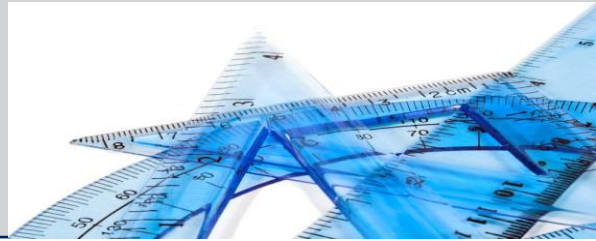
Cigarette Variability (CVAR) Task Force
CORESTA 2017 Update

- **Task Force Coordinator: Jason Flora**
  - Altria Client Services LLC, Richmond VA
- **Secretary and Study Coordinator: Rana Tayyarah**
  - ITG Brands, LLC, Greensboro NC
- **Statistical Analysis: Michael Morton**
  - Altria Client Services LLC, Richmond VA

CVAR – October 2017, Kitzbühel, Austria

Background

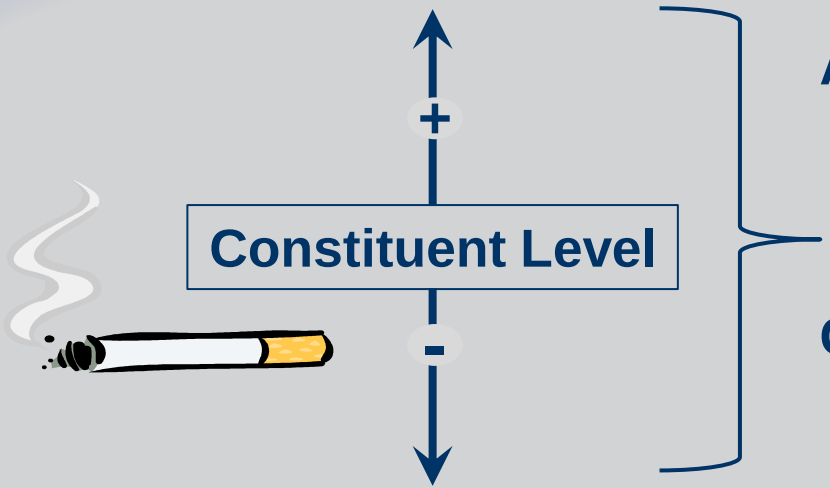
- Scientists measure tobacco and smoke constituents for a variety of reasons
- There is variability associated with measuring these constituents*
- In order for the scientific community to make science-based decisions regarding tobacco and smoke constituents, they need to fully understand this variability



*ISO 8243

Sources of Measurement Variability

- Tobacco and smoke analyte variability results from multiple sources:



Analytical Testing Variability

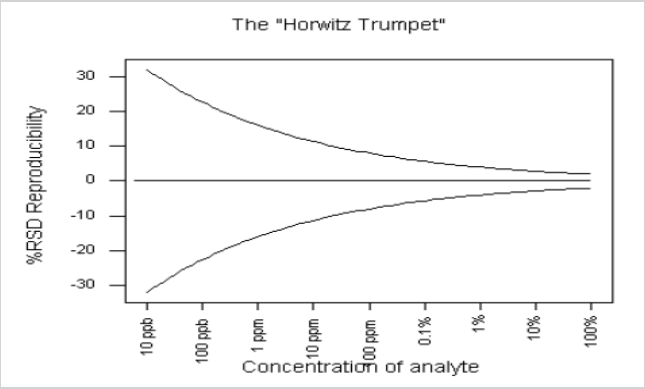
- Different operators and laboratories
- Methodologies
- Temporal changes

Commercial Cigarette Variability

- Raw materials (e.g., tobacco)
- Equipment
- Temporal Change

Analytical Testing

- Generally, analytes present in a higher concentration have lower variability than lower concentration analytes

