ENTHALPY ANALYTICAL

Reference Product Characterization

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Introduction

- Purpose of Reference Products:
  - Method Validation and Qualification
    - Certified values
    - Known repeatability
  - Quality Control Process Monitor
    - Method quality control, control charts
    - Data acceptance
  - Collaborative Study Material
    - Establish r and R values
  - Reporting of Results
    - Quality control check for clients and Regulators

Ideal Reference Products

- Features
  - Uniformity
    - Repeatable content and yield
  - Stability
    - Stable over time
  - Target Compounds
    - Contain all target compounds at quantifiable levels

Ideal Reference Products

- Controlling variability
  - Cigarettes
    - Simplified blend design (reduce natural variability)
    - Simplified product design (reduce product variability)
  - Smokeless Tobacco
    - Simplified blend design (reduce natural variability)
    - Packaging material selected to reduce water loss or uptake
    - Product Uniformity
      - Avoid pouched or whole leaf products

Current Reference Products

- Features
  - Uniformity
    - Tobacco is a natural product
      - Variability is expected
    - Design will impact variability
      - Banded paper
      - Filter Ventilation
  - Stability
    - Finite stability
    - Stability of target compounds might vary
  - Target Compounds
    - Target compounds range from % levels of <LOQ/LOD

1R6F Reference Product

- Features
  - Uniformity
    - Represents Commercial Blend
      - Flue Cured 34%
      - Burley 24%
      - Oriental 12%
      - Reconstituted 20%
      - Expanded Flue Cured 7%
      - Expanded Burley 3%
  - Design
    - Ventilated Filter
    - Banded Paper

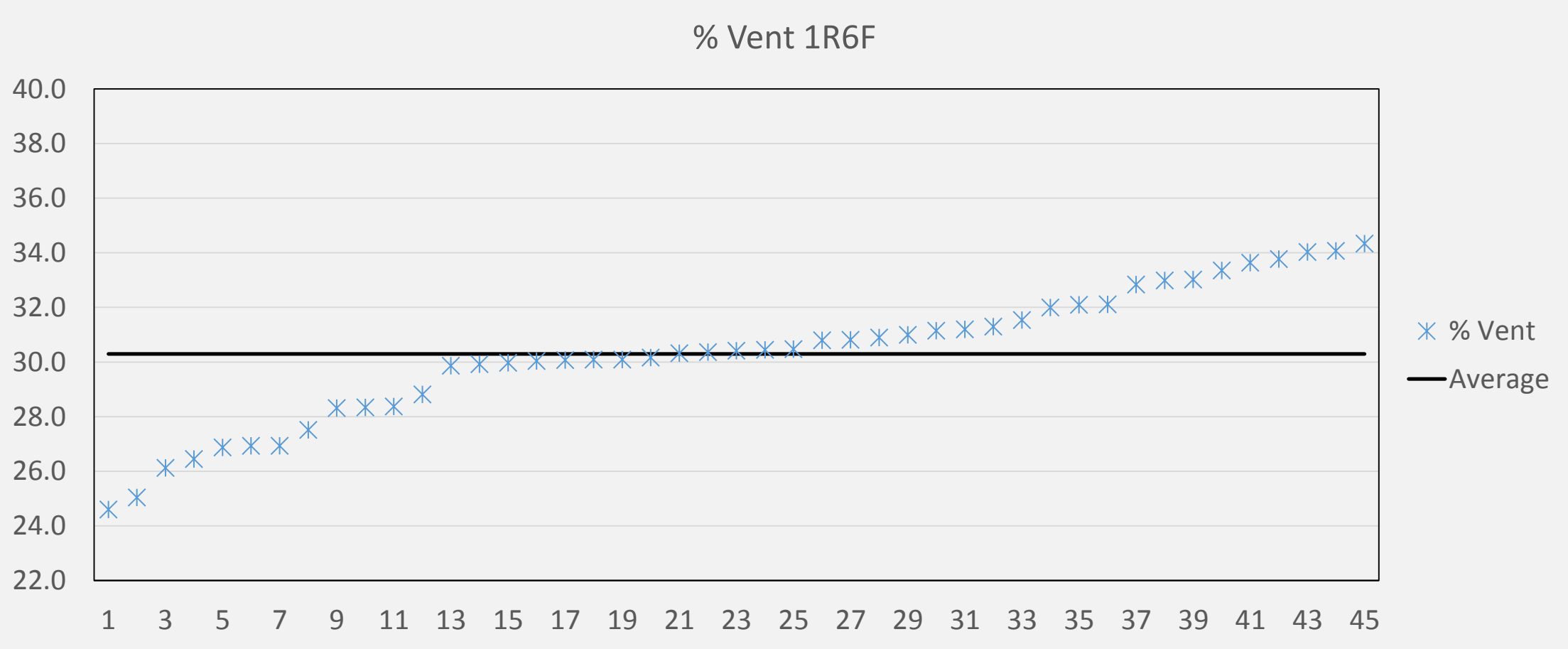
1R6F Reference Product

- Example data from the 2015 Characterization of the 1R6F Reference Product
  - Data collected under short term repeatability conditions
    - Short time frame
    - Same Technicians and equipment
    - 45 Production lots tested for TNCO and Physical Properties
    - Data blinded to remove production codes

