Product Stewardship as a Foundation for Science-Based Consensus Standards for Nicotine Pouches

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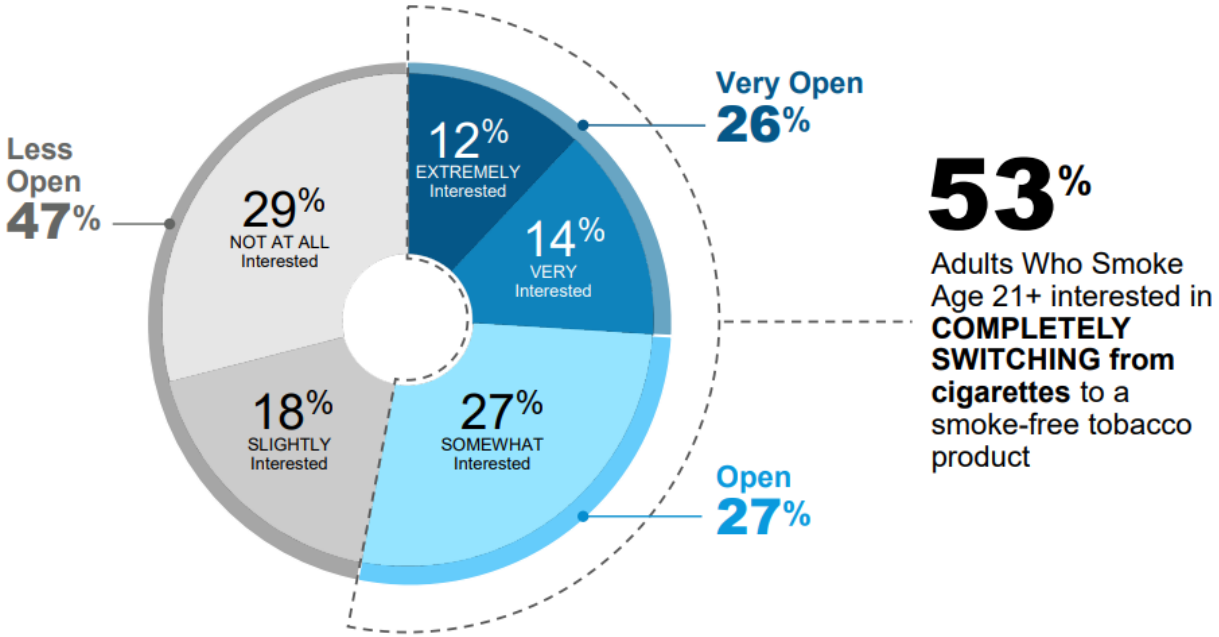
The Case for Product Standards for Reduced Risk Products (RRPs)



Adult Smokers, who cannot or will not quit, should have access to acceptable RRP alternatives that are substantiated through science and evidence[2]

- Compliance with product standards may facilitate the innovation of RRPs and allow such products to enter the market more rapidly by
  - Alleviating the amount of product-specific information required in a product application
  - Providing the basis for an accelerated marketing authorization pathway for RRPs
  - Creating industry-wide baselines for safety and quality
- Product standards could originate from
  - FDA under 907(a)(3)
  - Voluntary Consensus Standards

[1]Response to question – "In the next 6 months, how interested are you in completely switching all of your current cigarette usage occasions to a different tobacco product (such as e-vapor, smokeless tobacco, snus, or nicotine pouches)? ALCS Consumer Market Insights Data.
[2]Press Release, FDA announces comprehensive regulatory plan to shift trajectory of tobacco-related disease, death (July 27, 2017), available at https://www.fda.gov/news-events/press-announcements/fda-announces-comprehensive-regulatory-plan-shift-trajectory-tobacco-related-disease-death.

What is Product Stewardship?

"the act of minimizing the health, safety, environmental, and social impacts of a product and its packaging throughout all lifecycle stages …."

PRODUCT STEWARDSHIP INSTITUTE

https://www.productstewardship.us/page/Definitions

- Our product stewardship program focuses on the potential health impact – health and safety – to adult consumers independent of regulatory framework.
- We rely on core product stewardship principles that are practiced across the chemical, pharmaceutical, food and consumer packaged goods industries.

