

## Dosimetry tools, approaches and applications for tobacco and next generation product testing

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Measuring dose at the exposure interface may allow the comparison of biological data from different *in vitro* exposure systems and different nicotine delivery products (Figure 1). There are various *in vitro* exposure systems available, many summarised in Thorne and Adamson (2013). However, most of these commercially available systems were originally designed and intended for use with cigarettes only, well before e-cigarettes became commonplace. These exposure systems can easily be adapted to enable the assessment of new products: e-cigarettes, tobacco heating products (THP) or even medicinal nicotine inhalers. However, careful characterisation of the generated aerosol is required (at the point of generation and at the point of exposure) to enable comparisons before conclusions of any associated biological responses can be made.

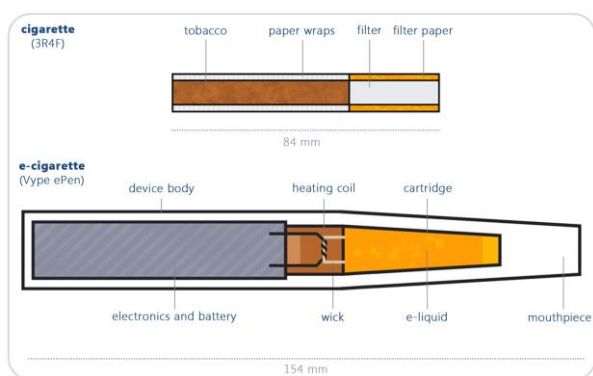


Figure 1. The cigarette (3R4F, University of Kentucky) and e-cigarette (Vype ePen containing 1.8% nicotine blended tobacco e-liquid)

Dosimetry tools and methods can assess many aspects of the test article aerosol and provide important data to confirm aerosol delivery in biological assay systems showing partial or no biological response to exposure. An example would be the direct mass measurement of total deposited particles at the exposure interface, using a quartz crystal microbalance (QCM) device (Adamson *et al.* 2012). Another example of a dosimetry method complementing QCMs is the quantification of a chemical marker within the surface deposit (of a QCM or a cell culture insert) identifying how much of a certain chemical/compound is being exposed to cells in culture. Nicotine quantification by UPLC-MS/MS (Jin *et al.* 2012) is a good example as it common amongst the inhalable products being assessed.

Diluted aerosols from a reference cigarette and a commercially available e-cigarette (Figure 1) were compared in two different commercially available *in*

*vitro* exposure systems: the Borgwaldt RM20S and the Vitrocell VC 10. Aerosols were assessed at source (generation), and deposited *in vitro* once diluted with air (4 dilutions/machine), by the methods just cited. The data show that the two exposure systems were able to generate and deliver cigarette and e-cigarette aerosols pre-dilution with no statistically significant difference between the same products and within analytically quantified nicotine concentration levels (Table 1).

Table 1. Cigarette (3R4F) and e-cigarette (ePen) nicotine concentration per puff at source on two machines

	Target (mg/puff)	RM20S (mg/puff)	VC 10 (mg/puff)
3R4F	0.189	0.177±0.056	0.193±0.055
ePen	0.056	0.049±0.006	0.053±0.012

Assessment of the diluted aerosol at the exposure interface showed that on a per puff basis and at a common dilution, nicotine delivery was much greater from the cigarette than from the e-cigarette. On the Borgwaldt RM20S system, QCM eluted nicotine ranged 1.9-13.0 ng/cm<sup>2</sup>/puff for the cigarette and 0.3-1.4 ng/cm<sup>2</sup>/puff for the e-cigarette. On the Vitrocell VC 10 system, nicotine concentration ranged 7.8-72.9 ng/cm<sup>2</sup>/puff for the cigarette and 3.8-9.5 ng/cm<sup>2</sup>/puff for the e-cigarette. In contrast, the e-cigarette aerosol deposited mass was greater than cigarette smoke mass on both exposure systems. The RM20S produced deposited mass ranging 0.1-0.5 µg/cm<sup>2</sup>/puff for cigarette and 0.1-0.9 µg/cm<sup>2</sup>/puff for e-cigarette; the VC 10 ranged 0.4-2.1 µg/cm<sup>2</sup>/puff for cigarette and 0.3-3.3 µg/cm<sup>2</sup>/puff for e-cigarette. Ratios for nicotine:mass differ between a cigarette and e-cigarette and this is to be expected based on the average mass output per puff for each product.

Our data demonstrate that the aerosol generated from a cigarette and e-cigarette using *in vitro* exposure systems are delivered consistently to the exposure interface despite compositional differences. It emphasises the importance of understanding and characterising different product aerosols using dosimetry tools prior to or in parallel with biological testing.

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