Tobacco Harm Reduction: A Chemistry Perspective of the Risk Continuum

Carlton Bequette[1], Amanda Hudson[2], Courtney Culbert[2]

[1] RJ Reynolds Tobacco Company, [2] RAI Services Company

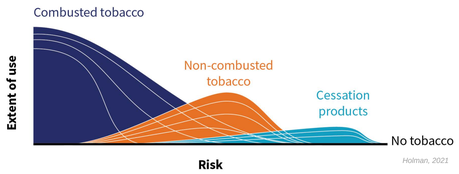
Abstract

Tobacco harm reduction (THR) is globally recognized in policy and regulation and is an important step in reducing the health impact of tobacco use. In 2001, the National Academies of Science stated "[tobacco] harm reduction refers to minimizing harms, decreasing total morbidity and mortality, without completely eliminating tobacco and nicotine use". A key pillar for Reynolds American is to reduce the health impact of our business by committing to providing adult tobacco consumers with a wide range of enjoyable and potentially less risky products, which aims to facilitate the migration of adult tobacco users down the risk continuum of tobacco and nicotine products. One of our priorities is supporting the science of THR through rigorous scientific assessment of potentially less harmful products (PLHPs) that have lower levels of harmful or potentially harmful constituents (HPHCs) as compared to combustible cigarettes. This study compares the analytical chemistry of tobacco and nicotine products across the continuum of risk to demonstrate the reduction of HPHCs as you move down the continuum.

Introduction

Tobacco harm reduction is an important public health approach that is an opportunity for adult tobacco users to move from combustible cigarettes to potentially less harmful products (PLHPs). One of our priorities is supporting the science of THR through rigorous scientific assessment of PLHPs that have lower levels of harmful or potentially harmful constituents as compared to combustible cigarettes. The aim of this study is to compare the analytical chemistry of tobacco and nicotine products across the continuum of risk to demonstrate the reduction of HPHCs as you move down the continuum. Products from Reynolds and competitors were analyzed for select HPHCs (carbonyls, TSNAs, metals) using validated methodology in an accredited laboratory. The levels of HPHCs were normalized to the unit of use for each tobacco product category, such as cigarettes (per cigarette), HTP (per stick), vapor (per 15 puffs), oral products (per pouch, per lozenge). Additionally, the levels of HPHCs were normalized per milligram of nicotine to demonstrate levels of analytes based solely on the amount of nicotine consumed.

Tobacco Harm Reduction – Risk Continuum



Study Design

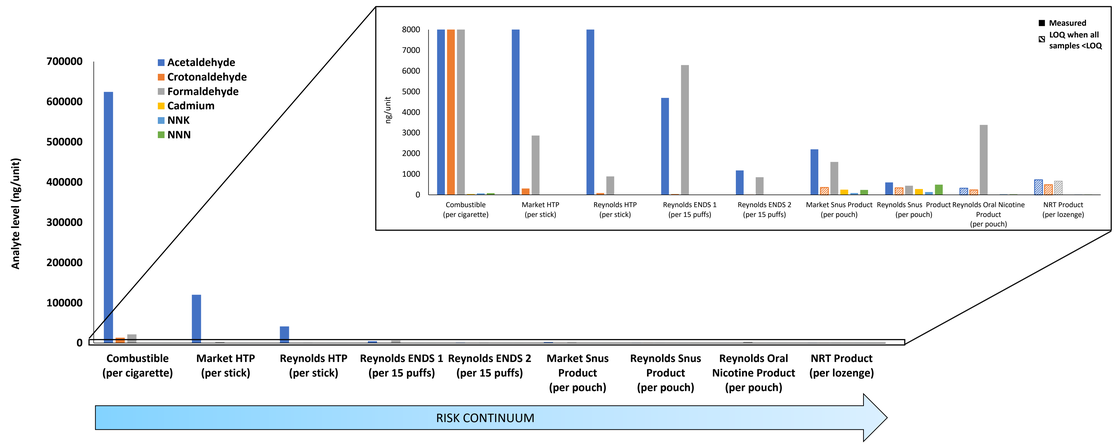
Tobacco products from across the risk continuum were evaluated for select HPHCs for comparison to combustible cigarettes.

