

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







Sources of Measurement Variability

Tobacco and smoke analyte variability results from multiple sources:





Analytical Testing



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



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)



CVAR TF Report

2018 Congress, Kunming – 181024

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 Regulatory Toxicolog	at Solverse ScienceOrect gy and Pharmacology				
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A review of curren of yield variability	t smoke constituent m	easurement activities and aspects	Ш			
*Imperial Tobacce Limited, P.D. Box 244 *JT International SA, 1, Bar de la Gabria	Southelite, Briand #1000 703 LBC 1, 1227 General, Switzerkend	no.				
ARTICLE INFO	ABSTRACT					
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Mainstream smoke NNN measured (ISO) in monitor (2007-2009)



Centre de Coopération pour les Recherches Scientifiques Relatives au Tabac Cooperation Centre for Scientific Research Relative to Tobacco



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

DETERMINATION OF BENZOIS PYRENE D	N MADNTREAM CIGARETTE	DETERMINATION OF SELECTED VOLATELE ORGANIC COMPOUNDS IN			
(July 2014)	10	(July 30.0)			
6. INTRODUCTI	ION	8. INTRODUCTION			
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		This method in applicable to the quantification of solected volatile inductions (1.3-batal toppers, arysteatrik, became and tobars) in maintenan tobars mode from cigar with BO-PIZPM valid, between 1 and 15 gar cigareet to GC-MS.			
2. NORMATIVE REFERENCES		The decembed method in specified using ISO 3508 and Health Canada T-115 measuremy. The use of these machine masking permaters reflects they include			
1.1. ISO 3308-3900 Routine analytical sandking machine - Definition	and studerd conditions.	reporting requirements of various notional regulations other than an endorsement appropriatement by CORESTA			
CRM No. 52 - July 2014	Page 12	C/884 No. 70 - July 2014			



- 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







- 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	Acetaldehvde			
		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, mediumterm, 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





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



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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-tosample 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

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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)

- S 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-tosample 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)





- 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?

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