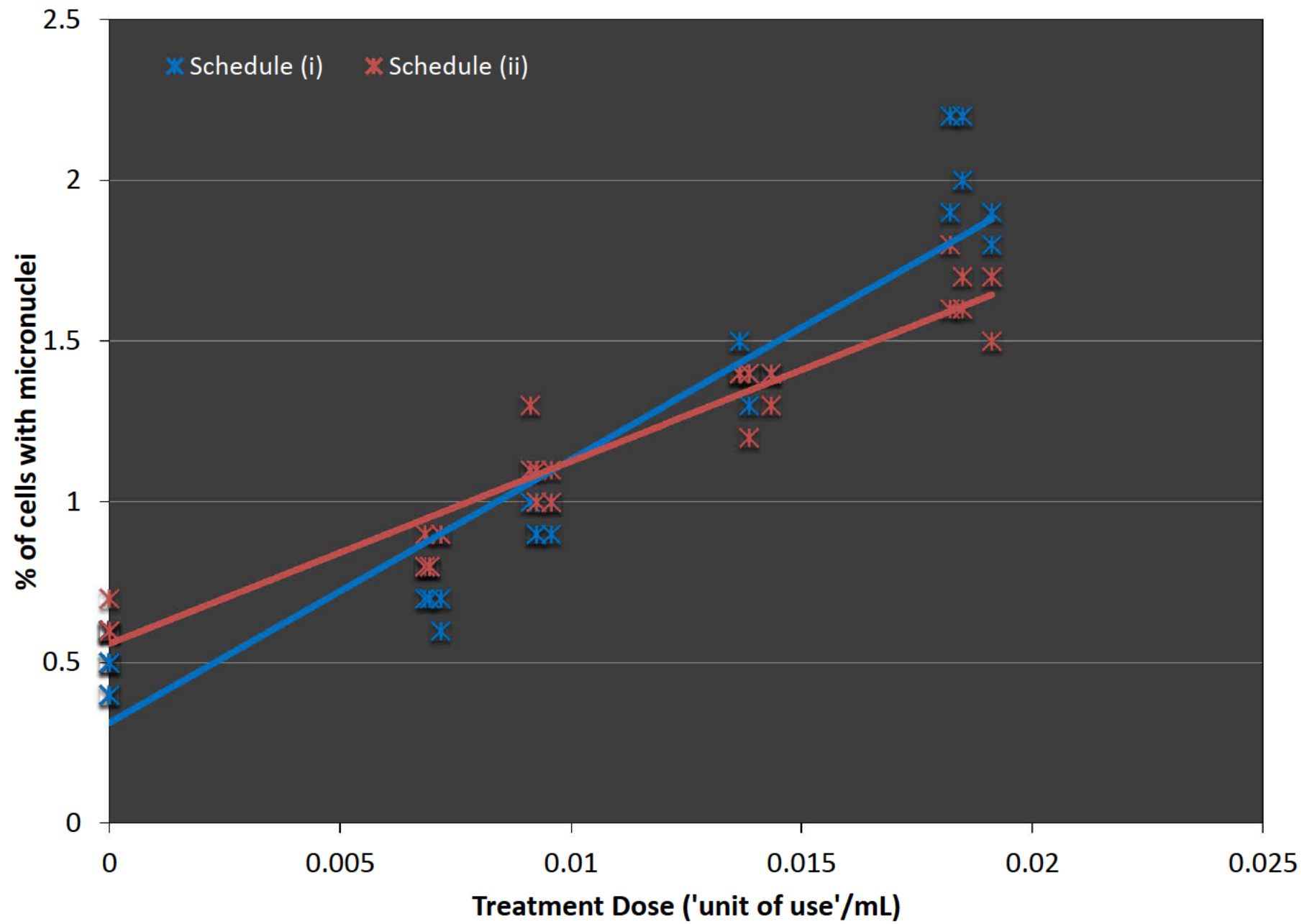
***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(Assay Information)**

Sample ID	Replicate Number	Assay Date	Treatment Schedule	Metabolic Activation	Treatment (hours)	Recovery (hours)	Before Treatment (Cells (x10 ⁵) per mL)		Negative Control (Cells (x10 ⁵) per mL)		Increase > 90%	
							Flask 1	Flask 2	Flask 1	Flask 2	Flask 1	Flask 2
084396	1	28-Nov-08	Schedule (i)	-S9	3	27	1.96	2.00	7.44	7.36	≥ 90%	≥ 90%
084396	2	04-Dec-08	Schedule (i)	-S9	3	27	1.96	2.00	6.40	6.64	≥ 90%	≥ 90%
084396	3	05-Dec-08	Schedule (i)	-S9	3	27	2.04	2.08	8.20	8.08	≥ 90%	≥ 90%
084396	1	11-Dec-08	Schedule (ii)	+S9	3	27	2.08	2.08	7.36	7.24	≥ 90%	≥ 90%
084396	2	12-Dec-08	Schedule (ii)	+S9	3	27	2.08	2.08	7.92	7.64	≥ 90%	≥ 90%
084396	3	17-Dec-08	Schedule (ii)	+S9	3	27	1.96	1.96	7.16	7.08	≥ 90%	≥ 90%

Slope Analysis of the Linear Portion of the Dose-Response Curve
[% of mononucleated cells with micronuclei/('unit of use'/mL)]

Treatment Schedule	Sample ID	Sample Description	% micronucleated cells/('unit of use'/mL)										
			Replicate 1		Replicate 2		Replicate 3		Statistics for Replicate 'Unit' Slope Estimates				
			Dose Range		Dose Range		Dose Range		Standard		t-test p-value (H ₀ : mean = 0)		
			('unit'/mL)	slope	('unit'/mL)	slope	('unit'/mL)	slope	Mean	Error	95% C.I.	p-value	significance
Schedule (i)	084396	Kentucky Reference 2R4F	0 - 0.018	88.3	0 - 0.018	82.5	0 - 0.019	76.0	82.3	3.5	67 - 97.5	0.002	significant
Schedule (ii)	084396	Kentucky Reference 2R4F	0 - 0.018	59.5	0 - 0.018	57.8	0 - 0.019	53.4	56.9	1.8	49.1 - 64.8	0.001	significant





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

Slope Analysis of the Linear Portion of the Dose-Response Curve for Smokeless Tobacco [%MNC*/('Unit of Use/mL)] and Smoked Tobacco [%MNC/(cigarettes/mL)] Samples

Treatment Schedule	Sample ID	Sample Description	% micronucleated cells /(cigarettes/mL) (KR 2R4F) or % micronucleated cells/('Unit of Use/mL)										
			Replicate 1		Replicate 2		Replicate 3		Statistics for Replicate 'Unit of Use' Slope Estimates				
			Dose Range		Dose Range		Dose Range		Standard		t-test p-value (H ₀ : mean = 0)		
			('Unit/mL)	slope	('Unit/mL)	slope	('Unit/mL)	slope	Mean	Error	95% C.I.	p-value	significance
Schedule (i)	084394	Camel SNUS Frost	0 - 0.0037	158	0 - 0.0037	161	0 - 0.0037	152	157	2	147 - 168	0.000	significant
Schedule (i)	084395	2S3	0 - 0.0009	692	0 - 0.0009	577	0 - 0.0009	636	635	33	492 - 777	0.003	significant
Schedule (i)	084396	KR 2R4F	0 - 0.0182	88.3	0 - 0.0185	82.5	0 - 0.0191	76.0	82.3	3.5	67 - 97.5	0.002	significant
Schedule (i)	084454	Fresh Strips	0 - 0.0178	44.5	0 - 0.0178	48.9	0 - 0.0178	40.7	44.7	2.4	34.5 - 54.8	0.003	significant
Schedule (i)	084455	Mellow Sticks	0 - 0.0043	203	0 - 0.0043	176	0 - 0.0043	161	180	12	127 - 233	0.005	significant
Schedule (i)	084456	Copenhagen Long Cut	0 - 0.0009	814	0 - 0.0009	858	0 - 0.0009	552	742	95	331 - 1152	0.016	significant
Schedule (i)	084457	Ariva Wintergreen	0 - 0.0079	144	0 - 0.0079	101	0 - 0.0079	79.7	108	19	27 - 189	0.029	significant
Schedule (i)	084458	Fresh Orbs	0 - 0.0099	112	0 - 0.0099	79.2	0 - 0.0099	81.2	90.9	10.8	44.6 - 137	0.014	significant
Schedule (ii)	084394	Camel SNUS Frost	0 - 0.0037	96.2	0 - 0.0037	143	0 - 0.0037	134	124	14	63 - 185	0.013	significant
Schedule (ii)	084395	2S3	0 - 0.0009	469	0 - 0.0009	389	0 - 0.0009	530	463	41	286 - 639	0.008	significant
Schedule (ii)	084396	KR 2R4F	0 - 0.0182	59.5	0 - 0.0185	57.8	0 - 0.0191	53.4	56.9	1.8	49.1 - 64.8	0.001	significant
Schedule (ii)	084454	Fresh Strips	0 - 0.0178	31.4	0 - 0.0178	30.8	0 - 0.0178	30.4	30.9	0.3	29.7 - 32.1	0.000	significant
Schedule (ii)	084455	Mellow Sticks	0 - 0.0043	93.3	0 - 0.0043	119	0 - 0.0043	138	117	13	61.3 - 172	0.012	significant
Schedule (ii)	084456	Copenhagen Long Cut	0 - 0.0009	486	0 - 0.0009	460	0 - 0.0009	445	464	12	411 - 516	0.001	significant
Schedule (ii)	084457	Ariva Wintergreen	0 - 0.0079	49.8	0 - 0.0079	76.4	0 - 0.0079	81.1	69.1	9.7	27.3 - 111	0.019	significant
Schedule (ii)	084458	Fresh Orbs	0 - 0.0099	85.4	0 - 0.0099	67.7	0 - 0.0099	71.7	75.0	5.3	51.9 - 98	0.005	significant

* MNC = micronucleated cells

Cigarette smoke condensate (CSC) test sample with cigarettes/mL dose basis

Evaluation of Ratio (Max ÷ Min) of Standard Deviations of 'Unit of Use' Slope Estimates and Corresponding Method of Comparison

One-Way ANOVA of Mean 'Unit of Use' Slope Estimates

Schedule (i)

Source	Sum of Squares	Degrees of Freedom	Mean Square	F-Ratio	P-Value
Among Samples	1556508	7	222358	54.62	0.000
Within Samples	65139	16	4071		
Total (Corr.)	1621646	23			

Treatment Schedule	Std. Dev. Ratio (Max ÷ Min)	Method of Comparison
Schedule (i)	40.4	Pairwise T-test (unequal variance)
Schedule (ii)	145.9	Pairwise T-test (unequal variance)

Schedule (ii)

Source	Sum of Squares	Degrees of Freedom	Mean Square	F-Ratio	P-Value
Among Samples	684414	7	97773	112.13	0.000
Within Samples	13951	16	872		
Total (Corr.)	698365	23			

One-way ANOVA analysis indicates significant differences (at $\alpha = 0.05$) among mean 'Unit of Use' specific activity slope estimates for smoked and smokeless tobacco test samples under both Treatment Schedules (i) and (ii).

ANOVA-Based Comparisons of Smokeless Tobacco Mean 'Unit of Use' Slopes to Control Brand KR 2R4F (084396) Mean 'Cigarette' Slope using Bonferroni-adjusted p-values

ANOVA-Based Comparison	Schedule (i)			Schedule (ii)		
	f-ratio	p-value	significance at $\alpha = 0.05$	f-ratio	p-value	significance at $\alpha = 0.05$
084394 vs. 084396	2.070	0.1695	not significant	7.783	0.0131	not significant
084395 vs. 084396	112	1.2E-08	significant	283	1.3E-11	significant
084454 vs. 084396	0.520	0.4810	not significant	1.167	0.2960	not significant
084455 vs. 084396	3.515	0.0792	not significant	6.151	0.0246	not significant
084456 vs. 084396	160	9.5E-10	significant	285	1.3E-11	significant
084457 vs. 084396	0.246	0.6270	not significant	0.255	0.6202	not significant
084458 vs. 084396	0.028	0.8699	not significant	0.559	0.4655	not significant

ANOVA-based comparison p-values less than the Bonferroni-adjusted $\alpha = 0.05$ indicate that significant differences were detected between the mean 'cigarette' slope of the KR 2R4F (084396) smoked tobacco samples and the mean 'unit of use' slope of the following smokeless tobacco samples under each Treatment Schedule:

Treatment Schedules (i) and (ii)

{2S3 (084395), Copenhagen Long Cut (084456)}

Pairwise T-test Comparisons of Smokeless Tobacco Mean 'Unit of Use' Slope to Control Brand KR 2R4F (084396) Mean 'Cigarette' Slope using Bonferroni-adjusted p-values

Pairwise T-Test Comparison	Schedule (i)			Schedule (ii)		
	t-statistic	p-value	significance at $\alpha = 0.05$	t-statistic	p-value	significance at $\alpha = 0.05$
084394 vs. 084396	17.37	0.0001	significant	4.691	0.0094	not significant
084395 vs. 084396	16.57	0.0001	significant	9.888	0.0006	significant
084454 vs. 084396	8.835	0.0009	significant	14.12	1.5E-04	significant
084455 vs. 084396	7.680	0.0015	significant	4.593	0.0101	not significant
084456 vs. 084396	6.903	0.0023	significant	33.08	5.0E-06	significant
084457 vs. 084396	1.346	0.2497	not significant	1.231	0.2857	not significant
084458 vs. 084396	0.7638	0.4875	not significant	3.190	0.0332	not significant

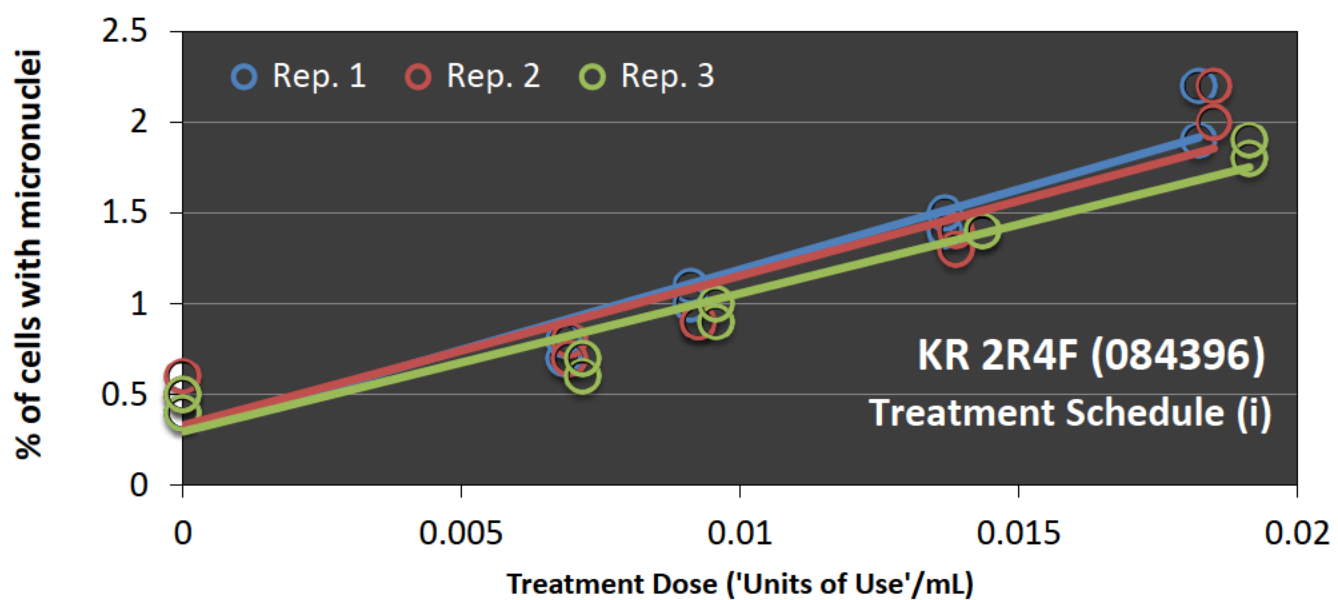
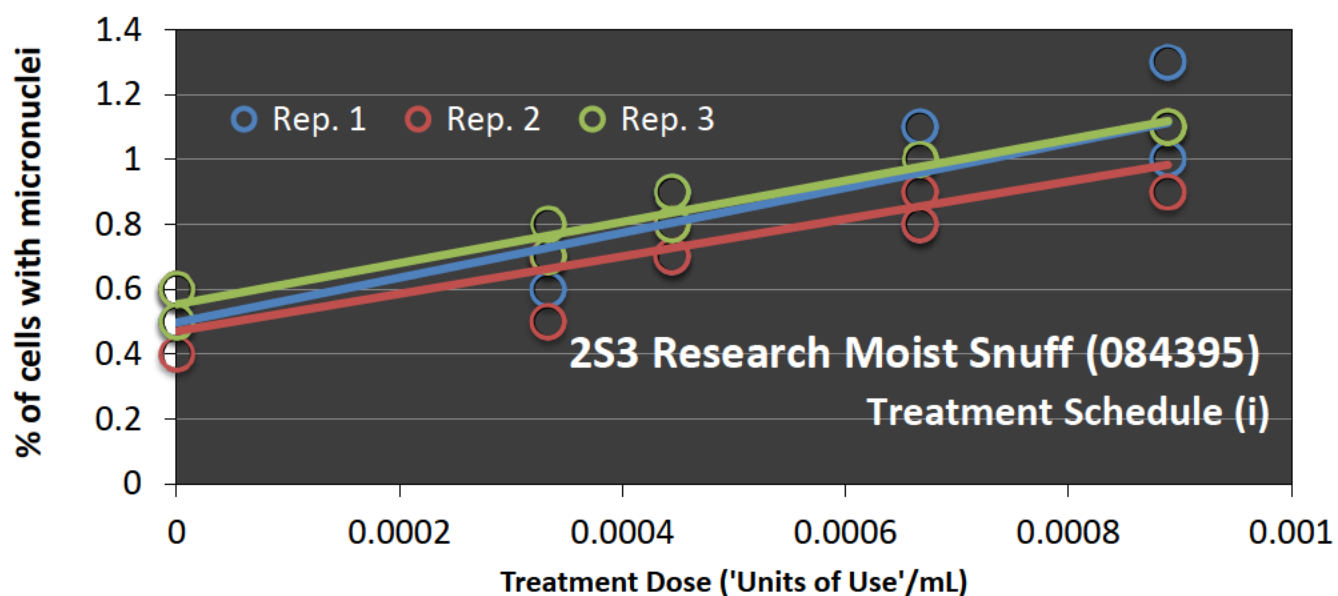
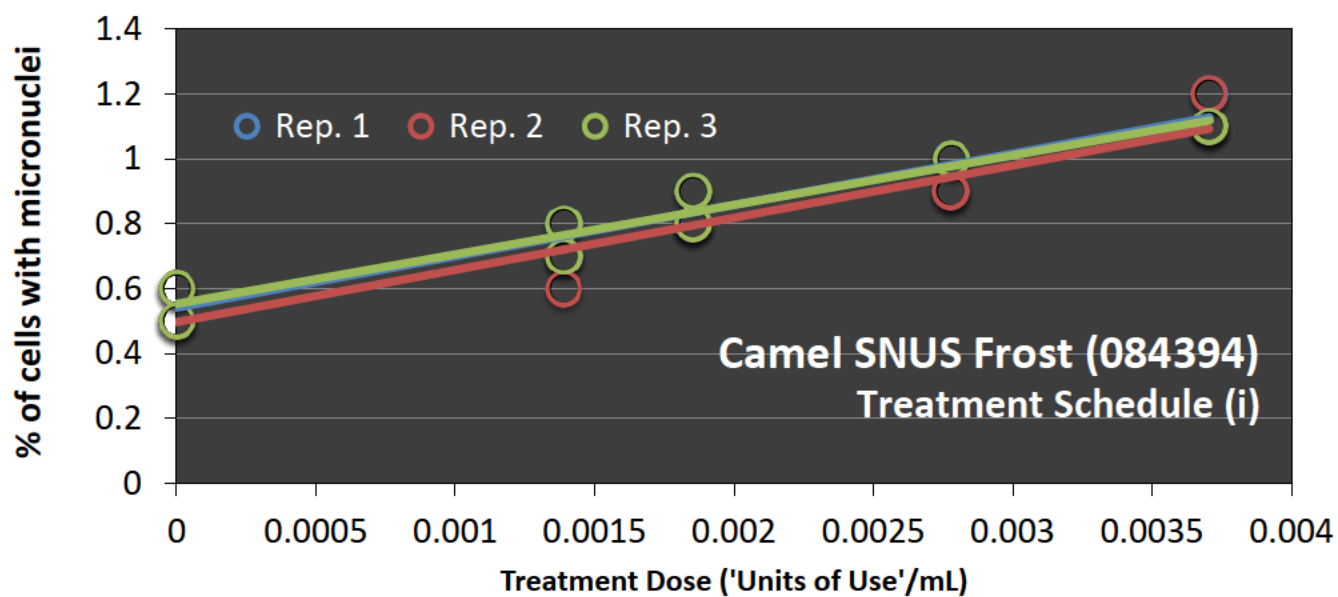
Pairwise t-test comparison p-values less than the Bonferroni-adjusted $\alpha = 0.05$ indicate that significant differences were detected between the mean 'cigarette' slope of the KR 2R4F (084396) smoked tobacco samples and the mean 'unit of use' slope of the following smokeless tobacco samples under each Treatment Schedule:

