



# Nonclinical Toxicity Assessment of Oral Tobacco- Derived Nicotine Products: I. Framework

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**CORESTA Smoke-Techno (SSPT) Conference - [ST 57]**

October 27, 2021





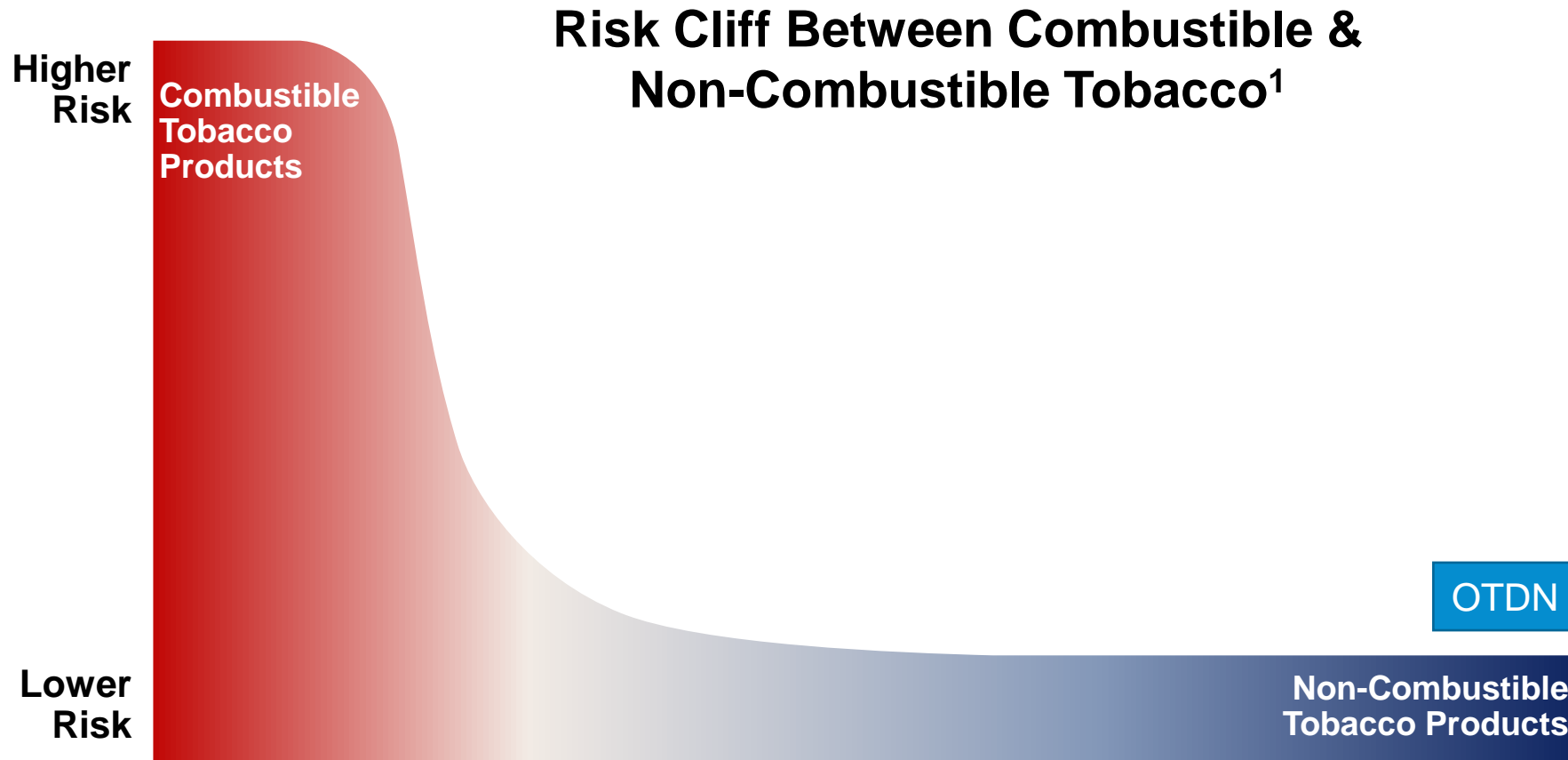
# Agenda

- Tobacco Harm Reduction
- Key Questions for oral tobacco derived nicotine (OTDN) Toxicity Assessment
- Nonclinical Toxicity Assessment Framework
- Summary





