INTRODUCTION

The Family Smoking Prevention and Tobacco Control Act (2009) gives the Food and Drug Administration (FDA) regulatory authority over the manufacture, marketing, and distribution of tobacco products. With the goal of improving public health and as a part of the required information in new pre-market tobacco product applications, information must be provided regarding potential health risks associated with a new product.

Respiratory toxicity is specifically洽谈 by the FDA for Center for Tobacco Products (CTP) as an important human health effect that can result from using inhalable product constituents. In vitro models that are human-relevant. Many available in vitro models for product applications, information must be provided regarding potential health risks associated with a new product. In summary, PG, a common E-vapor product ingredient, at 1.2% had a significant effect on cell viability. All PG concentrations were statistically different from the untreated control (UC) group. Significant differences were noted between day 8 and 16. HuPCLS were exposed via media to positive controls (Phortress and Phorsett), the human-relevant reference material. UC lost 30% viability while WST-8 results indicated no loss over 16 days in culture.

RESULTS

Viability & Osmolality

All treatment media were tested for osmolality and included airways and respiratory parenchyma. Histology Results:

• Positive Controls elicited tissue damage as assessed by the reference materials (PC) performed as expected. The high osmolality of the exposure media containing the 1.2% PG is hypothesized to be the cause of the significant loss of WST-8 viability – it is expected that a longer culture would have shown this effect histologically.

Osmolality Results:

• All treatment media were tested for osmolality and compared to the accepted human physiological range (275-295 mOsm/kg). Of all exposure media, only the 0.1% and 1.2% PG groups had measured values higher than the normal human range. Of these, only 1.2% PG caused tissue damage in the WST-8 viability assay.

CONCLUSIONS

For 16-days post-exposure, HuPCLS exhibited characteristic retention of overall health and viability, as measured using the WST-8 viability assay, tissue culture conditions, and criteria for evaluating in vitro models.

Combining the histomorphological and histosurgical assessment of HuPCLS viability allows for a more thorough assessment of treatment impact on human health. The decision process for regulatory clearance will be significantly impacted.

The respiratory media (PM) performed as expected. The high osmolality of the exposure media containing the 1.2% PG is hypothesized to be the cause of the significant loss of WST-8 viability – it is expected that a longer culture would have shown this effect histologically.

Development and Validation of HuPCLS as a cytotoxicity assay has made a significant amount of additional replicate experiments, testing all end points.

REFERENCES

Behring, H. P., et al. (2013). "In vitro exposure of precision-cut lung slices to 2,6-4-tert-amyl-3-methylphenyl-5-fluoroanthranilic acid (pentafluoroanthranilic acid)." Toxicol In Vitro 27(7): 1236-43.


Table 3: Osmolality Readings

<table>
<thead>
<tr>
<th>Exposure Group</th>
<th>0.1% PG</th>
<th>0.5% PG</th>
<th>1.2% PG</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 harvest</td>
<td>277 ± 7</td>
<td>284 ± 6</td>
<td>278 ± 0</td>
</tr>
<tr>
<td>8 harvest</td>
<td>274 ± 8</td>
<td>290 ± 7</td>
<td>276 ± 7</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>275 ± 6</td>
<td>287 ± 6</td>
<td>277 ± 4</td>
</tr>
</tbody>
</table>

* Significantly lower than untreated control (UC; p<0.05)

EXPERIMENTAL:

1. HuPCLS culture, UC lost 30% viability while WST-8 results indicated no loss over 16 days in culture.

2. PK (0-4)

3. Average derived from 4-7 PCLS/time point

4. 1.7 ± 0.2 73832 0.12 0.0 ± 0.0

5. Bleomycin or Phortress, UC lost 30% viability while WST-8 results indicated no loss over 16 days in culture.

RESULTS

Viability & Osmolality

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