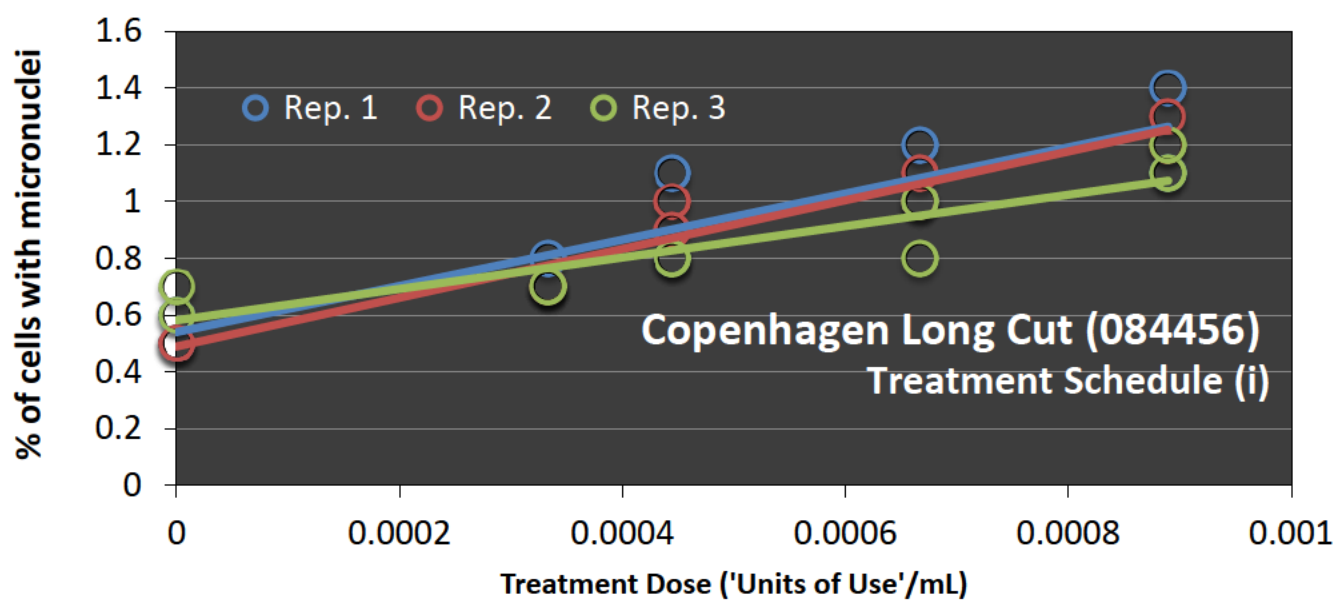
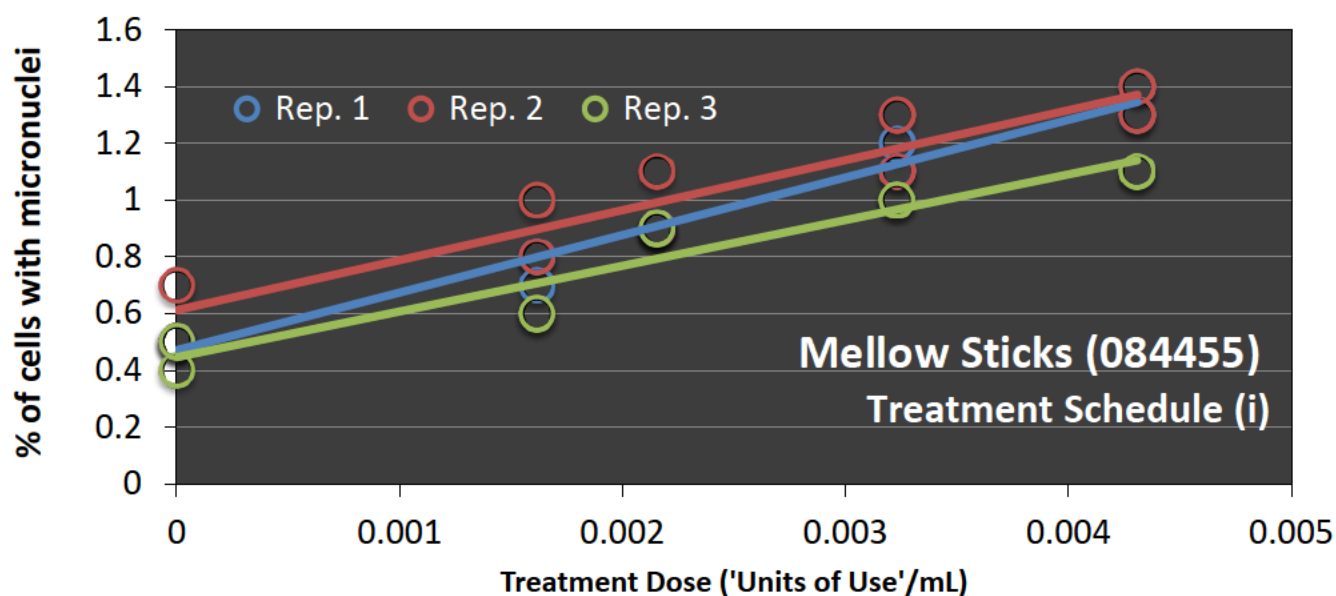
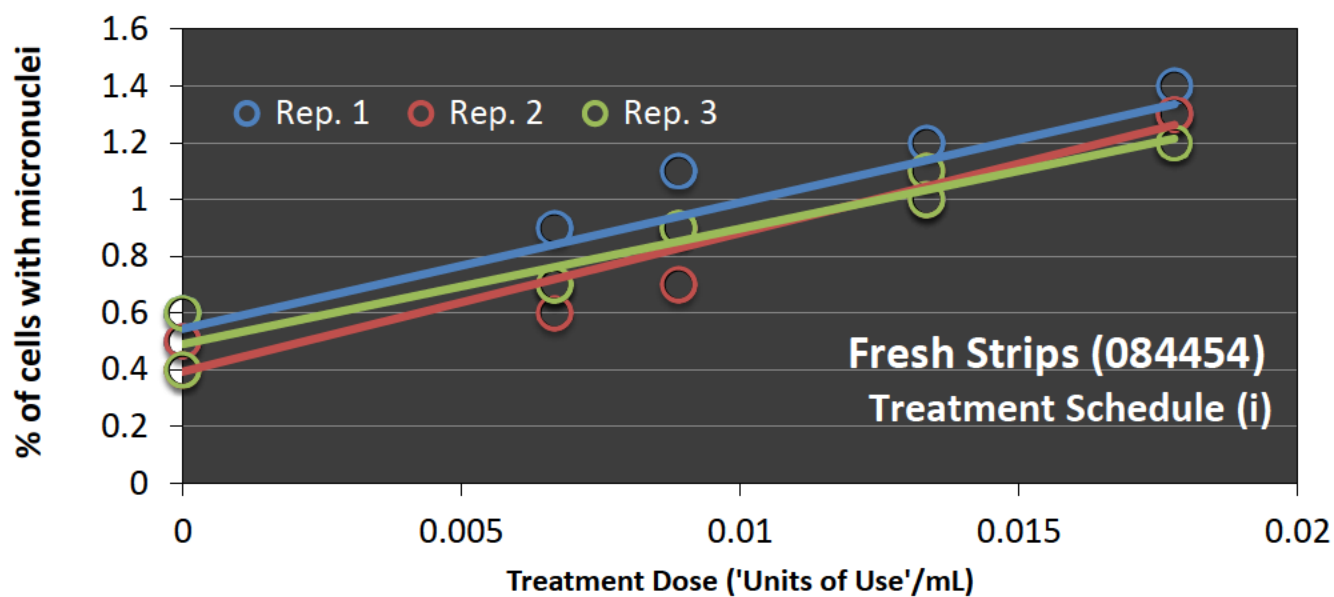
Treatment Schedule (i)

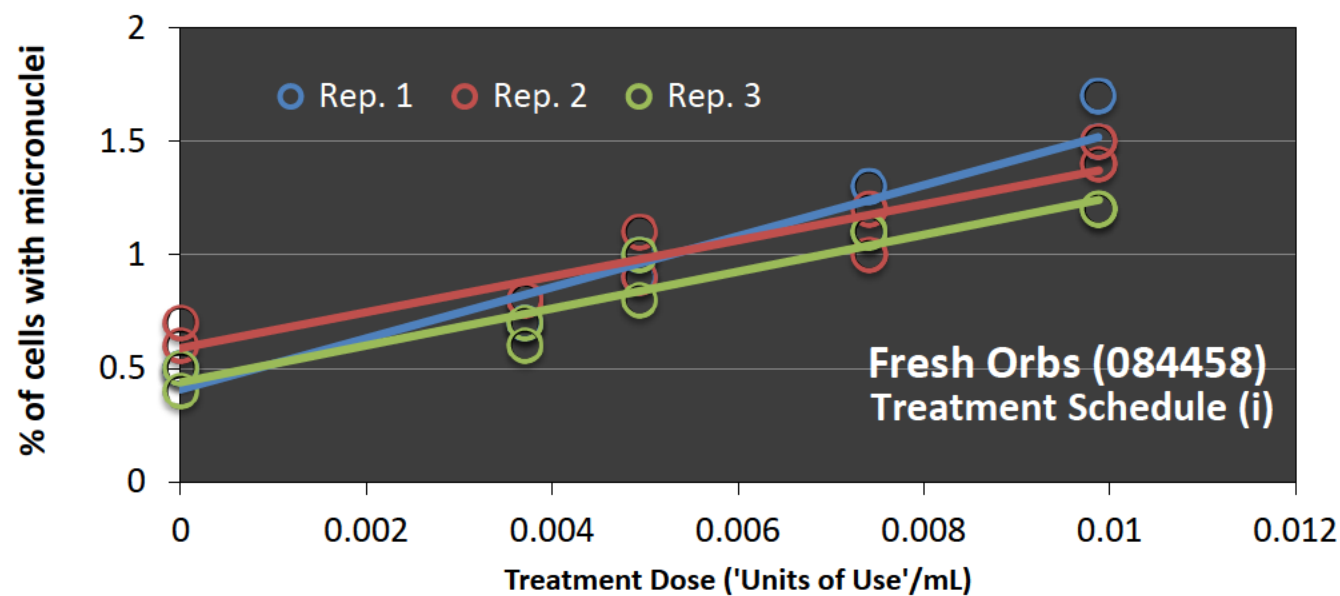
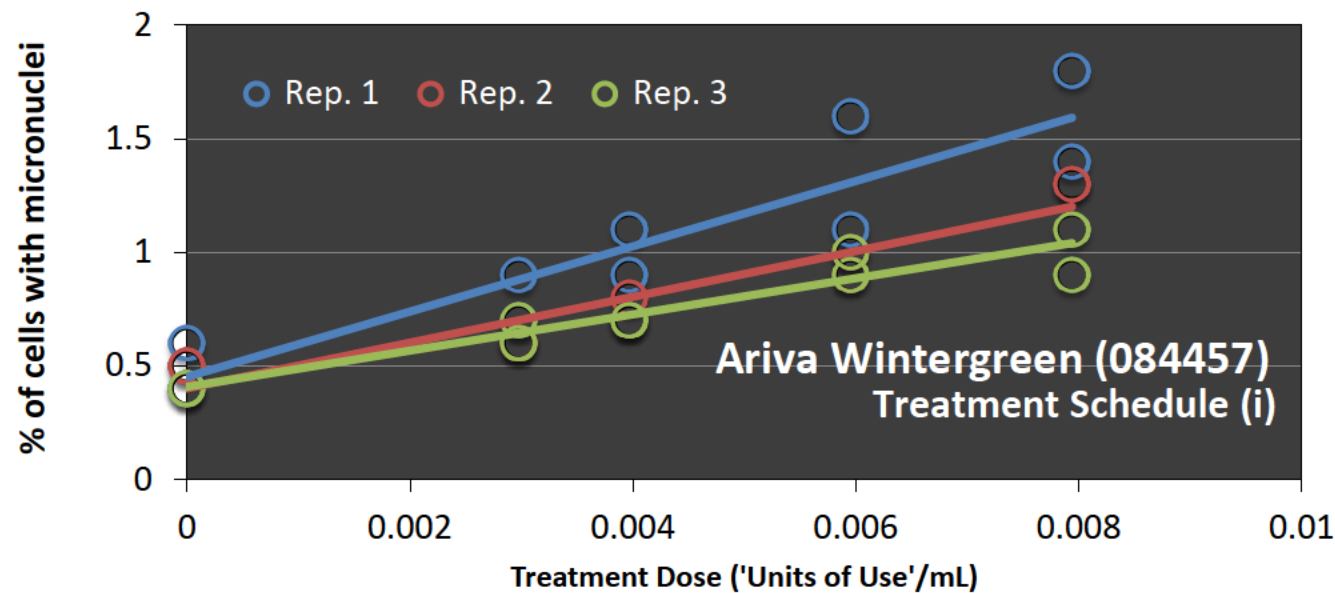
{Camel SNUS Frost (084394), 2S3 (084395), Fresh Strips (084454), Mellow Sticks (084455), Copenhagen Long Cut (084456)}

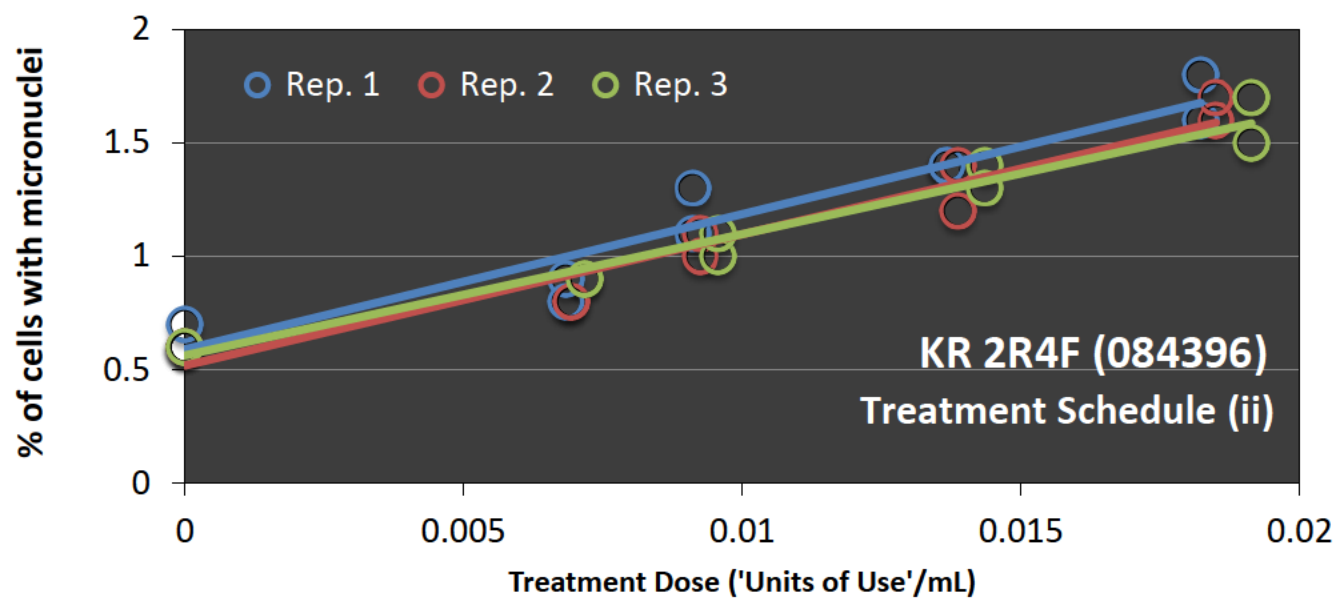
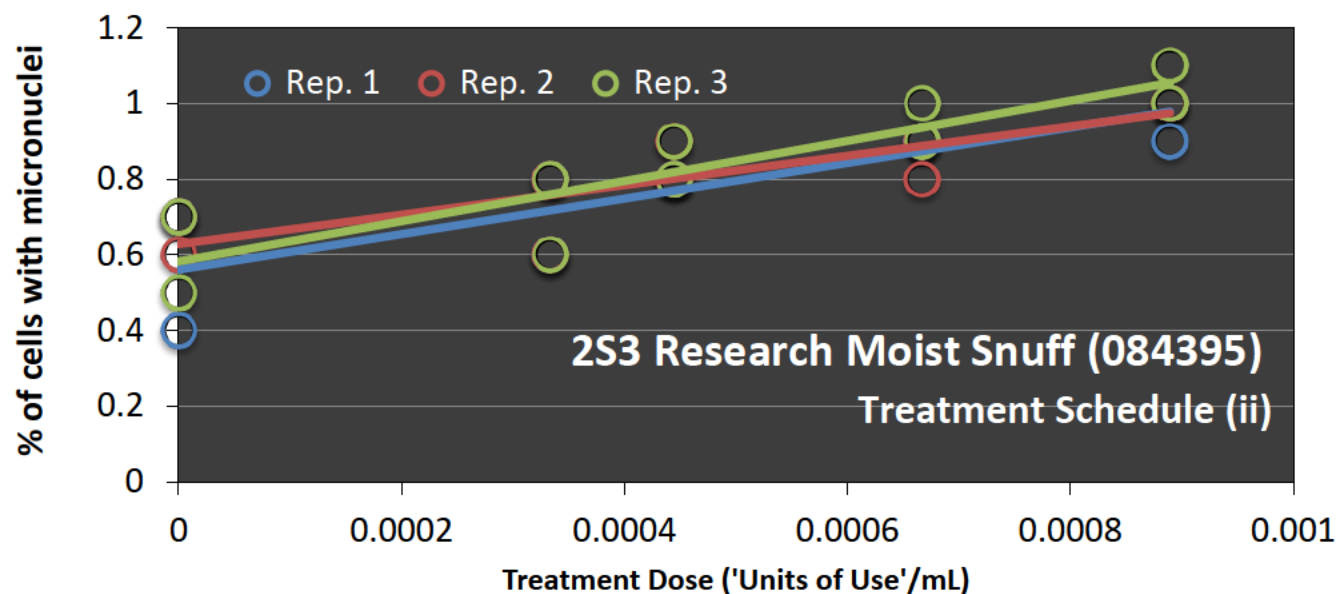
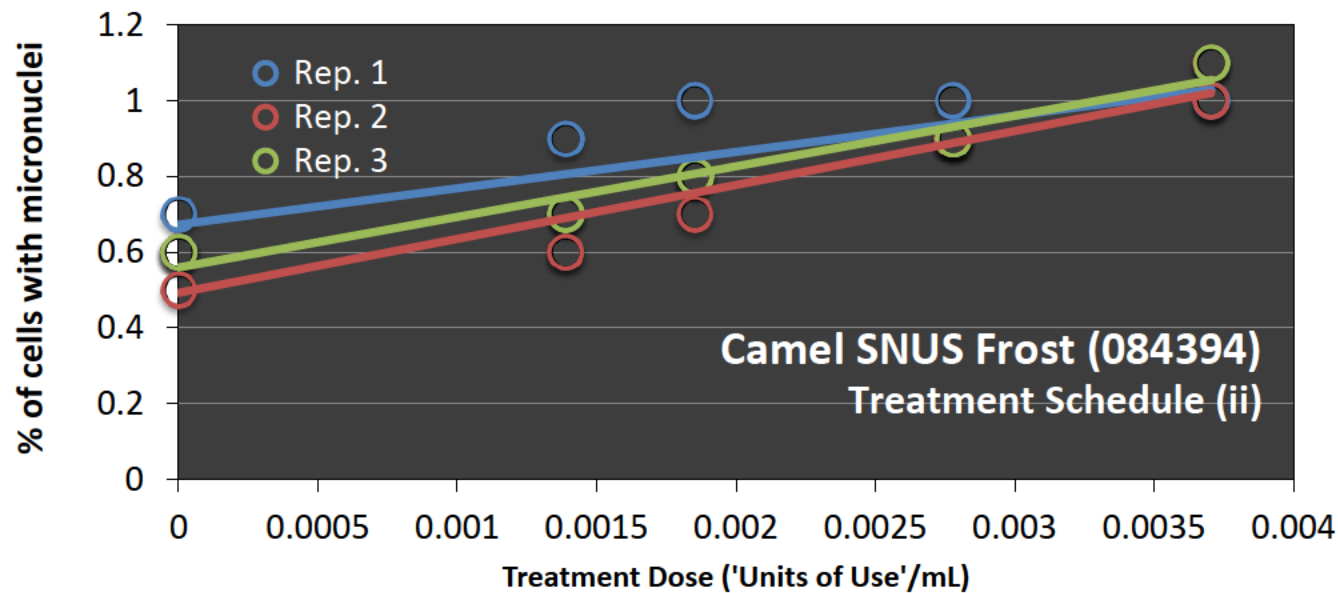
Treatment Schedule (ii)