- Combustible Cigarettes – Market survey (60+ commercial cigarettes)
- Heated Tobacco Product (HTP) – RJR and a market comparator product
- Electronic Nicotine Delivery System (ENDS) – two RJR vapor products
- Snus – RJR and a market comparator product
- Oral Product – RJR oral nicotine product
- Nicotine replacement therapy (NRT) – Commercially available product

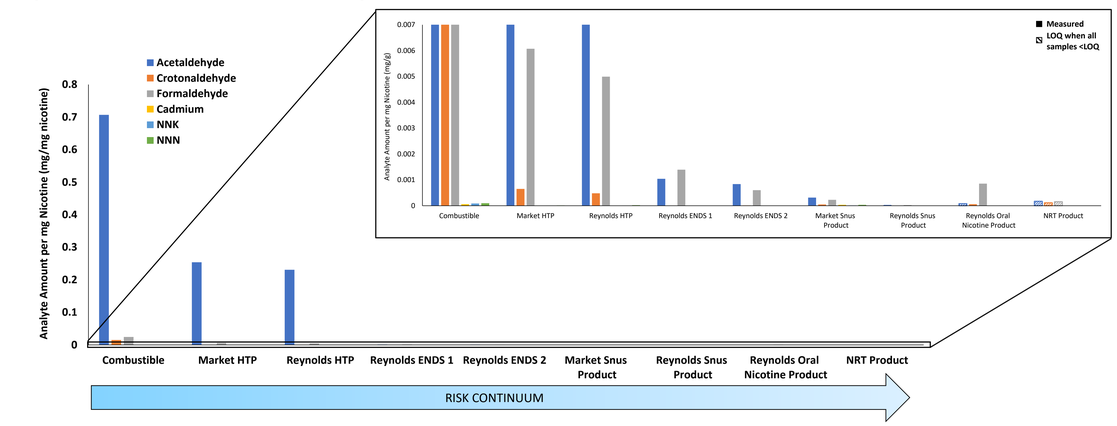
All mainstream smoke (MSS) and aerosol were generated using ISO or non-intense aerosolization regimens.

Results

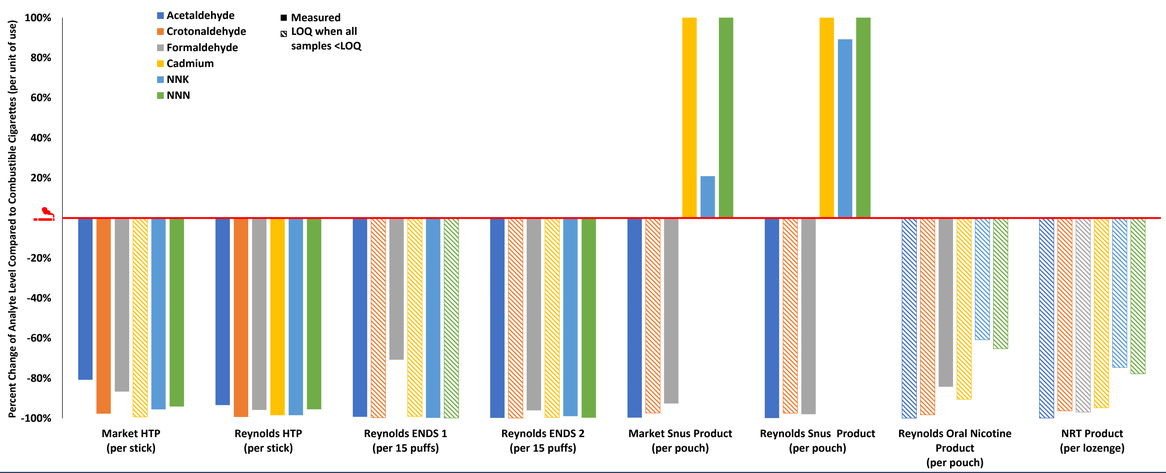
Analyte Levels Across the Risk Continuum – Analyte Level Per Unit of Product Use



Analyte Levels Across the Risk Continuum – Analyte Level Normalized to Nicotine



Percent Change of Analyte Levels Compared to Combustible Cigarettes – Per Unit of Use



Objectives and Endpoints

Objective:

To demonstrate and compare the levels of specific HPHCs as you move down the continuum of risk from combustible cigarettes to nicotine replacement therapies.

