

Supplementary Tables: Risk Perception CROMs health risks items and item stems.

Supplementary Table 1. Health risks evaluated in Risk Perception CROMs.

Health risks (absolute or relative)	ABOUT – Perceived Risk (v3.0)	PBI Survey	FDA CTP instrument		Number of items across CROMs
			e-cigarettes	smokeless tobacco products	
Breathing	●	●	●	●	6
Coughing	●	●		●	4
Lung cancer	●	●	●	●	4
Mouth cancer	●	●	●	●	4
Heart disease	●	●	●	●	4
Teeth		●	●	●	4
Lung disease				●	3
Emphysema	●	● [§]		●	3
Earlier death	●		●		2
Life-threatening disease	●		●		2
Respiratory infections	●			●	2
Other minor illnesses	●		●		2
Gum	●			●	2
Mouth sores	●			●	2
Asthma				●	1
Exercise capacity	●				1
Fatigue	●				1
Other types of cancer	●				1
Stomach cancer				●	1
Stomach ulcers				●	1
Mouth irritation				●	1
Taste	●				1
Aging	●				1

§ in [11,12].

Supplementary Table 2. Risk Perception CROMs item stems.

Risk Perception CROM	Item Stem Formulation*
ABOUT – Perceived Risk (v3.0)	What do you think is YOUR lifetime health risk, because you use [product] ... If you started using [product] again tomorrow, what do you think would be YOUR lifetime health risk of ... What do you think is the lifetime health risk to [product] users of ...
PBI Survey	In your opinion, how harmful are [product] to your general health? In your opinion, to what extent do [product] cause ... Please rate each item for the risk you feel it could pose to a person's health. How likely is it that these things will happen to a person who exclusively uses [product] daily?
FDA CTP instrument	If you were to use [product] every day, how likely is it that you would ... If you either used ... every day, which product would make it more likely that you would ... Imagine you used either ... every day, which product would make it more likely that you would ...

* Exact item stems are dependent on product, product use status (i.e., users and non-users), etc.



Supplementary Tables: Risk Perception CROMs psychometric validation output.

Supplementary Table 3. ABOUT – Perceived Risk psychometric validation output.

Data completeness (missing data)	Scaling assumptions (corrected item-total correlations)	Targeting (floor/ceiling effects)	Reliability (Cronbach's alpha & test-retest)	Construct validity (correlations with scales measuring similar constructs)	Known groups validity (different scores between groups of PPs)
Missing data was 0.1% at most at the item-level (however the proportion of don't know responses was between 11-15%)	Range of corrected item-total correlation Survey 1: Health Risk: 0.89-0.93 Addiction Risk: 0.90 – 0.93 Survey 2: Health Risk: 0.88-0.92 Addiction Risk: 0.92-0.95	Ceiling / Floor Survey 1: Health Risk – 7% / 10% Addiction risk – 8% / 20% Survey 2: Health Risk – 5% / 10% Addiction risk – 6% / 18%	Surveys 1&2: Health Risk: α 0.99 Addiction Risk: α 0.98	For the assessment objects cigarettes, THS 2.2, E-cigarettes and NRT, all correlations between the VAS scores and instrument's measures for both Perceived Health Risk and Perceived Addiction Risk were in the range of 0.52 to 0.68 across both types of risk Assuming a reliability of the VAS of 0.6 and applying the Spearman Brown formula for diattenuation imply correlations in the order of 0.68 and 0.89.	All mean differences were in the expected direction. In terms of the effect sizes (Cohen's d), differences between smokers and never smokers (0.51-0.84) were more pronounced than differences between personal and general risk among current smokers (0.23-0.34) The risk perception of cigarettes was higher than that of IQOS across all countries and years ^[13] . After adjustment for covariates, the relative risk between cigarettes and IQOS was higher in 2018 than in 2019 (0.93; standard error, 0.33; P = 0.005). This was driven by an increase in the risk perception of IQOS over time in Italy (2018: 42.6 [95% CI, 41.6–43.5]; 2019: 44.4 [43.4–45.4]) and Japan (2017: 44.0 [43.1–44.9]; 2018: 45.9 [45.2–46.7]; 2019: 48.6 [47.9–49.4]), while the risk perception of cigarettes remained stable

Supplementary Table 4. PBI Survey psychometric validation output.