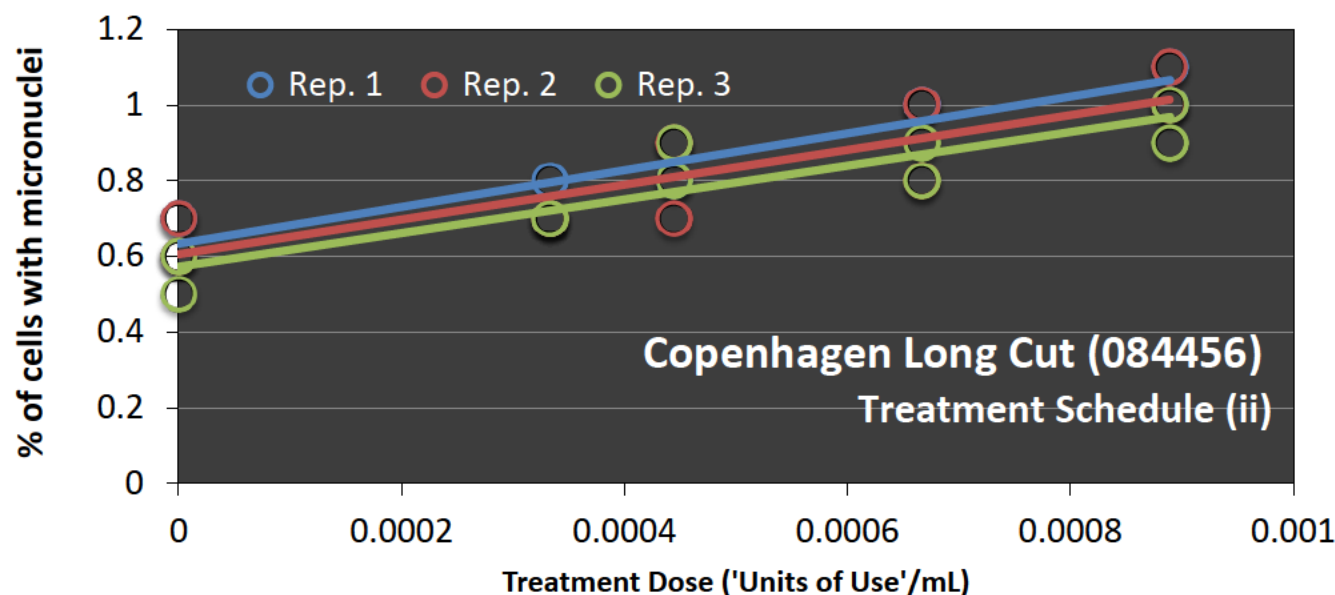
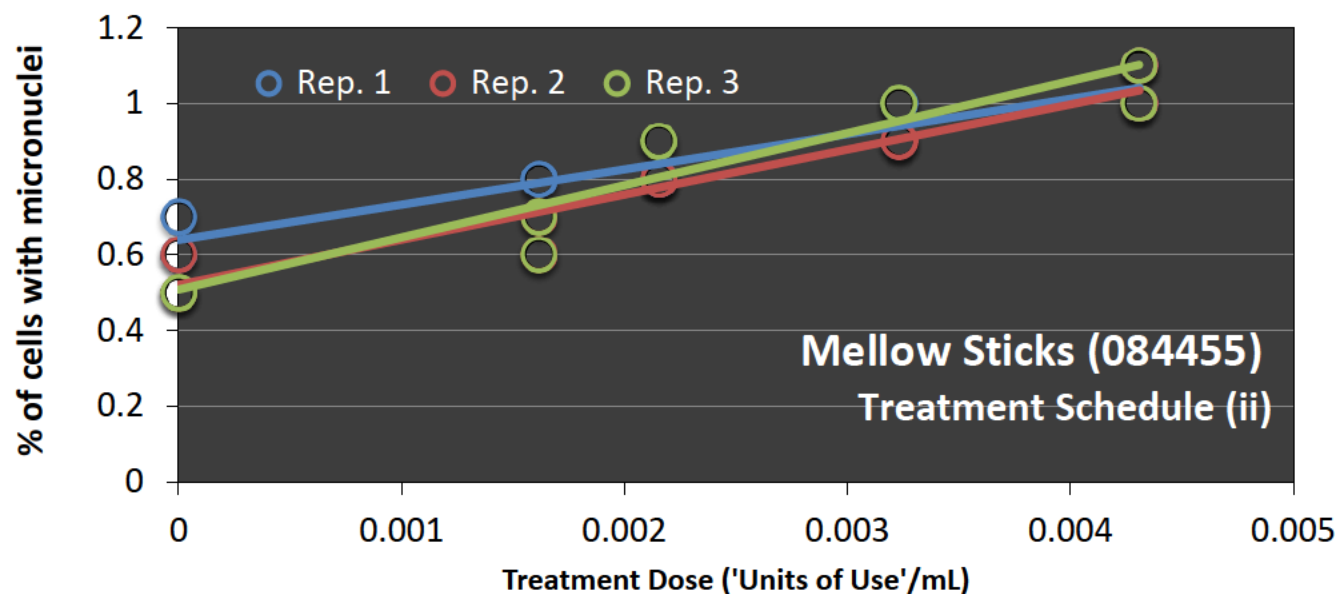
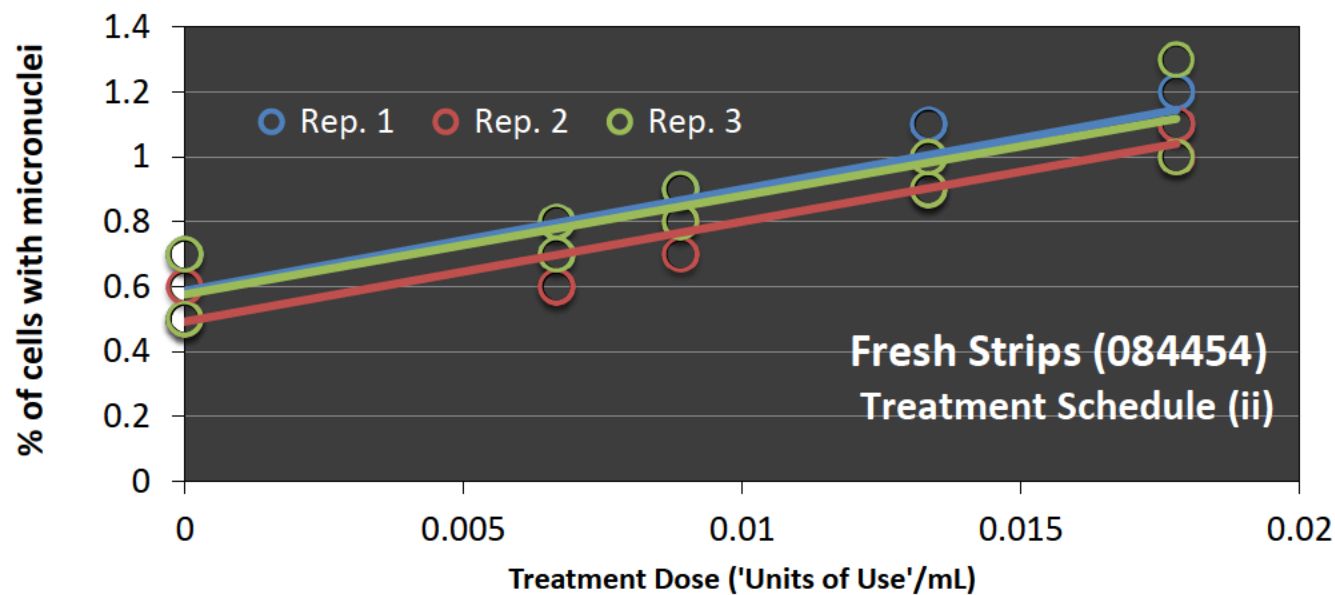
{2S3 (084395), Fresh Strips (084454), Copenhagen Long Cut (084456)}

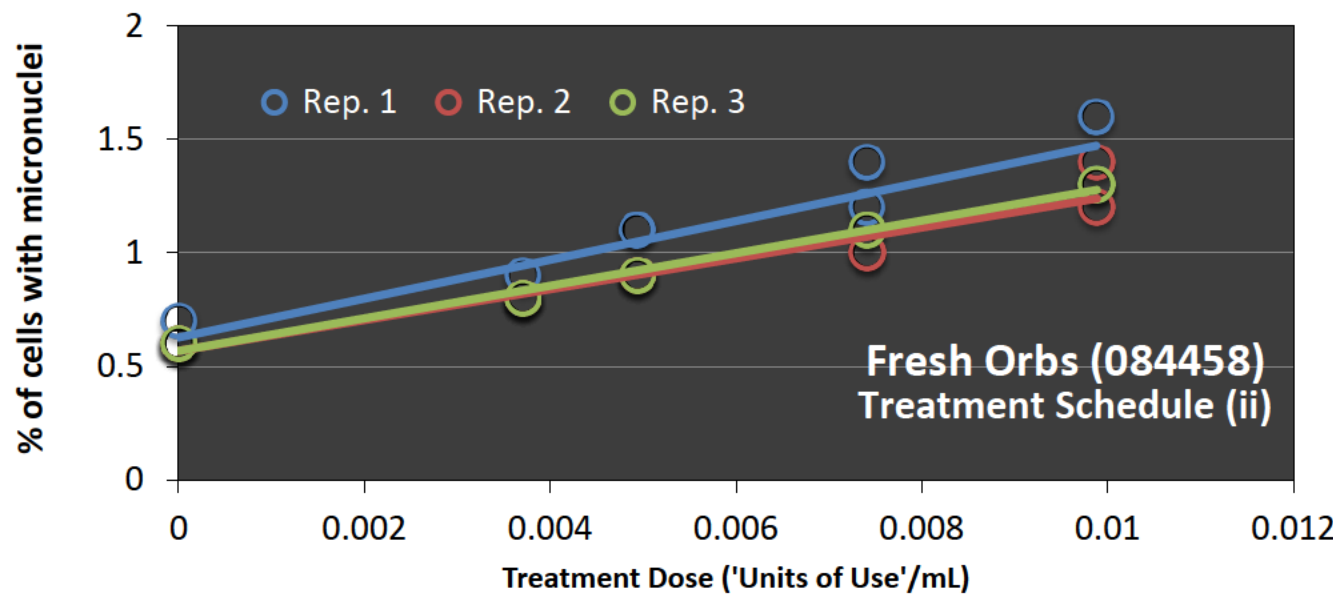
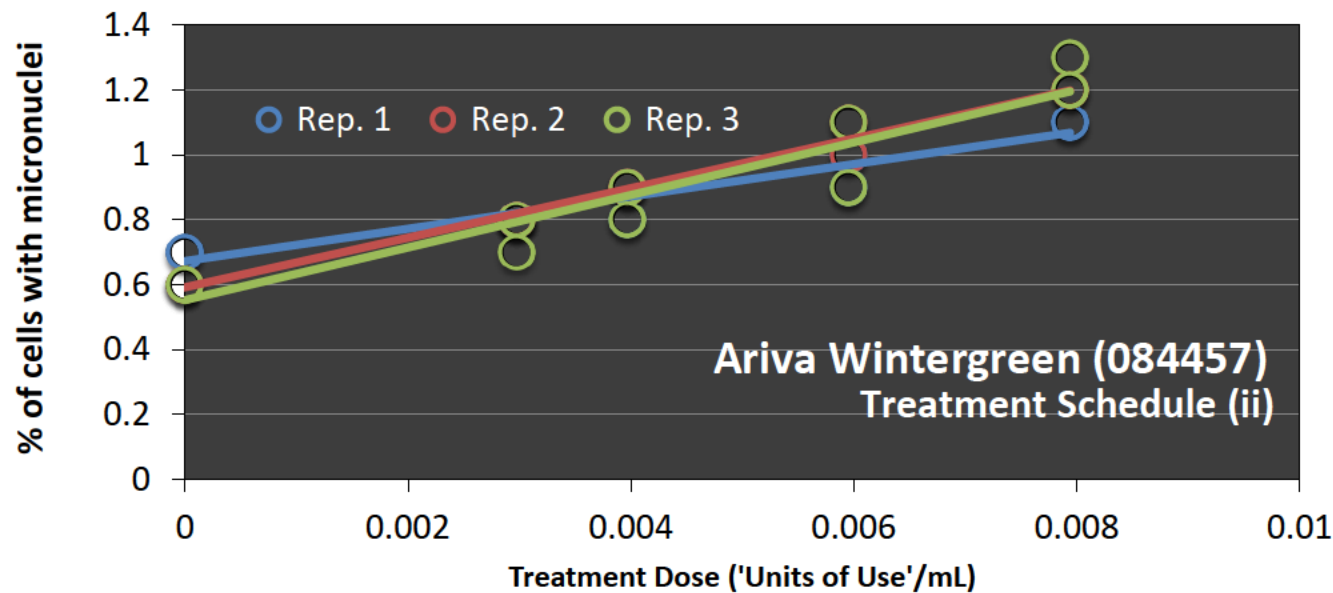


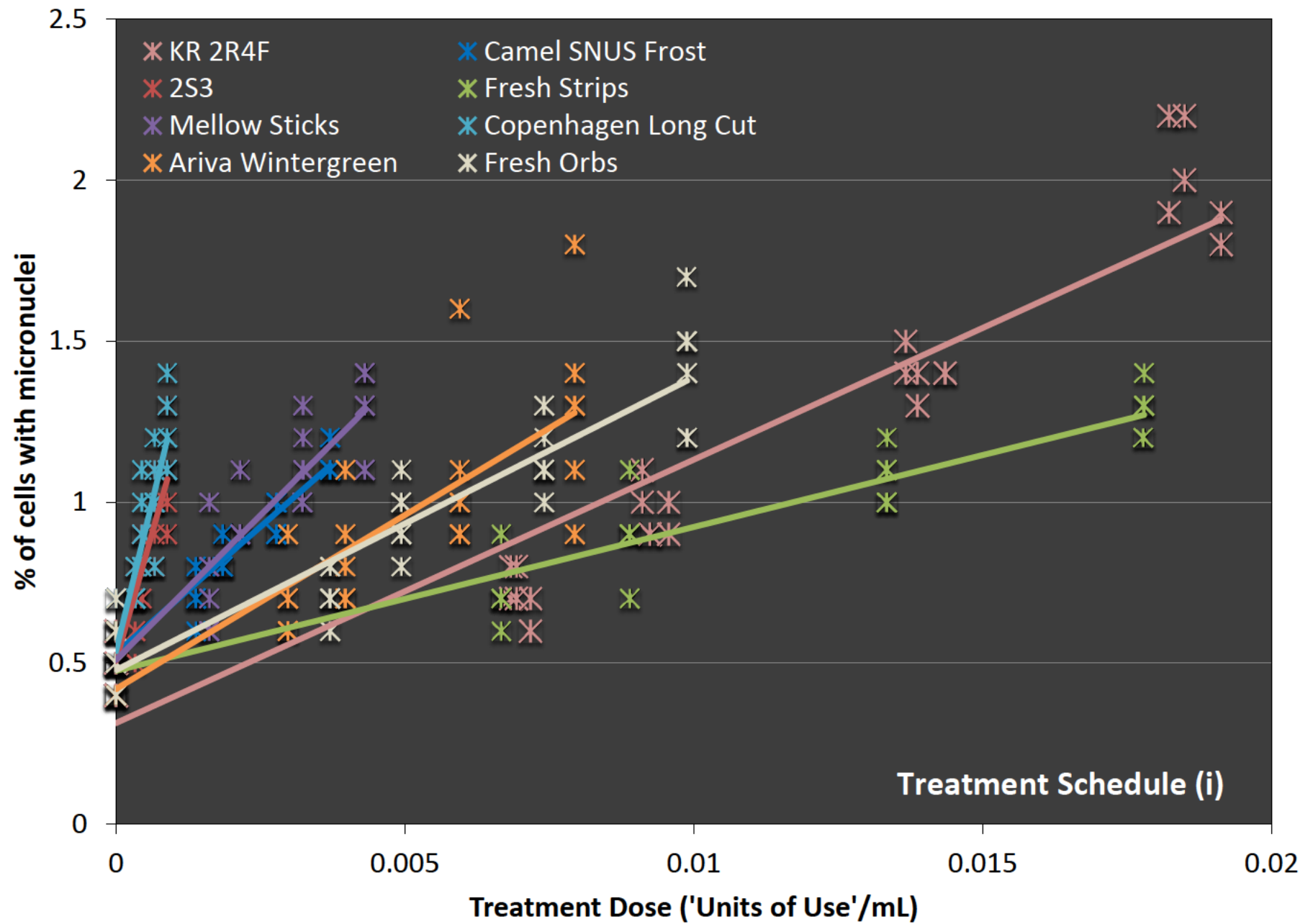


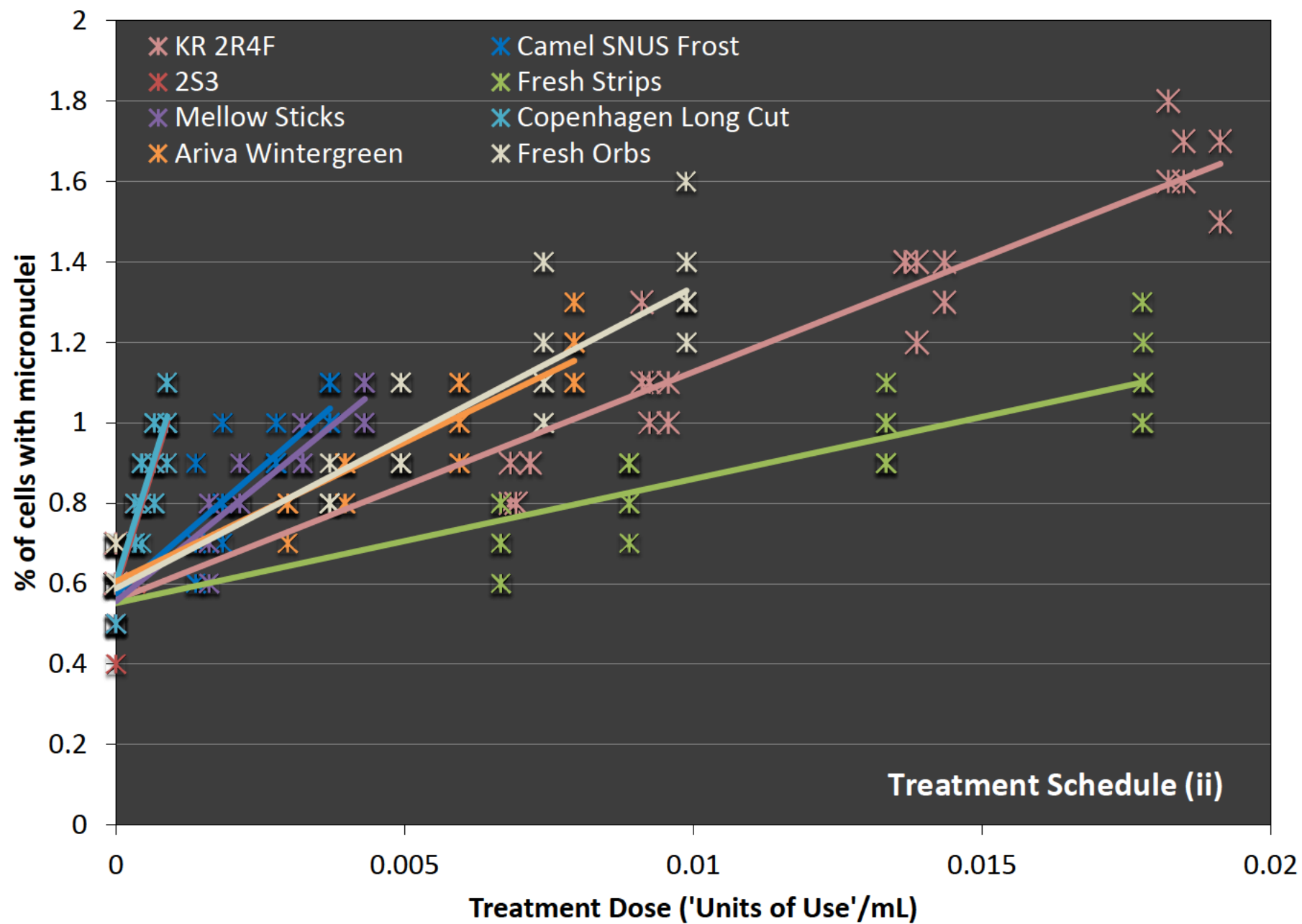












Sample ID	Sample Description
084394	Camel SNUS Frost
084395	2S3 Research Moist smokeless tobacco
084454	Fresh Strips
084455	Mellow Sticks
084456	Copenhagen Long Cut
084457	Ariva Wintergreen
084458	Fresh Orbs

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Project: M100
 Period: November 13 - 19, 2008