Endpoints:

Specific HPHCs from tobacco products across the continuum of risk:
Carbonyls – Acetaldehyde, Crotonaldehyde, Formaldehyde
Metals – Cadmium
TSNAs – n-nitrosonornicotine (NNN), 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK)

Materials and Methods

Aerosolization and Smoking:

ENDS: Aerosolization was performed on a linear smoking machine with a 55 mL volume puffs of 3 second duration every 30 seconds with a square wave puff profile.
HTP: Smoking was performed on a linear or rotary smoking machine with a 35 mL volume puffs of 2 second duration every 60 seconds with a bell-shaped puff profile and no vent blocking.
Cigarettes: Smoking was performed on a linear or rotary smoking machine with a 35 mL volume puffs of 2 second duration every 60 seconds with a bell-shaped puff profile and no vent blocking.

Analytical Methods

1. **Carbonyls –** Sample was extracted in DNPH (2,4-dinitrophenylhydrazine) solution on a shaker. MSS/Aerosol samples collected using an impinger. After derivatization, the solution was filtered and analyzed by high performance liquid chromatography with UV detection (HPLC-UV).
2. **Metals –** Sample digested in nitric acid by closed vessel microwave. MSS/aerosol was passed through an impinger containing nitric acid and analyzed by inductively coupled plasma mass spectroscopy.
3. **Nicotine –** Sample was extracted using an alcohol solution and analyzed by gas chromatography with a flame ionization detector. MSS/aerosol samples collected onto a CFP before extraction.
4. **TSNAs –** Sample was extracted using an ammonium acetate solution containing deuterated internal standards and analyzed by liquid chromatography coupled with quadrupole mass spectroscopy (LC/MS-MS) using positive electrospray ionization. MSS/aerosol samples collected onto a CFP before extraction.

Statistical Methods

1. **Unit of Use –** All data was converted from the reported value to per unit of use, if necessary:
   Combustible Cigarette – Per Cigarette
   HTP – Per Stick
   ENDS – Per 15 puffs (see Ref. 2)
   Snus, Oral Nicotine Product – Per pouch
   NRT – Per Lozenge
2. **Normalization to Nicotine –** Data converted from reported value to amount per milligram of nicotine.
   Ex. Market Snus – 7mg/g nicotine, 90 ng/g NNK
   Normalization: 90/7 = 12.85 ng NNK per 1mg nicotine
3. **Percent Change –** Calculation: (Value 1 – Value 2) / Value 1 * 100

Conclusions

Select HPHCs were evaluated in tobacco products that represent the continuum of risk: combustible cigarettes, heated tobacco products, electronic nicotine delivery systems, snus, oral nicotine products, and nicotine replacement therapies.

Analyte levels of specific harmful and potentially harmful constituents are reduced as you move down the risk continuum for each unit of use and per milligram of nicotine.

Tobacco harm reduction is an important opportunity for adult tobacco users to move from combustible cigarettes to potentially less harmful products, which have lower levels of select HPHCs.

References

1. Holman, M. R. (2021). "FDA Perspective: Opportunities for Harm Reduction The Need for Science and Engagement." Tobacco Science Research Conference, Boston, MA, USA.
2. In K. Stratton, L. Y. Kwan, & D. L. (2018) "Public Health Consequences of E-cigarettes". National Academies of Sciences, Engineering, and Medicine.

To see more of our scientific research visit ReynoldsScience.com

RAI SERVICES COMPANY