CORESTA Electronic Cigarette Task Force

Dr. Rob Stevens

Secretary, Smoke Science Study Group, CORESTA Scientific Commission
Secretary, CORESTA E-Cigarette Task Force

FDA Public Workshop – Electronic Cigarettes and the Public Health
December 10 – 11, 2014, Silver Spring, MD
Introduction & Purpose of CORESTA

- CORESTA is the Cooperation Centre for Scientific Research Relative to Tobacco

- It is an Independent Association:
  - Founded in 1956
  - Headquartered in Paris
  - Governed under French law

- Purpose of CORESTA:
  - Encourage international cooperation to actively work on tobacco-related areas of research
CORESTA Membership (by Geographic Region)

- Europe: 55%
- North America: 19%
- Latin America: 6%
- Asia: 17%
- Africa: 3%
CORESTA Membership
(by core activity)

- Consumer Products: 29%
- Academics & NPO: 18%
- Analyses: 16%
- Agrochemicals: 5%
- Leaf & Seeds: 11%
- Equipment & Components: 21%

FDA e-cigarette Workshop:
Dec. 10-11, 2014

Centre de Coopération pour les Recherches Scientifiques Relatives au Tabac
Cooperation Centre for Scientific Research Relative to Tobacco
First TF meeting was on May 2013

TF Coordinator
- Dr. Charles Garner - RJ Reynolds Tobacco

TF Secretary
- Dr. Rob Stevens - Lorillard Tobacco Company

TF membership continues to expand
- ≈ 55 people from more than 45 different organizations
- 15 countries
- North America, Europe, Asia
1. To create a document on worldwide product definition and definitions of terms to support harmonization of nomenclature.

2. To gather and share preliminary data on analysis relevant to e-cigarettes worldwide with a view to making recommendations for product testing.

3. To define the relevant categories of products for potential further CORESTA studies.
E-Cigarette Task Force Studies

- **E-Liquid Proficiency Study**
  - Major Ingredients
  - Methods Comparison

- **Aerosol Proficiency Study**
  - Major Ingredients
  - Puff by Puff and Total Yields
  - Selection of Puffing Parameters
  - Methods Comparison
To determine consistency of results between labs using their own methods for analysis of the same set of e-liquid samples

9 Labs tested the same 11 samples including a study control

Analytes Tested:

- Nicotine (0 – 1.6%)
- Glycerin (0 – ~100%)
- Propylene Glycol (0 – ~100%)
- Water (0 – 10%)
### General Information across Methods

<table>
<thead>
<tr>
<th>Sample Prep</th>
<th>Analysis</th>
</tr>
</thead>
</table>
| • Weigh 100 – 1000 mg*  
• Dilute with alcohol (10 – 100 mL)  
• Mix/Shake (10s – 3 hours)  
• Weight and volume used varied by analyte | • GC-TCD or Karl Fischer for water  
  • Packed column if TCD (most)  
  • GC-FID for other analytes  
  • Capillary column  
  • DB-Wax columns for most  
• 4 – 12 calibration standards (GC)  
• Linear (IS) calibration  
• r² >0.99 |

*Lab 6 measured by volume (25 – 100 µL) and diluted with 1mL solvent
%Error for Control Sample

<table>
<thead>
<tr>
<th></th>
<th>Nicotine</th>
<th>Glycerin</th>
<th>PG</th>
<th>Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error range for all labs</td>
<td>0.2 – 4.5 %</td>
<td>1.6 – 13%</td>
<td>0.2 – 10%</td>
<td>2.1 – 18%</td>
</tr>
</tbody>
</table>

- A Study Control was made by directly weighing analytical grade chemicals into tared sample vessels using a 5-place analytical balance.
- Precision for each lab was high (<5% RSD).
- Error from Actual value was low for all labs for each analyte.
- Error was highest for water (<18% error).