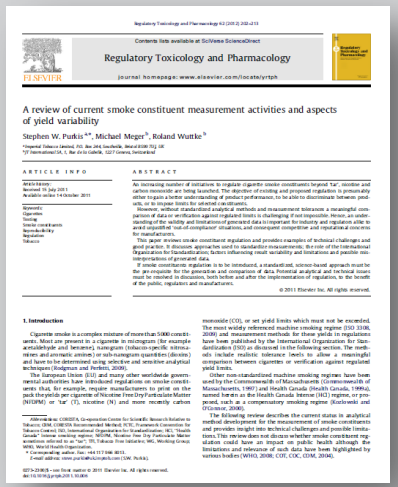


W Horwitz, L R Kamps, K W Boyer, J Assoc Off Anal Chem, 1980, 63, 1344.

- Generally, standardized methods show lower variability (e.g., tar, nicotine, CO, and TSNAs)

Analytical Testing

- **High levels of variability are observed within experienced laboratories over time (e.g., 3 years) even when measuring the same product with the same validated method**



Contents lists available at SciVerse ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

A review of current smoke constituent measurement activities and aspects of yield variability

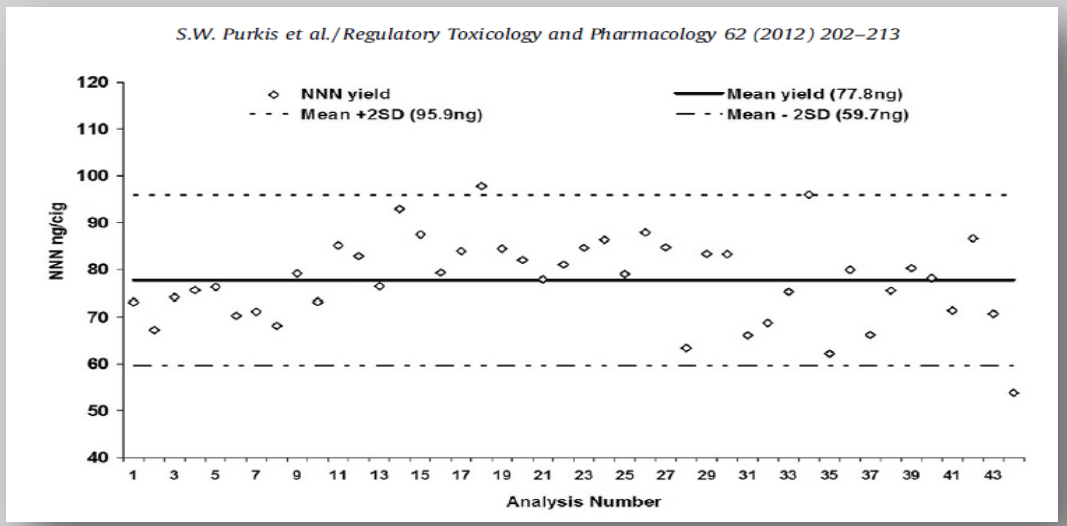
Stephen W. Purkis, Michael Meger, Roland Wuttke

ARTICLE INFO

ABSTRACT

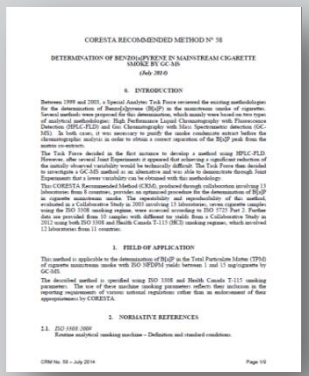
1. Introduction

Mainstream smoke NNN measured (ISO) in monitor (2007-2009)



Analytical Testing

- **CORESTA has focused on developing consensus standardized methods**
  - **Collaborative studies have elucidated repeatability and reproducibility of CORESTA recommended methods (CRMs)**
  - **Analytical testing has used single batch commercial and/or reference products**



