A consortium approach for consumer-reported outcome measures for assessing tobacco and/or nicotine-containing products

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INTRODUCTION

- In tobacco harm reduction research, it is essential to understand people's behaviors, intentions, and motivations related to initiation, continuation, or quitting the use of tobacco- and/or nicotine-containing products (TNP) in order to measure the effects of these products (objective and subjective) on population health. Consumer-reported outcome measures (CROM) form part of the methods used for assessing subjective effects, behaviors, and motivations and inform on the switching behaviors of users and non-users. Regulatory agencies, such as the U.S. Food and Drug Administration (FDA) [1], have established robust standards on the type of science-based evidence required to demonstrate that a modified risk tobacco product (MRTP) can benefit public health. To support regulatory decision-making on such products, there is a need for developing scientifically credible standards to ensure that CROM are valid and reliable.
- A consortium is being built under the auspices of CORESTA to establish best practices and guidelines for the use of CROM in the tobacco regulatory process. The main objective of the consortium is to provide guidance on how to develop, validate, identify, access and use CROM to evaluate TNP for pre-market and post-market studies.
- Here we present the preliminary work conducted by the CROM consortium to define the research questions and scope of work agreed through a qualitative review.

METHODS

- A qualitative review of key literature on MRTP was initiated in November 2018, which included the U.S. FDA MRTP briefing documents (in the context of applications submitted by Altria Client Services (ALCS), Philip Morris International (PMI), Reynolds American Services Company, and Swedish Match North America (SMNA)), regulatory documents, selected review papers, and public health reports. See detailed list in Table 1.
- A data extraction form with definitions for each field was developed in order to ensure harmonized data extraction among the different CROM Task Force (TF) members, who reviewed one document each. Data relating to self-reported measures were extracted in pre-market and post-market contexts – that is, concepts to be measured (e.g., risk perceptions, dependence), populations to be assessed, methods recommended and/or used, psychometric information, and weight of self-reported data in decision-making.

Table 1. List of documents reviewed by CROM TF members

Type of document	Title/source	
Briefing documents	February 6, 2019 – TPSAC meeting MRTPA - MR0000108 Altria Client Services LLC on behalf of US Smokeless Tobacco Company for Copenhagen® Snuff Fine Cut	February 6, 2019 – TPSAC meeting MRTPAs - MR0000020-22; MR0000024-25; MR000027-29 Swedish Match North America (amendment) for General Snus Products
	September 13–14, 2018 – TPSAC meeting MRTPAs - MR0000068-MR0000073 Reynolds American Incorporated Services Company on behalf of R.J. Reynolds Tobacco (RJRT) for Camel Snus	January 24–25, 2018 – TPSAC meeting MRTPAs - MR0000059-MR0000061 Philip Morris Products S.A. for IQOS
	April 9-10, 2015 – TPSAC meeting MRTPAs - MR0000020-MR0000029 Swedish Match North America (SMNA) for General Snus Products	
Regulatory documents	US Department of Health and Human Services, FDA, CTP. Guidance for Industry. Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems – Draft Guidance. May 2016. https://www.fda.gov/media/97652/download	
	US Department of Health and Human Services, FDA, CTP. Guidance for Industry. Guidance for Industry. Modified Risk Tobacco Product Applications – Draft Guidance. March 2012. https://www.fda.gov/media/83300/download	
	US Department of Health and Human Services, FDA, CTP. Guidance for Industry. Applications for Premarket Review of New Tobacco Products - Draft guidance. September 2011. https://www.fda.gov/media/81821/download	
	US Department of Health and Human Services, FDA, CDER. Guidance for Industry Label Comprehension Studies for Nonprescription Drug Products. August 2010. https://www.fda.gov/media/75626/download	
	DIRECTIVE 2014/40/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco and related products and repealing Directive 2001/37/EC. Official Journal of the European Union 29.4.2014. https://ec.europa.eu/health/sites/health/files/tobacco/docs/dir_201440_en.pdf	
Review papers	Berman ML et al. Consortium on Methods Evaluating Tobacco: Research Tools to Inform US Food and Drug Administration Regulation of Snus. Nicotine Tob Res. 2018;20(11):1292-1300.	
	O'Connor RJ. Postmarketing surveillance for "modified-risk" tobacco products. Nicotine Tob Res. 2012;14(1):29-42.	
Reports	Institute of Medicine. Scientific Standards for Studies on Modified Risk Tobacco Products The National Academies Press: Washington DC, USA. https://www.nap.edu/catalog/13294	
	CTP. Tobacco Regulatory Science Research Program at FDA's Center for Tobacco Products: Summary and Highlights. FISCAL YEARS 2010 2017. June 2018. https://www.fda.gov/media/114538/download	

Abbreviations: CDER: Centre for Drug Evaluation and Research; CTP: Centre for Tobacco Products; TPSAC: Tobacco Products Scientific Advisory Committee

RESULTS

Analysis of the qualitative review led to three main outcomes: 1) development of a consensus definition of consumer-reported outcomes (CRO); 2) a categorization scheme for the concepts of interest identified for assessing TNP; and 3) development of a common taxonomy and definitions to qualify them.