Scientific Framework to Demonstrate APPH

CONSTITUENT REDUCTION

Product Design and Control

Chemical and Physical Characterization

THE PRODUCT

- Chemistry Manufacturing and Controls
- Product Stability
- Chemical characterization

INDIVIDUAL RISK REDUCTION

Toxicology and Risk Assessment

Studies in Adult Human Subjects

EXPOSURE and HEALTH RISK

- Toxicology & Risk Assessment
- Health risk assessment (absolute and relative)
- Human Studies
- Human Factors Assessment

POPULATION HARM REDUCTION

Perception and Behavior Assessment

Risks and Benefits to Health of the Population

IMPACT on the POPULATION

- Risk perceptions (absolute and relative)
- Impact of product on users
- Impact on non-users
- Overall impact on the population
- Environmental Assessment

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Components of Product Stewardship

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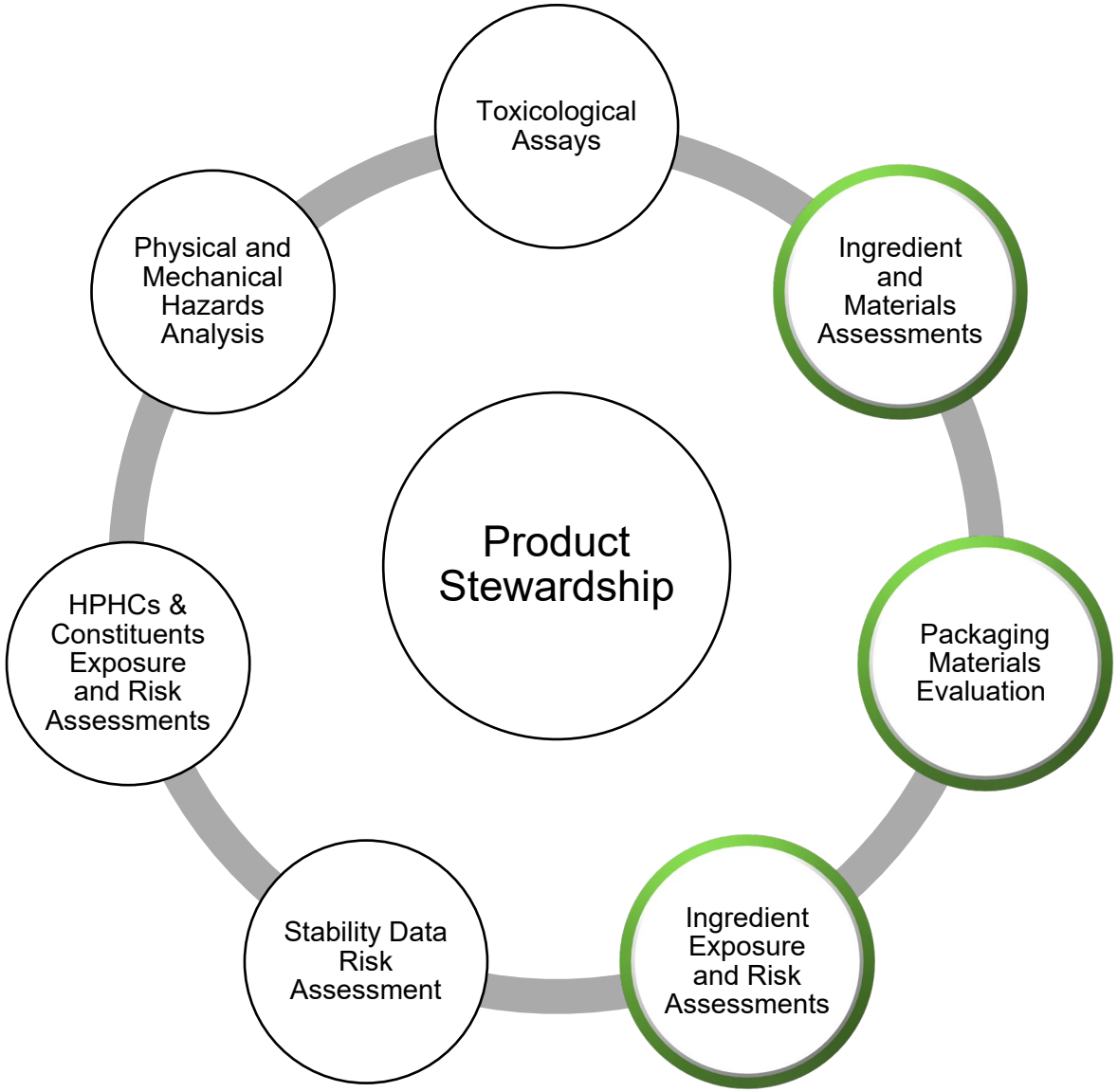
Components of Product Stewardship for a Consensus Standard