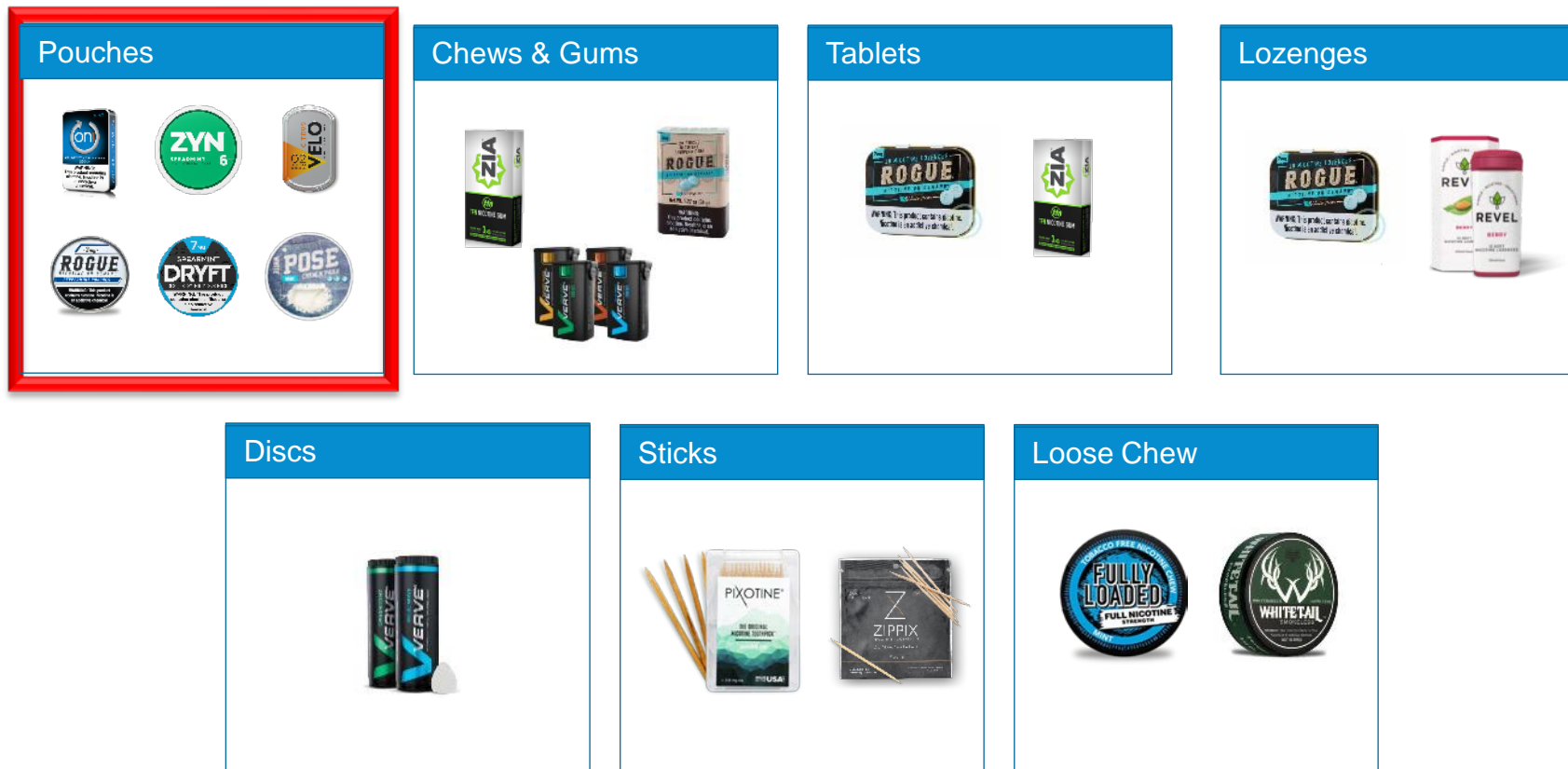
# Tobacco Harm Reduction



<sup>1</sup> Adapted from Nutt, et. Al Estimating the Harms of Nicotine-Containing Products Using the MCDA Approach. Eur. Addict Res 2014; 20:218-225. Evaluation criteria include; product specific mortality; product related mortality; product specific morbidity; dependence; loss of tangibles; loss of relationships; injury; crime; environmental damage; family adversities; international damage; economic cost; and community.



