A New Nicotine Inhaler Device: Delivered Dose, Composition and Stability of Formulation

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INTRODUCTION

- Tobacco harm reduction has been part of the UK tobacco control policy since 2010.[1] It aims to help smokers who may be unable to quit smoking in one step, who may want to stop smoking without necessarily giving up nicotine, or who may simply want to reduce the amount that they smoke with a view to quitting later.[2]
  - Tobacco harm reduction may or may not include temporary or long-term use of licensed nicotine-containing products.[2]
- A novel nicotine inhaler (Voke® [Nicovations Limited]; 0.056% w/w nicotine) has been developed to deliver 0.43 mg nicotine per charge of the stick device and has been licensed in the UK as an aid to cutting down or quitting cigarettes.[3]

Figure 1. The Voke® inhaler and pack.

- Voke® is a breath-operated system, similar to an asthma inhaler, consisting of a stick device and a pack containing a pressurized formulation of nicotine (**Figure 1**).
  - During device charging, the formulation is transferred from the pack to the stick.
  - Charging of the device takes 5 seconds.
- The formulation now contained in the stick can then be inhaled by the user in a similar manner as a cigarette.
  - Each charge provides 6–8 puffs, depending on the user's style of puffing.
  - Each pack provides 20 charges of the stick device.[3]
- All ingredients used in the formulation are of pharmaceutical grade and the formulation and device are manufactured under current Good Manufacturing Practice regulations.
  - Unlike electronic cigarettes, this device requires no heat to vaporize the nicotine, thus avoiding the generation of harmful carbonyls.[4]
- Functional performance, consistency of delivered dose and stability of the formulation are key features for consumer acceptance of the device.

OBJECTIVE

- To assess key performance characteristics of the new nicotine inhaler, including the consistency of the delivered dose of nicotine and the impurity profile during stability studies.

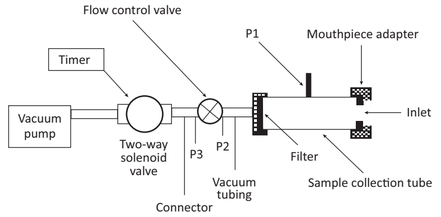
METHODS

Study design

Dose delivery

- Uniformity of dose delivery from the device was measured using standard pharmaceutical equipment (**Figure 2**).

Figure 2. Pharmacopoeal sampling apparatus for dry powder inhalers.



P1, P2, P3, pressure taps
Source: http://www.pharmacopeia.cn/v29240/usp29nf24s0_c601_viewall.html

- Dose deliveries from single charges of the novel inhaler were evaluated over a range of in-use conditions including: single-day use intra-device; single-day use inter-device; and 7-day use (with the device both upright and inverted).
- Performance of the device following 10-day temperature cycling (with the device both upright and inverted) and following long-term (to 18 months) storage were also evaluated.
- Three batches of devices were manufactured and tested.

Formulation stability

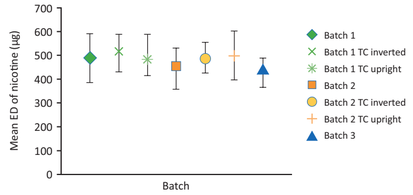
- The levels of impurities were monitored throughout storage at 25°C/60% relative humidity (RH) and 30°C/65% RH over an 18-month period and evaluated using high-performance liquid chromatography.
- The mean nicotine dose delivered by the inhaler was collected and quantified using gas chromatography against an external nicotine standard.
- Three batches of devices were manufactured and tested.

RESULTS

Dose delivery

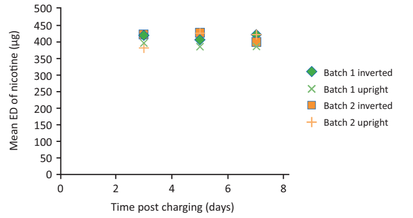
- The uniformity of the nicotine dose emitted was within the acceptance limits of the European Pharmacopoeia guidelines (**Figure 3**).
- After 10-day temperature cycling, the device continued to function properly and deliver the correct nicotine dose (**Figure 4**).

Figure 3. Mean emitted nicotine dose per charge of the device.



Error bars represent the actual range observed
ED, emitted dose; TC, temperature cycled

Figure 4. Mean emitted nicotine dose per charge of the device following temperature cycling.



ED, emitted dose

Table 1. Formulation stability of the Voke® nicotine inhaler* at 25°C and 60% relative humidity.

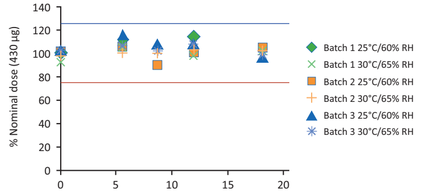
Impurity	Product specification (0.1%) NMT, %	Time, months					
		0	3	6	9	12	18
Anatabine	0.3	ND	ND	ND	ND	ND	ND
β-nicotyrine	0.3	ND	ND	ND	ND	BRT	BRT
Cotinine	0.3	BRT	ND	ND	ND	BRT	BRT
Myosmine	0.3	BRT	BRT	ND	BRT	BRT	0.1
Nicotine N-oxide	0.3	ND	0.1	0.2	0.1	0.2	0.2
Nornicotine	0.3	ND	ND	ND	ND	BRT	BRT
Anabasine	0.3	ND	ND	ND	ND	ND	BRT
Unspecified individual unknown impurities	0.1 each	ND	ND	ND	ND	BRT	BRT
Carboxylic acid impurity	0.3	ND	0.1	0.2	0.1	0.2	0.2
Specified unknown impurities (RRT ~1.03–1.08)	0.2	ND	ND	ND	ND	ND	ND
Total impurities	1.0	0	0.2	0.4	0.2	0.4	0.5

*Manufacturer batch number: BK0444780
BRT, below reporting threshold; ND, not detected; NMT, not more than; RRT, relative retention time

Formulation stability

- In all cases, the device performed well after long-term (to 18 months) storage and within the acceptance criteria (**Figure 5**).
  - Low levels of nicotine N-oxides and a carboxylate impurity were observed over time, but levels of these impurities were within product specification (**Table 1**).
  - Toxicity assessment of the results indicated that impurities were within limits recommended in the International Conference on Harmonisation Q3B guidelines on impurities in new drug products.

Figure 5. Stability of emitted nicotine dose per charge of the device following long-term storage at 25°C and 60% RH and at 30°C and 65% RH.



Blue and red lines represent upper and lower European Pharmacopoeia limits for uniformity of delivered dose (125% and 75%, respectively)
RH, relative humidity

CONCLUSIONS

- **The delivered dose of nicotine was consistent across a range of in-use conditions.**
- **No deterioration in performance was observed through the lifetime of the nicotine inhaler.**
- **No significant levels of impurities were detected after 18 months' storage of the inhaler.**

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DISCLOSURES

Alan Silcock is an employee of Nicovations Limited. Rene Gonzalez, Ritika Gupta, David Hackett and Alex Hearn are employees of Kind Consumer Limited.