CORESTA RECOMMENDED METHOD N° 58

DETERMINATION OF BENZO(a)PYRENE IN MAINSTREAM CIGARETTE SMOKE BY GC-MS

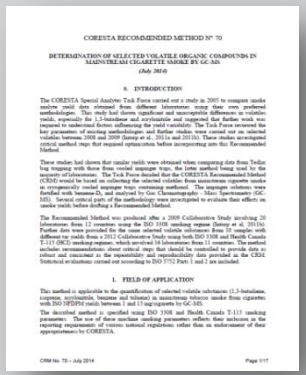
(July 2014)

6. INTRODUCTION

1. FIELD OF APPLICATION

2. NORMATIVE REFERENCES

CRM#58: B[a]P, 2014



CORESTA RECOMMENDED METHOD N° 70

DETERMINATION OF SELECTED VOLATILE ORGANIC COMPOUNDS IN MAINSTREAM CIGARETTE SMOKE BY GC-MS

(July 2014)

9. INTRODUCTION

1. FIELD OF APPLICATION

CRM#70: VOCs, 2014

Cigarette Manufacturing Variability

- CORESTA has not systematically addressed cigarette manufacturing variability
- In 2014, the CORESTA Scientific Commission created the Cigarette Manufacturing Variability (CVAR) Task Force
  - ✓ Coordinator: Jason Flora - ALCS
  - ✓ Secretary: Rana Tayyarah – ITG Brands

CVAR Objectives

1. To develop an appropriate experimental plan to explore commercial cigarette variability
2. To conduct a collaborative study to enhance the understanding of overall tobacco and smoke analyte variability relevant to commercial cigarette design features
3. To create a CORESTA technical report

CVAR Study Plan Summary

- Physicals and TNCO
- WHO priority list
- Abbreviated US FDA harmful and potentially harmful constituents (HPHC) list
- Hydrogen cyanide (HCN)

Measurement Type	Analyte Class	Measure/Analyte
Physicals		Pack moisture (as packed)
		Cigarette weight (as packed)
		Cigarette weight (post conditioning)
		Filler/tobacco Weight (post conditioning)
		Filter Tip Ventilation
		Circumference
		Length
		Resistance to Draw (Open/Closed)
		Paper porosity
Filler[10]	Alkaloids	Nicotine
	TSNAs	NNN
		NNK
	Ammonia	Ammonia (Reported as NH_3)
	Metals	Arsenic
		Cadmium
Smoke	TNCO	TPM
		Nicotine
		Water
		Carbon Monoxide
		NFDPM ("tar")
	Carbonyls	Acetaldehyde
		Acrolein
		Crotonaldehyde
		Formaldehyde
	Volatiles	Acrylonitrile
		Benzene
		1,3-Butadiene
		Isoprene
		Toluene
	Ammonia	Ammonia
	PAA	4-Aminobiphenyl
		1-Aminonaphthalene
		2-Aminonaphthalene
	PAH	Benzo[a]pyrene
	TSNA	NNN
		NNK
	HCN	HCN

