



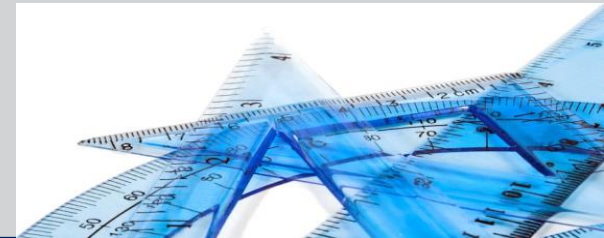
# **Cigarette Variability (CVAR) Task Force CORESTA 2019 Update**

- **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 2019, Hamburg, Germany**

- ❖ **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**



## ❖ Tobacco and smoke analyte variability results from multiple sources:

### Analytical Testing Variability

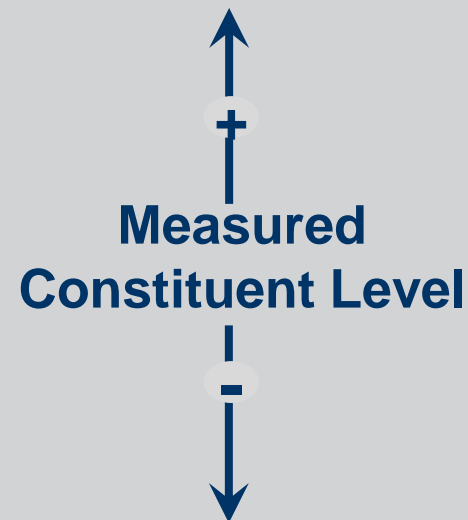
- Operators
- Laboratories
- Methods
- Temporal

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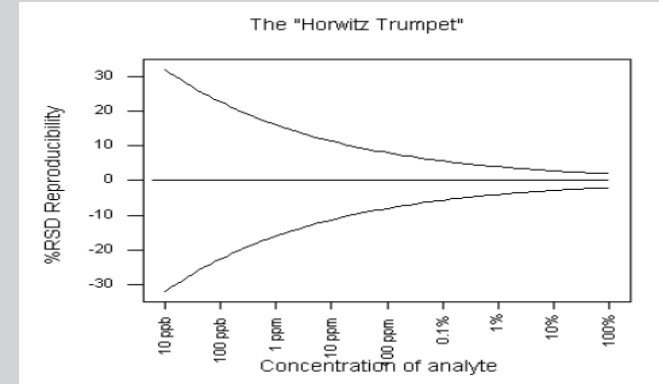
### Commercial Cigarette Variability

- Tobacco
  - Growing Conditions
  - Farmers
  - Geography
- Equipment
- Temporal

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- ❖ Generally, analytes present in a higher concentration have lower variability than lower concentration analytes
- ❖ Generally, standardized methods show lower variability (e.g., tar, nicotine, CO, and TSNAs)



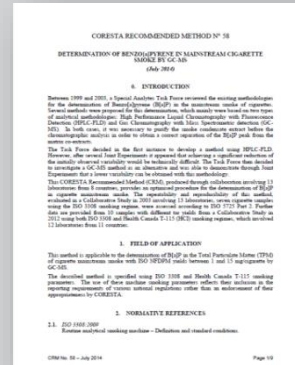
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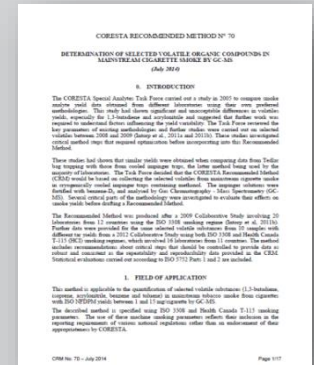


## ❖ CORESTA has focused on developing consensus standardized methods

- Collaborative studies have elucidated repeatability and reproducibility of CORESTA recommended methods (CRMs)
- Analytical testing in these collaborative studies used single batches of commercial and/or reference products



