Standardization of a Puff from Electronic Nicotine Delivery Systems (ENDS)

The Crown JUULs of ENDS

Ana Coutinho
Angela Lee
Bryan Eng
Dongyue Yu
Sharmila Das
Yuwei Lu

Acknowledgements: Dr. Richard Dalby & Dr. James Polli

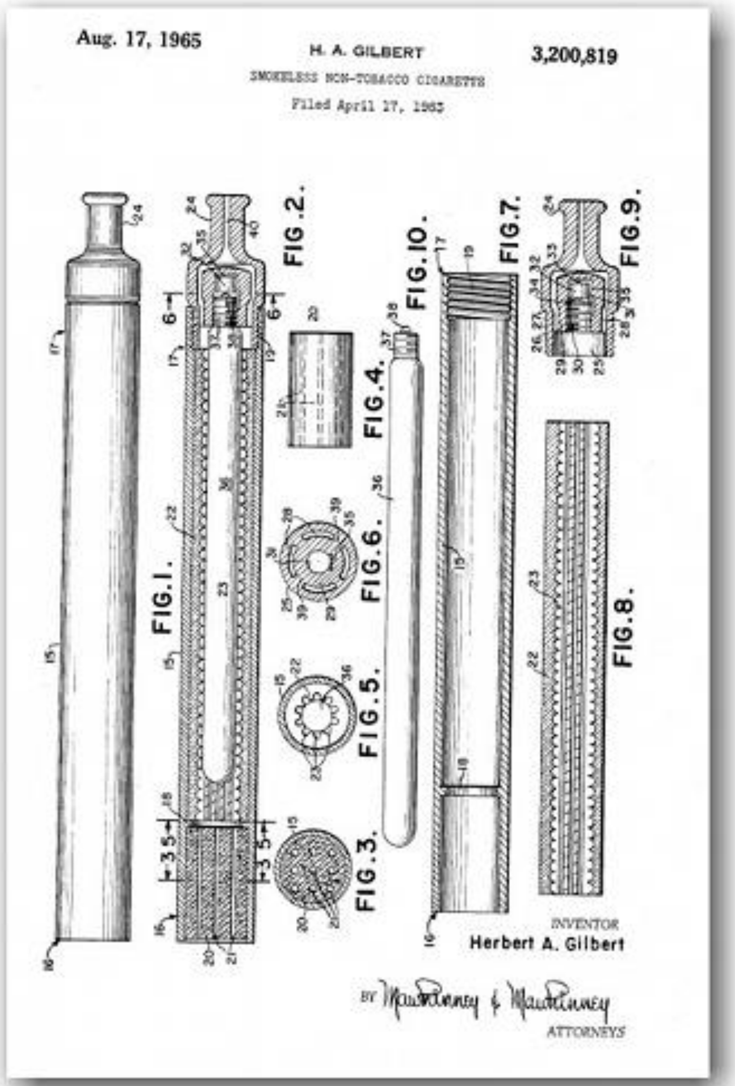
Background

Invented in 1965 by Herbert Gilbert

Since 2003 the technology has evolved to 5 generations

Over 500 brands of e-cigarettes

37.3 % of high school seniors reported to using e-cigarettes in the past 12 months (NIDA)