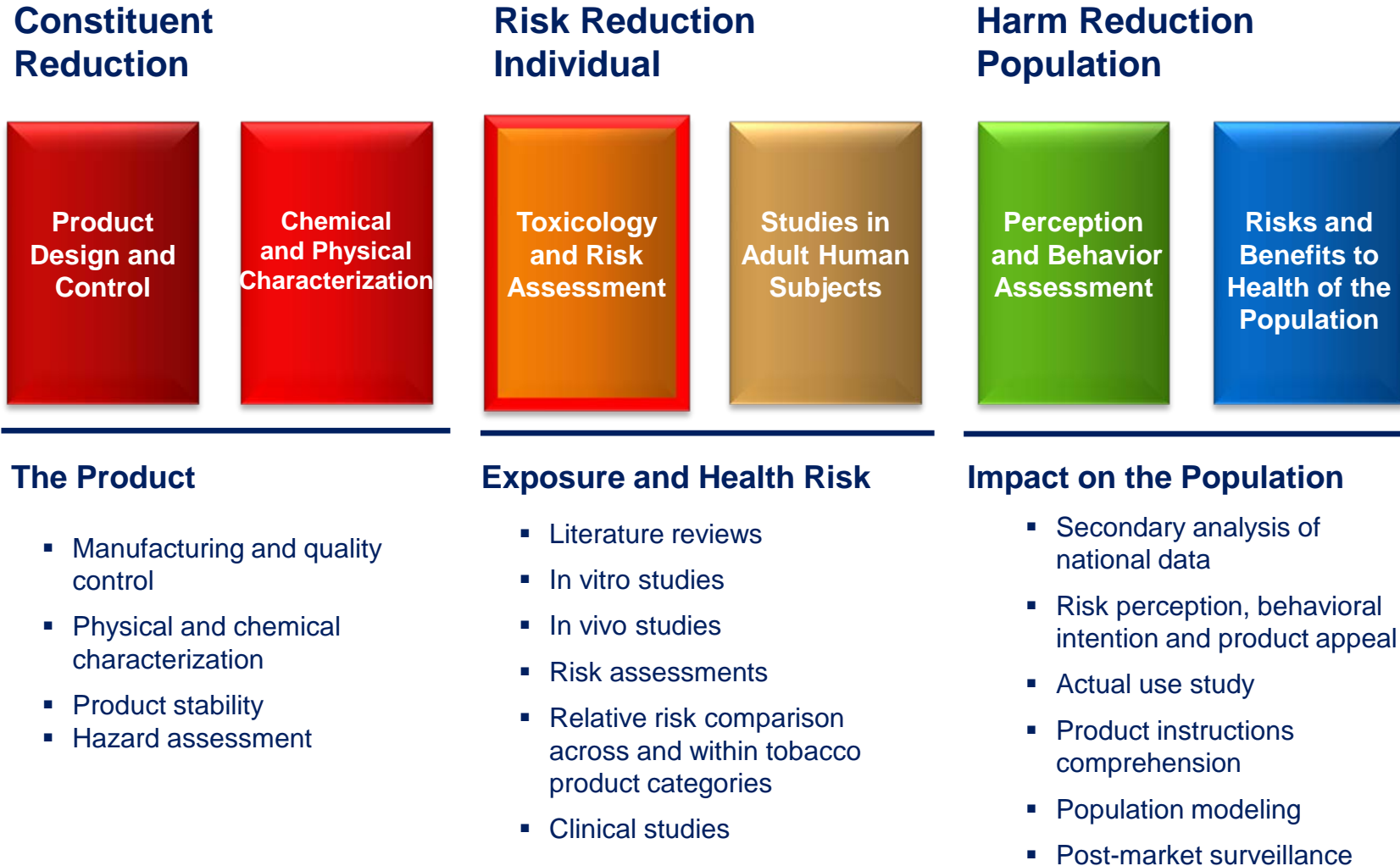
# Evolving Landscape of OTDN Products



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# Tobacco