Reliability (Cronbach's alpha & test-retest)	Construct validity (correlations with scales measuring similar constructs)	Sensitivity to change
Perceived Harm of MarkTen[®]XL: Validation sample: α .876; ICC .870 (<.001) Cross-validation sample: α .888; ICC.798 (<.001)	Perceived Harm of MarkTen[®]XL: Validation sample: correlation with Behavioral Selection -.309 (<.001) Cross-validation sample: correlation with Behavioral Selection -.387 (<.001)	Correlations between residualised change scores of Perceived Harm of MarkTen[®]XL scales and behavioral selection: Validation sample: Pearson .016 (.784) Cross-validation sample: Pearson .066 (.266)
Perceived Harm of E-Vapor/E-Cigs: Validation sample: α .864; ICC .856 (<.001) Cross-validation sample: α .871; ICC .792 (<.001)	Perceived Harm of E-Vapor/E-Cigs: Validation sample: correlation with Behavioral Selection -.314 (<.001) Cross-validation sample: correlation with Behavioral Selection -.387 (<.001)	Perceived Harm of E-Vapor/E-Cigs scales and behavioral selection task: Validation sample: Pearson .023 (.700) Cross-validation sample: Pearson .067 (.258)
Relative Risk: Validation sample: items Risk1-Risk10 ICC range .527-.747 (<.001); average .603 (<.001) Cross-validation sample: items Risk1-Risk10 ICC range .390-.723 (<.001); average .597 (<.001) Full sample: items Risk1-Risk10 ICC range .462-.731 (<.001)	Relative Risk: Validation sample: correlation with Behavioral Selection items Risk2-Risk6 range -.282 - -.163 (<.001) Cross-validation sample: correlation with Behavioral Selection items Risk2-Risk6 range -.334 - -.214 (<.001)	Relative Risk scales and behavioral selection task (Not Selecting MarkTen[®]XL): Validation sample: items Risk2-Risk6 Pearson range .023-.116 (>.053) Cross-validation sample: items Risk2-Risk6 Pearson range .133-.206 (<.05)
Specific Risk of Cigarettes: Validation sample: items RiskC1-RiskC9 ICC range .637-.795 (<.001) Cross-validation sample: items RiskC1-RiskC9 ICC range .560-.782 (<.001)	Specific Risk of Cigarettes: Validation sample: correlation with being a tobacco user items RiskC1-RiskC9 range -1.580 - -.041 (<.001; RiskC5 p.115) Cross-validation sample: correlation with being a tobacco user items RiskC1-RiskC9 range -.221 - -.075 (<.001; RiskC5 p .005)	Specific risk of MarkTen[®]XL scales and behavioral selection task (Not Selecting MarkTen[®]XL): Validation sample: items RiskV1-RiskV9 Pearson range -.022 - -.103 (>.08) Cross-validation sample: items RiskV2, RiskV3, RiskV4, RiskV9 range .210-.232 (<.001); RiskV6 .197 (.001); RiskV1, RiskV7, RiskV8 range .131-.137 (>.02); RiskV5 .071 (.234)
Specific Risk of MarkTen[®]XL: Validation sample: items RiskV1-RiskV9 ICC range .682-.835 (<.001) Cross-validation sample: items RiskV1-RiskV9 ICC range .652 - .768 (<.001)	Specific Risk of MarkTen[®]XL: Validation sample: correlation with Behavioral Selection items RiskV1-RiskV9 -.298 - -.194 (<.001) Cross-validation sample: correlation with Behavioral Selection items RiskV1-RiskV9 -.378 - -.227 (<.001)	Full sample: items RiskV4, RiskV6, RiskV9 range .114-.130 (<.01); items RiskV1- RiskV2- RiskV3, RiskV8 range .093-.109 (<.05); items RiskV5, RiskV7 .048, .078 (>.05)

Supplementary Table 5. FDA CTP instrument psychometric validation output.

FDA CTP instrument	Structural validity Factorial analyses (EFA/exploratory factorial analysis, CFA/confirmatory factorial analysis), ITC (item-to-total correlation), IRT (item-response theory)	Reliability (Cronbach's alpha & test-retest)
e-cigarettes	Absolute health risk: # factors: 1, % var. explained: 71.6 Factor loadings: .76–.86, Communalities: .57–.74 Health risk of e-cigarettes compared with cigarettes: # factors: 1, % var. explained: 47.4 Factor loadings: .68–.75 (except common cold or flu, pancreatic cancer, diabetes, stomach ulcers, stomach cancer <.3). Communalities: .46–.62 Addiction risk of e-cigarettes compared with cigarettes: # factors: 1, % var. explained: 66.7 Factor loadings: .72–.79, Communalities: .52–.58 Pregnancy risk of e-cigarettes compared with cigarettes: # factors: 1, % var. explained: 70.4 Factor loadings: .61–.66, Communalities: .55–.62 Health risk of e-cigarettes relative to NRT: # factors: 1, % var. explained: 77.2 Factor loadings: .73–.97, Communalities: .56–.72 Health risk of e-cigarettes relative to cessation: # factors: 1, % var. explained: 91.5 Factor loadings: .81–.99, Communalities: .77–.80	Absolute health risk: correlation between this single item and all items = .82 Health risk of e-cigarettes compared with cigarettes: (Final scale: The overall harm item had a correlation with the overall scale of .75, therefore, the core 8-item scale was used to represent the construct. The average of these items has a .93 correlation with the 23 remaining items.) Addiction risk of e-cigarettes compared with cigarettes: α .83 Pregnancy risk of e-cigarettes compared with cigarettes: α .90 Health risk of e-cigarettes relative to NRT: Used overall harm item to represent scale; correlation between this and all items = .92. Health risk of e-cigarettes relative to cessation: Used overall harm item to represent scale; correlation between this and all items = .98.
smokeless tobacco (ST) products	Absolute risk of ST product: Health Risk: 2 factor solution, var. explained: 71.7% Factor loadings: 0.68–0.92, Factor correlation: 0.59 Risk of ST products relative to cigarettes: Health Risk: 2 factor solution, var. explained: 50.7% Factor loadings: 0.64–0.83, Factor correlation: 0.22 Addiction risk: # factors: 1, var. explained: 59.5% Factor loadings: 0.65–0.70 Pregnancy risk: # factors: 1, var. explained: 67.5% Factor loadings: 0.74–0.79 Risk of ST product compared to cessation - Health risk relative to NRT: # factors: 1, Variance explained: 82.4% Factor loadings: 0.76–0.85 Health risk relative to cessation: # factors: 1, var. explained: 87.8% Factor loadings: 0.85–0.88	Absolute health risk of ST product: α 0.75-0.85 Health risk of ST product relative to cigarettes: α 0.93 Addiction risk of ST product relative to cigarettes: α 0.78 Pregnancy risk of ST product relative to cigarettes: α 0.88 Risk of ST products compared to NRT/cessation: α 0.93/0.94 between single items and all items