Current Federal Regulations

Child Nicotine Poison Prevention Act of 2015

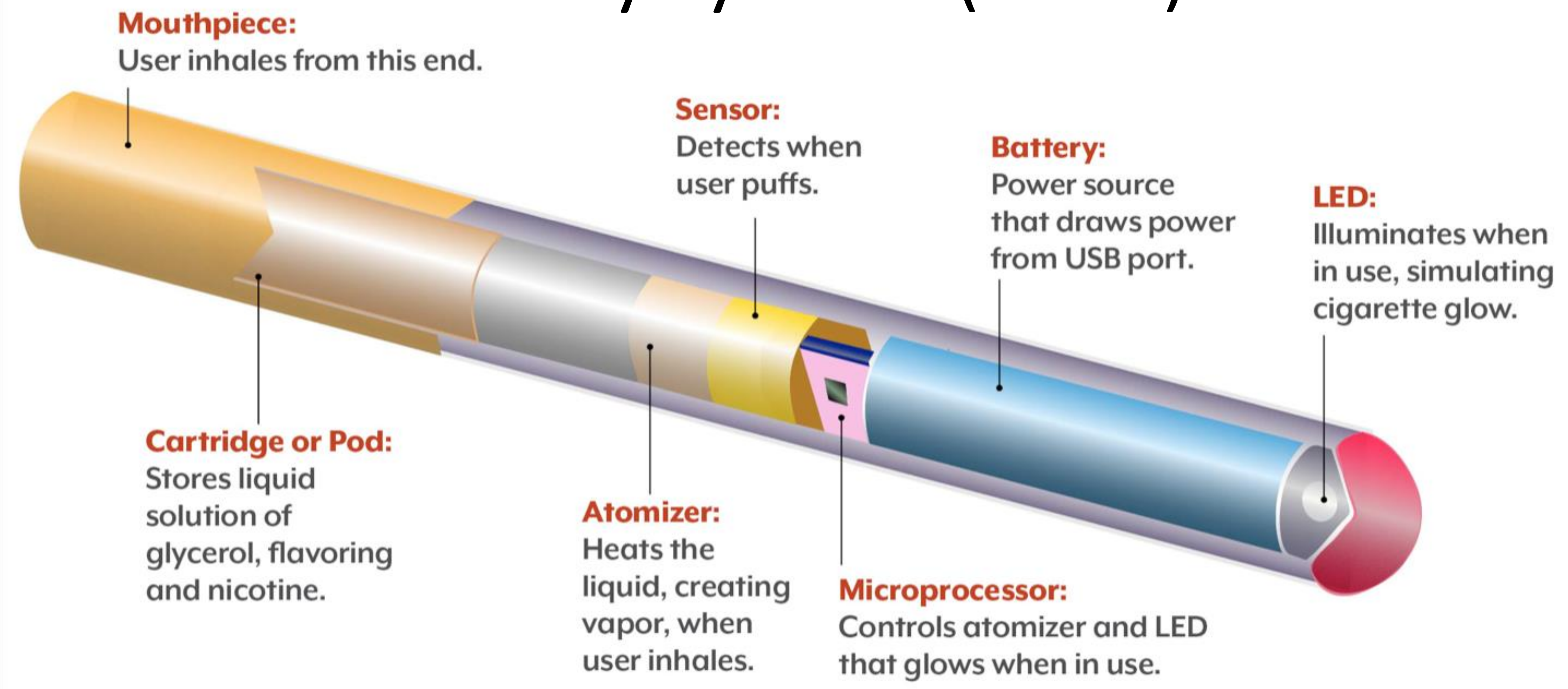
FDA’s Tobacco Rule: extending FDA’s regulatory power to include e-cigarettes as tobacco products in 2016