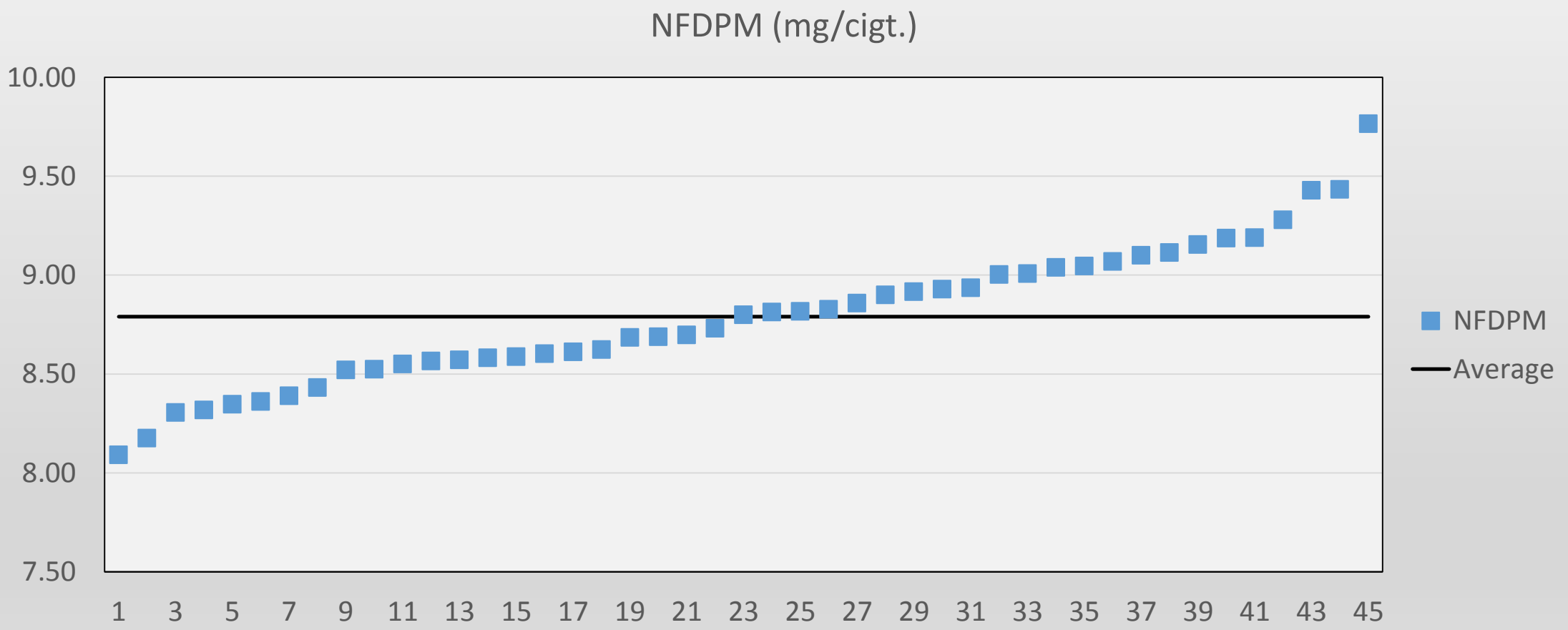
1R6F Reference Product

- Impact of Filter Ventilation
  - Filter Ventilation
    - Portion of the puff is directed through the filter
    - Variability in filter ventilation will directly impact smoke yields under ISO smoking conditions
  - Data
    - Collected to support the Certification of the 1R6F
      - 45 unique production lots
    - Data collected in a short time frame
      - Short Term Repeatability (r)

1R6F Reference Product-% Vent



1R6F Reference Product-NFDPM



1R6F Reference Product Summary Data for Physical Properties

	Length (mm)	Weight (g)	Circum. (mm)	Filter Vent (%)	Pressure Drop Open (mm WG)	Pressure Drop Closed (mm WG)
Average	83.1	0.9	24.8	30.3	107.4	137.5
SD	0.1	0	0	2.4	2.7	2.3
% RSD	0.1	0.8	0.2	8.1	2.5	1.6

3R4F TSNAs in Filler

- Samples were obtained from four lots of 3R4F cigarettes.
- 200 cigarette were composited from each lot.
- Ground composites analyzed for TSNA content by LC-MS/MS.