CVAR Study Plan Summary

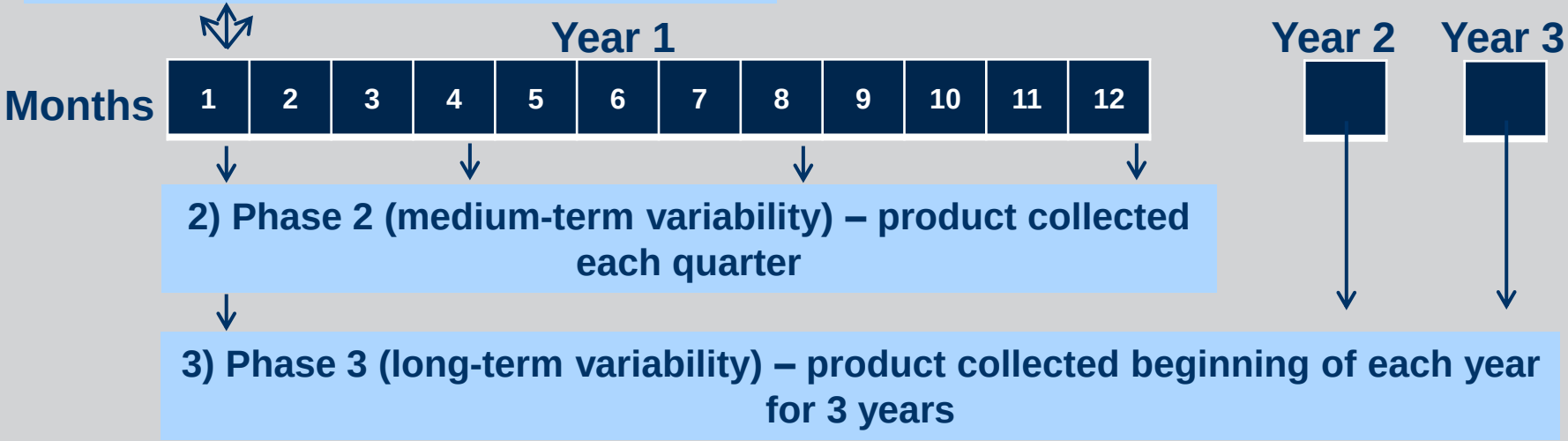
- **Analytical testing variability is minimized by:**
  - **Tested at one time (ISO and HC)**
  - **Single laboratory per constituent**
  - **Statistically balanced run order**
  - **Reference products (3R4F and 1R6F)**

- **Samples are stored at -20°C to -24°C until time of testing to minimize product changes over time**

CVAR Study Plan Summary

- **The study is designed to allow the estimation of short-term, medium-term, and long-term variability for a range of cigarette types available across the world-wide market**

1) Phase 1 (short-term variability): 3 collections within 1 week



Volunteer CVAR Participants

Volunteer Manufacturers

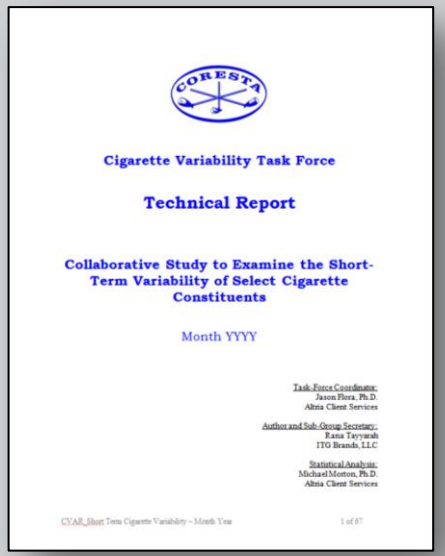
- Altria Client Services
- Beijing Cigarette Factory, CNTC
- British American Tobacco (Germany) GmbH
- China Tobacco Hunan Industrial Co., Ltd.,
- Imperial Tobacco Group
- Japan Tobacco Inc.
- JT International
- Philip Morris Int.
- RAI Services Company

Volunteer Laboratories

- Altria Client Services
- British American Tobacco (Germany) GmbH
- China Tobacco Anhui Industrial Co., Ltd.
- China Tobacco Hunan Industrial Co., Ltd.,
- Imperial Tobacco Group
- Japan Tobacco Inc.
- JT International
- JTI Research & Development, Okolab
- Liggett Group LLC
- ITG Brands, LLC
- RAI Services Company

CVAR Accomplishments

- **Phase 1 - Short-term variability:**
  - Sample collection and analysis is complete
  - Draft Phase 1 Technical Report complete
- **Phase 2 – Mid-term variability**
  - Sample collection and analysis is complete
  - Preliminary data analysis complete
  - Draft Phase 2 Technical Report in-progress
- **Phase 3 - Long-term variability**
  - Sample collection complete and shipping in-progress