Stopping Appealing Flavors in E-Cigarettes for Kids Act – Current Bill

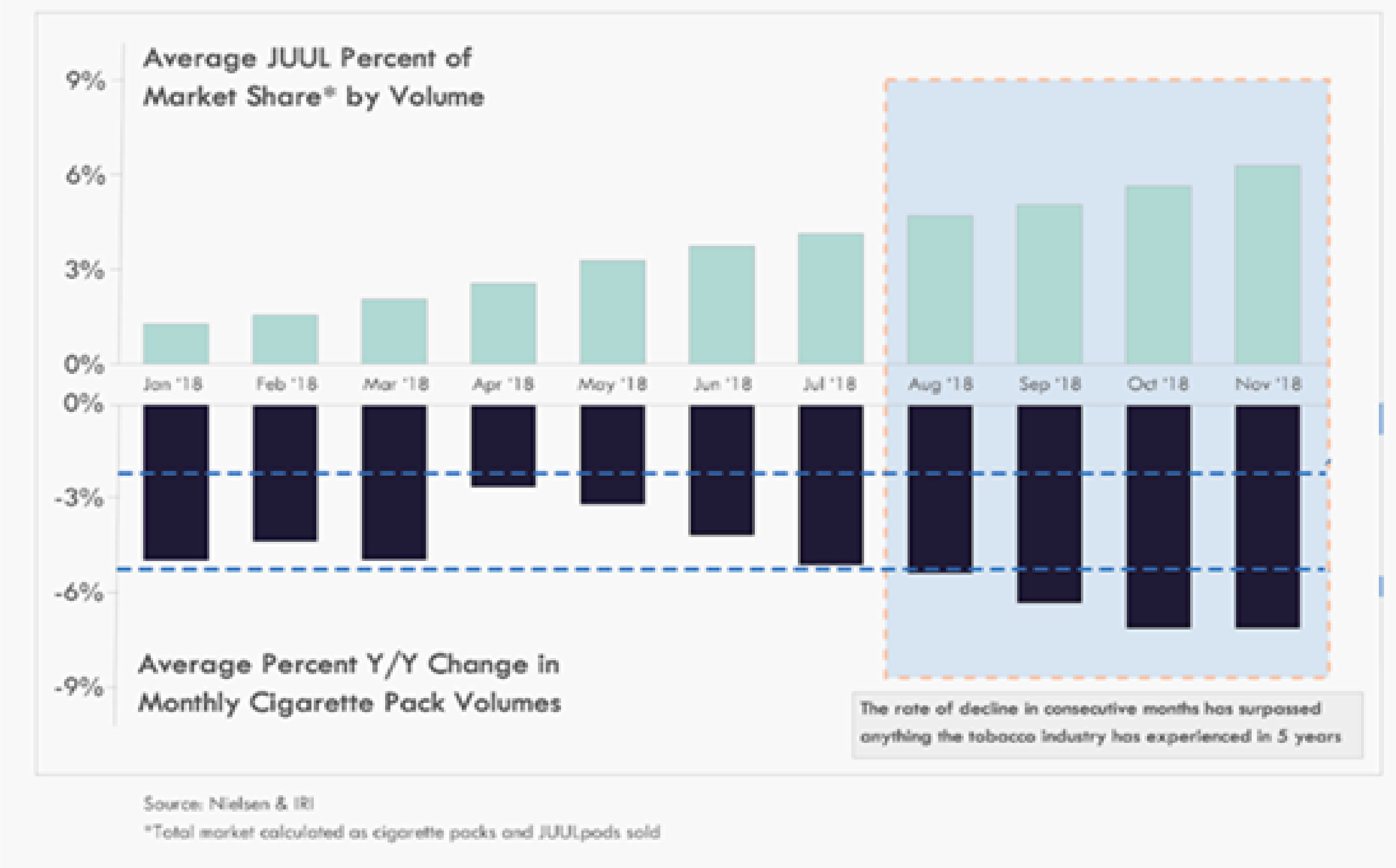
Marketing order required for new tobacco products

- Substantial equivalence (SE) for new tobacco products under FD&C Act

First Generation Electronic Nicotine Delivery Systems (ENDS)