Sample Generation Data for *In Vitro* Micronucleus Assay

'Units of Use' Dosing Data

Set-Run	Sample ID	Replicate Number	Extraction Date	Tobacco Weight (g)	Volume (mL) ¹	mg Tobacco per mL	Dry Matter (%)	Nicotine (mg/g)	mg (Tobacco-H ₂ O) per mL	Calculated Nicotine in Extraction Solution (mg/mL)	Units of Use			'Units of Use'/mL media				
											Unit	Weight (g)	Units/mL	1	2	3	4	5
3-4	084394	1	19-Nov-08	2.5013	22.5	111.169	68.27	12.5	75.900	1.39	1 pouch	0.6	0.185	0	0.0014	0.0019	0.0028	0.0037
3-6	084394	2	19-Nov-08	2.5002	22.5	111.120		12.9	75.867	1.44	1 pouch	0.6	0.185	0	0.0014	0.0019	0.0028	0.0037
3-13	084394	3	19-Nov-08	2.5018	22.5	111.191		13.3	75.916	1.47	1 pouch	0.6	0.185	0	0.0014	0.0019	0.0028	0.0037
3-9	084395	1	19-Nov-08	2.5008	22.5	111.147	45.98	13.5	51.108	1.50	2.5 grams	2.5	0.044	0	0.0003	0.0004	0.0007	0.0009
3-11	084395	2	19-Nov-08	2.5005	22.5	111.133		13.2	51.102	1.47	2.5 grams	2.5	0.044	0	0.0003	0.0004	0.0007	0.0009
3-15	084395	3	19-Nov-08	2.5014	22.5	111.173		14.1	51.121	1.57	2.5 grams	2.5	0.044	0	0.0003	0.0004	0.0007	0.0009
3-2	084454	1	19-Nov-08	2.5018	22.5	111.191	88.90	3.69	98.845	0.411	1	0.125	0.890	0	0.0067	0.0089	0.0133	0.0178
3-10	084454	2	19-Nov-08	2.5016	22.5	111.182		3.60	98.837	0.400	1	0.125	0.889	0	0.0067	0.0089	0.0133	0.0178
3-12	084454	3	19-Nov-08	2.5006	22.5	111.138		3.45	98.798	0.383	1	0.125	0.889	0	0.0067	0.0089	0.0133	0.0178
3-1	084455	1	19-Nov-08	2.5017	22.5	111.187	93.93	3.97	104.434	0.442	1 stick	0.516	0.215	0	0.0016	0.0022	0.0032	0.0043
3-3	084455	2	19-Nov-08	2.5015	22.5	111.178		4.83	104.426	0.537	1 stick	0.516	0.215	0	0.0016	0.0022	0.0032	0.0043
3-7	084455	3	19-Nov-08	2.5003	22.5	111.124		3.63	104.375	0.403	1 stick	0.516	0.215	0	0.0016	0.0022	0.0032	0.0043
2-7	084456	1	13-Nov-08	2.5011	22.5	111.160	44.63	12.7	49.614	1.42	2.5 grams	2.5	0.044	0	0.0003	0.0004	0.0007	0.0009
2-9	084456	2	13-Nov-08	2.5000	22.5	111.111		12.3	49.592	1.37	2.5 grams	2.5	0.044	0	0.0003	0.0004	0.0007	0.0009
2-10	084456	3	13-Nov-08	2.5012	22.5	111.164		12.2	49.616	1.36	2.5 grams	2.5	0.044	0	0.0003	0.0004	0.0007	0.0009
2-3	084457	1	13-Nov-08	2.5004	22.5	111.129	96.32	5.63	107.044	0.625	1	0.28	0.397	0	0.0030	0.0040	0.0060	0.0079
2-5	084457	2	13-Nov-08	2.5004	22.5	111.129		5.61	107.044	0.624	1	0.28	0.397	0	0.0030	0.0040	0.0060	0.0079
2-6	084457	3	13-Nov-08	2.5002	22.5	111.120		5.62	107.036	0.625	1	0.28	0.397	0	0.0030	0.0040	0.0060	0.0079
2-2	084458	1	13-Nov-08	2.5000	22.5	111.111	94.86	2.08	105.400	0.231	1	0.225	0.494	0	0.0037	0.0049	0.0074	0.0099
2-4	084458	2	13-Nov-08	2.5019	22.5	111.196		2.35	105.480	0.262	1	0.225	0.494	0	0.0037	0.0049	0.0074	0.0099
2-8	084458	3	13-Nov-08	2.5014	22.5	111.173		2.22	105.459	0.247	1	0.225	0.494	0	0.0037	0.0049	0.0074	0.0099

1. Samples extracted in appropriate solvent control to give a final concentration of 111.1 mg/mL

Tobacco Extract in Solvent (μL/mL media)				
1	2	3	4	5
0	7.5	10	15	20

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(% Micronuclei and % Cytotoxicity as determined by Relative Increase in Cell Counts (RICC))**

Set Number	Run Number	Sample ID	Replicate Number	Treatment Schedule	Unit of Use Dose (units/mL)	Treatment Time (h)	Metabolic Activation	% Cytotoxicity (by RICC)			% Micronuclei		
								Flask 1	Flask 2	Average	Flask 1	Flask 2	Average
3	4	084394	1	Schedule (i)	0	3	-S9	0	0	0	0.60	0.50	0.55
3	4	084394	1	Schedule (i)	0.0014	3	-S9	13.0	13.4	13.2	0.80	0.70	0.75
3	4	084394	1	Schedule (i)	0.0019	3	-S9	24.6	26.1	25.3	0.90	0.80	0.85
3	4	084394	1	Schedule (i)	0.0028	3	-S9	39.9	45.8	42.8	1.00	1.00	1.00
3	4	084394	1	Schedule (i)	0.0037	3	-S9	58.0	54.2	56.1	1.10	1.30	1.20
3	6	084394	2	Schedule (i)	0	3	-S9	0	0	0	0.60	0.60	0.60
3	6	084394	2	Schedule (i)	0.0014	3	-S9	13.8	10.9	12.4	0.70	0.60	0.65
3	6	084394	2	Schedule (i)	0.0019	3	-S9	28.3	27.3	27.8	0.90	0.80	0.85
3	6	084394	2	Schedule (i)	0.0028	3	-S9	45.7	39.8	42.7	1.10	0.90	1.00
3	6	084394	2	Schedule (i)	0.0037	3	-S9	60.9	55.5	58.2	1.20	1.20	1.20
3	13	084394	3	Schedule (i)	0	3	-S9	0	0	0	0.60	0.50	0.55
3	13	084394	3	Schedule (i)	0.0014	3	-S9	5.2	8.7	7.0	0.80	0.70	0.75
3	13	084394	3	Schedule (i)	0.0019	3	-S9	9.3	16.0	12.7	0.90	0.80	0.85
3	13	084394	3	Schedule (i)	0.0028	3	-S9	30.1	27.7	28.9	1.00	1.00	1.00
3	13	084394	3	Schedule (i)	0.0037	3	-S9	43.0	38.3	40.7	1.30	1.10	1.20
3	9	084395	1	Schedule (i)	0	3	-S9	0	0	0	0.50	0.60	0.55
3	9	084395	1	Schedule (i)	0.0003	3	-S9	23.4	20.0	21.7	0.60	0.80	0.70
3	9	084395	1	Schedule (i)	0.0004	3	-S9	33.1	37.1	35.1	0.80	0.90	0.85
3	9	084395	1	Schedule (i)	0.0007	3	-S9	46.2	47.1	46.7	1.00	1.10	1.05
3	9	084395	1	Schedule (i)	0.0009	3	-S9	57.9	55.0	56.5	1.10	1.40	1.25
3	11	084395	2	Schedule (i)	0	3	-S9	0	0	0	0.60	0.40	0.50
3	11	084395	2	Schedule (i)	0.0003	3	-S9	9.6	10.1	9.8	0.80	0.50	0.65
3	11	084395	2	Schedule (i)	0.0004	3	-S9	14.7	19.5	17.1	0.80	0.80	0.80
3	11	084395	2	Schedule (i)	0.0007	3	-S9	26.9	24.5	25.7	1.00	0.90	0.95
3	11	084395	2	Schedule (i)	0.0009	3	-S9	35.9	35.2	35.6	1.10	1.00	1.05
3	15	084395	3	Schedule (i)	0	3	-S9	0	0	0	0.60	0.50	0.55
3	15	084395	3	Schedule (i)	0.0003	3	-S9	8.2	5.7	6.9	0.70	0.80	0.75
3	15	084395	3	Schedule (i)	0.0004	3	-S9	11.4	6.9	9.1	0.80	0.90	0.85
3	15	084395	3	Schedule (i)	0.0007	3	-S9	17.4	17.1	17.3	1.10	1.00	1.05
3	15	084395	3	Schedule (i)	0.0009	3	-S9	26.6	32.0	29.3	1.10	1.10	1.10
3	2	084454	1	Schedule (i)	0	3	-S9	0	0	0	0.50	0.70	0.60
3	2	084454	1	Schedule (i)	0.0067	3	-S9	22.8	22.4	22.6	0.70	1.00	0.85
3	2	084454	1	Schedule (i)	0.0089	3	-S9	36.6	34.7	35.6	0.90	1.20	1.05
3	2	084454	1	Schedule (i)	0.0133	3	-S9	46.9	50.3	48.6	1.10	1.20	1.15
3	2	084454	1	Schedule (i)	0.0178	3	-S9	64.1	70.1	67.1	1.40	1.50	1.45

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(% Micronuclei and % Cytotoxicity as determined by Relative Increase in Cell Counts (RICC))**

Set Number	Run Number	Sample ID	Replicate Number	Treatment Schedule	Unit of Use Dose (units/mL)	Treatment Time (h)	Metabolic Activation	% Cytotoxicity (by RICC)			% Micronuclei		
								Flask 1	Flask 2	Average	Flask 1	Flask 2	Average
3	10	084454	2	Schedule (i)	0	3	-S9	0	0	0	0.50	0.50	0.50
3	10	084454	2	Schedule (i)	0.0067	3	-S9	6.9	10.7	8.8	0.70	0.70	0.70
3	10	084454	2	Schedule (i)	0.0089	3	-S9	16.0	20.8	18.4	0.90	1.00	0.95
3	10	084454	2	Schedule (i)	0.0133	3	-S9	26.4	26.8	26.6	1.10	1.20	1.15
3	10	084454	2	Schedule (i)	0.0178	3	-S9	34.7	39.6	37.2	1.30	1.50	1.40
3	12	084454	3	Schedule (i)	0	3	-S9	0	0	0	0.50	0.60	0.55
3	12	084454	3	Schedule (i)	0.0067	3	-S9	6.2	7.2	6.7	0.70	0.80	0.75
3	12	084454	3	Schedule (i)	0.0089	3	-S9	13.8	10.8	12.3	0.90	0.90	0.90
3	12	084454	3	Schedule (i)	0.0133	3	-S9	22.6	20.0	21.3	1.20	1.20	1.20
3	12	084454	3	Schedule (i)	0.0178	3	-S9	29.2	26.7	27.9	1.40	1.30	1.35
3	1	084455	1	Schedule (i)	0	3	-S9	0	0	0	0.60	0.50	0.55
3	1	084455	1	Schedule (i)	0.0016	3	-S9	17.1	23.9	20.5	0.80	0.80	0.80
3	1	084455	1	Schedule (i)	0.0022	3	-S9	35.7	34.5	35.1	1.00	0.90	0.95
3	1	084455	1	Schedule (i)	0.0032	3	-S9	54.3	50.7	52.5	1.20	1.30	1.25
3	1	084455	1	Schedule (i)	0.0043	3	-S9	63.6	69.7	66.6	1.50	1.40	1.45
3	3	084455	2	Schedule (i)	0	3	-S9	0	0	0	0.60	0.70	0.65
3	3	084455	2	Schedule (i)	0.0016	3	-S9	15.7	14.0	14.8	0.80	1.00	0.90
3	3	084455	2	Schedule (i)	0.0022	3	-S9	36.4	33.1	34.8	1.00	1.10	1.05
3	3	084455	2	Schedule (i)	0.0032	3	-S9	44.3	45.6	44.9	1.10	1.30	1.20
3	3	084455	2	Schedule (i)	0.0043	3	-S9	64.3	64.7	64.5	1.40	1.40	1.40
3	7	084455	3	Schedule (i)	0	3	-S9	0	0	0	0.40	0.50	0.45
3	7	084455	3	Schedule (i)	0.0016	3	-S9	6.7	9.4	8.1	0.60	0.70	0.65
3	7	084455	3	Schedule (i)	0.0022	3	-S9	17.1	19.3	18.2	1.00	0.90	0.95
3	7	084455	3	Schedule (i)	0.0032	3	-S9	28.1	28.8	28.4	1.00	1.00	1.00
3	7	084455	3	Schedule (i)	0.0043	3	-S9	37.1	34.4	35.8	1.10	1.20	1.15
2	7	084456	1	Schedule (i)	0	3	-S9	0	0	0	0.60	0.50	0.55
2	7	084456	1	Schedule (i)	0.0003	3	-S9	22.8	26.0	24.4	0.90	0.80	0.85
2	7	084456	1	Schedule (i)	0.0004	3	-S9	31.7	34.9	33.3	1.10	0.90	1.00
2	7	084456	1	Schedule (i)	0.0007	3	-S9	44.8	41.8	43.3	1.20	1.00	1.10
2	7	084456	1	Schedule (i)	0.0009	3	-S9	60.0	58.2	59.1	1.40	1.30	1.35
2	9	084456	2	Schedule (i)	0	3	-S9	0	0	0	0.50	0.50	0.50
2	9	084456	2	Schedule (i)	0.0003	3	-S9	17.9	16.4	17.1	0.70	0.80	0.75
2	9	084456	2	Schedule (i)	0.0004	3	-S9	28.5	22.4	25.4	1.10	1.00	1.05
2	9	084456	2	Schedule (i)	0.0007	3	-S9	32.5	31.9	32.2	1.20	1.10	1.15
2	9	084456	2	Schedule (i)	0.0009	3	-S9	47.2	42.2	44.7	1.30	1.20	1.25

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(% Micronuclei and % Cytotoxicity as determined by Relative Increase in Cell Counts (RICC))**

Set Number	Run Number	Sample ID	Replicate Number	Treatment Schedule	Unit of Use Dose (units/mL)	Treatment Time (h)	Metabolic Activation	% Cytotoxicity (by RICC)			% Micronuclei		
								Flask 1	Flask 2	Average	Flask 1	Flask 2	Average
2	10	084456	3	Schedule (i)	0	3	-S9	0	0	0	0.60	0.70	0.65
2	10	084456	3	Schedule (i)	0.0003	3	-S9	12.3	11.2	11.7	0.70	0.80	0.75
2	10	084456	3	Schedule (i)	0.0004	3	-S9	19.6	15.5	17.6	0.80	0.90	0.85
2	10	084456	3	Schedule (i)	0.0007	3	-S9	27.0	24.2	25.6	1.00	1.10	1.05
2	10	084456	3	Schedule (i)	0.0009	3	-S9	31.3	32.3	31.8	1.20	1.20	1.20
2	3	084457	1	Schedule (i)	0	3	-S9	0	0	0	0.60	0.50	0.55
2	3	084457	1	Schedule (i)	0.0030	3	-S9	17.1	15.8	16.5	0.90	0.80	0.85
2	3	084457	1	Schedule (i)	0.0040	3	-S9	27.1	28.6	27.9	1.10	1.00	1.05
2	3	084457	1	Schedule (i)	0.0060	3	-S9	45.0	41.4	43.2	1.60	1.20	1.40
2	3	084457	1	Schedule (i)	0.0079	3	-S9	54.3	50.4	52.3	1.90	1.40	1.65
2	5	084457	2	Schedule (i)	0	3	-S9	0	0	0	0.50	0.50	0.50
2	5	084457	2	Schedule (i)	0.0030	3	-S9	9.7	19.8	14.8	0.70	0.60	0.65
2	5	084457	2	Schedule (i)	0.0040	3	-S9	29.2	28.9	29.1	0.80	0.80	0.80
2	5	084457	2	Schedule (i)	0.0060	3	-S9	38.9	38.8	38.9	1.00	1.00	1.00
2	5	084457	2	Schedule (i)	0.0079	3	-S9	46.9	52.1	49.5	1.40	1.40	1.40
2	6	084457	3	Schedule (i)	0	3	-S9	0	0	0	0.40	0.40	0.40
2	6	084457	3	Schedule (i)	0.0030	3	-S9	12.2	10.5	11.3	0.70	0.60	0.65
2	6	084457	3	Schedule (i)	0.0040	3	-S9	21.8	21.6	21.7	0.80	0.80	0.80
2	6	084457	3	Schedule (i)	0.0060	3	-S9	34.0	32.7	33.3	0.90	1.00	0.95
2	6	084457	3	Schedule (i)	0.0079	3	-S9	44.9	41.2	43.0	1.10	1.10	1.10
2	2	084458	1	Schedule (i)	0	3	-S9	0	0	0	0.50	0.50	0.50
2	2	084458	1	Schedule (i)	0.0037	3	-S9	9.7	9.4	9.5	0.90	0.70	0.80
2	2	084458	1	Schedule (i)	0.0049	3	-S9	27.6	26.6	27.1	1.10	0.90	1.00
2	2	084458	1	Schedule (i)	0.0074	3	-S9	51.0	45.3	48.2	1.40	1.20	1.30
2	2	084458	1	Schedule (i)	0.0099	3	-S9	58.6	61.9	60.2	1.80	1.60	1.70
2	4	084458	2	Schedule (i)	0	3	-S9	0	0	0	0.60	0.70	0.65
2	4	084458	2	Schedule (i)	0.0037	3	-S9	17.0	22.4	19.7	0.80	0.80	0.80
2	4	084458	2	Schedule (i)	0.0049	3	-S9	36.8	35.5	36.2	1.00	1.10	1.05
2	4	084458	2	Schedule (i)	0.0074	3	-S9	49.1	51.4	50.2	1.10	1.30	1.20
2	4	084458	2	Schedule (i)	0.0099	3	-S9	62.3	70.1	66.2	1.50	1.50	1.50
2	8	084458	3	Schedule (i)	0	3	-S9	0	0	0	0.50	0.40	0.45
2	8	084458	3	Schedule (i)	0.0037	3	-S9	12.4	7.5	10.0	0.70	0.70	0.70
2	8	084458	3	Schedule (i)	0.0049	3	-S9	15.5	13.2	14.4	1.00	0.90	0.95
2	8	084458	3	Schedule (i)	0.0074	3	-S9	24.2	23.3	23.7	1.20	1.10	1.15
2	8	084458	3	Schedule (i)	0.0099	3	-S9	33.5	33.3	33.4	1.40	1.30	1.35

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(% Micronuclei and % Cytotoxicity as determined by Relative Increase in Cell Counts (RICC))**

Set Number	Run Number	Sample ID	Replicate Number	Treatment Schedule	Unit of Use Dose (units/mL)	Treatment Time (h)	Metabolic Activation	% Cytotoxicity (by RICC)			% Micronuclei		
								Flask 1	Flask 2	Average	Flask 1	Flask 2	Average
3	4	084394	1	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.70	0.65
3	4	084394	1	Schedule (ii)	0.0014	3	+S9	6.8	5.5	6.1	0.70	0.90	0.80
3	4	084394	1	Schedule (ii)	0.0019	3	+S9	10.5	7.8	9.2	0.90	1.00	0.95
3	4	084394	1	Schedule (ii)	0.0028	3	+S9	22.6	21.9	22.2	1.00	1.00	1.00
3	4	084394	1	Schedule (ii)	0.0037	3	+S9	36.8	31.3	34.0	1.10	1.00	1.05
3	6	084394	2	Schedule (ii)	0	3	+S9	0	0	0	0.50	0.60	0.55
3	6	084394	2	Schedule (ii)	0.0014	3	+S9	8.1	11.6	9.9	0.60	0.70	0.65
3	6	084394	2	Schedule (ii)	0.0019	3	+S9	18.7	20.2	19.4	0.80	0.80	0.80
3	6	084394	2	Schedule (ii)	0.0028	3	+S9	29.3	28.7	29.0	0.90	0.90	0.90
3	6	084394	2	Schedule (ii)	0.0037	3	+S9	40.7	43.4	42.0	1.10	1.00	1.05
3	13	084394	3	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.60	0.60
3	13	084394	3	Schedule (ii)	0.0014	3	+S9	15.7	8.9	12.3	0.70	0.70	0.70
3	13	084394	3	Schedule (ii)	0.0019	3	+S9	29.9	22.8	26.3	0.90	0.90	0.90
3	13	084394	3	Schedule (ii)	0.0028	3	+S9	35.4	33.3	34.4	1.00	0.90	0.95
3	13	084394	3	Schedule (ii)	0.0037	3	+S9	47.2	46.3	46.8	1.10	1.20	1.15
3	9	084395	1	Schedule (ii)	0	3	+S9	0	0	0	0.40	0.70	0.55
3	9	084395	1	Schedule (ii)	0.0003	3	+S9	11.4	13.3	12.3	0.60	0.80	0.70
3	9	084395	1	Schedule (ii)	0.0004	3	+S9	16.3	21.9	19.1	0.80	0.80	0.80
3	9	084395	1	Schedule (ii)	0.0007	3	+S9	30.1	31.3	30.7	0.90	1.00	0.95
3	9	084395	1	Schedule (ii)	0.0009	3	+S9	37.4	37.5	37.4	1.00	1.00	1.00
3	11	084395	2	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.70	0.65
3	11	084395	2	Schedule (ii)	0.0003	3	+S9	8.1	3.6	5.9	0.70	0.80	0.75
3	11	084395	2	Schedule (ii)	0.0004	3	+S9	12.5	11.7	12.1	0.90	0.90	0.90
3	11	084395	2	Schedule (ii)	0.0007	3	+S9	26.5	21.9	24.2	0.90	1.00	0.95
3	11	084395	2	Schedule (ii)	0.0009	3	+S9	29.4	30.7	30.0	1.00	1.00	1.00
3	15	084395	3	Schedule (ii)	0	3	+S9	0	0	0	0.50	0.70	0.60
3	15	084395	3	Schedule (ii)	0.0003	3	+S9	15.4	4.0	9.7	0.60	0.80	0.70
3	15	084395	3	Schedule (ii)	0.0004	3	+S9	20.0	21.6	20.8	0.80	0.90	0.85
3	15	084395	3	Schedule (ii)	0.0007	3	+S9	35.4	28.0	31.7	0.90	1.00	0.95
3	15	084395	3	Schedule (ii)	0.0009	3	+S9	43.1	42.4	42.7	1.00	1.10	1.05
3	2	084454	1	Schedule (ii)	0	3	+S9	0	0	0	0.50	0.70	0.60
3	2	084454	1	Schedule (ii)	0.0067	3	+S9	9.4	10.3	9.8	0.70	0.80	0.75
3	2	084454	1	Schedule (ii)	0.0089	3	+S9	26.6	27.8	27.2	0.90	0.90	0.90
3	2	084454	1	Schedule (ii)	0.0133	3	+S9	39.8	35.7	37.8	1.00	1.10	1.05
3	2	084454	1	Schedule (ii)	0.0178	3	+S9	47.7	50.0	48.8	1.20	1.20	1.20