CRM#58: B[a]P, 2014



CRM#70: VOCs, 2014



# Cigarette Manufacturing Variability

- ❖ **CORESTA had not systematically addressed commercial cigarette variability**
- ❖ **In 2014, the CORESTA Scientific Commission created the Cigarette 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 <sup>10</sup>	Alkaloids	Nicotine
	TSNAs	NNN
		NNK
	Ammonia	Ammonia (Reported as NH <sub>3</sub> )
	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

- ❖ 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



Year 1

Months



2) Phase 2 (medium-term variability) – product collected each quarter



3) Phase 3 (long-term variability) – product collected beginning of each year for 3 years

Year 2



Year 3





# 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**



# 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



# Study Cigarette Design Features

Sample Code	Blend	Approx. ISO Tar	Comment
1	American	>10 mg	
2	American	3 mg	Charcoal Filter
3	Virginia	10 mg	
4	American	10 mg	
6	American	16 mg	
7	American	1 mg	
8	Virginia	8 mg	
9	American	7 mg	
10 (3R4F)	American	10 mg	Study Reference
11 (1R6F) (phase 2 and 3)	American	10 mg	Study Reference



# 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 week's 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 per analyte group**

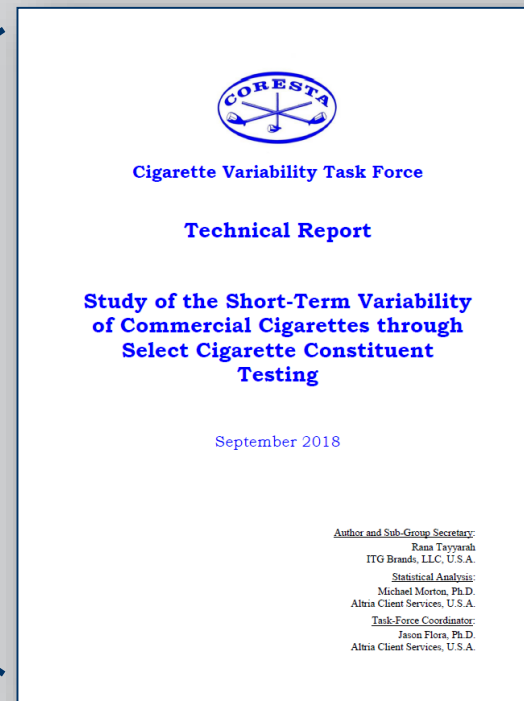
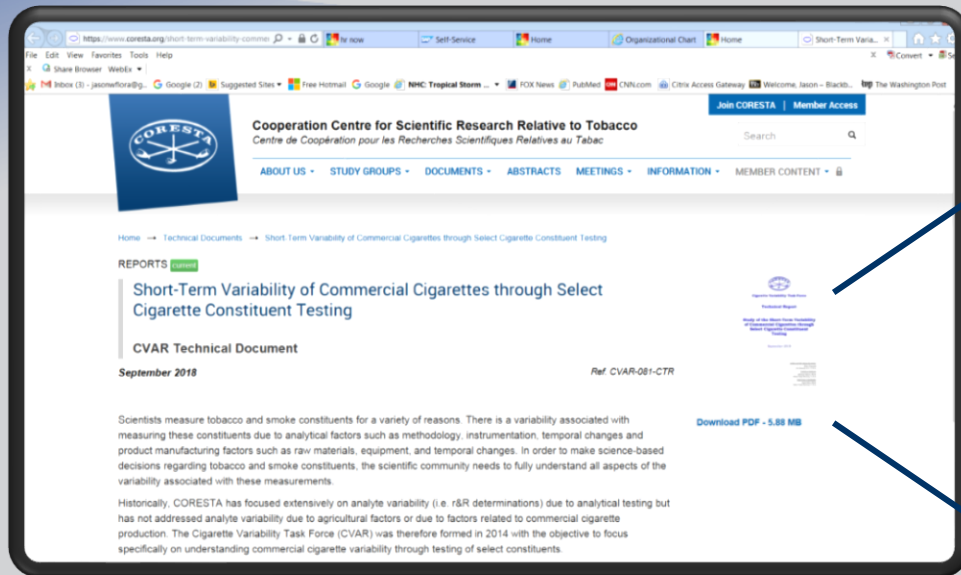