JUUL Rises as Cigarettes Fall



FDA Priority Areas

Priority Area 1:
Modernize Toxicology to Enhance Product Safety

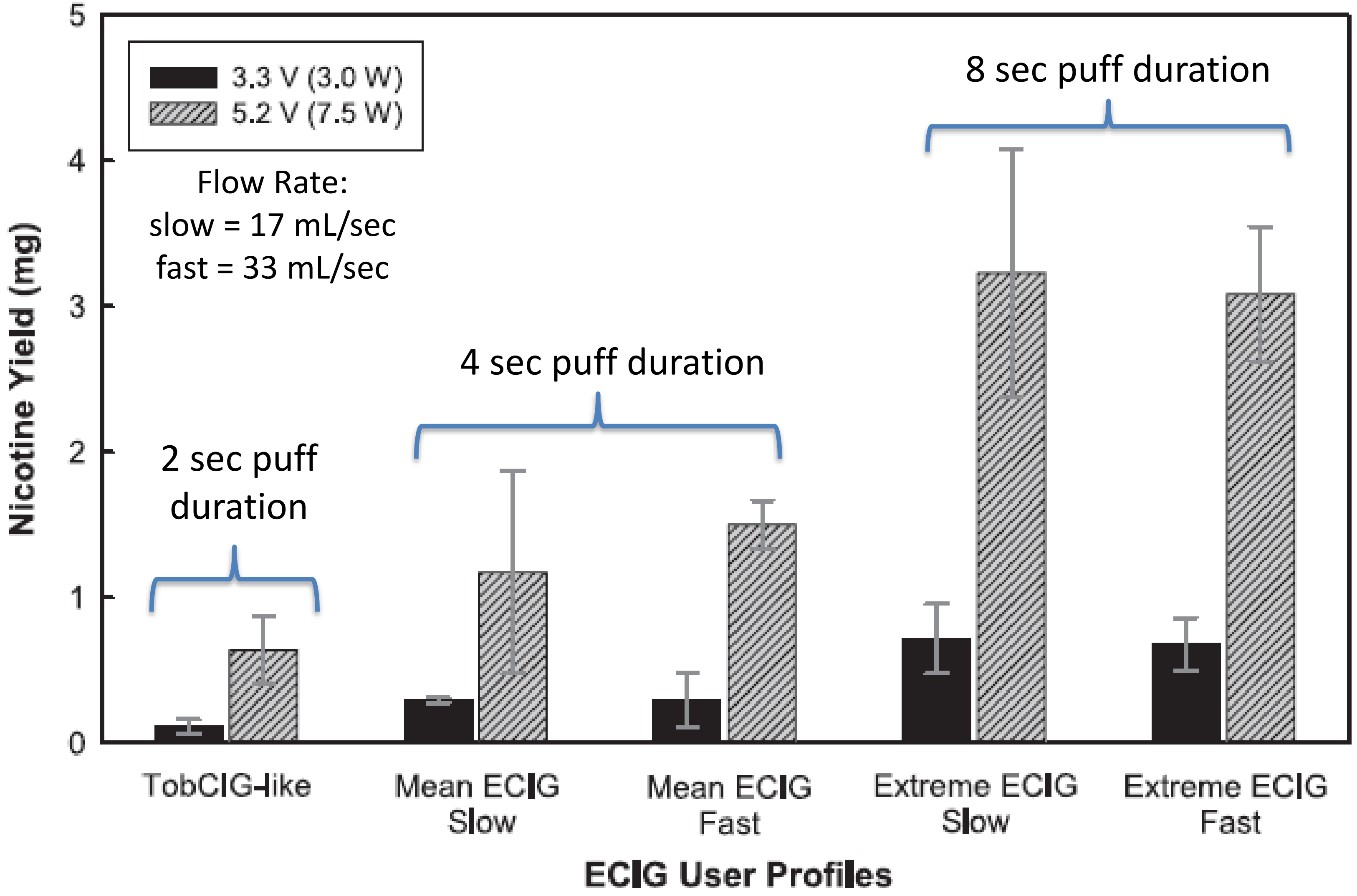
Priority Area 4:
Ensure FDA Readiness to Evaluate Innovative Emerging Technologies, Strategic Plan for Regulatory Science

Priority Area 8:
Strengthen Social and Behavioral Science to Help Consumers and Professionals Make Informed Decisions about Regulated Products: Strategic Plan for Regulatory Science