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(% Micronuclei and % Cytotoxicity as determined by Relative Increase in Cell Counts (RICC))**

Set Number	Run Number	Sample ID	Replicate Number	Treatment Schedule	Unit of Use Dose (units/mL)	Treatment Time (h)	Metabolic Activation	% Cytotoxicity (by RICC)			% Micronuclei		
								Flask 1	Flask 2	Average	Flask 1	Flask 2	Average
3	10	084454	2	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.50	0.55
3	10	084454	2	Schedule (ii)	0.0067	3	+S9	2.9	3.6	3.3	0.60	0.60	0.60
3	10	084454	2	Schedule (ii)	0.0089	3	+S9	10.1	7.3	8.7	0.70	0.80	0.75
3	10	084454	2	Schedule (ii)	0.0133	3	+S9	23.0	21.2	22.1	0.90	1.00	0.95
3	10	084454	2	Schedule (ii)	0.0178	3	+S9	26.6	27.7	27.2	1.10	1.20	1.15
3	12	084454	3	Schedule (ii)	0	3	+S9	0	0	0	0.70	0.50	0.60
3	12	084454	3	Schedule (ii)	0.0067	3	+S9	6.6	5.6	6.1	0.80	0.70	0.75
3	12	084454	3	Schedule (ii)	0.0089	3	+S9	9.9	11.3	10.6	1.00	0.90	0.95
3	12	084454	3	Schedule (ii)	0.0133	3	+S9	28.9	29.0	29.0	1.10	1.00	1.05
3	12	084454	3	Schedule (ii)	0.0178	3	+S9	37.2	41.1	39.2	1.20	1.30	1.25
3	1	084455	1	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.70	0.65
3	1	084455	1	Schedule (ii)	0.0016	3	+S9	17.5	16.4	16.9	0.80	0.80	0.80
3	1	084455	1	Schedule (ii)	0.0022	3	+S9	33.3	27.9	30.6	0.90	0.90	0.90
3	1	084455	1	Schedule (ii)	0.0032	3	+S9	42.1	36.9	39.5	1.00	1.00	1.00
3	1	084455	1	Schedule (ii)	0.0043	3	+S9	54.0	50.8	52.4	1.10	1.10	1.10
3	3	084455	2	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.50	0.55
3	3	084455	2	Schedule (ii)	0.0016	3	+S9	9.4	16.5	13.0	0.80	0.70	0.75
3	3	084455	2	Schedule (ii)	0.0022	3	+S9	23.4	27.8	25.6	0.80	0.80	0.80
3	3	084455	2	Schedule (ii)	0.0032	3	+S9	32.0	33.1	32.6	0.90	0.90	0.90
3	3	084455	2	Schedule (ii)	0.0043	3	+S9	40.6	42.9	41.7	1.20	1.10	1.15
3	7	084455	3	Schedule (ii)	0	3	+S9	0	0	0	0.50	0.50	0.50
3	7	084455	3	Schedule (ii)	0.0016	3	+S9	17.1	17.7	17.4	0.70	0.70	0.70
3	7	084455	3	Schedule (ii)	0.0022	3	+S9	24.8	29.8	27.3	0.90	0.90	0.90
3	7	084455	3	Schedule (ii)	0.0032	3	+S9	36.8	41.9	39.3	1.00	1.00	1.00
3	7	084455	3	Schedule (ii)	0.0043	3	+S9	48.7	47.6	48.1	1.10	1.10	1.10
2	7	084456	1	Schedule (ii)	0	3	+S9	0	0	0	0.70	0.60	0.65
2	7	084456	1	Schedule (ii)	0.0003	3	+S9	14.7	13.1	13.9	0.80	0.70	0.75
2	7	084456	1	Schedule (ii)	0.0004	3	+S9	25.7	23.8	24.8	0.90	0.80	0.85
2	7	084456	1	Schedule (ii)	0.0007	3	+S9	27.2	28.5	27.8	1.00	1.00	1.00
2	7	084456	1	Schedule (ii)	0.0009	3	+S9	34.6	30.8	32.7	1.10	1.10	1.10
2	9	084456	2	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.70	0.65
2	9	084456	2	Schedule (ii)	0.0003	3	+S9	10.0	5.5	7.8	0.70	0.70	0.70
2	9	084456	2	Schedule (ii)	0.0004	3	+S9	14.7	15.9	15.3	0.90	0.80	0.85
2	9	084456	2	Schedule (ii)	0.0007	3	+S9	27.3	22.8	25.0	1.00	0.80	0.90
2	9	084456	2	Schedule (ii)	0.0009	3	+S9	34.0	31.0	32.5	1.10	1.00	1.05

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(% Micronuclei and % Cytotoxicity as determined by Relative Increase in Cell Counts (RICC))**

Set Number	Run Number	Sample ID	Replicate Number	Treatment Schedule	Unit of Use Dose (units/mL)	Treatment Time (h)	Metabolic Activation	% Cytotoxicity (by RICC)			% Micronuclei		
								Flask 1	Flask 2	Average	Flask 1	Flask 2	Average
2	10	084456	3	Schedule (ii)	0	3	+S9	0	0	0	0.50	0.60	0.55
2	10	084456	3	Schedule (ii)	0.0003	3	+S9	13.3	19.7	16.5	0.70	0.70	0.70
2	10	084456	3	Schedule (ii)	0.0004	3	+S9	22.1	29.9	26.0	0.80	0.90	0.85
2	10	084456	3	Schedule (ii)	0.0007	3	+S9	34.5	33.3	33.9	0.90	1.00	0.95
2	10	084456	3	Schedule (ii)	0.0009	3	+S9	46.0	51.3	48.6	1.00	1.10	1.05
2	3	084457	1	Schedule (ii)	0	3	+S9	0	0	0	0.70	0.70	0.70
2	3	084457	1	Schedule (ii)	0.0030	3	+S9	6.2	5.6	5.9	0.80	0.80	0.80
2	3	084457	1	Schedule (ii)	0.0040	3	+S9	16.3	16.7	16.5	0.90	0.90	0.90
2	3	084457	1	Schedule (ii)	0.0060	3	+S9	20.2	21.4	20.8	1.10	1.00	1.05
2	3	084457	1	Schedule (ii)	0.0079	3	+S9	27.9	25.4	26.7	1.20	1.20	1.20
2	5	084457	2	Schedule (ii)	0	3	+S9	0	0	0	0.70	0.60	0.65
2	5	084457	2	Schedule (ii)	0.0030	3	+S9	2.1	8.3	5.2	0.80	0.80	0.80
2	5	084457	2	Schedule (ii)	0.0040	3	+S9	14.3	20.1	17.2	1.00	0.90	0.95
2	5	084457	2	Schedule (ii)	0.0060	3	+S9	20.7	24.3	22.5	1.10	1.10	1.10
2	5	084457	2	Schedule (ii)	0.0079	3	+S9	24.3	29.9	27.1	1.20	1.30	1.25
2	6	084457	3	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.60	0.60
2	6	084457	3	Schedule (ii)	0.0030	3	+S9	5.6	15.9	10.8	0.80	0.70	0.75
2	6	084457	3	Schedule (ii)	0.0040	3	+S9	23.4	21.2	22.3	0.90	0.90	0.90
2	6	084457	3	Schedule (ii)	0.0060	3	+S9	33.1	34.1	33.6	1.10	1.00	1.05
2	6	084457	3	Schedule (ii)	0.0079	3	+S9	41.9	48.5	45.2	1.30	1.20	1.25
2	2	084458	1	Schedule (ii)	0	3	+S9	0	0	0	0.70	0.60	0.65
2	2	084458	1	Schedule (ii)	0.0037	3	+S9	6.1	5.4	5.7	0.90	0.80	0.85
2	2	084458	1	Schedule (ii)	0.0049	3	+S9	10.7	8.5	9.6	1.20	1.10	1.15
2	2	084458	1	Schedule (ii)	0.0074	3	+S9	14.5	15.4	14.9	1.40	1.30	1.35
2	2	084458	1	Schedule (ii)	0.0099	3	+S9	23.7	19.2	21.4	1.60	1.50	1.55
2	4	084458	2	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.60	0.60
2	4	084458	2	Schedule (ii)	0.0037	3	+S9	6.9	8.2	7.5	0.80	0.80	0.80
2	4	084458	2	Schedule (ii)	0.0049	3	+S9	12.2	12.7	12.5	1.00	0.90	0.95
2	4	084458	2	Schedule (ii)	0.0074	3	+S9	13.0	17.2	15.1	1.10	1.10	1.10
2	4	084458	2	Schedule (ii)	0.0099	3	+S9	29.8	34.3	32.0	1.30	1.40	1.35
2	8	084458	3	Schedule (ii)	0	3	+S9	0	0	0	0.60	0.60	0.60
2	8	084458	3	Schedule (ii)	0.0037	3	+S9	13.5	15.3	14.4	0.80	0.80	0.80
2	8	084458	3	Schedule (ii)	0.0049	3	+S9	27.0	32.4	29.7	0.90	0.90	0.90
2	8	084458	3	Schedule (ii)	0.0074	3	+S9	45.9	40.5	43.2	1.10	1.10	1.10
2	8	084458	3	Schedule (ii)	0.0099	3	+S9	52.3	46.8	49.5	1.30	1.40	1.35

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Project: M100

Period: November 28 - December 17, 2008

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(Assay Information)**

Sample ID	Replicate Number	Assay Date	Treatment Schedule	Metabolic Activation	Treatment (hours)	Recovery (hours)	Before Treatment (Cells (x10 ⁵) per mL)		Negative Control (Cells (x10 ⁵) per mL)		Increase > 90%	
							Flask 1	Flask 2	Flask 1	Flask 2	Flask 1	Flask 2
084394	1	28-Nov-08	Schedule (i)	-S9	3	27	1.92	2.00	7.44	7.68	≥ 90%	≥ 90%
084394	2	04-Nov-08	Schedule (i)	-S9	3	27	1.92	2.08	7.44	7.20	≥ 90%	≥ 90%
084394	3	05-Nov-08	Schedule (i)	-S9	3	27	2.12	2.04	9.84	10.28	≥ 90%	≥ 90%
084395	1	28-Nov-08	Schedule (i)	-S9	3	27	1.92	1.96	7.72	7.56	≥ 90%	≥ 90%
084395	2	04-Nov-08	Schedule (i)	-S9	3	27	1.96	1.96	8.20	8.32	≥ 90%	≥ 90%
084395	3	05-Nov-08	Schedule (i)	-S9	3	27	2.04	2.04	9.40	9.04	≥ 90%	≥ 90%
084454	1	28-Nov-08	Schedule (i)	-S9	3	27	1.96	1.96	7.76	7.84	≥ 90%	≥ 90%
084454	2	04-Nov-08	Schedule (i)	-S9	3	27	2.08	2.04	7.84	8.00	≥ 90%	≥ 90%
084454	3	05-Nov-08	Schedule (i)	-S9	3	27	2.08	2.04	9.88	9.84	≥ 90%	≥ 90%
084455	1	28-Nov-08	Schedule (i)	-S9	3	27	1.92	1.96	7.52	7.64	≥ 90%	≥ 90%
084455	2	04-Nov-08	Schedule (i)	-S9	3	27	2.04	1.96	7.64	7.40	≥ 90%	≥ 90%
084455	3	05-Nov-08	Schedule (i)	-S9	3	27	2.08	2.12	10.48	10.60	≥ 90%	≥ 90%
084456	1	28-Nov-08	Schedule (i)	-S9	3	27	1.92	1.96	7.72	7.80	≥ 90%	≥ 90%
084456	2	04-Nov-08	Schedule (i)	-S9	3	27	1.96	2.08	6.88	6.72	≥ 90%	≥ 90%
084456	3	05-Nov-08	Schedule (i)	-S9	3	27	2.12	2.04	8.64	8.48	≥ 90%	≥ 90%
084457	1	28-Nov-08	Schedule (i)	-S9	3	27	1.96	2.00	7.56	7.32	≥ 90%	≥ 90%
084457	2	04-Nov-08	Schedule (i)	-S9	3	27	2.04	1.96	6.56	6.80	≥ 90%	≥ 90%
084457	3	05-Nov-08	Schedule (i)	-S9	3	27	2.00	2.12	8.24	8.24	≥ 90%	≥ 90%
084458	1	28-Nov-08	Schedule (i)	-S9	3	27	1.92	1.96	7.72	7.52	≥ 90%	≥ 90%
084458	2	04-Nov-08	Schedule (i)	-S9	3	27	1.96	2.08	6.20	6.36	≥ 90%	≥ 90%
084458	3	05-Nov-08	Schedule (i)	-S9	3	27	2.08	2.00	8.52	8.36	≥ 90%	≥ 90%

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Project: M100

Period: November 28 - December 17, 2008

***In Vitro* Micronucleus Assay of CHO cells with (+) and without (-) S9 Metabolic Activation
(Assay Information)**

Sample ID	Replicate Number	Assay Date	Treatment Schedule	Metabolic Activation	Treatment (hours)	Recovery (hours)	Before Treatment (Cells (x10 ⁵) per mL)		Negative Control (Cells (x10 ⁵) per mL)		Increase > 90%	
							Flask 1	Flask 2	Flask 1	Flask 2	Flask 1	Flask 2
084394	1	11-Dec-08	Schedule (ii)	+S9	3	27	2.04	2.04	7.36	7.16	≥ 90%	≥ 90%
084394	2	12-Dec-08	Schedule (ii)	+S9	3	27	2.08	2.00	7.00	7.16	≥ 90%	≥ 90%
084394	3	17-Dec-08	Schedule (ii)	+S9	3	27	2.04	2.00	7.12	6.92	≥ 90%	≥ 90%
084395	1	11-Dec-08	Schedule (ii)	+S9	3	27	2.12	2.12	7.04	7.24	≥ 90%	≥ 90%
084395	2	12-Dec-08	Schedule (ii)	+S9	3	27	2.04	1.92	7.48	7.40	≥ 90%	≥ 90%
084395	3	17-Dec-08	Schedule (ii)	+S9	3	27	2.00	1.96	7.20	6.96	≥ 90%	≥ 90%
084454	1	11-Dec-08	Schedule (ii)	+S9	3	27	2.08	2.00	7.20	7.04	≥ 90%	≥ 90%
084454	2	12-Dec-08	Schedule (ii)	+S9	3	27	2.00	2.04	7.56	7.52	≥ 90%	≥ 90%
084454	3	17-Dec-08	Schedule (ii)	+S9	3	27	1.96	1.96	6.80	6.92	≥ 90%	≥ 90%
084455	1	11-Dec-08	Schedule (ii)	+S9	3	27	2.04	2.04	7.08	6.92	≥ 90%	≥ 90%
084455	2	12-Dec-08	Schedule (ii)	+S9	3	27	1.96	2.00	7.08	7.32	≥ 90%	≥ 90%
084455	3	17-Dec-08	Schedule (ii)	+S9	3	27	2.04	1.96	6.72	6.92	≥ 90%	≥ 90%
084456	1	11-Dec-08	Schedule (ii)	+S9	3	27	2.08	2.12	7.52	7.32	≥ 90%	≥ 90%
084456	2	12-Dec-08	Schedule (ii)	+S9	3	27	2.08	2.12	8.08	7.92	≥ 90%	≥ 90%
084456	3	17-Dec-08	Schedule (ii)	+S9	3	27	2.00	2.04	6.52	6.72	≥ 90%	≥ 90%
084457	1	11-Dec-08	Schedule (ii)	+S9	3	27	2.04	2.08	7.20	7.12	≥ 90%	≥ 90%
084457	2	12-Dec-08	Schedule (ii)	+S9	3	27	2.04	2.08	7.64	7.84	≥ 90%	≥ 90%
084457	3	17-Dec-08	Schedule (ii)	+S9	3	27	2.00	1.96	6.96	7.24	≥ 90%	≥ 90%
084458	1	11-Dec-08	Schedule (ii)	+S9	3	27	2.08	2.00	7.32	7.20	≥ 90%	≥ 90%
084458	2	12-Dec-08	Schedule (ii)	+S9	3	27	2.12	2.16	7.36	7.52	≥ 90%	≥ 90%
084458	3	17-Dec-08	Schedule (ii)	+S9	3	27	2.00	2.00	6.44	6.44	≥ 90%	≥ 90%

Slope Analysis of the Linear Portion of the Dose-Response Curve
[% of mononucleated cells with micronuclei/('Unit of Use'/mL)] (Unit of Use)

Treatment Schedule	Sample ID	Sample Description	% micronucleated cells/('Unit of Use'/mL)									
			Replicate 1		Replicate 2		Replicate 3		Statistics for Replicate 'Unit of Use' Slope Estimates			
			Dose Range		Dose Range		Dose Range		Standard		t-test p-value (H ₀ : mean = 0)	
			('Unit'/mL)	slope	('Unit'/mL)	slope	('Unit'/mL)	slope	Mean	Error	95% C.I.	p-value
Schedule (i)	084394	Camel SNUS Frost	0 - 0.0037	158	0 - 0.0037	161	0 - 0.0037	152	157	2	147 - 168	0.000
Schedule (i)	084395	2S3	0 - 0.0009	692	0 - 0.0009	577	0 - 0.0009	636	635	33	492 - 777	0.003
Schedule (i)	084454	Fresh Strips	0 - 0.0178	44.5	0 - 0.0178	48.9	0 - 0.0178	40.7	44.7	2.4	34.5 - 54.8	0.003
Schedule (i)	084455	Mellow Sticks	0 - 0.0043	203	0 - 0.0043	176	0 - 0.0043	161	180	12	127 - 233	0.005
Schedule (i)	084456	Copenhagen Long Cut	0 - 0.0009	814	0 - 0.0009	858	0 - 0.0009	552	742	95	331 - 1152	0.016
Schedule (i)	084457	Ariva Wintergreen	0 - 0.0079	144	0 - 0.0079	101	0 - 0.0079	79.7	108	19	27 - 189	0.029
Schedule (i)	084458	Fresh Orbs	0 - 0.0099	112	0 - 0.0099	79.2	0 - 0.0099	81.2	90.9	10.8	44.6 - 137	0.014
Schedule (ii)	084394	Camel SNUS Frost	0 - 0.0037	96.2	0 - 0.0037	143	0 - 0.0037	134	124	14	63 - 185	0.013
Schedule (ii)	084395	2S3	0 - 0.0009	469	0 - 0.0009	389	0 - 0.0009	530	463	41	286 - 639	0.008
Schedule (ii)	084454	Fresh Strips	0 - 0.0178	31.4	0 - 0.0178	30.8	0 - 0.0178	30.4	30.9	0.3	29.7 - 32.1	0.000
Schedule (ii)	084455	Mellow Sticks	0 - 0.0043	93.3	0 - 0.0043	119	0 - 0.0043	138	117	13	61.3 - 172	0.012
Schedule (ii)	084456	Copenhagen Long Cut	0 - 0.0009	486	0 - 0.0009	460	0 - 0.0009	445	464	12	411 - 516	0.001
Schedule (ii)	084457	Ariva Wintergreen	0 - 0.0079	49.8	0 - 0.0079	76.4	0 - 0.0079	81.1	69.1	9.7	27.3 - 111	0.019
Schedule (ii)	084458	Fresh Orbs	0 - 0.0099	85.4	0 - 0.0099	67.7	0 - 0.0099	71.7	75.0	5.3	51.9 - 98	0.005

One-Way ANOVA of Mean 'Unit of Use' Slope Estimates Among Test Samples

Schedule (i)

Source	Sum of Squares	Degrees of Freedom	Mean Square	F-Ratio	P-Value
Among Samples	1454272	6	242379	52.15	0.000
Within Samples	65064	14	4647		
Total (Corr.)	1519336	20			

Evaluation of Ratio (Max ÷ Min) of Standard Deviations of 'Unit of Use' Slope Estimates and Corresponding Method of Comparison

Treatment Schedule	Std. Dev. Ratio (Max ÷ Min)	Method of Comparison
Schedule (i)	40.4	Pairwise T-test (unequal variance)
Schedule (ii)	145.9	Pairwise T-test (unequal variance)

Schedule (ii)

Source	Sum of Squares	Degrees of Freedom	Mean Square	F-Ratio	P-Value
Among Samples	636679	6	106113	106.64	0.000
Within Samples	13931	14	995		
Total (Corr.)	650610	20			

One-way ANOVA analysis indicates significant differences (at $\alpha = 0.05$) among mean 'Unit of Use' specific activity slope estimates for test samples under both Treatment Schedules (i) and (ii).