Cigarette Variability Task Force

Technical Report

Collaborative Study to Examine the Short-Term Variability of Select Cigarette Constituents

Month YYYY

Task Force Coordinator:
Jason Flora, Ph.D.
Altria Client Services

Author and Sub-Group Secretary:
Rana Tayyarah
ITG Brands, LLC

Statistical Analysis:
Michael Morton, Ph.D.
Altria Client Services

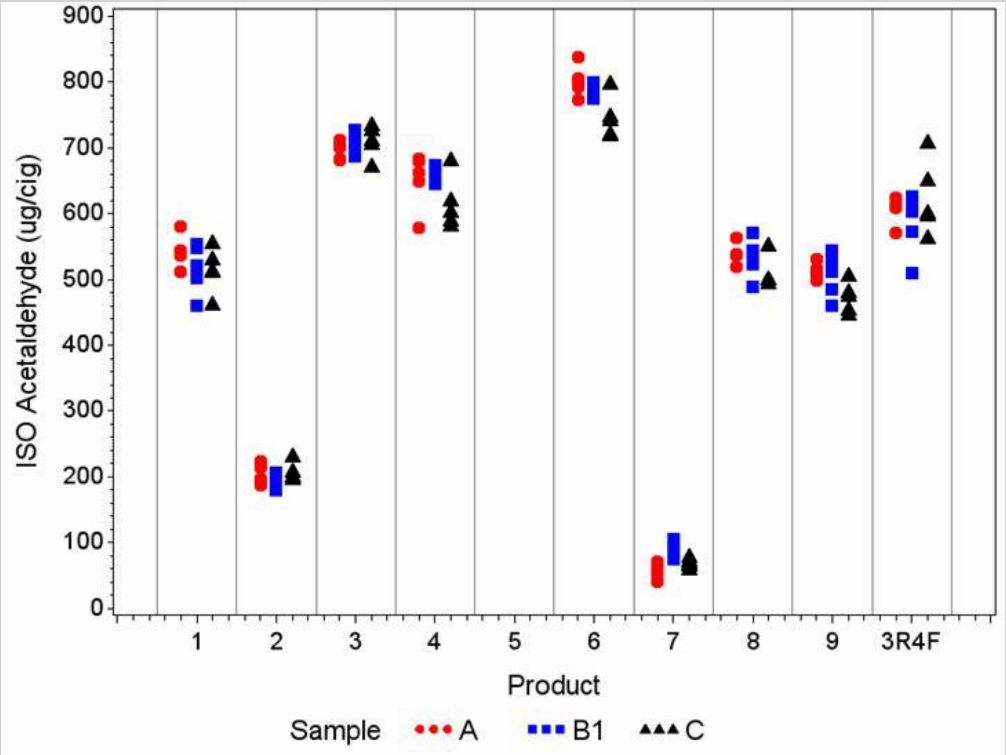
CVAR_Short Term Cigarette Variability – Month Year 1 of 67

Summary of Phase 1: Short-term Variability

- 8 commercial cigarette products + 3R4F and 8 volunteer laboratories
- 3 sample times for each commercial product (within 1 weeks time span)
- TNCO measured at all participating labs to evaluate sample-to-sample vs. lab-to-lab variation
- All other measurements were conducted in a single lab

Observations from Phase 1: Short-term Variability

- Smoke constituent analysis conducted on all 8 test products at a single laboratory
  - Example: Acetaldehyde measured under ISO conditions for all products collected at 3 times within 1 week
  - Short-term variability is not typically large



Overall Product Ranges Phase 1

Average of the Batch-to-Batch Relative Ranges of all Analytes for each Product Compared to Repeat Testing Variability for 3R4F