Lack of Standardization of Puff Profiles in Literature

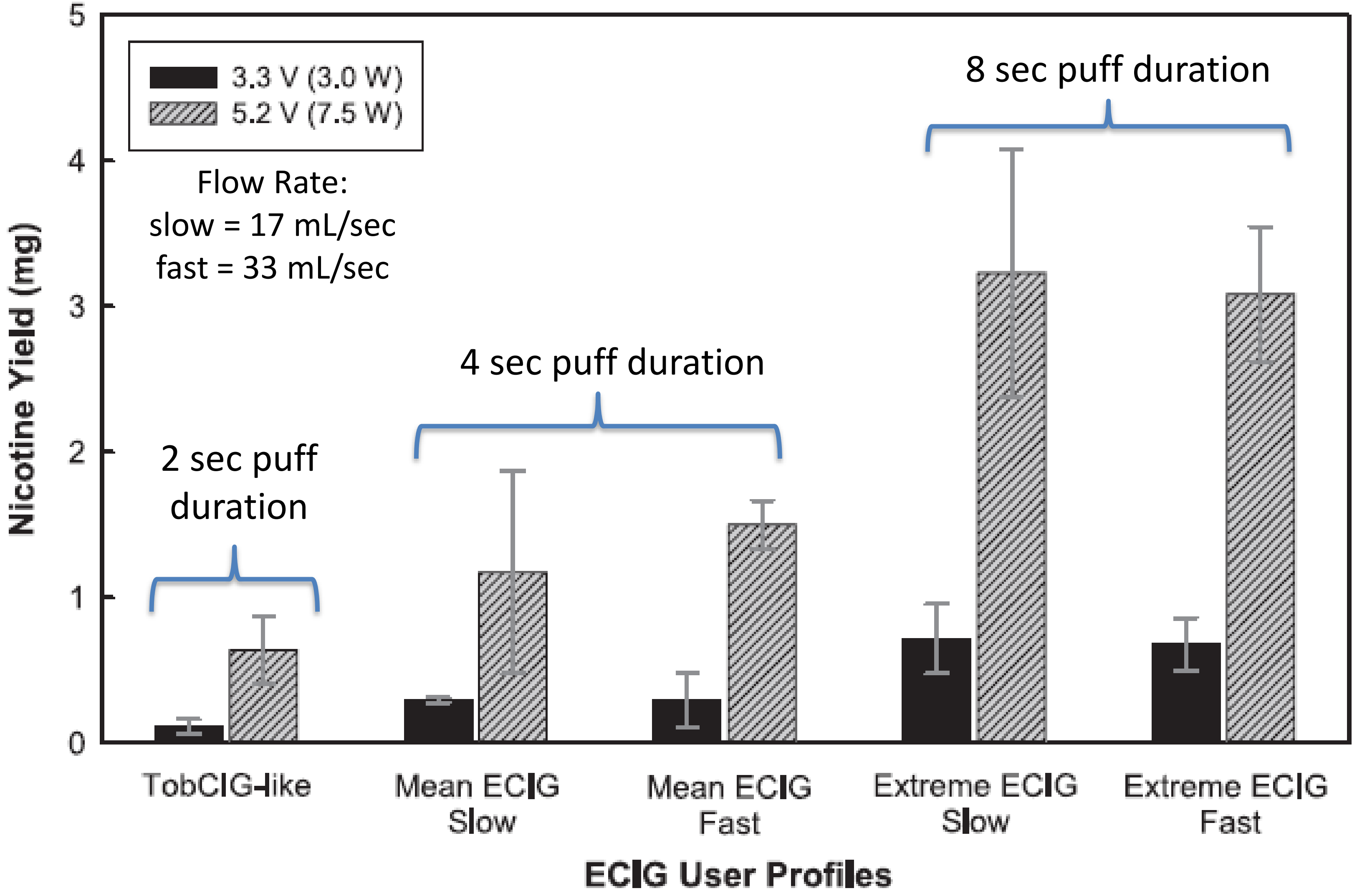
Authors	Year	Puff Definition			
		Puff duration (seconds)	**Inter-puff Interval (seconds)**	**Volume (mL)**	**Flow Rate**
Flora et al	2016	4	30	55	-
Romagna et al	2013	2	60	-	-
Ingrebrethsen et al.	2012	2, 3, and 4	30	55	-
Belka et al.	2017	4	90	60	0.3 L/min
Olmedo et al.	2016	4	30	-	1.0 L/min
Goniewicz et al	2012	1.8	10	70	-
Kosmider et al	2014	1.8	17	70	-
Trehy et al	2011	4	60	100	-

Variability in Yield by Puffing Profile



Karaoghlanian et al. (2014). Effects of User Puff Topography, Device Voltage, and Liquid Nicotine Concentration on Electronic Cigarette Nicotine Yield: Measurements and Model Predictions. Nicotine & Tobacco Research, 17(2), 150-157.