ANOVA-Based Comparisons of Mean 'Unit of Use' Slope for Contrasts of Interest using Bonferroni-adjusted p-values

ANOVA-Based Comparison	Schedule (i)			Schedule (ii)		
	f-ratio	p-value	significance at $\alpha = 0.05$	f-ratio	p-value	significance at $\alpha = 0.05$
084394 vs. 084395	73.62	0.0000	significant	172.91	0.0000	significant
084394 vs. 084454	4.09	0.0627	not significant	13.12	0.0028	not significant
084394 vs. 084455	0.17	0.6894	not significant	0.08	0.7762	not significant
084394 vs. 084456	110.23	0.0000	significant	173.78	0.0000	significant
084394 vs. 084457	0.78	0.3922	not significant	4.57	0.0506	not significant
084394 vs. 084458	1.42	0.2535	not significant	3.65	0.0766	not significant
084395 vs. 084454	112.40	0.0000	significant	281.31	0.0000	significant
084395 vs. 084455	66.78	0.0000	significant	180.61	0.0000	significant
084395 vs. 084456	3.68	0.0756	not significant	0.00	0.9742	not significant
084395 vs. 084457	89.55	0.0000	significant	233.72	0.0000	significant
084395 vs. 084458	95.47	0.0000	significant	226.83	0.0000	significant
084454 vs. 084455	5.91	0.0291	not significant	11.11	0.0049	not significant
084454 vs. 084456	156.78	0.0000	significant	282.41	0.0000	significant
084454 vs. 084457	1.30	0.2738	not significant	2.20	0.1599	not significant
084454 vs. 084458	0.69	0.4199	not significant	2.93	0.1091	not significant
084455 vs. 084456	101.83	0.0000	significant	181.50	0.0000	significant
084455 vs. 084457	1.67	0.2176	not significant	3.42	0.0857	not significant
084455 vs. 084458	2.56	0.1321	not significant	2.63	0.1272	not significant
084456 vs. 084457	129.55	0.0000	significant	234.73	0.0000	significant
084456 vs. 084458	136.66	0.0000	significant	227.83	0.0000	significant
084457 vs. 084458	0.09	0.7626	not significant	0.05	0.8238	not significant

ANOVA-based comparison p-values less than the Bonferroni-adjusted $\alpha = 0.05$ indicate that significant differences in mean 'unit of use' slope were as follows under treatment schedules (i) and (ii):

Schedule (i)

Sample Description	Sample ID	Mean Slope	Homogenous Groupings
Fresh Strips	084454	44.7	X
Fresh Orbs	084458	90.9	X
Ariva Wintergreen	084457	108	X
Camel SNUS Frost	084394	157	X
Mellow Sticks	084455	180	X
2S3	084395	635	X
Copenhagen Long Cut	084456	742	X

Schedule (ii)

Sample Description	Sample ID	Mean Slope	Homogenous Groupings
Fresh Strips	084454	30.9	X
Ariva Wintergreen	084457	69.1	X
Fresh Orbs	084458	75.0	X
Mellow Sticks	084455	117	X
Camel SNUS Frost	084394	124	X
2S3	084395	463	X
Copenhagen Long Cut	084456	464	X

Statistical Analysis (Unit)

Revision: 0

Pairwise T-Test Comparisons of Mean 'Unit of Use' Slope for Contrasts of Interest using Bonferroni-adjusted p-values

Pairwise T-Test Comparison	Schedule (i)			Schedule (ii)		
	t-statistic	p-value	significance at $\alpha = 0.05$	t-statistic	p-value	significance at $\alpha = 0.05$
084394 vs. 084395	14.3657	0.0001	significant	7.8018	0.0015	significant
084394 vs. 084454	32.9417	0.0000	significant	6.5598	0.0028	not significant
084394 vs. 084455	1.8226	0.1424	not significant	0.3889	0.7172	not significant
084394 vs. 084456	6.1201	0.0036	not significant	18.1445	0.0001	significant
084394 vs. 084457	2.5845	0.0610	not significant	3.1968	0.0330	not significant
084394 vs. 084458	5.9935	0.0039	not significant	3.2403	0.0317	not significant
084395 vs. 084454	17.7552	0.0001	significant	10.5321	0.0005	significant
084395 vs. 084455	12.8742	0.0002	significant	8.0512	0.0013	significant
084395 vs. 084456	1.0571	0.3501	not significant	0.0198	0.9851	not significant
084395 vs. 084457	13.8106	0.0002	significant	9.3413	0.0007	significant
084395 vs. 084458	15.6008	0.0001	significant	9.3784	0.0007	significant
084454 vs. 084455	10.8712	0.0004	significant	6.6582	0.0026	not significant
084454 vs. 084456	7.2989	0.0019	significant	35.5799	0.0000	significant
084454 vs. 084457	3.3363	0.0289	not significant	3.9290	0.0171	not significant
084454 vs. 084458	4.1906	0.0138	not significant	8.2282	0.0012	significant
084455 vs. 084456	5.8366	0.0043	not significant	19.5802	0.0000	significant
084455 vs. 084457	3.1986	0.0329	not significant	2.9487	0.0420	not significant
084455 vs. 084458	5.4628	0.0055	not significant	2.9930	0.0402	not significant
084456 vs. 084457	6.5112	0.0029	not significant	25.3401	0.0000	significant
084456 vs. 084458	6.7735	0.0025	not significant	29.2606	0.0000	significant
084457 vs. 084458	0.7894	0.4740	not significant	0.5266	0.6263	not significant

Pairwise t-test comparison p-values less than the Bonferroni-adjusted $\alpha = 0.05$ indicate that significant differences in mean 'unit of use' slope were detected in the following cases:

Schedule (i):

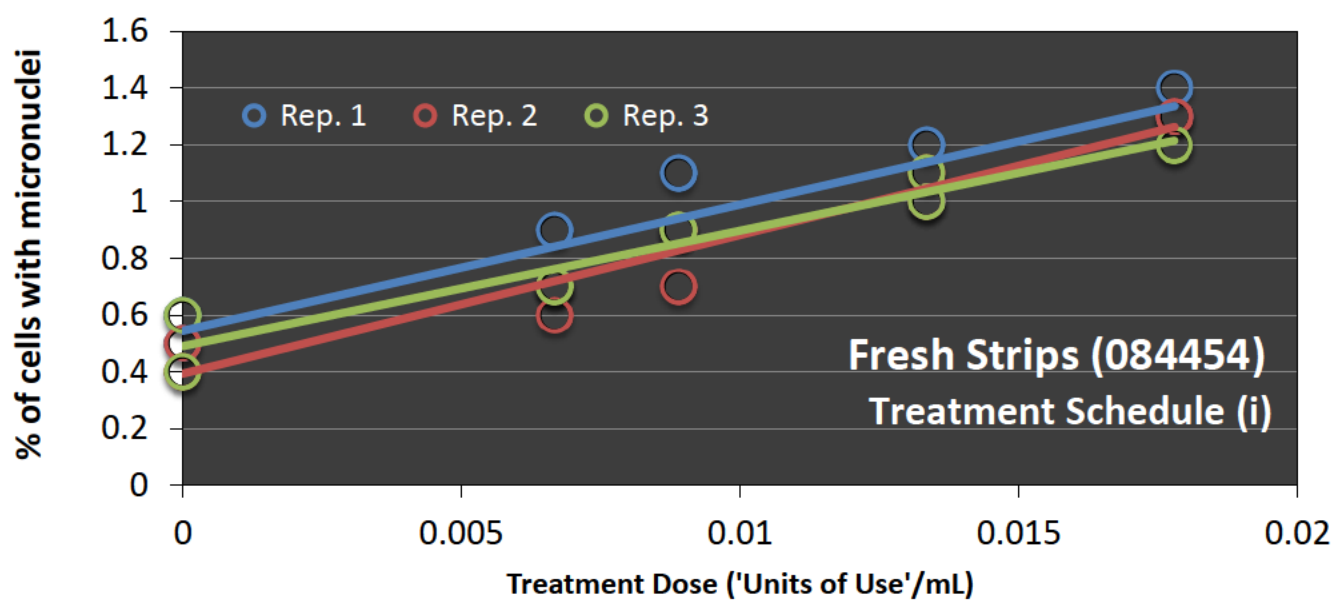
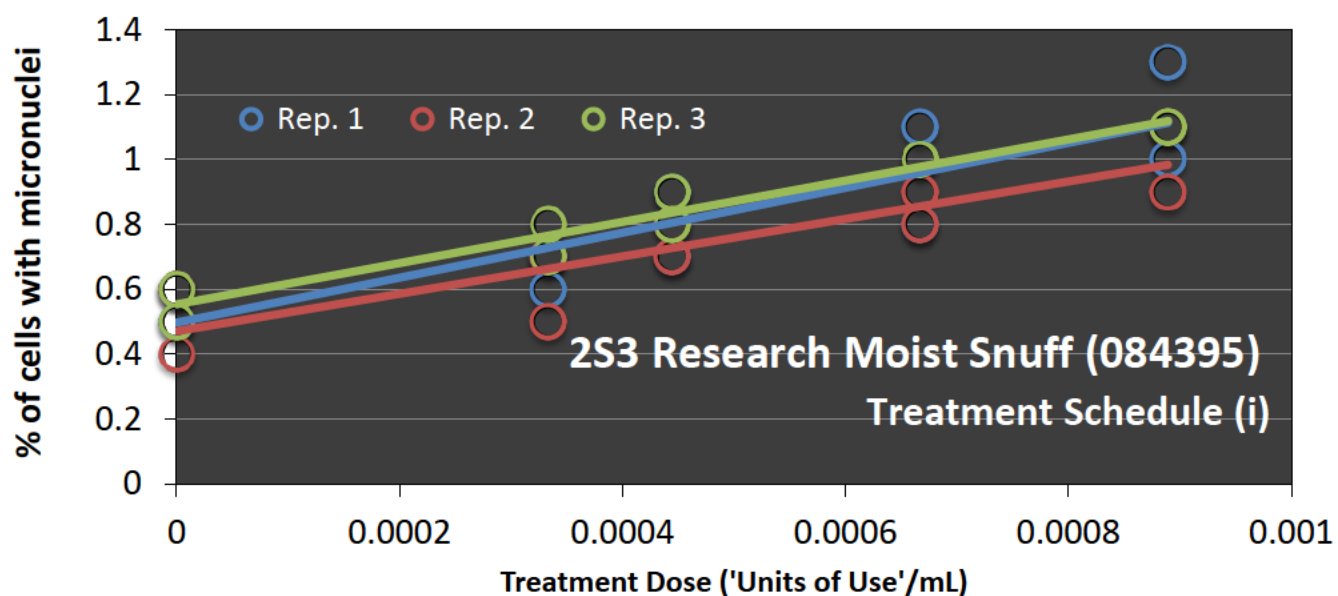
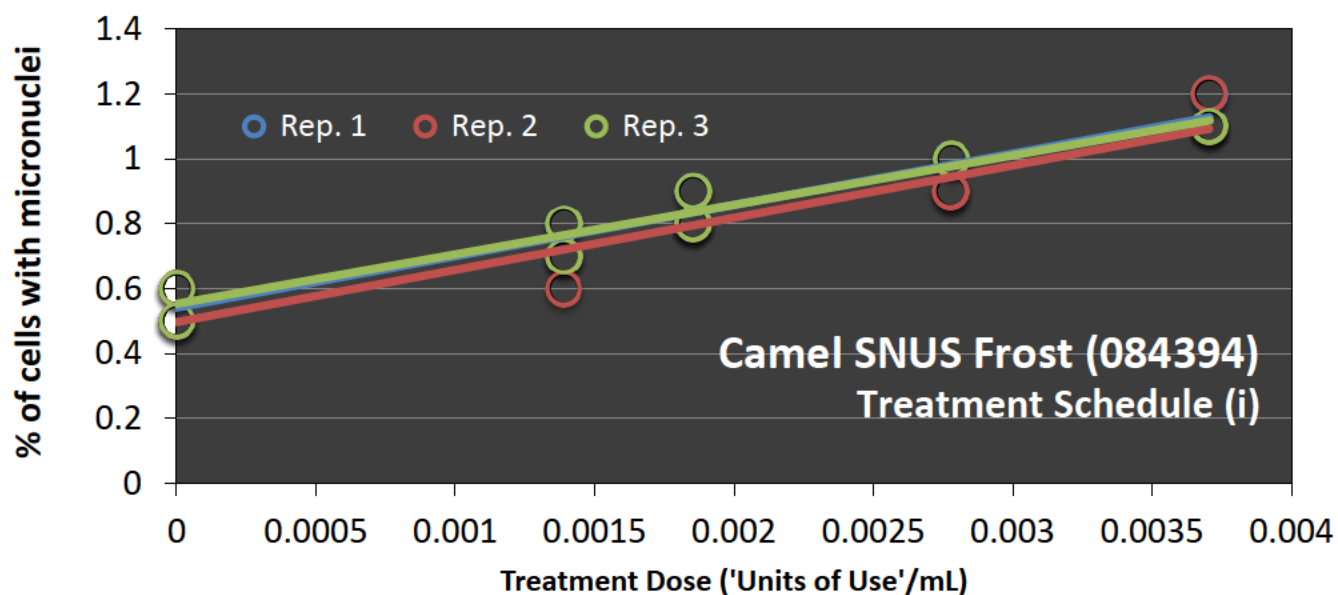
Fresh Strips (084454) and each of {Camel SNUS Frost (084394), Mellow Sticks (084455), 2S3 (084395), Copenhagen Long Cut (084456)}

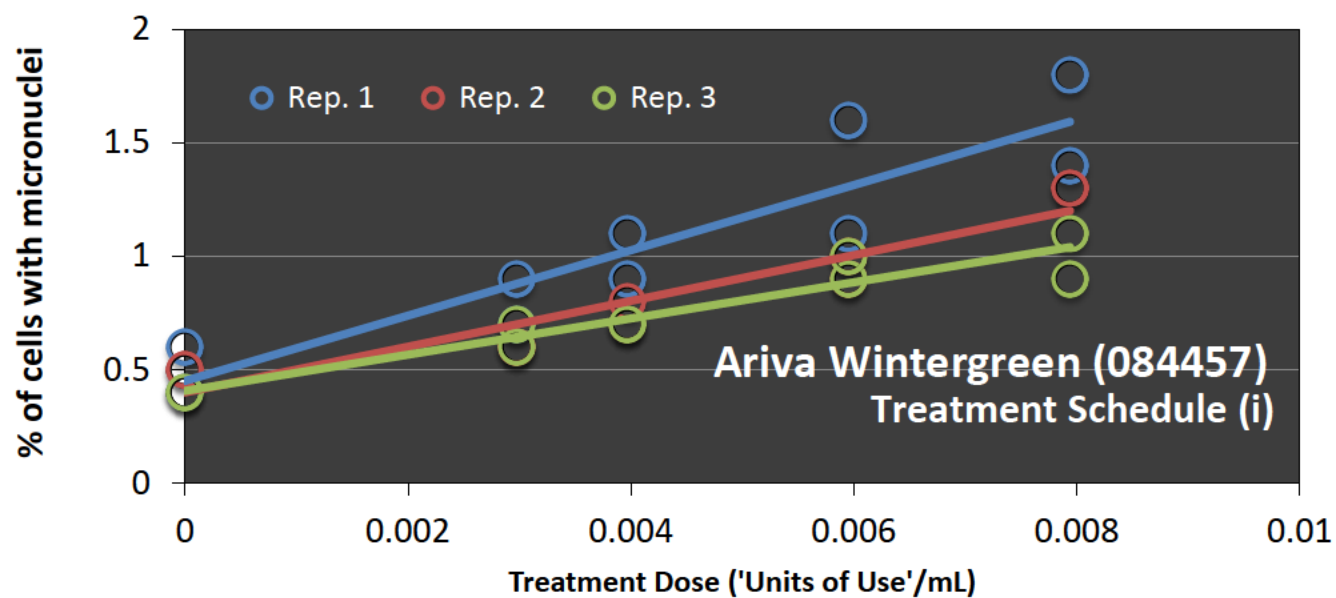
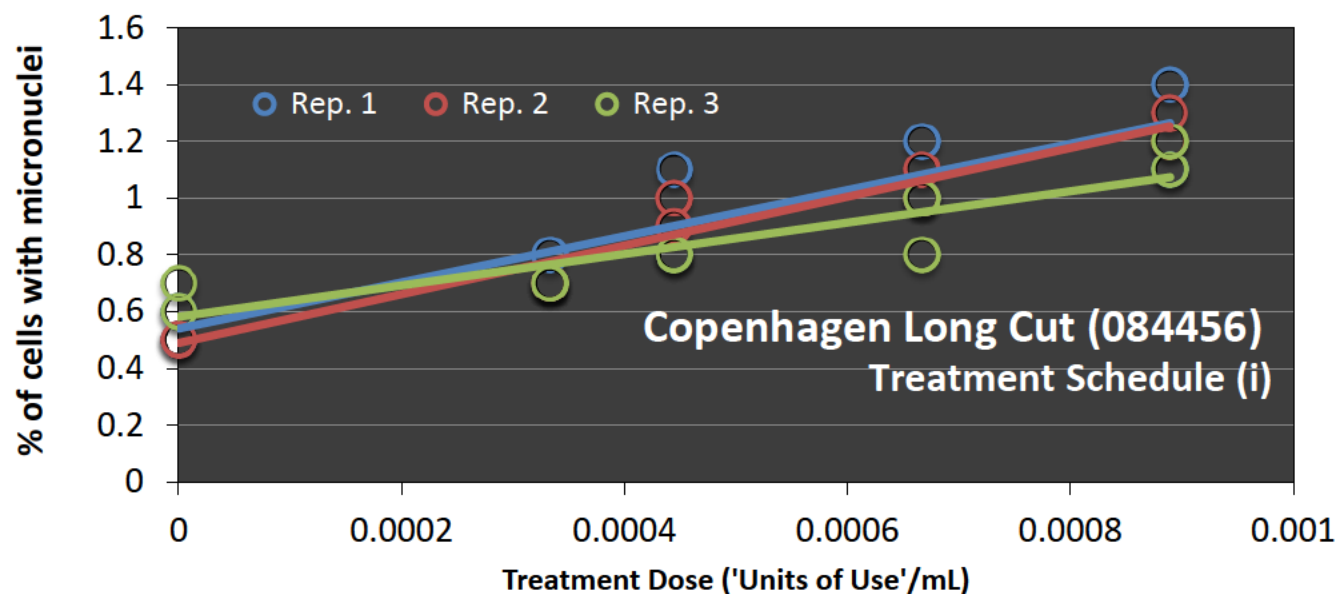
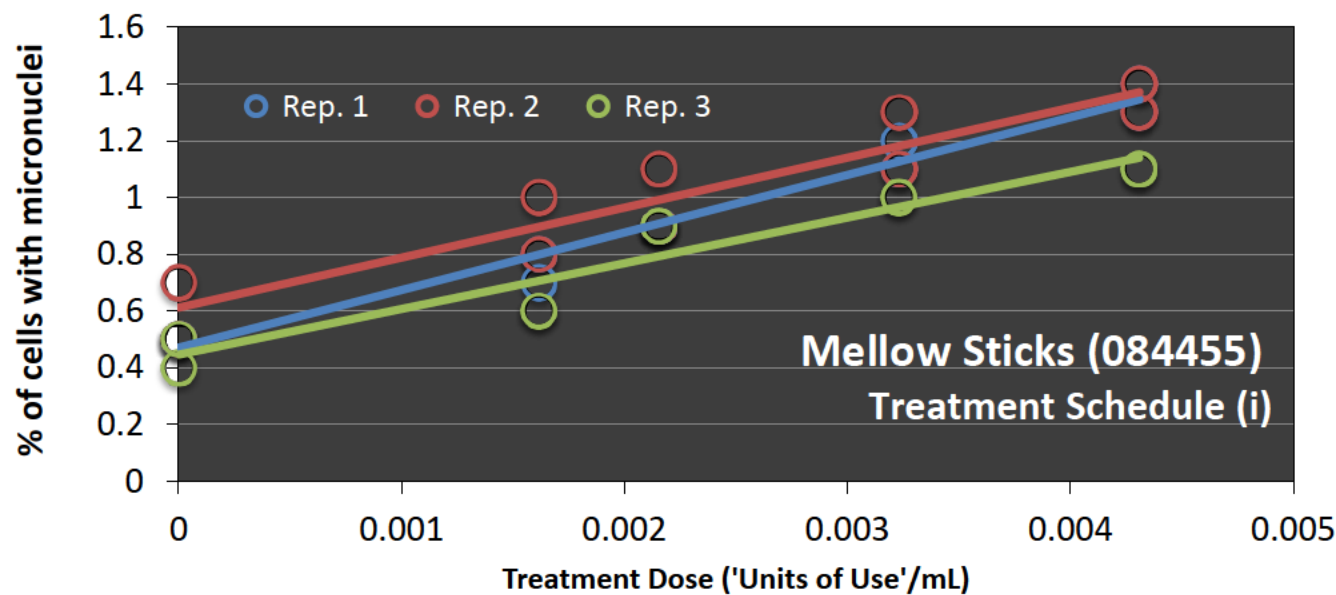
2S3 (084395) and each of {Fresh Orbs (084458), Ariva Wintergreen (084457), Camel SNUS Frost (084394), Mellow Sticks (084455)}

