



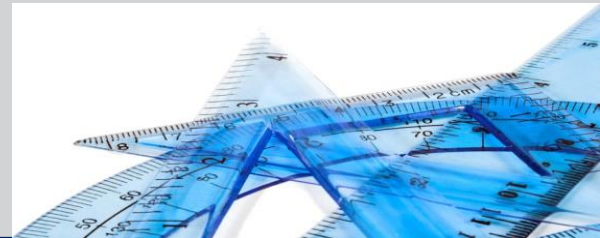
Cigarette Variability (CVAR) Task Force CORESTA 2018 Update

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

CVAR – October 2018, Kunming, China

- ❖ **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

+

Commercial Cigarette Variability

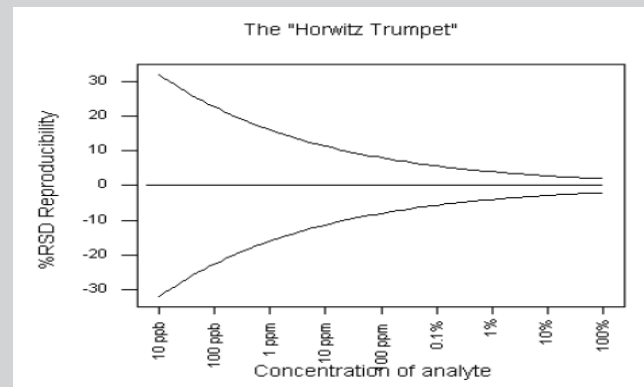
- Tobacco
 - Growing Conditions
 - Farmers
 - Geography
- Equipment
- Temporal

=

Measured Constituent Level



- ❖ 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)

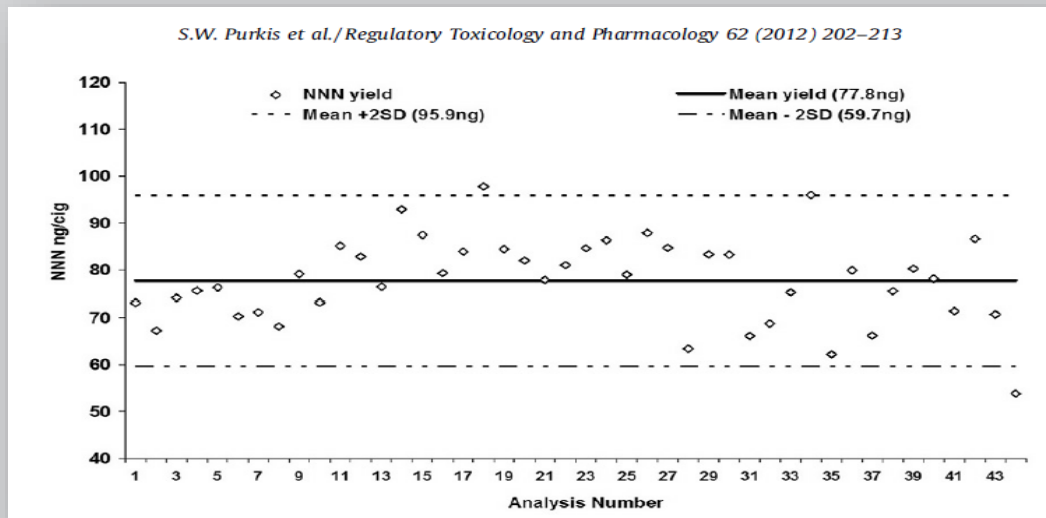
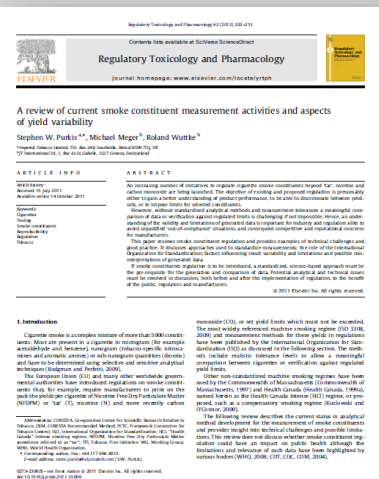


W Horwitz, L R Kamps, K W Boyer, J Assoc Off Anal Chem, 1980, 63, 1344.