Variability in Yield by Puffing Profile



Nicotine yields from 15 puffs varied by more than **50-fold** across conditions.

Karaoghlanian et al. (2014). Effects of User Puff Topography, Device Voltage, and Liquid Nicotine Concentration on Electronic Cigarette Nicotine Yield: Measurements and Model Predictions. Nicotine & Tobacco Research, 17(2), 150-157.

Why define a puff for a *first generation* product?

Lack of standardization among current literature

Allows for comparison of experiments

Sets the standard for regulation of future generations

Improves comparison between products for premarket tobacco approval and substantial equivalence

Gives a guideline for the measure of exposure

Literature Review of Puff Topography

Reference	Subjects	Puff Duration (sec)	Puff Interval (sec)	Flow Rate (mL/sec)
Norton et al., 2014	18	3	29.6	-
Lee et al., 2015	20	2.9	22.1	24.8
Robinson et al., 2015	21	3.5	42.7	37
Behar et al., 2015	20	2.75	16.9	21
St. Helen et al., 2016	2	5.2	319	-
Strasser et al., 2016	28	2.1	11.2	-
Robinson et al., 2016	20	2	-	34.4
Cunningham et al., 2016	64	2.2	23.2	39
Lee et al., 2017	6	1.8	21.7	30.5
	14	3.3	38.1	26.6
Weighted Average		2.57	27.51	30.67

Proposed Standard Puff Definition for First Generation Products

Puff Duration	2.5 seconds
Inter-Puff Interval	30 seconds
Volume	75 mL
Air Flow Rate	30 mL/sec

Voltage to be matched to that of the stock battery

Implementation

Guidance documentation to researchers and industry detailing standard puff

A standard puff would allow the FDA to stay better informed and well-equipped to evaluate all first generation e-cigarettes

Suggesting that FDA-sponsored studies utilize the puff standard definition

Inter-institutional cross-talk

CORESTA vs UMB Puff Definitions

	UMB	CORESTA
Puff Duration	2.5 seconds	3 seconds
Inter-Puff Interval	30 seconds	30 seconds
Volume	75 mL	55 mL
Air Flow Rate	30 mL/sec	18 mL/sec

Advantages of the UMB puff definition:

Study citing average user air flow rates : 20-39 mL/sec

Focus on first generation e-cigarette products

Definition based on literature

Summary

We propose a standardized puff definition to:

- Characterize HPHCs
- To have comparable scientific literature
- As a gateway to regulate the newer generation of products

Our proposal would improve methods to convey complex scientific and quantitative information about product risk and benefits to consumers and professionals

References

FDA Resources

U.S. Food and Drug Administration (FDA) Center for Tobacco Products. Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems - Draft Guidance for Industry (May 2016). https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM499352.pdf

U.S. Food and Drug Administration (FDA) Center for Tobacco Products. Applications for Premarket Review of New Tobacco Products - Draft Guidance for Industry (Sept 2011). https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM273425.pdf

U.S. Food and Drug Administration (FDA) Center for Tobacco Products. Section 905(j) Reports: Demonstrating SubstantialEquivalence for Tobacco Products - Draft Guidance for Industry and FDA staff (Jan 2011). https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM239021.pdf

U.S. Food and Drug Administration (FDA) Center for Tobacco Products. (2018). Strategic Plan for Regulatory Science. Retrieved from https://www.fda.gov/scienceresearch/specialtopics/regulatoryscience/ucm267719.htm

U.S. Food and Drug Administration (FDA) Center for Tobacco Products. (2019a). Manufacturing. Retrieved from https://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Manufacturing/default.htm

U.S. Food and Drug Administration (FDA) Center for Tobacco Products. (2019b). Market and Distribute a Tobacco Product. Retrieved from https://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/default.htm