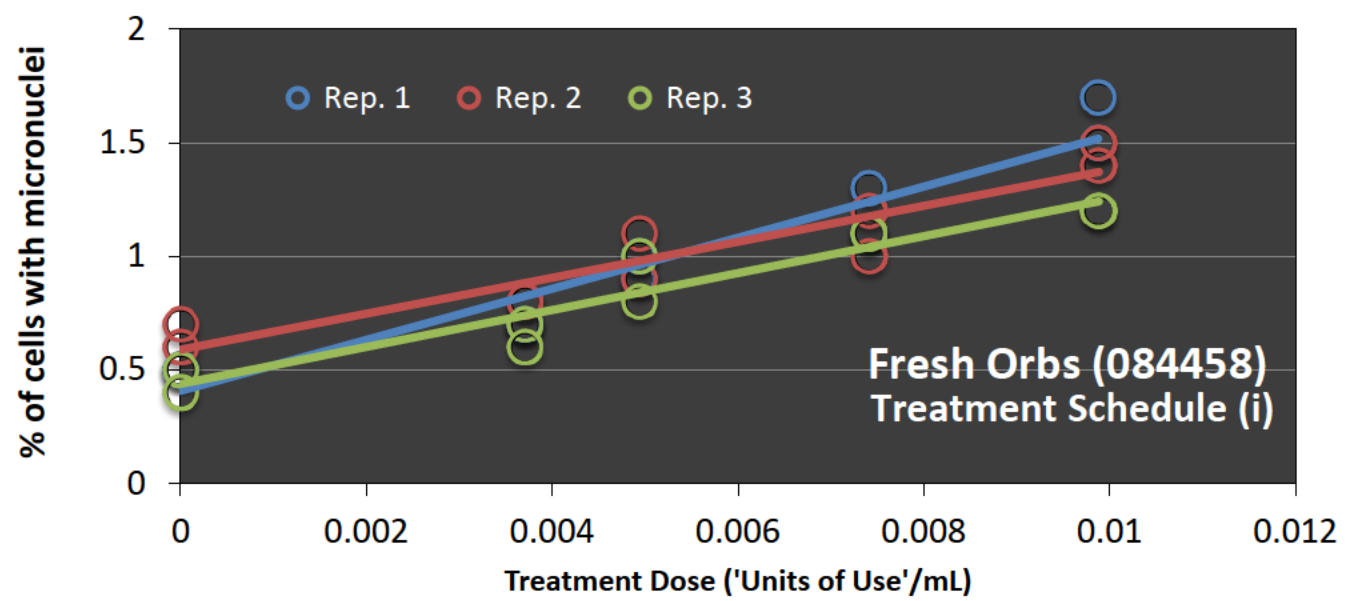
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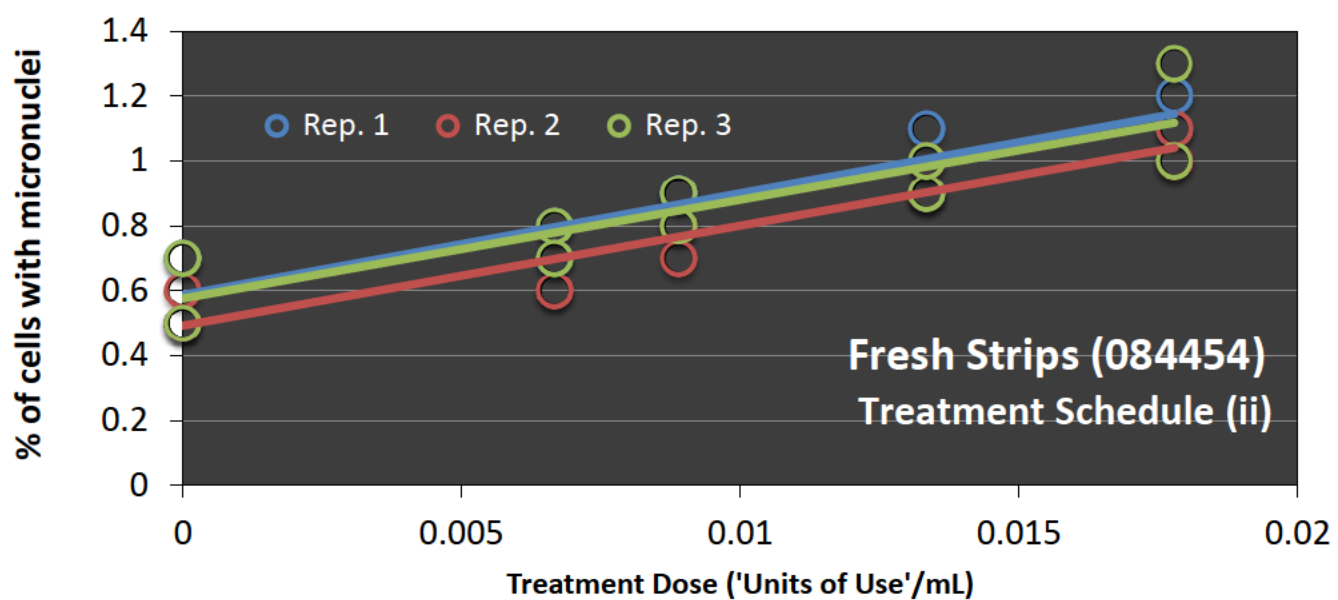
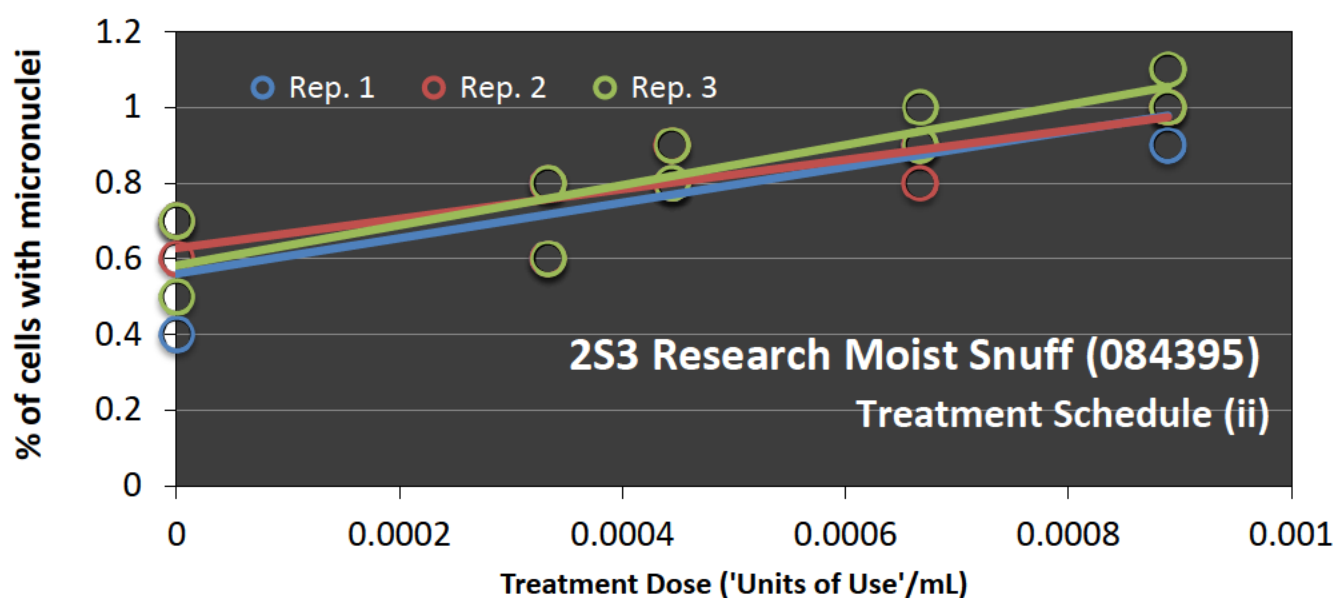
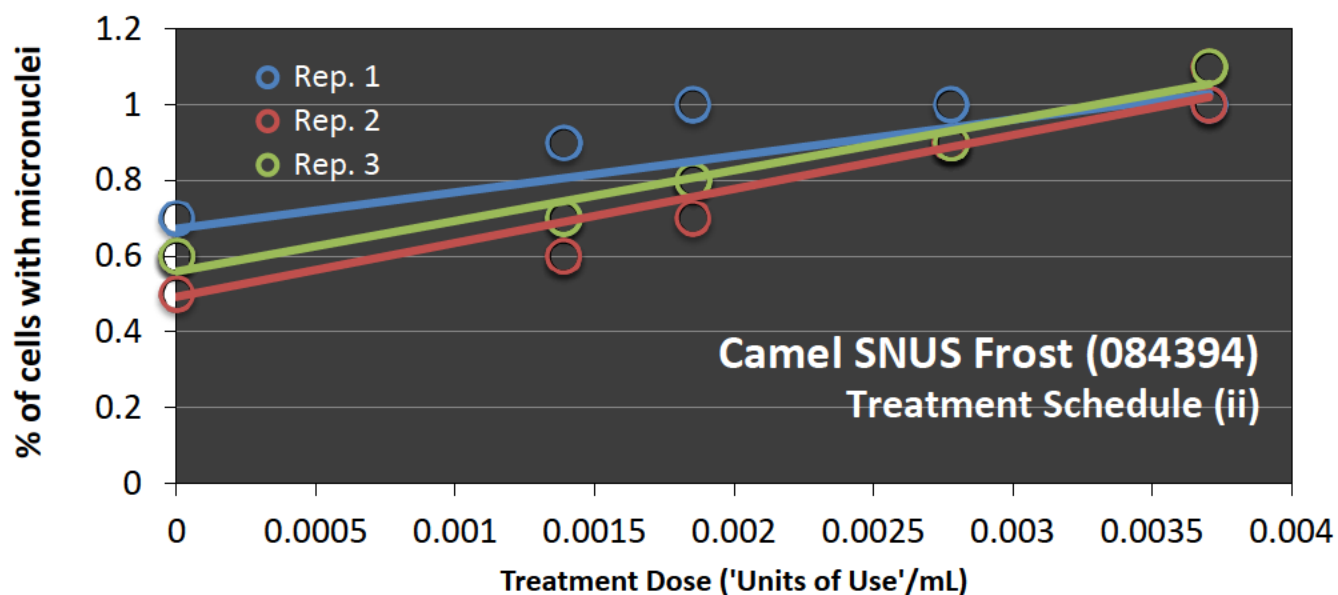
2S3 (084395) and Copenhagen Long Cut (084456) and each of {Camel SNUS Frost (084394), Mellow Sticks (084455), Fresh Orbs (084458), Ariva Wintergreen (084457), Fresh Strips (084454)}

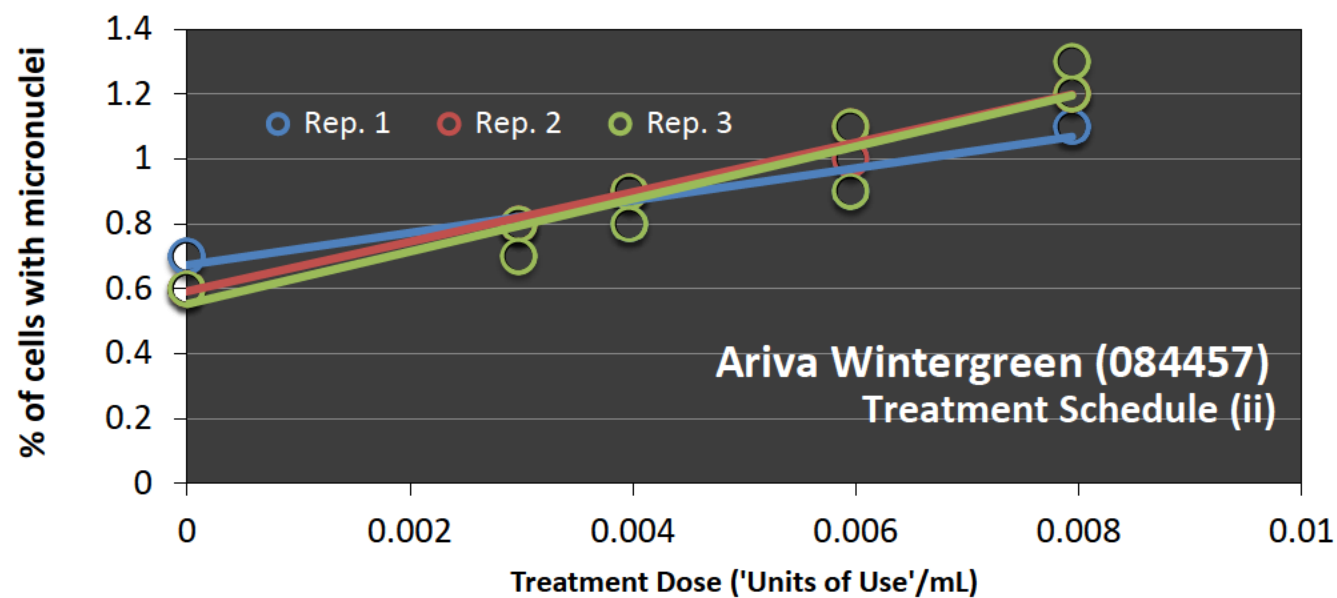
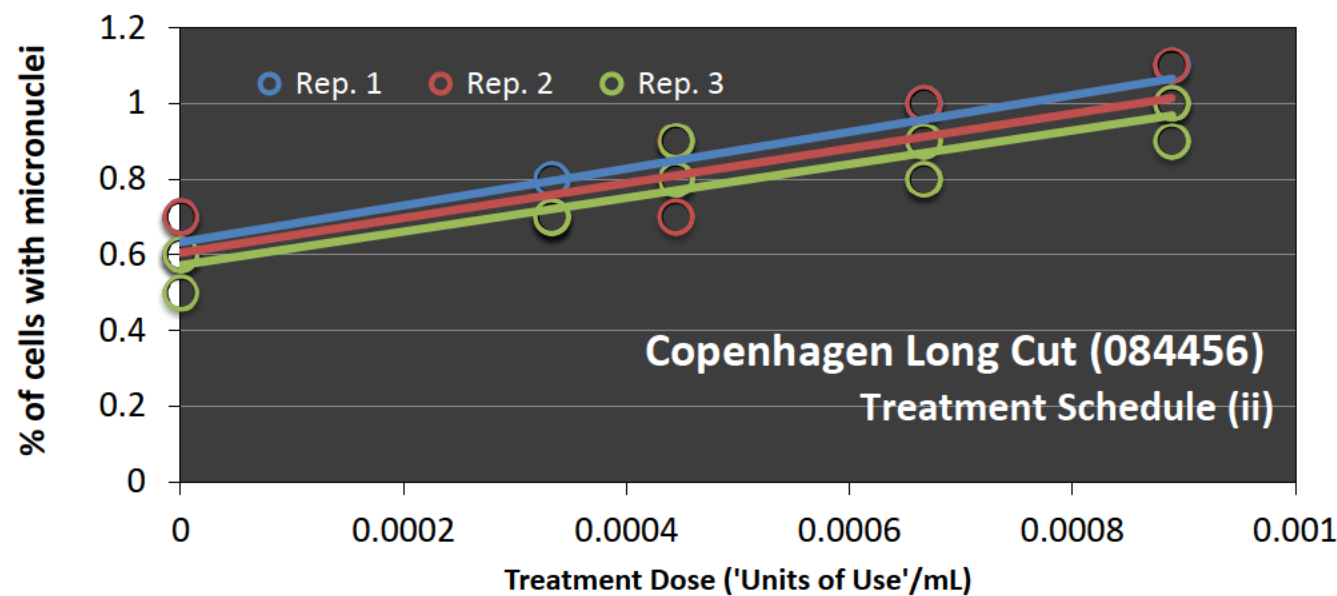
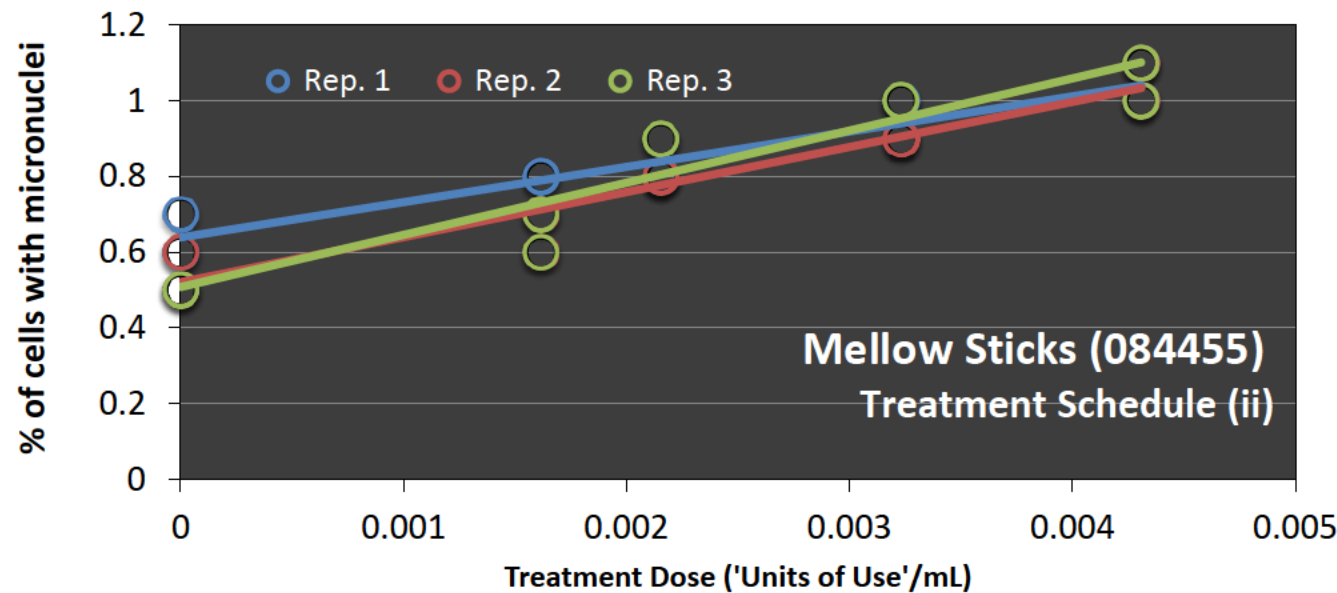
Fresh Strips (084454) and Fresh Orbs (084458)