References – EPH82 (ISPOR 2024)

- [1] FDA, *Final Rule: Premarket tobacco product applications and Recordkeeping requirements*. 2021.
- [2] FDA, *Guidance for Industry: Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies*. 2022.
- [3] McCaffrey, S., et al., *Best Practices and Guidelines with respect to Psychometric CROM for use in Research on Tobacco and Nicotine Containing Products*. CORESTA Technical Report, CROM-269-1-CTR, 2024.
- [4] FDA, *Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims*. 2009.
- [5] FDA, *Guidance for Industry: Principles for selecting, developing, modifying, and adapting patient reported outcome instruments for use in medical device evaluation*. 2020.
- [6] Chrea, C., et al., *Developing fit-for-purpose self-report instruments for assessing consumer responses to tobacco and nicotine products: the ABOUT™ Toolbox initiative*. F1000Res, 2018. 7:1878.
- [7] 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, 2018. 16(1): p. 192.
- [8] ALCS, *Validation of the Perception and Behavioral Intentions (PBI) Survey Instrument for use in the Perceptions and Behavioral Intentions PMTA Study – Final Report*. USSTC MRTP Application for Copenhagen® Snuff Fine Cut (Module 7, Appendix 7.3.3-8), 2017. [Available from: <https://www.fda.gov/tobacco-products/advertising-and-promotion/us-smokeless-tobacco-company-modified-risk-tobacco-product-mrtp-application>]
- [9] O'Brien, E.K., S.A. Baig, and A. Persoskie, *Developing and Validating Measures of Absolute and Relative E-Cigarette Product Risk Perceptions: Single Items Can Be Surprisingly Comprehensive*. Nicotine & Tobacco Research, 2022. 24(3): p. 316-323.
- [10] O'Brien, E.K., S.A. Baig, and A. Persoskie, *Absolute and Relative Smokeless Tobacco Product Risk Perceptions: Developing and Validating New Measures that are Up-to-Snuff*. Nicotine & Tobacco Research, 2022. 24(2): p. 265-269.
- [11] McKinney, D., Lewis, J., and Becker, E., *Reduced Risk Claims Comprehension and Risk Perceptions in Adult Tobacco Users and Nonusers for an Oral Tobacco-Derived Nicotine Product After Exposure to Promotional Materials*. in Symposium presented at the Tobacco Science Research Conference. 2022. New Orleans, LA, USA.
- [12] McKinney, D. and Becker, E., *Promotional Materials for a Novel Heated Tobacco Capsule System Do Not Alter Risk Perceptions*. in Poster presented at the Tobacco Science Research Conference. 2023. New Orleans, LA, USA.
- [13] AIMoosawi, S., et al., *Risk perception of IQOS™ and cigarettes: Temporal and cross-country comparisons*. SSM Popul Health, 2022. 18:101123.
- [14] O'Brien, E.K., Persoskie, A., and Tam, J., *Multi-item Measures of Tobacco Health Perceptions: A Review*. Am J Health Behav. 2019;43(2):266-278.
- [15] Kaufman, A.R., et al., *A review of risk perception measurement in tobacco control research*. Tobacco Control, 2020;29:s50-s58.
- [16] Kaufman, A.R., et al., *Measuring Cigarette Smoking Risk Perceptions*. Nicotine Tob Res. 2020;22(11):1937-1945.