Images (in order of appearance):

https://westcoastvapesupply.com/blogs/updates/an-in-depth-look-juul-pods
https://cytus.fandom.com/wiki/File:Crown.png
http://www.jrsmarcom.com/content-is-king/crown
https://patents.google.com/patent/US3200819
https://www.coloradohealthinstitute.org/sites/default/files/download_files/Figure1.jpg
https://brandspurng.com/2019/01/07/cigarette-decline-rates-accelerate-as-juul-share-grows
https://www.vaporfi.com/blog/wp-content/uploads/2015/01/Chalice_Setup24-1.jpg
https://patch.com/img/cdn20/users/22947209/20170730/080654/styles/T800x600/public/processed_images/e-cig-1501459571-2674.jpg

References

Literature Review:

Anderson et al. (2017). Method for the Determination of Carbonyl Compounds in E-Cigarette Aerosols. Journal of Chromatographic Science, 55(2), 142-148.

Behar et al. (2015). Puffing Topography and Nicotine Intake of Electronic Cigarette Users. PloS one, 10(2), e0117222.

Belk et al. (2017). Measurement of an electronic cigarette aerosol size distribution during a puff. EPJ Web of Conferences, 143, 02006.

Cunningham et al. (2016). Development, validation and application of a device to measure e-cigarette users' puffing topography. Scientific reports, 6, 35071.

DeVito et al. (2018). E-cigarettes: Impact of E-Liquid Components and Device Characteristics on Nicotine Exposure. Current neuropharmacology, 16(4), 438-459.

Gauthey et al. (2019). Poisoning with malicious or criminal intent: characteristics and outcome of patients presenting for emergency care. Clinical Toxicology, 1-4.

Goniewicz et al. (2012). Nicotine Levels in Electronic Cigarettes. Nicotine & Tobacco Research, 15(1), 158-166. doi:10.1093/ntr/nts103

Helen et al. (2016). Nicotine Delivery and Vaping Behavior during ad libitum E-cigarette Access. Tobacco Regulatory Science, 2(4), 363-376.

Ingebrethsen et al. (2012). Electronic cigarette aerosol particle size distribution measurements. Inhal Toxicol, 24(14), 976-984.

Karaoghlanian et al. (2014). Effects of User Puff Topography, Device Voltage, and Liquid Nicotine Concentration on Electronic Cigarette Nicotine Yield: Measurements and Model Predictions. Nicotine & Tobacco Research, 17(2), 150-157.

Kurek et al. (2014). Carbonyl Compounds in Electronic Cigarette Vapors: Effects of Nicotine Solvent and Battery Output Voltage. Nicotine & Tobacco Research, 16(10), 1319-1326.

Lee et al. (2015). Changes in puffing behavior among smokers who switched from tobacco to electronic cigarettes. Addictive Behaviors, 48, 1-4.

Lee et al. (2017). Examining Daily Electronic Cigarette Puff Topography Among Established and Nonestablished Cigarette Smokers in their Natural Environment. Nicotine & Tobacco Research, 20(10), 1283-1288.

Norton et al. (2014). Initial puffing behaviors and subjective responses differ between an electronic nicotine delivery system and traditional cigarettes. Tobacco Induced Diseases, 12(October).

Olmedo et al. (2016). A direct method for e-cigarette aerosol sample collection. Environ Res, 149, 151-156.

Robinson et al. (2015). Electronic Cigarette Topography in the Natural Environment. PloS one, 10(6), e0129296.

Robinson et al. (2016). Week Long Topography Study of Young Adults Using Electronic Cigarettes in Their Natural Environment. PloS one, 11(10), e0164038.

Romagna et al. (2013). Cytotoxicity evaluation of electronic cigarette vapor extract on cultured mammalian fibroblasts (ClearStream-LIFE): comparison with tobacco cigarette smoke extract. Inhal Toxicol, 25(6), 354-361.

Strasser et al. (2016). Nicotine Replacement, Topography, and Smoking Phenotypes of E-cigarettes. Tobacco Regulatory Science, 2, 352-362.

Trehy et al. (2011). Analysis of Electronic Cigarette Cartridges, Refill Solutions, and Smoke for Nicotine and Nicotine Related Impurities. Journal of Liquid Chromatography & Related Technologies, 34(14), 1442-1458.