# Observations from Phase 1: Short-term Variability

- 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



# Phase 1 Technical Report September 2018





## 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 per analyte group**



## 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-term 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)**



# Phase 2 Technical Report

## January 2019

The screenshot shows the CORESTA website interface. At the top, there is a navigation menu with links for ABOUT US, STUDY GROUPS, DOCUMENTS, ABSTRACTS, MEETINGS, INFORMATION, and MEMBER CONTENT. The main content area features the report title "Medium-Term Variability of Commercial Cigarettes through Select Cigarette Constituent Testing" and a "Download PDF - 8.95 MB" button. The text below the title discusses the variability associated with measuring tobacco and smoke constituents and mentions the formation of the Cigarette Variability Task Force (CVAR).

The cover page features the CORESTA logo at the top, followed by the text "Cigarette Variability Task Force" and "Technical Report". The main title is "Study of the Medium-Term Variability of Commercial Cigarettes through Select Cigarette Constituent Testing", and the date "January 2019" is listed below. At the bottom right, the author and sub-group secretary information is provided.

**Author and Sub-Group Secretary:**  
Rana Tyyarah  
ITG Brands, LLC, U.S.A.  
**Statistical Analysis:**  
Michael Morton, Ph.D.  
Altria Client Services, U.S.A.  
**Task-Force Coordinator:**  
Jason Flora, Ph.D.  
Altria Client Services, U.S.A.



## Summary of Phase 3: Long-term Variability (3 years)

- ❖ **8 commercial cigarette products + 3R4F and 1R6F and 8 volunteer laboratories**
- ❖ **3 sample times for each commercial product (sampled yearly)**
- ❖ **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 per analyte group**



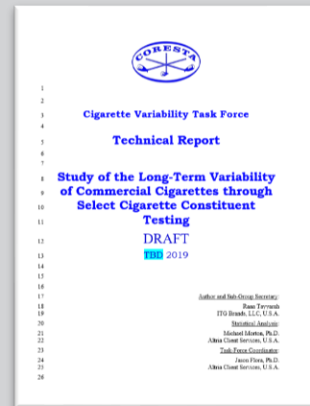
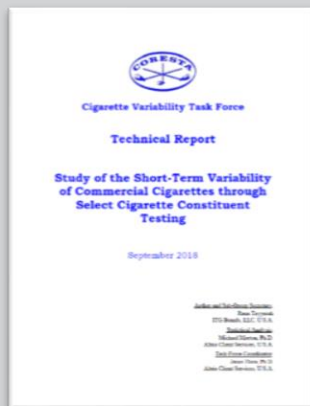
# Observations from Phase 3: Long-term Variability

- **For Long-term variability (collected over 3 years), batch-to-batch constituent variability is relatively:**
  - Large compared to short-term variability (1 week) for tobacco or agricultural specific constituents (e.g. Nicotine, NNN, NNK, Ammonia)
  - Similar compared to medium-term variability (collected quarterly for one year) for tobacco or agricultural specific constituents (e.g. Nicotine, NNN, NNK, Ammonia)
  - Similar compared to short-term and medium-term variability for combustion-related constituents (e.g., B[a]P, VOCs)
- **The draft Phase 3 Technical Report is complete**
- **We plan to submit this to the Scientific Commission ASAP**



# Collective Phase Findings

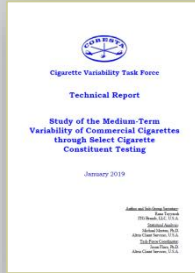
- ❖ **Combustion products such as benzene, tar, B[a]P, etc. have been much less variable**
  - **Most physical properties show small variation**
- ❖ **Large variation in tobacco-related compounds, such as TSNAs and Ammonia**





# How Can We Use This Information?

- ❖ **Most comparisons in the Technical Reports are conducted by determining the Range % of the Mean for the samples collected**
  - 3 batched collected over one week – Phase 1
  - 4 batched collected quarterly for one year – Phase 2
  - 3 batched collected over 3 years – Phase 3



$$\text{Range \% of the Mean} = \left( \frac{\text{Highest Batch Value} - \text{Lowest Batch Value}}{\text{Mean of the Batch Values}} \right) \times 100$$