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Product Stewardship Framework

Ingredient, Material and Packaging Assessments	Supplier Qualification Process Ingredient/Material Grade and Quality Determination
Toxicological Risk Assessments of Ingredients	Ingredient Exposure Assessments Ingredient Risk Assessments

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Ingredient, Material and Packaging Assessments – Supplier Qualification

- A robust supplier qualification process is the foundation upon which material and ingredient safety-in-use evaluations for finished products are based
- Determine that supplier has a comprehensive quality system (e.g., cGMP, etc.) to demonstrate appropriate control of their supply chain and manufacturing processes
- Systematically assess the ability of a supplier to deliver ingredients or materials of USP/food grade quality

Ingredient, Material and Packaging Assessments – Grade and Quality Determination

- Ingredient and Material Quality Assessment
  - Nicotine should be Pharmaceutical Grade (e.g., USP, EP)
  - Each ingredient (flavors, filler materials, etc.) should be GRAS and food grade quality
    - Ensures that each material contains the lowest levels of impurities/contaminants that are technically feasible and are in parallel with ingredients used in the food supply
  - Packaging materials should be appropriate for use in food packaging
    - Appropriate 21 CFR compliant for use as indirect food additives

Documentation from supplier

- ✓ Food/Pharma Grade Statement
- ✓ Allergen Statement
- ✓ Continuing Guarantee
- ✓ SDS
- ✓ Technical Data Sheet / Product Specifications

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Toxicological Risk Assessment of Ingredients

- Exposure assessment of each individual chemical in all ingredients
  - Requires full disclosure of all ingredients present in the product
  - This disclosure should be at the chemical level and, for almost all cases, each chemical should be identified with a CAS RN and a FEMA number (if applicable)
  - Estimates of daily exposure which are confirmed by consumer use data
- Risk assessment of each individual chemical in all ingredients
  - Established Acceptable Daily Intakes (ADIs) should not be exceeded
  - Exposure levels should be supported by the available data on which authoritative bodies (e.g., FDA, JECFA, etc.) made their GRAS determination, if available (i.e., Margins of Exposure > 1)
  - Hierarchy of health guidance values should be established

Toxicology and Risk Assessment

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Summary

- Product stewardship is paramount to the success of tobacco harm reduction
- A rigorous ingredient and material quality evaluation can significantly reduce the complexity of the overall product stewardship evaluation
- These principles should be institutionalized into product standards to help industry and FDA focus on the ultimate goal – developing and authorizing products that move smokers to reduced risk products by:
  - Alleviating the amount of product-specific information required in a product application
  - Providing the basis for an abbreviated marketing authorization pathway for RRPs
  - Creating industry-wide baselines for safety and quality