Harm Reduction Framework



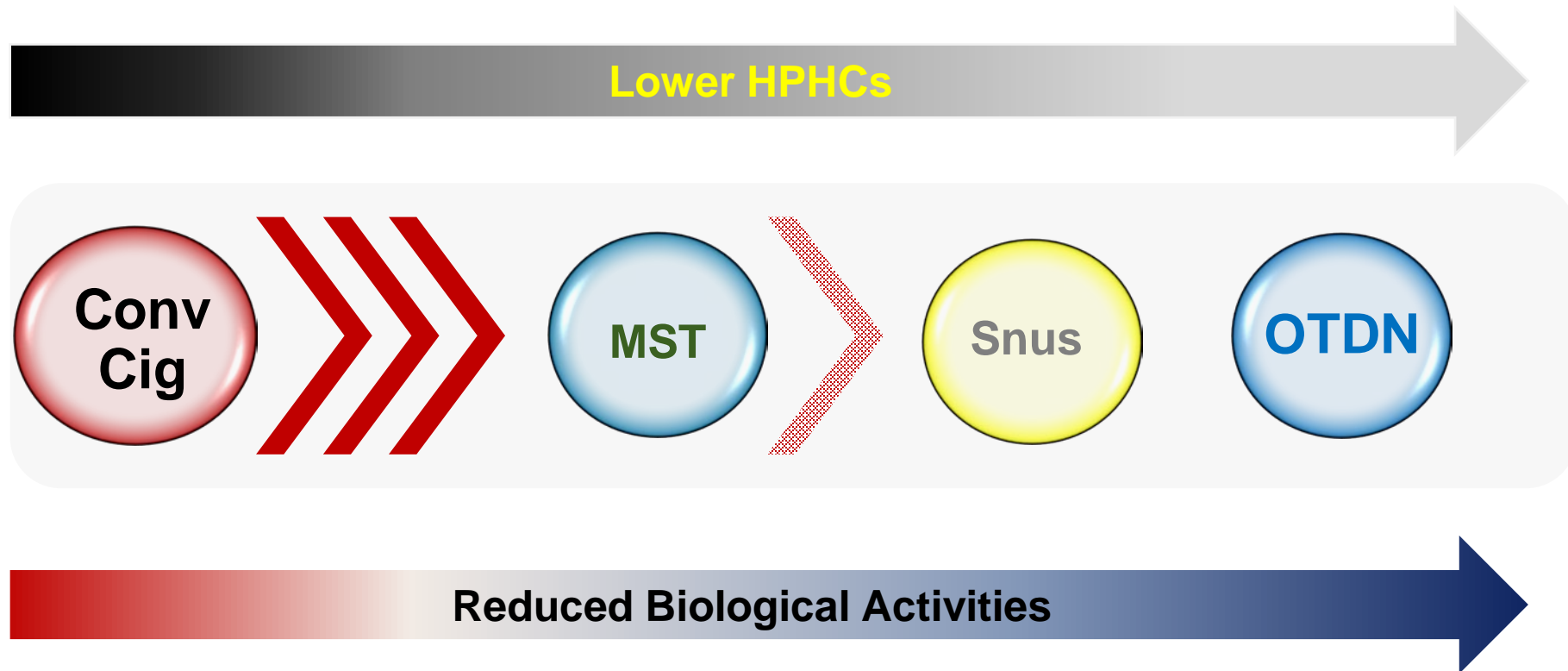
# Key Questions for OTDN Toxicity Assessment