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

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





Cigarette Manufacturing Variability

- ❖ **CORESTA has 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 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
	PAA	4-Aminobiphenyl
		1-Aminonaphthalene
		2-Aminonaphthalene
		PAH
	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**



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



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:

- Phase 1 Technical Report complete

❖ Phase 2 – Medium-term variability

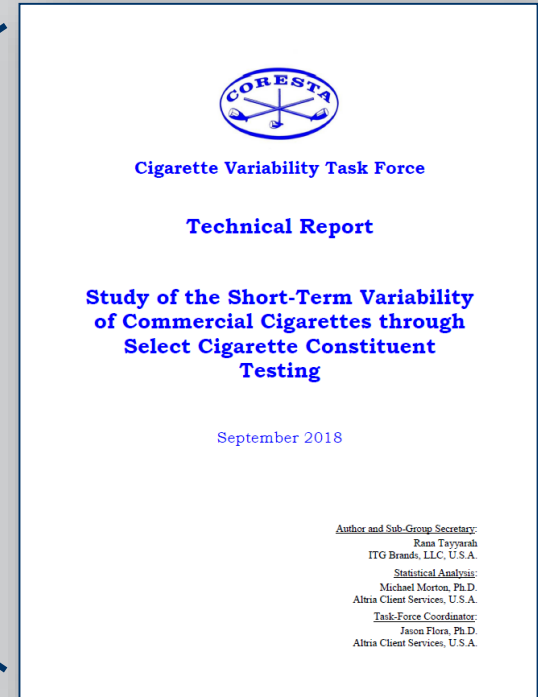
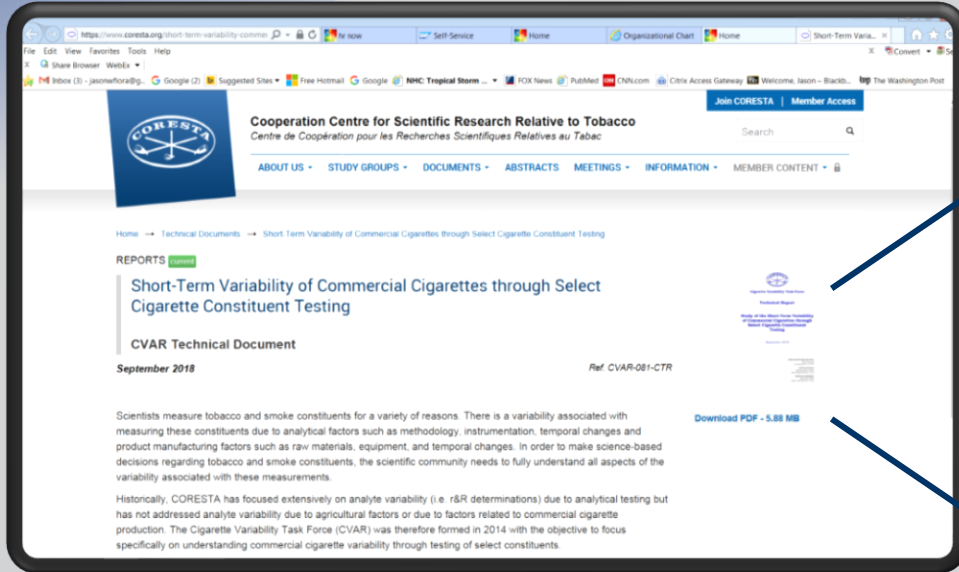
- Sample collection, testing and analysis is complete
- Phase 2 Technical Report is under review by the Scientific Commission

❖ Phase 3 - Long-term variability

- Sample collection and testing is complete
- Data analysis is in-progress



Phase 1 Technical Report





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**



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	American	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



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)**



Next Steps

- ❖ **Draft technical report for Phase 2 is being reviewed by the Scientific Commission. Final report expected to be on CORESTA website by December 2018.**
- ❖ **All Phase 3 (long-term variability) samples have been collected and tested and data analysis is in-progress**
- ❖ **Complete Phase 3 data analysis, technical report and draft publication is planned for 2019**



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**



Coming Up Next!

- ❖ **Paper IG02 - Mike Morton will discuss:**
 - **Considerations we made for the study design**
 - **Statistical versus practical differences**
 - **Key observations to date**



Thank You Questions?

CVAR TF Report

2018 Congress, Kunming – 181024