%Error Calculated as (Reported – Actual)/Actual * 100

The actual value is based on each lab’s control sample rather than on the target value.
Results for Control Sample - Water

- **Target Value = 9%**
- **Karl Fischer methods averaged 3% error**
- **GC/TCD methods averaged 13% error**
## Nicotine Results Compared to Nominal Value

<table>
<thead>
<tr>
<th>Sample</th>
<th>Nominal Value (w/w)</th>
<th>Avg. of all Labs (w/w)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample 1</td>
<td>1.6%</td>
<td>1.48 ± 0.07</td>
</tr>
<tr>
<td>Sample 2</td>
<td>1.6%</td>
<td>1.57 ± 0.07</td>
</tr>
<tr>
<td>Sample 3</td>
<td>0.0%</td>
<td>--</td>
</tr>
<tr>
<td>Sample 4</td>
<td>0.79%</td>
<td>0.73 ± 0.03</td>
</tr>
<tr>
<td>Sample 5</td>
<td>0.79%</td>
<td>0.72 ± 0.03</td>
</tr>
<tr>
<td>Sample 6</td>
<td>0.54%</td>
<td>0.55 ± 0.02</td>
</tr>
<tr>
<td>Sample 7</td>
<td>0.53%</td>
<td>0.53 ± 0.01</td>
</tr>
<tr>
<td>Sample 8</td>
<td>0.53%</td>
<td>0.54 ± 0.03</td>
</tr>
<tr>
<td>Sample 9</td>
<td>0.48%</td>
<td>0.46 ± 0.01</td>
</tr>
<tr>
<td>Sample 10</td>
<td>0.58%</td>
<td>0.58 ± 0.02</td>
</tr>
<tr>
<td>Sample 11 (Control)</td>
<td>1.0%</td>
<td>1.03 ± 0.03</td>
</tr>
</tbody>
</table>

* Reported as Average ± Standard Deviation
Analytical methods used across the 9 different labs were based on alcohol dilution and GC-FID analysis for nicotine, glycerin, and PG.

Water analyses were performed using either GC-TCD or Karl Fischer analysis.

The laboratory results showed high accuracy and precision.

Use of study controls and reporting in mg/mL and mg/mg are recommended.
To determine consistency of results between labs using the same puffing regimen and their own methods for analysis

4 laboratories conducted a puffing parameters evaluation

14 labs tested the same 8 samples using the recommended puffing parameters

Analytes Tested:

- Total Yield, Nicotine, Glycerin, Propylene Glycol, Water
## E-Cigarette Aerosol Studies Method Summary

<table>
<thead>
<tr>
<th>In Common (Most Labs)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sample Handling</strong></td>
</tr>
<tr>
<td>• Stored unopened under ISO conditions* prior to testing</td>
</tr>
<tr>
<td><strong>Collection</strong></td>
</tr>
<tr>
<td>• 20 port Conventional Linear Smoking machine</td>
</tr>
<tr>
<td>• 44mm CFP, Conditioned to ISO std*</td>
</tr>
<tr>
<td>• Room Conditioned to ISO smoking std*</td>
</tr>
<tr>
<td><strong>Sample Prep</strong></td>
</tr>
<tr>
<td>• Isopropanol with heptadecane and ethanol as IS, 20mL</td>
</tr>
<tr>
<td>• Shake to extract, 30min</td>
</tr>
<tr>
<td>• Possible additional dilution for Gly/PG</td>
</tr>
<tr>
<td><strong>Analysis</strong></td>
</tr>
<tr>
<td>• GC-TCD for water</td>
</tr>
<tr>
<td>• Packed column (most)</td>
</tr>
<tr>
<td>• GC-FID for other analytes</td>
</tr>
<tr>
<td>• Capillary column</td>
</tr>
<tr>
<td>• DB-Wax columns for most</td>
</tr>
<tr>
<td>• 6 – 12 calibration standards</td>
</tr>
<tr>
<td>• Linear (IS) calibration</td>
</tr>
<tr>
<td>• $r^2 &gt; 0.99$</td>
</tr>
</tbody>
</table>