- Reduced-risk potential – comparison to other tobacco products
  - Comparators across tobacco product categories
  - Comparators within OTDN category
- Inherent toxicity potential – risk assessment of ingredients
- Whole product toxicity evaluation – *in vitro* biological assays
  - Test material extraction and characterization
  - Standardized vs. mechanistic assays
  - Test systems and endpoints for *in vitro* assays for OTDN



# Comparator Products for Relative Toxicity Assessment

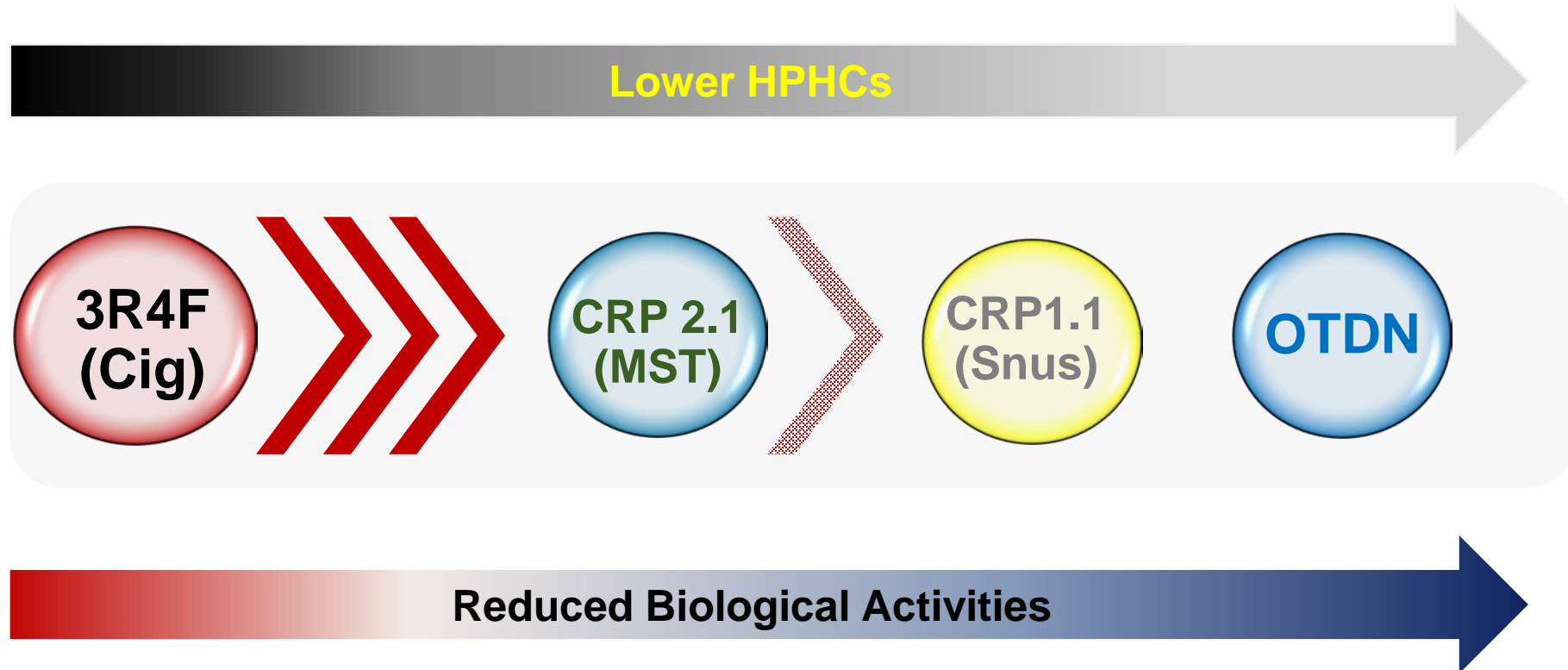
## Comparators across Tobacco Products Categories





