

Cigarette Variability (CVAR) Task Force CORESTA 2017 Update

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 - Altria Client Services LLC, Richmond VA
- Secretary and Study Coordinator: Rana Tayyarah
 - ITG Brands, LLC, Greensboro NC
- Statistical Analysis: Michael Morton
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CVAR – October 2017, Kitzbühel, Austria





- 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 Variability

- Different operators and laboratories
- Methodologies
- Temporal changes

Commercial Cigarette Variability

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



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)



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



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CVAR TF Report

SSPT2017, Kitzbühel - 171010

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



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 Nº	58	CORESTA RECOMMENDED METHOD Nº 70	
DETERMINATION OF BENZO(#PFRENT IN MAINSTREAM SMOKE BY CC MS	I CIGARETTE	DETERMINATION OF SELECTED VOLATILE ORGANIC COMPOUN MAINNTREAM CIGARETTE SMORE BY GC-MS	NDS IN
(July 2014)		(July 2014)	
6. INTRODUCTION		8. INTRODUCTION	
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Centre de Coopération pour les Recherches Scientifiques Relatives au Tabac Cooperation Centre for Scientific Research Relative to Tobacco 2014



- 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







- 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

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, 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





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

COREST	
Cigarette Variability T	ask Force
Technical Rep	oort
Collaborative Study to Exar Term Variability of Sele Constituents	nine the Short- ct Cigarette
Month YYYY	
	Task-Force Coordinator, Jason Flora, Ph.D. Altria Client Services
	suthor and Sub-Group Secretary. Rana Tayyarah ITO Brands, LLC
	Statistical Analysis; Michael Monton, Ph.D. Altria Client Services



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



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	00/	00/	00/	00/	407	407	00/	00/	
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%
may	1.09/	240/	1.09/	200/	220/	520/	210/	210/	150/
	1970	2470	1970	2070	2270	5270	2170	3170	10%
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

CVAR TF Report SSPT2017, Kitzbühel - 171010



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



Phase 2: Nicotine in Filler (as-is)

3R4F demonstrated low variability

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



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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			Pha	Relative Ranges			
Product	А	B1	С	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									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 y	ear			
Filler NNN		Phase 1			Pha	se 2		Relati	ve Ranges
Product	А	B1	С	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 ye					
CINNN		Phase 1			Pha	se 2		Relative Ranges		
Product	А	B1	С	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			Pha	se 2		Relative Ranges		
Product	А	B1	С	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)





- 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?