Exposure to cigarette smoke toxicants in smokers who switch to using the glo™
tobacco heating product

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Introduction
Tobacco heating products (THPs) represent a subset of the next-generation nicotine
and tobacco product category, in which tobacco is typically heated at temperatures
of less than 350°C instead of burning (600°C) and has the potential to significantly
reduce the majority of cigarette smoke toxicants. The use of THPs holds great
potential for reducing the harm associated with tobacco use but this needs to be
scientifically proven.

Objective
To examine changes in biomarkers of exposure (BoE) to cigarette smoke toxicants
when smokers switch to using the novel THP, THP1.0 (commercially known as glo™)
(Figure 1) for 5 days, compared with those seen in smokers who remain smoking
combustible tobacco cigarettes.

Approach and Methods
We performed a two-centre, in-clinic (confine), forced-switching, randomised
controlled clinical study in Fukuoka, Japan (UMIN000024988, ISRCTN14301365).
Baseline levels of BoE to selected gas and particulate phase cigarette smoke
toxicants in the exhaled breath and urine of 180 smokers were compared to those
seen when the smokers either remained smoking combustible cigarettes or switched
to using a mentholated or non-mentholated THP1.0 for 5 days. The study was IRB
approved and run in accordance with ICH-GCP. Subjects provided written informed
consent prior to study participation and were deemed healthy following medical
examination and clinical laboratory screening. Smoking status was verified by
exhaled carbon monoxide (eCO) and urinary cotinine measurements.

Subjects were healthy male or female smokers of Japanese origin aged 23-55.
Smoking status was verified by urinary cotinine and eCO at screening and admission.
Healthy status was verified by vital signs, clinical laboratory evaluations,
physical examination, ECG and lung function tests. Subjects typically smoked 10-30
cigarettes per day, within 6–8 mg ISO tar bands, with at least a 3-year smoking
history.

Main exclusion criteria were planning to quit smoking in next 12 months, regular use
of nicotine or tobacco products other than cigarettes, and non-inhalers (self-reported
or observed at admission). Female subjects were excluded if a positive pregnancy
test was performed at screening or admission.

All subjects smoked cigarettes for two consecutive 24-h periods, up to a limit of
120% of their self-reported usual daily consumption. All urine voided by each
subject was collected over each 24-h period and the urine tested for BoE. eCO was
also measured on both days.

At end of baseline period, subjects were randomised to either continued smoking or
THP1.0 use groups. They remained in the clinic for a further 5 days and 24-hour
urine samples were collected for BoE analysis. eCO was also measured on each day.

Table 1. Subject demographics in the regular and mentholated
cigarette and regular and
mentholated THP1.0

<table>
<thead>
<tr>
<th></th>
<th>Cigarette</th>
<th>THP1.0</th>
<th>Menthol cigarette</th>
<th>THP1.0 menthol</th>
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<tbody>
<tr>
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<td>Mean ± SD</td>
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<tr>
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<td>Female</td>
<td>17 ± 5.7</td>
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<td>15 ± 4.3</td>
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<tr>
<td>Sex, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range (days)</td>
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<td>10 – 30</td>
<td>10 – 20</td>
<td>10 – 20</td>
</tr>
</tbody>
</table>

Table 2. Mean levels (n=30 in each group) of biomarkers of exposure to carbon monoxide (eCO, left) and benzene (S-PMA, right). Baseline data were averaged from the two 24-h periods prior to randomisation.

Results
120 subjects completed the study in the regular cigarette, menthol cigarette, regular THP1.0 and mentholated THP1.0 groups; see Table 1 for demographics of participants in these groups. Subjects who switched from smoking to exclusive use of either THP1.0 variant (n=30 in each group) for 5 days showed reductions in levels of exhaled carbon monoxide and a range of urinary BoEs, compared to their levels at baseline. In contrast, the continued smoking groups (regular and mentholated; n=30 in each group) showed little change in BoE levels throughout the study. Data from these groups are presented in Figures 2 and 3.

Conclusions
• In this clinical study, we observed reductions in BoE in subjects who switched to using either regular or mentholated THP1.0.
• These findings are in accordance with the lower levels of toxicants measured in the machine emissions from THP1.0.
• Future studies will examine whether these reductions in exposure are preserved for prolonged, ambulatory periods and also whether these lead to any changes in health effects indicators in smokers.

References