# Comparator Products for Relative Toxicity Assessment

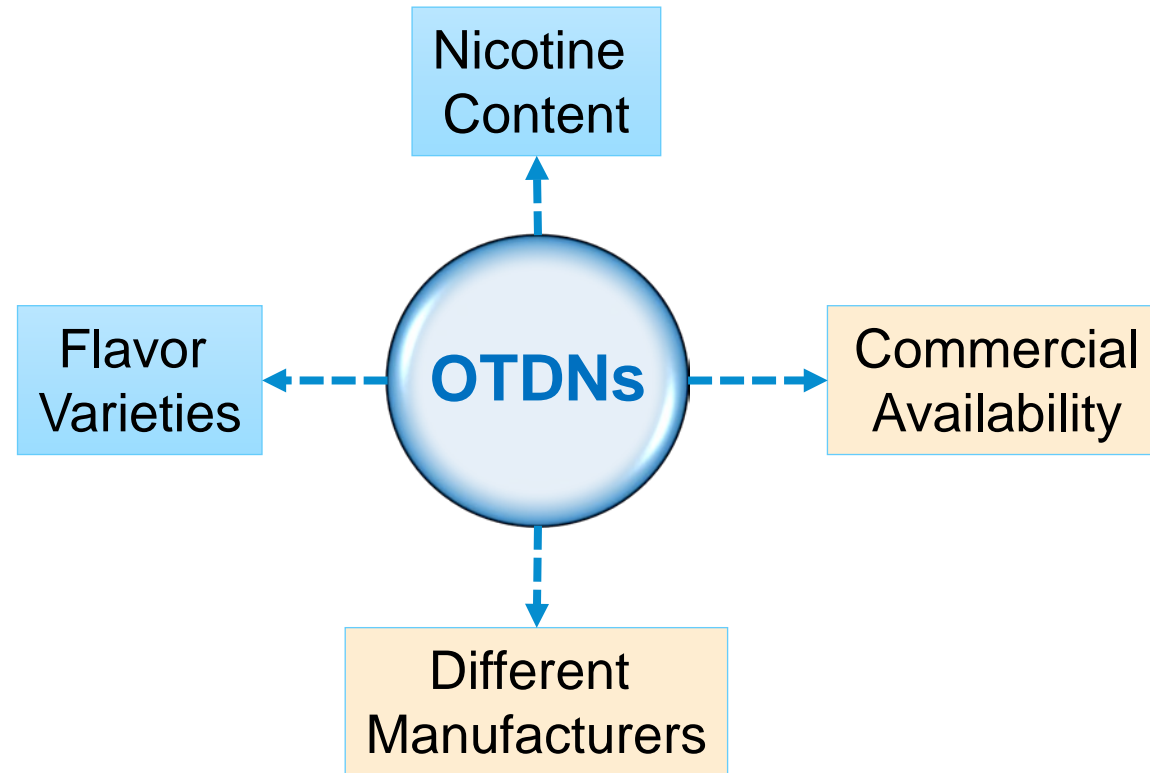
## Comparators across Tobacco Products Categories





# Comparator Products for Relative Toxicity Assessment

## Comparators within OTDN Category



**Low Biological Activities Compared to Cigarette**



# OTDN Nonclinical Toxicity Assessment Framework

I. Framework Overview

ST 57 - Zhang

II. Ingredient risk assessment

ST 58 – Morgan

Test products

III. Test product extraction and characterization

ST 59 - Smith

IV. *In vitro* OECD regulatory testing

ST 60 - Doshi

V. *In vitro* oral health mechanistic testing

ST 61 - Kumar





# Summary

- Thoughtful selection of comparator products for relative risk comparison across tobacco product categories and within OTDN product category
- A rigorous nonclinical toxicity assessment framework for OTDN
  - Comprehensive risk assessment on ingredients
  - Biologically relevant test product extraction for in vitro testing
  - Both standard OECD and new oral health mechanistic in vitro testing
- Preliminary data consistent with significantly lower *in vitro* toxicity between combustible & non-combustible oral products including OTDNs tested
- Reduced-risk potential upon complete switching





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