Originally Presented as ST27 CORESTA Congress 2014

TSNA Results-Ground Filler

	Lot # V348X61B5	Lot # V349Y61B5	Lot # V348Z61B5	Lot # 2013 Composite
	NNN ng/g	**NNN ng/g**	**NNN ng/g**	**NNN ng/g**
Average	2476.1	2593.9	2423.8	2351.1
SD	58.4	25.9	11.4	10.5
%RSD	2.4	1.0	0.5	0.4
% Diff*	5.2	9.8	3.0	NA

	Lot # V348X61B5	Lot # V349Y61B5	Lot # V348Z61B5	Lot # 2013 Composite
	NAB ng/g	**NAB ng/g**	**NAB ng/g**	**NAB ng/g**
Average	76.8	88.9	76.9	72.9
SD	1.3	3.9	1.3	0.6
%RSD	1.7	4.4	1.6	0.8
% Diff*	5.1	19.7	5.3	NA

	Lot # V348X61B5	Lot # V349Y61B5	Lot # V348Z61B5	Lot # 2013 Composite
	NAT ng/g	**NAT ng/g**	**NAT ng/g**	**NAT ng/g**
Average	1615.7	1869.1	1759.5	1713.8
SD	63.3	44.3	30.0	26.3
%RSD	3.9	2.4	1.7	1.5
% Diff*	-5.9	8.7	2.6	NA

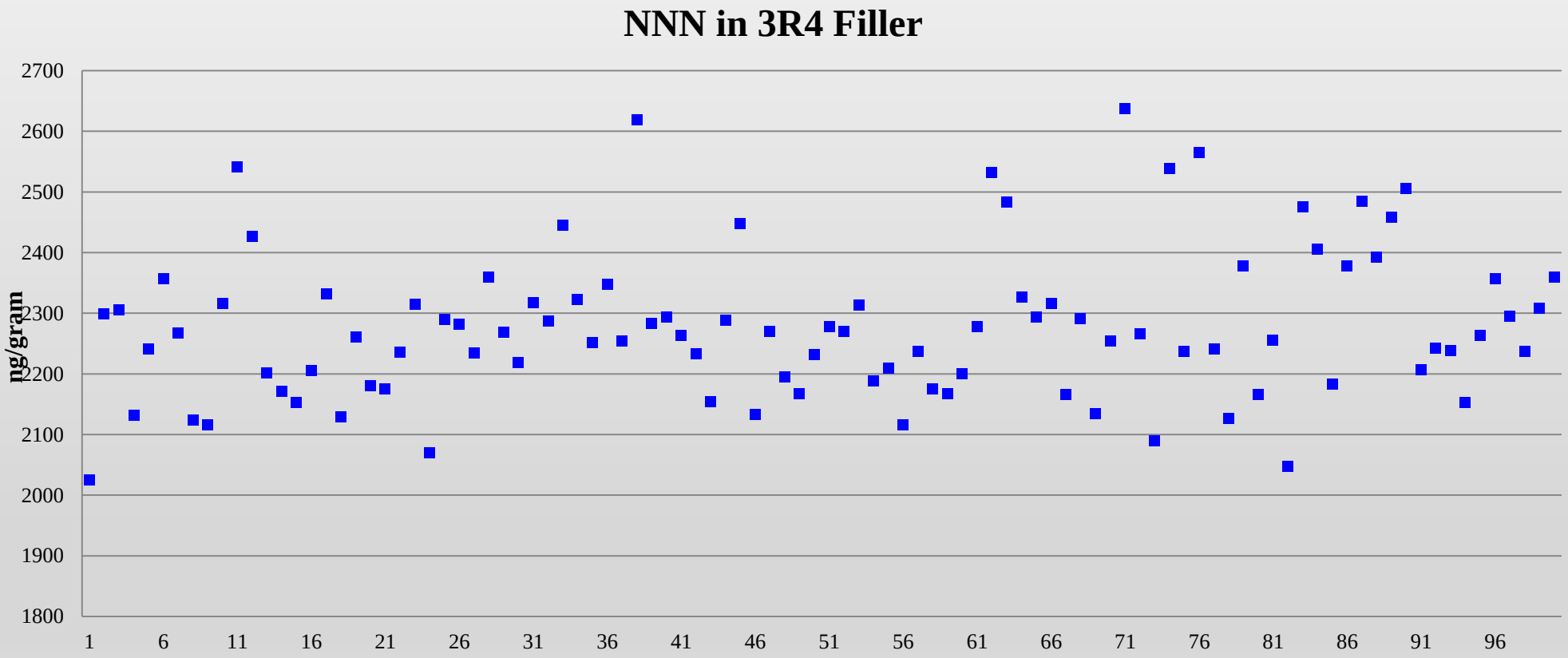
	Lot # V348X61B5	Lot # V349Y61B5	Lot # V348Z61B5	Lot # 2013 Composite
	NNK ng/g	**NNK ng/g**	**NNK ng/g**	**NNK ng/g**
Average	724.1	787.6	745.5	735.4
SD	13.3	13.0	17.4	7.6
%RSD	1.8	1.6	2.3	1.0
% Diff*	-1.5	6.9	1.4	NA

