Global Forum on Nicotine

Scientific assessment framework to quantify the risk reduction potential of next generation products

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Parallel 5, Science track: Reduced harm nicotine products and their role in tobacco smoking cessation
Warsaw, Poland
Agenda

• Approach to assessing risk profile of Tobacco Heating Products relative to cigarettes

• Summary of evidence gathered to date

• Assessing population health impact
A THREE-STEP SCIENTIFIC JOURNEY TO ASSESSING THE RISK PROFILE OF NEXT GENERATION PRODUCTS

01 EMISSIONS
- Chemical studies
- \textit{in vitro} toxicological studies

02 EXPOSURE
- Behavioral studies
- Short term clinical studies

03 RISK
- Individual risk studies
- Population risk studies

\textsuperscript{a}Murphy J \textit{et al} (2017) \textit{Reg Tox Pharm} doi.org/10.1016/j.yrtph.2017.09.008
## INTRODUCTION: TOBACCO HEATING PRODUCTS

### ORIGIN OF HARMFUL AND POTENTIALLY HARMFUL CONSTITUENTS

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>TOBACCO PRESENT</th>
<th>AEROSOL FORMATION MECHANISM</th>
<th>NUMBER OF COMPOUNDS IN AEROSOL</th>
<th>HPHC FORMATION MECHANISMS</th>
<th>UNTARGETED EMISSIONS(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3R4F reference cigarette</td>
<td>Yes</td>
<td>Combustion &amp; pyrolysis</td>
<td>&gt;6,500</td>
<td>• Transfer from tobacco • Pyrosynthesis of tobacco</td>
<td><img src="image1.png" alt="Image" /></td>
</tr>
<tr>
<td>glo</td>
<td>Yes</td>
<td>Distillation and elution</td>
<td>700-1000</td>
<td>• Transfer of toxicants from leaf • Thermal degradation of humectants • Extractables &amp; Leachables from device during storage or heating</td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
</tbody>
</table>

\(^a\)Rawlinson et al. (2017) J Chrom A, 1497, 144-154

![Image](image3.png)
glo heats but does NOT combust tobacco

Cigarettes burn tobacco at around 900°C\textsuperscript{a}
glo\textsuperscript{TM} heats tobacco up to a maximum of 240°C\textsuperscript{b}

5 step assessment\textsuperscript{c}

1) Thermogravimetric analysis
2) Temperature profiling
3) Combustion markers
4) Toxicants
5) Physical Integrity

\textsuperscript{b}Forster, M et al (2015) Chem Cent, 9, 20
\textsuperscript{c}Eaton et al (2018) Regul. Toxicol. Pharma., 93, 4-13
glo heats but does NOT combust tobacco

Forster M et al., Regulatory Toxicology Pharmacology, 2018b, 93, 14–33. https://doi.org/10.1016/j.yrtph.2017.10.006; Measured using the Health Canada Intense machine puffing regime. These qualities do not necessarily mean this product produces less adverse health effects than other tobacco products.
In laboratory tests, glo promotes substantially less disease relevant gene changes in comparison to a scientific reference cigarette, 3R4F\textsuperscript{a,b,c}

2. glo and a scientific reference cigarette (3R4F) puffed on machines using the Health Canada Intense (HCI) regime: The contents of glo vapour differ significantly from cigarette smoke, however, these qualities and the above responses do not necessarily mean this product produces less adverse health effects than other tobacco products;
3. Ingenuity Pathway Analysis (IPA) has broadly been adopted by the life science research community and is widely cited for the analysis, integration, and interpretation of data derived from ‘omics experiments.

In lab based tests, glo promotes substantially less disease relevant gene responses in comparison to a cigarette\textsuperscript{a,b}
- 3-D cellular system (Mucilair\textsuperscript{TM}) exposed to glo heated tobacco vapour and cigarette smoke
- Ingenuity Pathway Analysis\textsuperscript{c} of >22,000 gene responses grouped into disease relevant categories
The results indicated that smokers who switched completely from smoking cigarettes to using glo experienced similar reductions in exposure (to a number of smoke toxicants) as those who stopped smoking.\textsuperscript{a, b}
ASSESSING RISK: INDIVIDUAL & POPULATION LEVELS

INDIVIDUAL RISK = Risk posed to the user only

POPULATION RISK = Risk posed to the whole population*

*Population = smokers, NGP users, former smokers, never smokers, youth
ASSESSING RISK: INDIVIDUAL & POPULATION LEVELS

INDIVIDUAL RISK =
• ‘1 year’ clinical study (risk markers)
• Systems Biology

POPULATION RISK =
Population studies*

*Population = smokers, NGP users, former smokers, never smokers, youth
IN THE ABSENCE OF EPIDEMIOLOGY, WE WILL USE POPULATION STUDIES TO ASSESS THE IMPACT OF GLO ON POPULATION HEALTH EFFECTS.

Population risk assessment

Population modelling

Annual surveys + ER* estimates

Assess impact of glo on:
- Morbidity (disease incidence)
- Mortality (smoking related deaths)

*ER = Excess Risk
Population modelling challenges & opportunities

Challenges:
• Dose response curves are unknown for relating exposure to risk
• Estimation of Excess Risk (ER) for each smoking status particularly NGP solus and dual use
• Agreement on criteria of smokers, former smokers, NGP status etc.
• In the absence of agreed criteria, ER assumptions and methodological approaches - very different outcomes can be achieved

Opportunities:
• Multi-disciplinary approach allows for integration of toxicological and clinical data to estimate ER
• Adverse Outcome Pathways can organise data into disease relevant frameworks
• Delphi panel approach to confirmation of criteria, assumptions and ERs
• Expert ring trials with different models and same input data to align on criteria, assumptions and models
Summary

• We have a published framework for assessing reduced emissions, exposure and risk

• External review of THP science is only starting to emerge, but our glo data on emissions and exposure show their risk reduction potential

• Substantiation of reduced risk requires additional longer term clinical and population based studies

• Modelling techniques have the potential to assess population risk in the absence of epidemiology