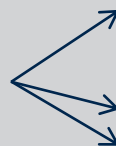


# How Can We Use This Information?

❖ “For medium-term variability (collected within 1 year), batch-to-batch constituent variability is relatively large compared to short-term variability (1 week) for tobacco or agricultural specific constituents (e.g. Nicotine, NNN, NNK, Ammonia)”

ISO NNN ng/cigarette						
Product	Sample				Range % of mean	p-value
	B2	D	E	F		
1	45.0	65.4	60.0	50.7	36.8 %	0.0065
2	14.5	14.9	13.2	14.6	11.7 %	0.3876
3	6.00	6.36	7.28	5.88	21.9 %	0.2870
4	91.6	93.8	89.9	88.6	5.7 %	0.6256
6	68.5	66.0	71.5	71.8	8.3 %	0.6425
7	7.88	4.80	5.12	4.84	54.4 %	<0.0001
8	4.48	6.16	4.20	3.84	49.7 %	0.0075
9	27.0	17.8	18.2	19.3	44.5 %	<0.0001
3R4F	113.0	110.4	124.5	105.8	16.5 %	0.1038

10 mg ISO tar



1 mg ISO tar



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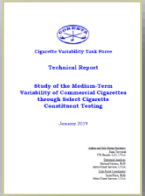
Virginia Blend



# How Can We Use This Information?

10 mg ISO tar

ISO NNN ng/cigarette						
	Sample					
Product	B2	D	E	F	Range % of mean	p-value
1	45.0	65.4	60.0	50.7	36.8 %	0.0065



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- ❖ As shown by the CORESTA CVAR Task Force, batch-to-batch constituent variability (e.g., same product with different batches of Tobacco) is relatively large for tobacco or agricultural specific constituents even when products are tested at the same lab at the same time.
- ❖ For example, ISO smoke NNN values for the same 10 mg tar commercial cigarette (product 1) manufactured 3 months apart and tested at the same lab at the same time showed a % difference of 37.0%. Additionally, the same product tested quarterly (same lab same time) also showed a range % of the mean of 36.8%.





# How Can We Use This Information?

1 mg ISO tar

ISO NNN ng/cigarette						
Sample						
Product	B2	D	E	F	Range % of mean	p-value
7	7.88	4.80	5.12	4.84	54.4 %	<0.0001



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- ❖ For a highly ventilated product example, ISO smoke NNN values for the same 1 mg tar commercial cigarette (product 7) manufactured 3 months apart and tested at the same lab at the same time showed a % difference of 48.6%. Additionally, the same product tested quarterly (same lab same time) showed a range % of the mean of 54.4%.
- ❖ Under the ISO smoking regime, we observed much greater variability compared to CI for highly ventilated products.
- ❖ However, under the CI regime, we still observed a % difference of 23.1% when comparing the same products manufactured 3 months apart and a range % of the mean of 23.8% for the commercial product sampled quarterly for 1 year.



# Key Points

- ❖ **Data from this study can be used in a variety of ways to explain product variability when tested at the same lab at the same time.**
  - **Product comparisons**
  - **Meeting product standards (internal or external)**
  
- ❖ **It is important to consider product design features when making comparisons to this data (e.g., ventilation).**
  
- ❖ **Single point in time constituent measurements of cigarette tobacco and smoke are not truly representative of the commercial product's constituent levels, particularly tobacco related constituents, which vary over time.**
  - **Analytical variability**
  - **Product variability**



- ❖ **Thanks to all Task Force members, companies, and laboratories for their devotion to this important work**
- ❖ **Special Thanks to Rana Tayyarah and Michael Morton**



# 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**
- ❖ **September 2018 – Phase 1 TR published on CORESTA website**
- ❖ **October 2018 – TF Meeting, CORESTA Congress presentation of Phase 1 and 2 observations**
- ❖ **April 2019 – Final TF Meeting – Reviewed observations from Phase 3**