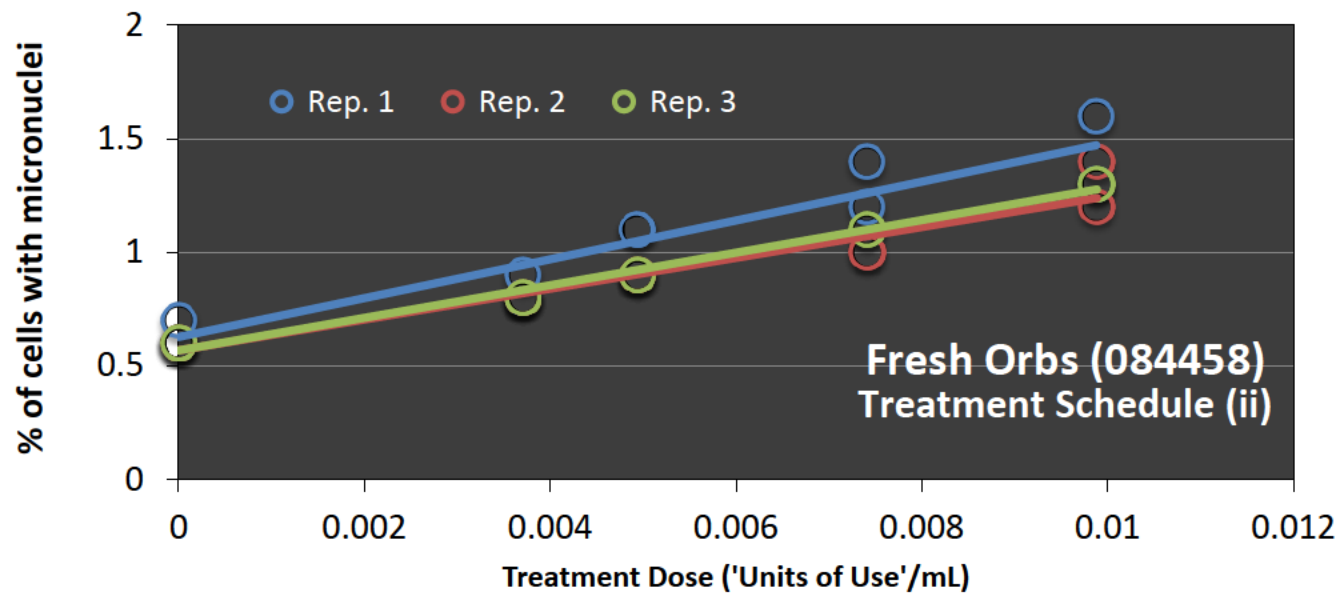


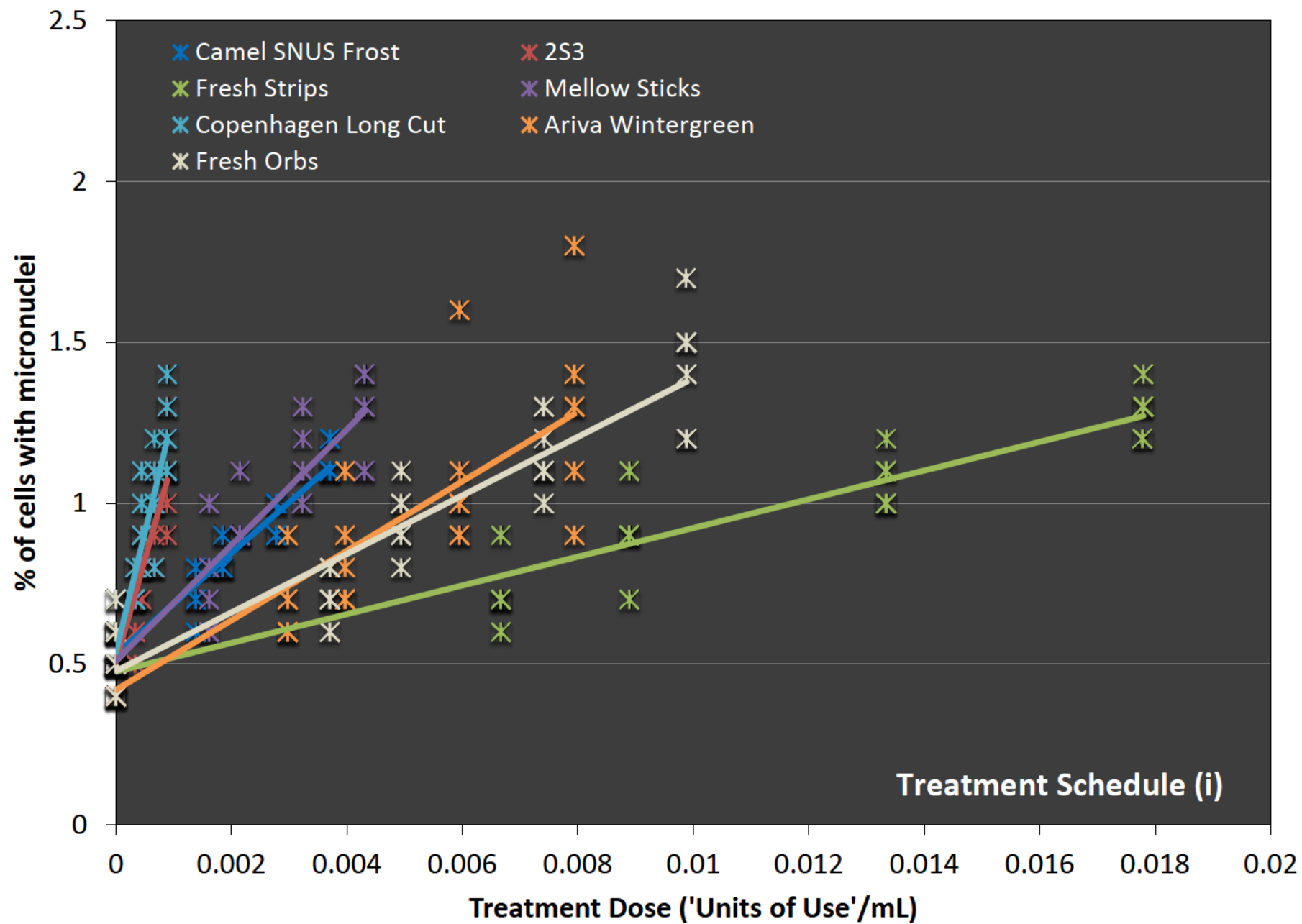


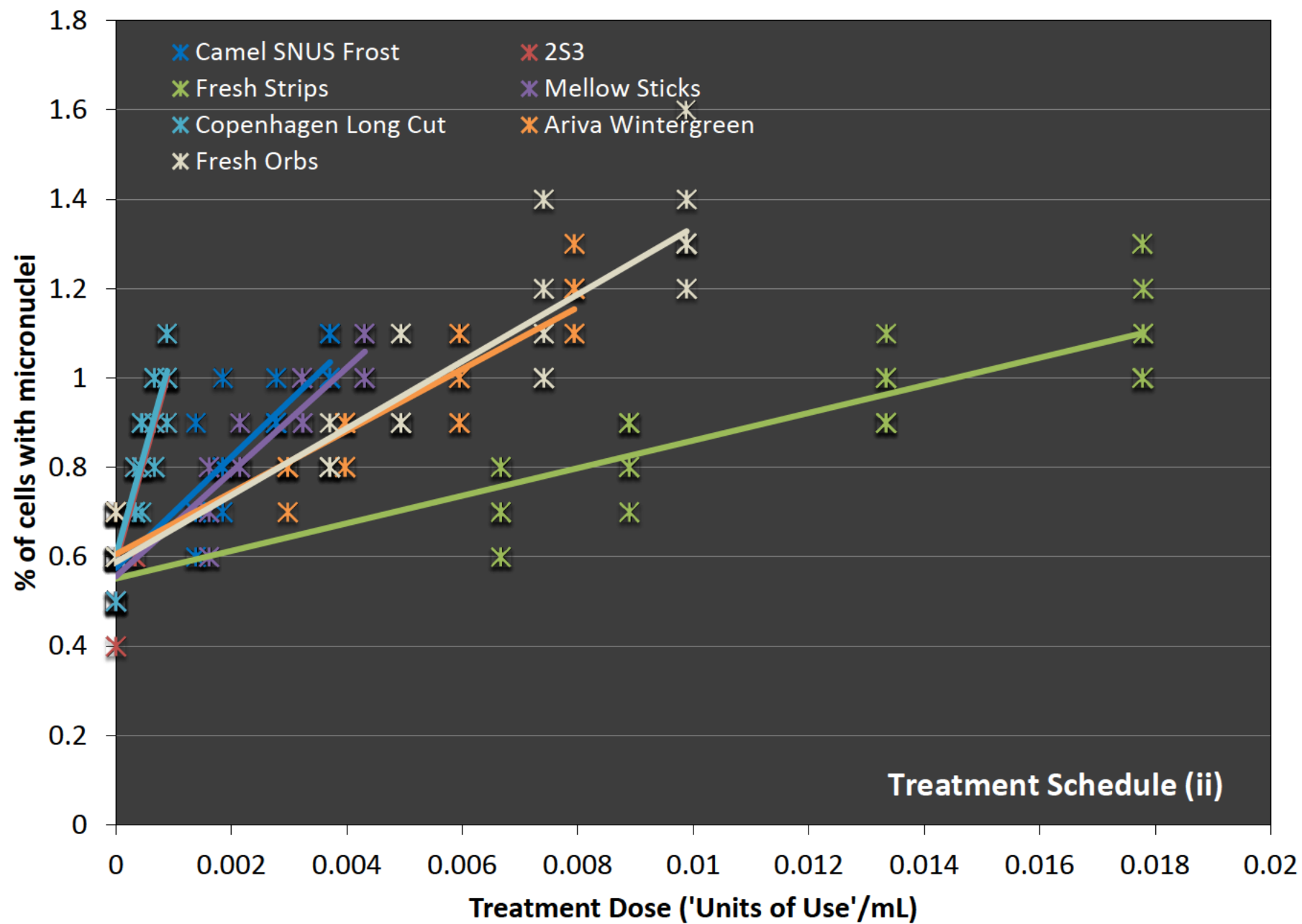












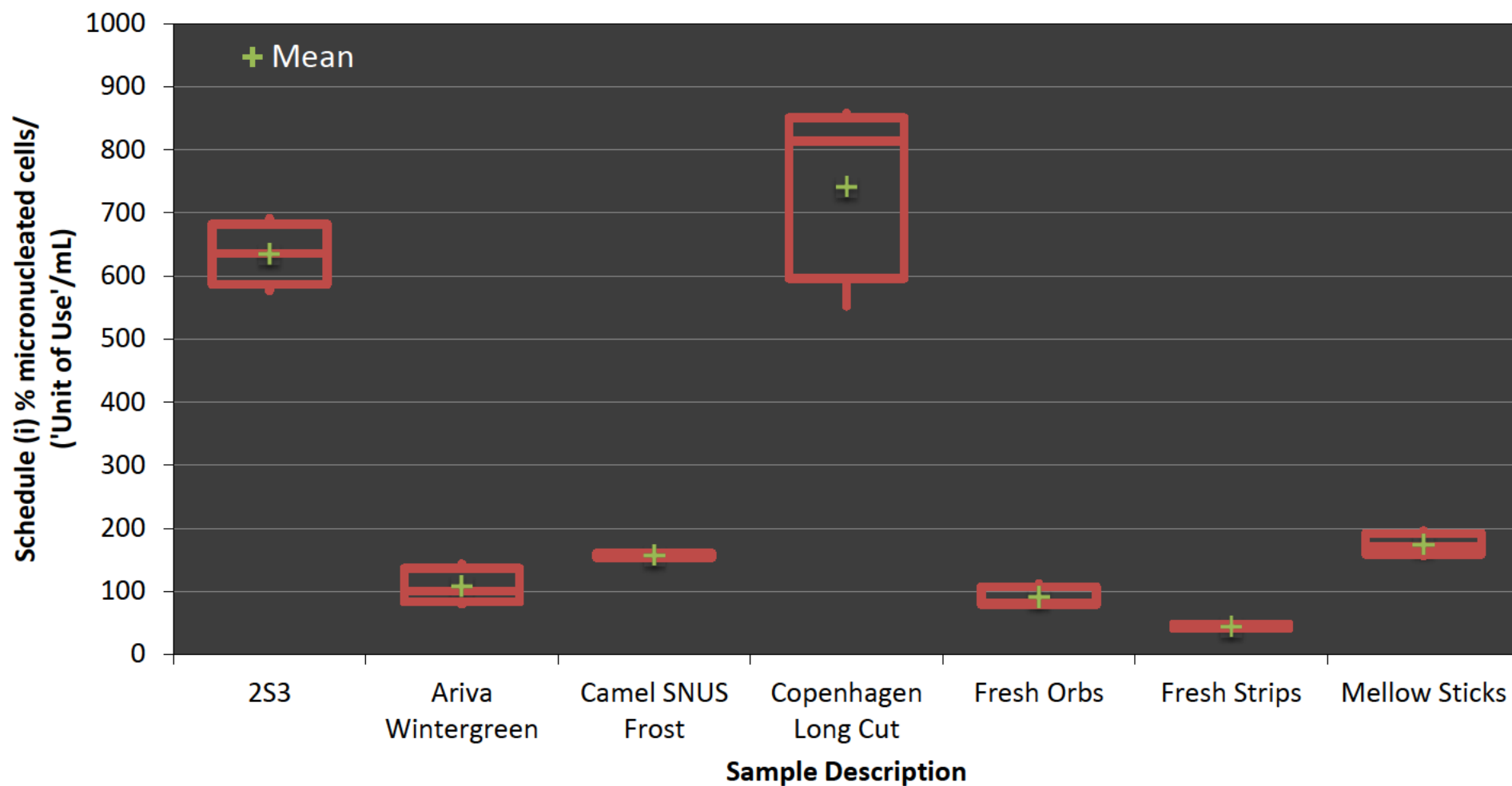
Test **Describe - Comparative**

Performed by

Schedule (i) % micronucleated cells/('Unit of Use'/mL) by Sample Description
Wendy Wagstaff

Date

8 December 2010



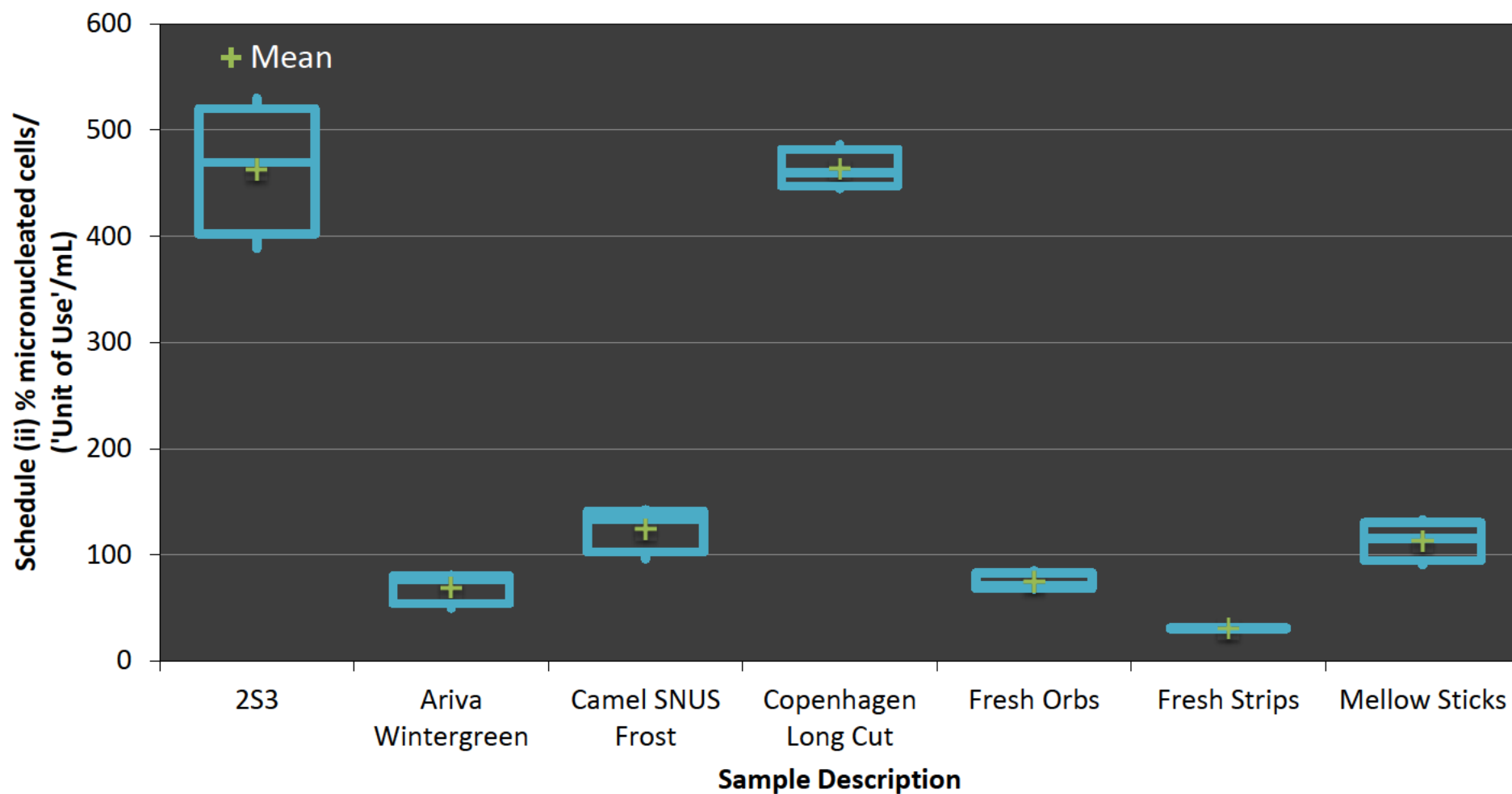
Test Describe - Comparative

Performed by

Schedule (ii) % micronucleated cells/('Unit of Use'/mL) by Sample Description
Wendy Wagstaff

Date

8 December 2010



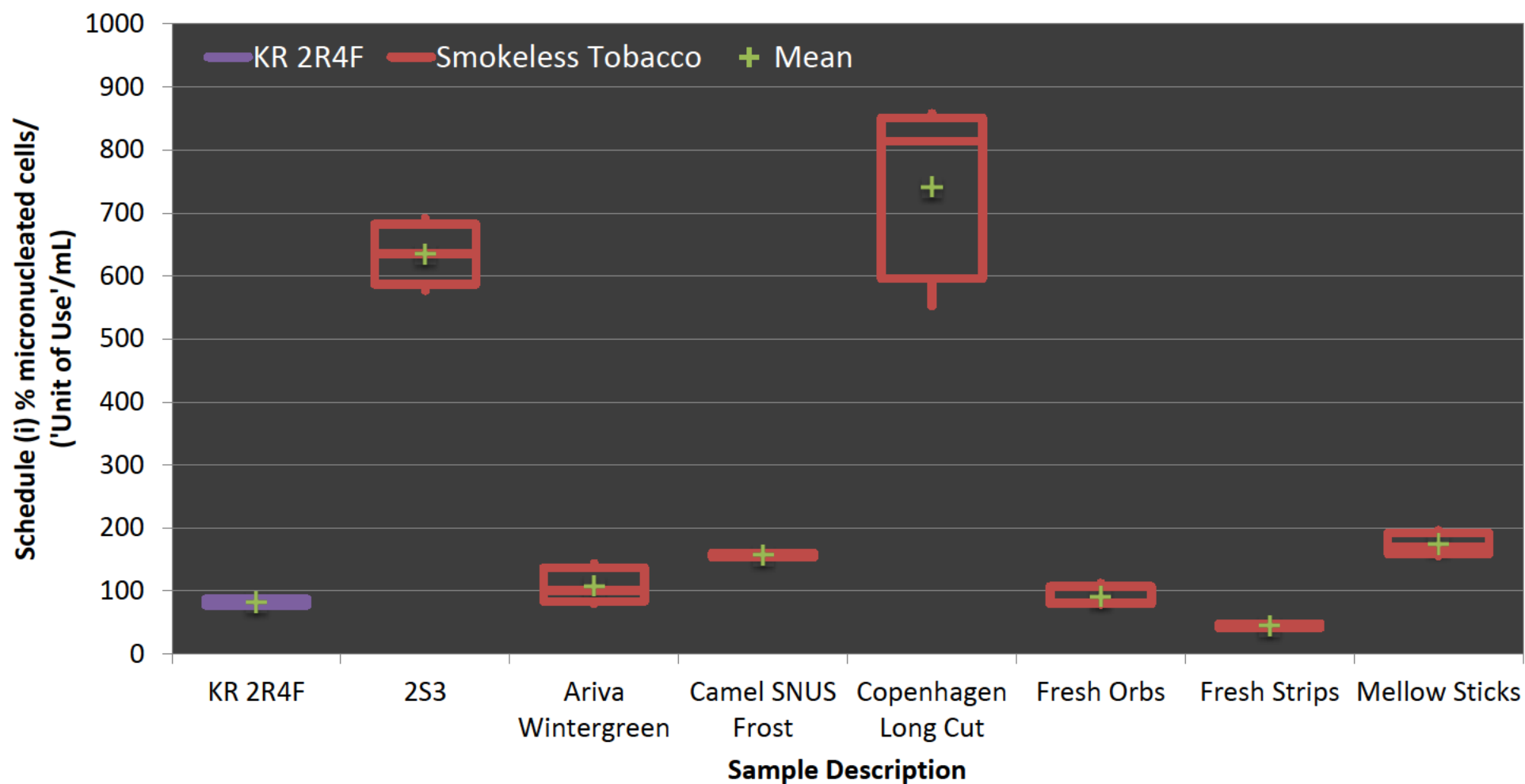
Test Describe - Comparative

Performed by

Schedule (i) % micronucleated cells/(cigarette/mL) (KR 2R4F) and % micronucleated cells/('Unit of Use'/mL) by Sample Description

Date

8 December 2010



Test Describe - Comparative

Performed by

Schedule (ii) % micronucleated cells/(cigarette/mL) (KR 2R4F) and % micronucleated cells/('Unit of Use'/mL) by Sample Description

Date

8 December 2010