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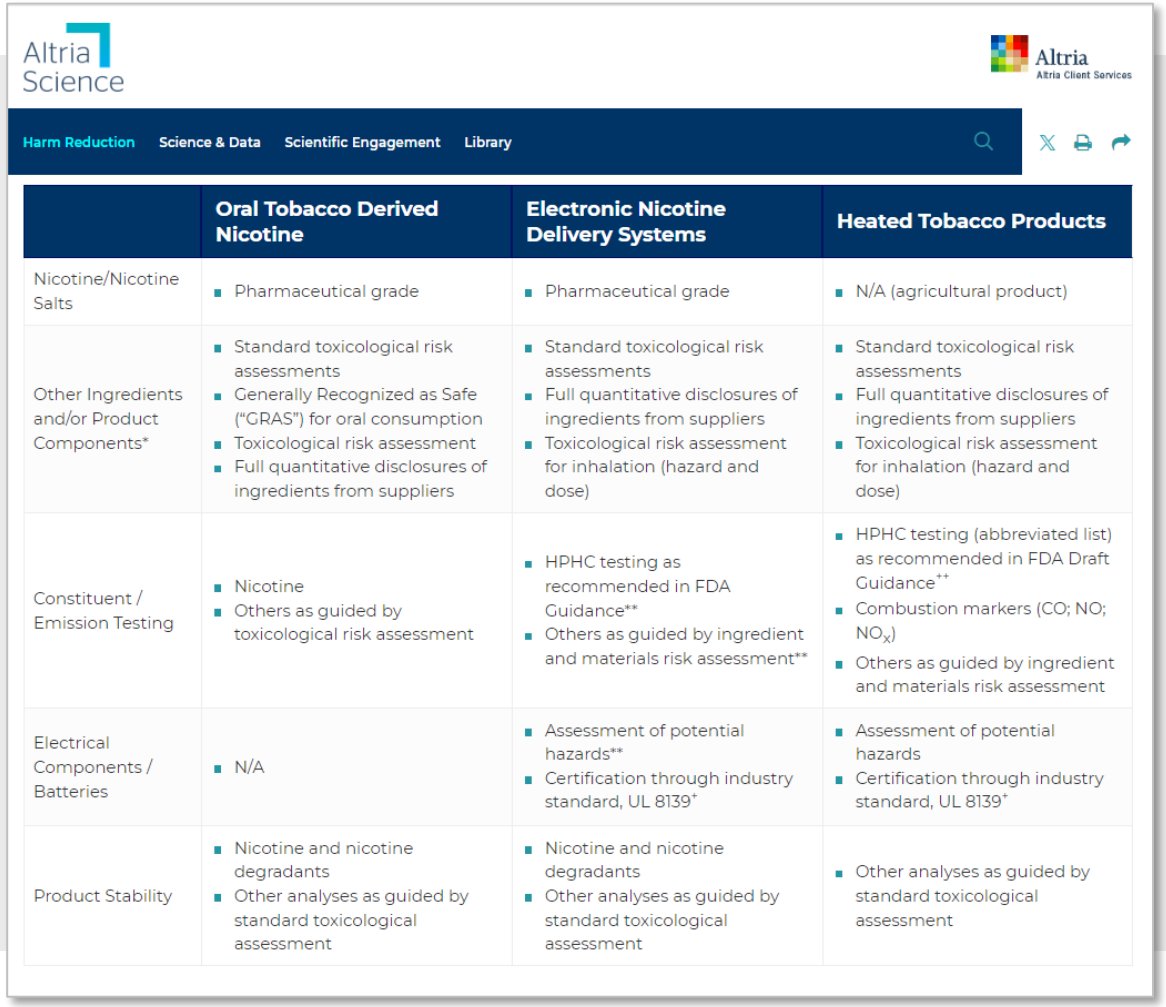
Smoke-Free Product Standards



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Harm Reduction | Science & Data | Scientific Engagement | Library

	Oral Tobacco Derived Nicotine	Electronic Nicotine Delivery Systems	Heated Tobacco Products
Nicotine/Nicotine Salts	▪ Pharmaceutical grade	▪ Pharmaceutical grade	▪ N/A (agricultural product)
Other Ingredients and/or Product Components*	▪ Standard toxicological risk assessments ▪ Generally Recognized as Safe ("GRAS") for oral consumption ▪ Toxicological risk assessment ▪ Full quantitative disclosures of ingredients from suppliers	▪ Standard toxicological risk assessments ▪ Full quantitative disclosures of ingredients from suppliers ▪ Toxicological risk assessment for inhalation (hazard and dose)	▪ Standard toxicological risk assessments ▪ Full quantitative disclosures of ingredients from suppliers ▪ Toxicological risk assessment for inhalation (hazard and dose)
Constituent / Emission Testing	▪ Nicotine ▪ Others as guided by toxicological risk assessment	▪ HPHC testing as recommended in FDA Guidance** ▪ Others as guided by ingredient and materials risk assessment**	▪ HPHC testing (abbreviated list) as recommended in FDA Draft Guidance++ ▪ Combustion markers (CO; NO; NO_x) ▪ Others as guided by ingredient and materials risk assessment
Electrical Components / Batteries	▪ N/A	▪ Assessment of potential hazards** ▪ Certification through industry standard, UL 8139+	▪ Assessment of potential hazards ▪ Certification through industry standard, UL 8139+
Product Stability	▪ Nicotine and nicotine degradants ▪ Other analyses as guided by standard toxicological assessment	▪ Nicotine and nicotine degradants ▪ Other analyses as guided by standard toxicological assessment	▪ Other analyses as guided by standard toxicological assessment

Learn more about our science and evidence based product standards