Can innovation in vapour products bring more satisfaction with lower toxicant levels?

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AGENDA

• Foundations of tobacco harm reduction
• The science of Vype e-pen
• Evolving coil and wick
• The science of i-switch
BAT’s Transforming Tobacco strategy and approach is underpinned by the concept of Tobacco Harm Reduction.
Scientific publications on VYPE e-cigarettes

The world’s largest published dataset on a single vapour product
What has this science programme told us so far?

- Chemical studies show that the aerosols from our vapour products are much simpler, and with fewer toxicants and far lower levels of toxicants, than tobacco smoke.

- Indoor air quality studies have shown very little impact of the use of vapour products on indoor air, in sharp contrast to cigarette smoking.

- *In vitro* biological studies have shown that the consequence of lower toxicants is much reduced biological response to the aerosols (such as no mutagenicity, no genotoxicity) compared to cigarette smoke (which is highly mutagenic and genotoxic).

- Human clinical studies have shown rapid reductions in biomarkers of exposure to toxicants.
COMPARISON OF THE CHEMICAL COMPOSITION OF CIGARETTE SMOKE AND THE VAPOUR FROM VYPE e-pen2*

*These results do not necessarily mean this product is less harmful than other tobacco products


= level in vapour is greater than 95% reduced compared to smoke
Vype e-pen 2 has reduced toxicity relative to cigarettes

OECD TG 471: Bacterial Reverse Mutation Test, S. typhimurium TA98

Exposure to reference cigarette smoke caused mutations in a dose dependent manner; e-cigarettes gave no response

These qualities do not necessarily mean this product produces less adverse health effects than tobacco products


Switching to Vype e-pen 2 following 2 weeks 3R4F exposure reversed biological effects \textit{in vitro}.

\textit{Inflammatory cytokine expression was greatly reduced compared to 4 week 3R4F exposure.}

These qualities do not necessarily mean this product produces less adverse health effects than other tobacco products.
iSwitch with PureTech blade technology gives improved consumer satisfaction with less nicotine, more aerosol and with much lower toxicants

- **ePen2**
  - Gen1 nicotine salt
  - Core flavours

- **ePen3**
  - + Gen2 nicotine salt
  - + Improved wicking
  - + Optimised power management

- **iSwitch**
  - + Tailored nicotine salt
  - + Increased particle size = high flavour impact with 18mg nicotine,
    satisfaction with 3mg liquid
  - + PureTech atomizer

Substantially reduced toxicants is not sufficient alone to determine reduced risk
A revolutionary advance from coil-and-wick to proprietary new-to-world PureTech blade technology

**EXISTING COIL-AND-WICK TECHNOLOGY**

› Absorbent wick
› Electrical heating coil
› Small surface area
› Risks of dry out
› Variable particle size

**PURETECH Blade**

› **10x** larger surface area vs. best-in-class cotton wick (ePen3)
› Large aerosol particle size range
› Advanced temperature control
› Dynamic wicking
› Improved sensory performance
› Improved consumer satisfaction
› Less e-liquid nicotine required

![Steel matrix x200 magnification](https://example.com/steel_matrix.jpg)
### Emissions chemistry

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Reference cigarette</th>
<th>E-pen 2</th>
<th>E-pen 3</th>
<th>i=Switch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaldehyde (µg/puff)</td>
<td>208</td>
<td>0.12</td>
<td>0.07</td>
<td>NQ</td>
</tr>
<tr>
<td>Acrolein (µg/puff)</td>
<td>14.9</td>
<td>0.15</td>
<td>0.02</td>
<td>BDL</td>
</tr>
<tr>
<td>Formaldehyde (µg/puff)</td>
<td>5.11</td>
<td>0.39</td>
<td>0.06</td>
<td>0.04</td>
</tr>
<tr>
<td>Benzo(a)pyrene (ng/puff)</td>
<td>1.26</td>
<td>NQ</td>
<td>NQ</td>
<td>BDL</td>
</tr>
<tr>
<td>Carbon Monoxide (mg/puff)</td>
<td>2.99</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
</tr>
<tr>
<td>NNK (ng/puff)</td>
<td>26.6</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
</tr>
<tr>
<td>NNN (ng/puff)</td>
<td>24.8</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
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<tr>
<td>1,3-butadiene (µg/puff)</td>
<td>11.1</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
</tr>
<tr>
<td>Benzene (µg/puff)</td>
<td>8.08</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
</tr>
</tbody>
</table>
**iSwitch - Unprecedented reductions in biological activity seen to date in our laboratory tests of vapour products**

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Number of lung-disease-relevant genes perturbed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air vs Reference Cigarette* (24 hrs)</td>
<td>5603</td>
</tr>
<tr>
<td>Air vs iSwitch (24 hrs)</td>
<td>0</td>
</tr>
</tbody>
</table>

Vapour from iSwitch had **no impact on lung-disease-relevant gene perturbations** in a 3D cellular system using human airway epithelial cells.

In extremis *in vitro* testing for cytotoxicity shows all Vype products are much less toxic than cigarette smoke, with **iSwitch the least toxic**.
First clinical study on iSwitch confirms large reduction in toxicant exposures

<table>
<thead>
<tr>
<th>Toxicant</th>
<th>% Reduction</th>
<th>iSwitch</th>
<th>Cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>-90%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>NNK</td>
<td>-80%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>NNN</td>
<td>-70%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>Acrolein</td>
<td>-60%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
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<tr>
<td>Crotonaldehyde</td>
<td>-40%</td>
<td><img src="chart.png" alt="Graph" /></td>
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</tr>
<tr>
<td>Benzene</td>
<td>-30%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>1,3 Butadiene</td>
<td>-20%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>Acrylamide</td>
<td>-10%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>o-Toluidine</td>
<td>-5%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>Pyrene</td>
<td>-20%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>Ethylene oxide</td>
<td>-30%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>Acrylamide (AAMA)</td>
<td>-50%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
<tr>
<td>Acrylamide (GMN)</td>
<td>-60%</td>
<td><img src="chart.png" alt="Graph" /></td>
<td></td>
</tr>
</tbody>
</table>

14 BoEs for cigarette smoke toxicants measured

All **BoEs significantly reduced** for subjects switching to iSwitch*

In most cases **BoEs reduced to levels similar to cessation**

*o-Toluidine significant after one inexplicably high value removed from cessation arm (sensitivity test)

These substantially reduced toxicant exposures are not sufficient alone to determine reduced risk
Nicotine salts help drive satisfaction through increased nicotine delivery closer to that of a cigarette.

![Graph showing mean plasma nicotine concentration over time for different nicotine delivery methods (Cigarette ad libitum, Vype ePen 3 (30 mg/mL; protonated) ad libitum, Vype ePen 3 (18 mg/mL; protonated) ad libitum, Vype ePen 3 (18 mg/mL; unprotonated) ad libitum, Vype ePen 2 (18 mg/mL; unprotonated) ad libitum).]

Ebajemito, JK et al., unpublished data.
SUMMARY

• Vaping products continue to evolve

• All vaping products are likely to generate much lower levels of toxicants than found in cigarette smoke

• The latest technologies that improve wicking and manage aerosol generation can provide both better satisfaction and even lower toxicant levels in emissions
THANK YOU