* ISO 3402:1999
## Methods Summary

<table>
<thead>
<tr>
<th>Differences</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Collection</strong></td>
<td>Lab E – used a rotary machine, condition during vaping: 40% RH, pad conditioning: 40% RH</td>
</tr>
</tbody>
</table>
| **Sample Prep** | Lab C – 25mL solvent  
Labs F, G, H, L – 10mL solvent  
Shake time 20min - 60min among labs  
IS anethole, octadecane, quinoline and methanol also used |
| **Analysis** | A range of columns and conditions were used; most labs used 2 GC runs some used 3, one used 4  
Sometimes dual column (2 runs in one) |
Impact of Puffing Parameters on Total Yield

Lab 2 – Disposable Product

Lab 3 – Disposable Product

Lab 4 – Disposable Product

- No difference in total aerosol collected matter (ACM) yield between puffing regimes
- Precision is similar among test sets
### Range in Total Yield across all Puffing Regimes

<table>
<thead>
<tr>
<th>Lab</th>
<th>(%) Total PG</th>
<th>(%) Total Nicotine</th>
<th>(%) Total Glycerin</th>
<th>(%) Total Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab 1 - Rechargeable</td>
<td>47 - 48</td>
<td>1.21 - 1.24</td>
<td>26 - 27</td>
<td>11 - 13</td>
</tr>
<tr>
<td>Lab 2 - Disposable</td>
<td>56 - 58</td>
<td>1.8 - 1.9</td>
<td>28 - 29</td>
<td>8 - 11</td>
</tr>
<tr>
<td>Lab 2 - Rechargeable</td>
<td>57 - 59</td>
<td>1.8 - 1.9</td>
<td>28 - 29</td>
<td>8 - 12</td>
</tr>
<tr>
<td>Lab 3 - Disposable</td>
<td>0</td>
<td>1.60 - 1.61</td>
<td>71 - 76</td>
<td>19.6 - 20.3</td>
</tr>
<tr>
<td>Lab 3 - Rechargeable</td>
<td>0</td>
<td>1.3 - 1.4</td>
<td>72 - 76</td>
<td>15 - 16</td>
</tr>
<tr>
<td>Lab 4 - Disposable</td>
<td>42 - 47</td>
<td>1.0 - 1.2</td>
<td>33 - 39</td>
<td>15 - 18</td>
</tr>
<tr>
<td>Lab 4 - Rechargeable</td>
<td>34 - 41</td>
<td>1.4 - 1.5</td>
<td>41 - 44</td>
<td>11 - 13</td>
</tr>
</tbody>
</table>

Analytes trended with aerosol collected matter (ACM) for all regimes

% Composition was not affected by varying the regime
Recommendation:

- 55 ml puff volume, 3 second puff duration, 30 second puff interval, and square wave puff profile

E-Cigarette Aerosol Proficiency Study:

- 14 labs tested the same 8 samples using the recommended puffing parameters
- Analytes Tested:
  - Total Yield, Nicotine, Glycerin, Propylene Glycol, Water
PG, % of Aerosol Collected
Product 3 – Cumulative and per pad Aerosol yields
E-cig Mass Loss: ACM Ratio as Function of ACM

Product 3

E-cig Mass Loss : ACM Ratio

Total Pad ACM (mg)

0 20 40 60 80 100 120 140 160

E-cig Mass Loss : TPM Ratio

Total Pad TPM (mg)

0 20 40 60 80 100 120 140 160
Aerosol methods were similar among the participating labs

- Alcohol extraction followed by GC-FID and GC-TCD analysis

Results across most labs were very consistent for Nicotine, Glycerin, PG and Water

E-cig mass loss to ACM ratios were good metrics to verify results
Preliminary proficiency study for e-liquids

- Nicotine, water, glycerin and propylene glycol: Inter-lab study completed (May 2014)

Puffing parameters to collect e-cigarette aerosol

- Preliminary study completed in May 2014 and recommendation made: (55 ml puff volume, 3 second puff duration, 30 second puff interval, and square wave puff profile)

Preliminary proficiency study for e-cigarette aerosol

- Nicotine, water, glycerin and propylene glycol: Inter-lab study completed (October 2014)
Global interdisciplinary expertise from different sectors

Focus on advancing scientific knowledge

Well established procedures for developing methods

Leadership and coordination of inter-lab studies to recommend analytical methods
Questions?