	1	2	3	4	6	7	8	9	3R4F
Blend	Virginia	American	Virginia	American	American	American	Virginia	American	American
Approx ISO tar	>10mg	~3mg	~10mg	~10mg	~16mg	~1mg	~8mg	~7mg	~10mg
Physical Measurements	2%	3%	3%	6%	4%	4%	2%	2%	--
Filler Constituents	5%	10%	9%	7%	4%	4%	12%	19%	2%
ISO Smoke Constituents	7%	12%	4%	7%	7%	27%	8%	8%	5%
CI Smoke Constituents	6%	6%	7%	5%	6%	5%	6%	8%	3%
average of all	5%	8%	6%	6%	5%	10%	7%	9%	4%
max	19%	24%	19%	28%	22%	52%	21%	31%	15%
min	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%

Batch-to-batch constituent variability is generally larger for commercial cigarettes manufactured within the same week as compared to a single batch of 3R4F reference cigarettes

Observations from Phase 1: Short-term Variability

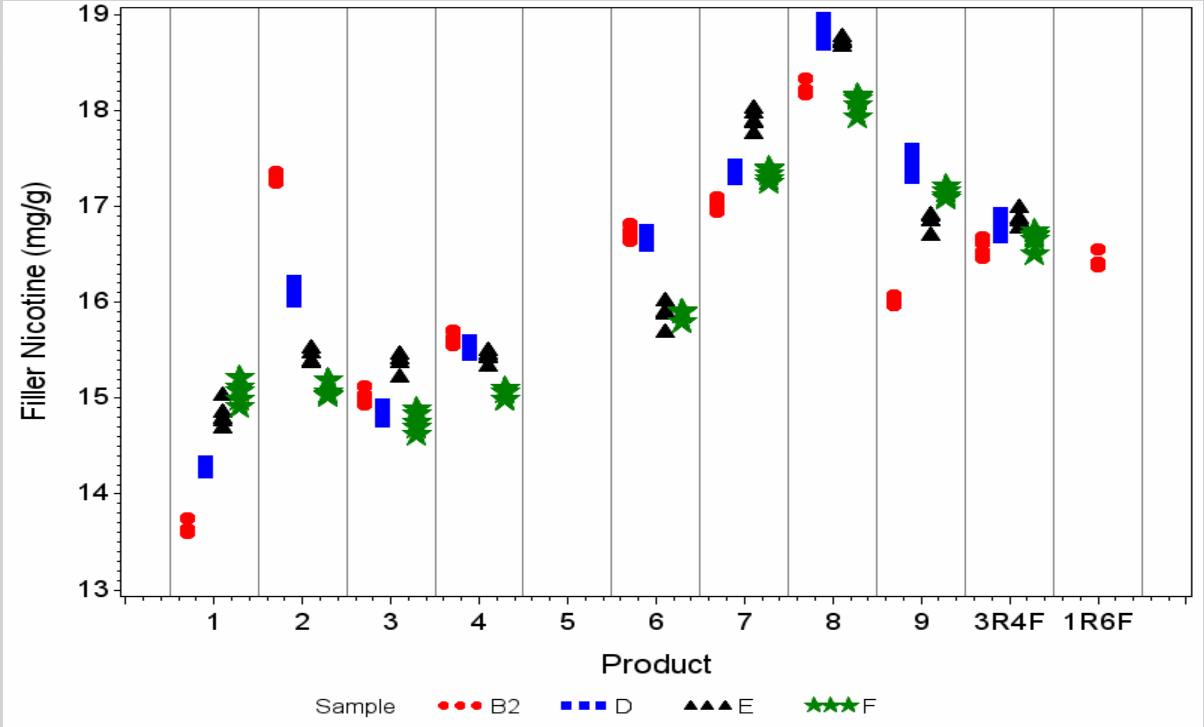
- For short-term variability (collected within 1 week), batch-to-batch constituent variability is typically small
- Batch-to-batch constituent variability is generally larger for commercial cigarettes manufactured within the same week as compared to a single batch of 3R4F reference cigarettes
- There is less variability observed under CI than ISO smoking because CI eliminates ventilation with 100% vent blocking and thereby eliminates a potential contributing source of sample-to-sample variation