* %difference from 2013 composite sample

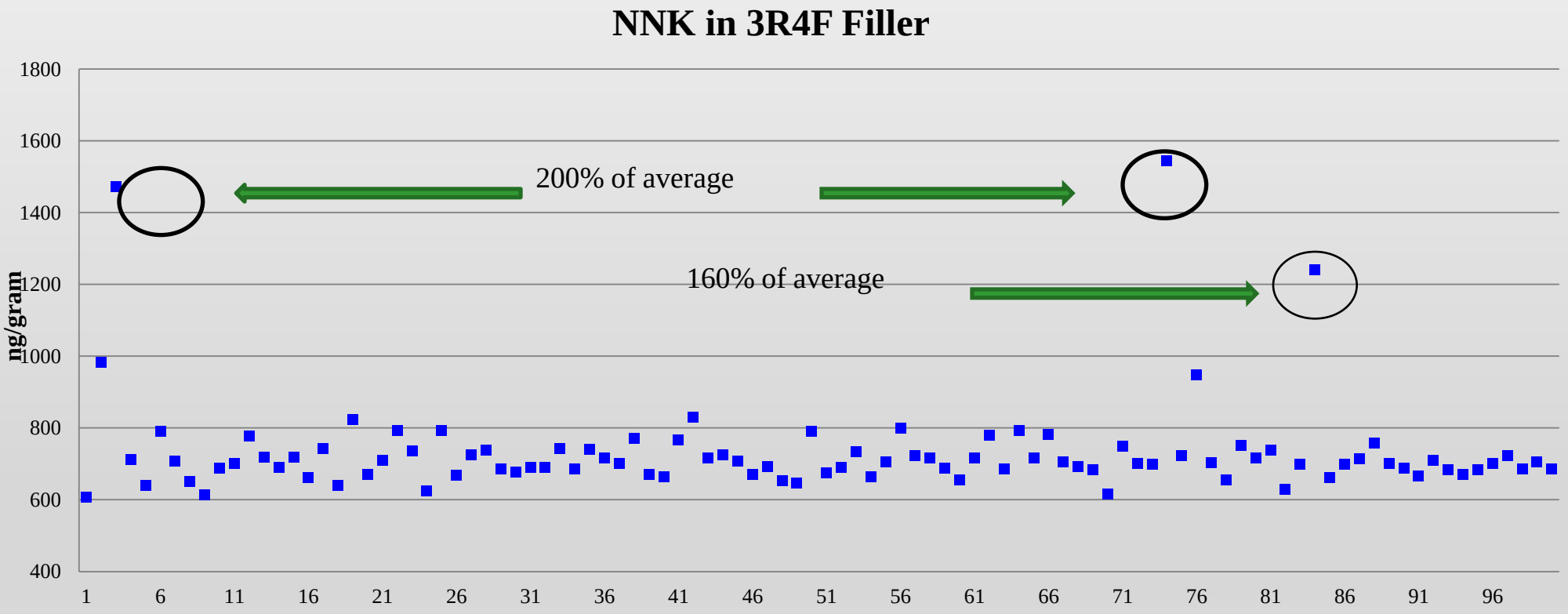
TSNAs in 3R4F- Individual cigarette

- TSNAs were determined from 100 individual cigarettes selected from lot of 5000.
- Filler from one cigarette was extracted and analyzed by LC-MS/MS.

Individual cigarette results-NNN



Individual cigarette results-NNK



TSNA Summary

	NNN	NAT	NAB	NNK
	ng/g	ng/g	ng/g	ng/g
Average	2277.5	1668.0	81.0	732.9
Stdev	123.5	155.2	5.3	136.4
% RSD	5.4	9.3	6.6	18.6

TSNAs in 100 individual cigarettes

4% of the samples had NNK or NAT greater than 150% of the average of all samples

Conclusion

- Design of Reference products will impact method repeatability (r) and reproducibility (R) values
- Factors that impact product variably should be reduced and controlled during the design of Reference products
  - Simplified blend or pre-production analysis of blend components
  - Particle size (smokeless)
  - Filter ventilation
- Long term stability of the product requires on-going analysis
  - Stability of target compounds over time
  - Reduce product moisture changes
    - Commercial versus custom packaging