CROM Definition

The CROM TF adopted the following definition: ***Consumer-reported outcomes are data collected by self-report from the subject of research, whether it concerns perceived states, reports of behavior, or the combination of both, and understanding of messages.***

Categorization Scheme and Taxonomy

A consensus taxonomy and related categorization (see Table 2) were developed. Basically, concepts were distributed within eight categories, including Product Perceptions, Behavioral Intentions, Responses to Product, Consumer Comprehension, Health Literacy, Believability, Product Use Behavior, and Impact on Health and Functioning. The development of definitions for each category and concept is currently on-going.

Of note, the list of concepts is not exhaustive of all concepts measured in tobacco research – only those found in the reviewed documents are listed.

How is risk perception measured?

To illustrate the heterogeneity identified across documents for the same concept, we present in Table 3 how risk perceptions for health in general and for specific diseases have been assessed in four distinct MRTPAs, in comparison to the recommendations made by the U.S. FDA and the Institute of Medicine on this specific type of assessment.

Table 2. Consensus taxonomy and categorization for CRO concepts used in TNP evaluation

Category	Subcategory	Concepts
Product Perceptions	Risk Perceptions	Risk Perceptions – Health (own personal risk); Risk Perceptions – Diseases (own personal risk); Risk Perceptions – Health (general risk); Risk Perceptions – Diseases (general risk); Risk Perceptions – Addiction (own personal risk); Risk Perceptions – Addiction (general risk); Risk Perceptions – Harm to Others (risk linked to personal behaviour); Risk Perceptions – Harm to Others (risk linked to others' behaviour)
	Ease of use	Ease of use
	Product appeal	Product appeal
	Outcome expectancies	Expectations of quitting; Positive reinforcement - Sensory satisfaction; Negative reinforcement - Negative affect reduction; Appetite/Weight control; Negative consequences
Behavioral Intentions		Likelihood to try; Likelihood to use; Likelihood to dual use; Likelihood to poly-use; Likelihood to initiate; Likelihood to quit; Likelihood to switch
		Purchase intent
Responses to Product	Linked to the use of the product	Dependence, Liking/Satisfaction; Taste/Sensory effects; Reinforcing Effects
	Linked to the absence of the product	Craving; Withdrawal symptoms
Consumer Comprehension		Comprehension of messages
Health Literacy		Health literacy
Believability		Believability of messages
Product Use Behaviour		Cessation; Initiation; Product use pattern; Use not as intended; Use as intended; Tobacco use status; Purchase experience; Purchase behaviour
Impact on Health and Functioning	Health-related Quality of Life	Health-related quality of life
	Physical Functioning	Activities of daily living; Physical activities
	Mental Health	Anxiety; Depression; Irritability; Anhedonia; Mood states
	Cognitive Functioning	Attention; Decision-making; Memory
	Social Functioning	Social activities
	Health Status	Health status/health; Mental health status; Physical health status
	Symptoms	Fatigue; Pain; Sleep disorders

References

1. U.S. Department of Health and Human Services, FDA, CTP. Guidance for Industry. Guidance for Industry. Modified Risk Tobacco Product Applications – Draft Guidance. March 2012. https://www.fda.gov/media/83300/download
2. Cano, S. et al. Development and validation of a new instrument to measure perceived risks associated with the use of tobacco and nicotine-containing products. *Health Qual. Life Outcomes* **16** (1), 192 (2018).

Table 3. Assessment of risk perception (health in general and specific diseases)

Source	Types of risks: Health in general	Specific diseases	Own personal risk	Risk in general	Relative*	Absolute	Measures recommended or used: One single item	Multi-items measure	None specified	Example provided (guidance and reports only)
FDA Guidance – PMTA	✓			✓	✓	✓			✓	
FDA Guidance – MRTPA	✓			✓	✓				✓	
IOM Report 2012	✓	✓	✓	✓	✓					✓ Likelihood estimates assessed through numerical scales
MRTPA submission: PMI – IQOS	✓	✓	✓		✓	✓		✓ Perceived Health Risk calibrated scale of the ABOUT–Perceived Risk[2]		
MRTPA submission: RJRT – Camel Snus	✓	✓		✓	✓	✓	✓ One single item for each product / disease combination			
	✓	✓		✓		✓		✓ ALCS's Specific (Absolute) Risk Scales		
MRTPA submission: ALCS – Copenhagen Snuff	✓			✓	✓			✓ ALCS's (Indirect) Relative Risk Scales		
	✓			✓		✓	✓ Adapted from CDC (NATS, 2013-2014)			
MRTPA original submission: SMNA– Snus	✓	✓	✓			✓	✓ Ad hoc item			
	✓		✓		✓		✓ Ad hoc item			
MRTPA submission - amendment: SMNA– Snus	✓	✓		✓		✓	✓ Adapted from the item used in the NCI HINTS			
	✓	✓		✓	✓		✓ Adapted from the item used in the NCI HINTS			

Abbreviations: ABOUT: Assessment of Behavioral OUtcomes related to Tobacco and Nicotine Products; ALCS: Altria Clients Services; CDC: Center for Disease Control; NATS: National Adult Tobacco Survey; NCI HINTS: National Cancer Institute (NCI) Health Information National Trends Survey.

* Relative is defined as relative to risk perceptions associated with using other tobacco products, nicotine replacement therapy, quitting, and never using tobacco products.

CONCLUSIONS

- The key outcomes presented here form the foundations of the CROM consortium to address the needs for developing common terminology, standards, and best practices for CROM in tobacco and nicotine research.
- The consortium might be used as a platform between the tobacco industry, academia, and regulatory and public health stakeholders to enhance harmonization in CROM-related science.