Summary of Phase 2: Medium-term Variability (1 year)

- 8 commercial cigarette products + 3R4F and 1R6F and 8 volunteer laboratories
- 4 sample times for each commercial product (sampled quarterly)
- TNCO measured at all participating labs to evaluate sample-to-sample vs. lab-to-lab variation
- All other measurements were conducted in a single lab

Phase 2: Nicotine in Filler (as-is)

- 3R4F demonstrated low variability
- Greater variability was observed for products collected over 1 year compared to 3R4F



Filler Nicotine (mg/g) (as-is) Phase 1 vs. Phase 2

- **Filler Nicotine values showed greater variability over 1 year compared to over 1 week (Percent Relative Ranges)**

	1 week			1 year					
Filler Nic.	Phase 1			Phase 2				Relative Ranges	
Product	A	B1	C	B2	D	E	F	Phase 1	Phase 2/1.21
1	13.8	14.1	13.9	13.7	14.3	14.8	15.1	2.1%	8.2%
2	16.6	16.8	16.6	17.3	16.1	15.4	15.1	1.0%	11.2%
3	16.4	15.8	15.6	15.0	14.9	15.4	14.8	4.9%	3.3%
4	15.1	15.4	15.6	15.6	15.5	15.5	15.0	3.1%	3.1%
6	16.4	16.5	16.4	16.7	16.7	15.9	15.9	1.0%	4.2%
7	16.8	17.6	17.2	17.0	17.4	17.9	17.4	4.7%	4.3%
8	18.5	18.4	18.1	18.2	18.8	18.7	18.1	2.1%	3.2%
9	15.5	15.3	15.9	16.0	17.5	16.9	17.2	3.7%	7.3%
3R4F	16.9	16.9	16.9	16.6	16.8	16.9	16.7	0.4%	1.4%
							Average Relative Ranges	2.8%	5.6%

Filler NNN (ng/g) (as-is) Phase 1 vs. Phase 2

- Filler NNN values showed greater variability over 1 year compared to over 1 week

	1 week			1 year					
Filler NNN	Phase 1			Phase 2				Relative Ranges	
Product	A	B1	C	B2	D	E	F	Phase 1	Phase 2/1.21
1	727	726	717	791	1257	1248	1149	1.1%	40.7%
2	774	833	785	739	690	550	765	8.1%	24.2%
3	132	117	128	139	121	112	82	12.6%	40.3%
4	2308	2238	2283	2090	2416	2188	2247	3.1%	12.0%
6	1163	1155	1129	1091	1282	1132	1456	2.8%	25.1%
7	814	870	856	825	750	1059	949	6.3%	29.2%
8	93	105	108	108	107	98	78	15.1%	24.7%
9	571	675	751	671	431	306	383	33.4%	55.7%
3R4F	2817	2712	2742	2690	2767	2712	2754	3.8%	2.3%
							Average Relative Ranges	10.3%	31.5%

CI Smoke NNN (ng/cig) Phase 1 vs. Phase 2

- **Smoke NNN values showed greater variability over 1 year compared to over 1 week**

	1 week			1 year					
CI NNN	Phase 1			Phase 2				Relative Ranges	
Product	A	B1	C	B2	D	E	F	Phase 1	Phase 2/1.21
1	114	112	112	105	154	159	155	1.0%	33.8%
2	60	63	71	61	61	46	53	18.9%	20.6%
3	18.1	17.2	14.9	14.1	17.5	13.0	9.1	21.6%	46.5%
4	260	216	221	216	219	209	213	19.8%	3.7%
6	175	166	168	151	164	142	175	5.5%	16.7%
7	84	82	81	82	65	68	71	3.8%	18.5%
8	10.9	11.5	12.1	10.7	10.7	9.5	9.3	11.4%	10.9%
9	76	70	69	72	55	46	43	11.8%	38.2%
3R4F	304	317	305	267	277	268	250	4.7%	8.0%
							Average Relative Ranges	11.7%	23.6%

CI Smoke B[a]P (ng/cig) Phase 1 vs. Phase 2

- Smoke B[a]P values showed analogous variability over 1 year compared to over 1 week

	1 week			1 year					
CI B[a]P	Phase 1			Phase 2				Relative Ranges	
Product	A	B1	C	B2	D	E	F	Phase 1	Phase 2/1.21
1	16.0	16.3	16.4	16.8	17.4	16.8	17.2	2.1%	3.2%
2	6.6	6.6	6.5	6.8	6.8	6.7	6.9	2.8%	3.0%
3	13.1	13.4	13.4	13.1	14.0	13.7	13.7	2.7%	6.0%
4	15.7	15.8	16.0	15.2	14.9	15.3	15.0	2.1%	1.7%
6	10.8	11.0	11.0	11.7	11.5	11.3	11.9	1.8%	4.7%
7	6.5	6.5	6.5	7.0	7.0	6.8	7.0	0.4%	2.2%
8	12.6	13.1	13.0	12.1	12.6	12.4	12.3	3.8%	3.5%
9	10.0	10.3	10.4	10.3	10.3	10.0	10.7	3.1%	6.1%
3R4F	15.0	15.1	15.3	16.2	16.2	15.7	15.3	2.3%	5.2%
							Average Relative Ranges	2.4%	3.8%

Observations from Phase 2: Medium-term Variability

- **For medium-term variability (collected within 1 year), batch-to-batch constituent variability is relatively:**
  - **Large compared to short-tem variability (1 week) for tobacco or agricultural specific constituents (e.g. Nicotine, NNN, NNK, Ammonia)**
  - **Similar compared to short-term variability for combustion-related constituents (e.g., B[a]P, VOCs)**

Next Steps

- Draft technical report for Phase 1 is being finalized after review at the October 2017 CVAR Task Force meeting (Q4 2017)
- Draft technical report for Phase 2 is being drafted and was discussed at the October 2017 CVAR Task Force meeting (Q4 2017)
- Technical reports will be reviewed by the Scientific Commission and published on the CORESTA website
- All Phase 3 (long-term variability) samples have been collected and shipping is in-progress
- Completion of Phase 3 technical report and draft publication is planned for Q4 2018

CVAR Task Force Timeline

- Sept 2012 – First round of HPHCs submissions
- Feb 2013 – U.S. manufacturers met with FDA to discuss variability of HPHC data
- Jan 2014 – U.S. manufacturers met to formulate a plan to address HPHC variability (Follow-up meeting in March 2014)
- April 2014 – *Ad hoc* CORESTA meeting in Nuremberg to discuss proposal for a Task Force (TF) – Led by Steve Purkis of Imperial Tobacco
- June 2014 – Scientific Commission approved the CVAR TF
- July 2014 – Invitation letter sent to all CORESTA Delegates in July 2014
- As of Nov 2014 – 13 member companies as TF participants
- Nov 2014 – First CVAR TF Meeting
- March 2015 – CVAR TF Meeting
- April/June 2015 – Study 1 launched
- Aug 2015 – Webpage posted
- Oct 2015 – TF Meeting
- April 2016 – TF Meeting, preliminary report out for Phase 1 and Phase 3 study was developed
- May 2016 – CVAR was described at a Waters Tobacco Symposium, Raleigh NC
- October 2017 – TF Meeting, status for Phase 2 and Phase 3
- October 2017 – CORESTA Congress presentation of Phase 1 observations
- May 2017 – TF Meeting, Phase 1 TR Review, Preliminary report out Phase 2, status for Phase 3
- October 2017 – TF Meeting, Phase 1 TR finalize, Preliminary report Phase 2, status for Phase 3

Thank You

Questions?