




## NEXT GENERATION NICOTINE DELIVERY CONFERENCE 2016

Demonstrating risk reduction in the fast paced world of next generation tobacco and nicotine products

**James Murphy** | Research and Development, British American Tobacco




# Agenda

- Insight into BAT R&D
  - Evolution of next generation products across the risk spectrum
  - Multidisciplinary approach to demonstrate the reduced risk potential of next generation products
  - Source of emission toxicants and data on e-cigarettes
  - Bridging data between product variants: A new requirement in the fast paced world of next generation products
- 

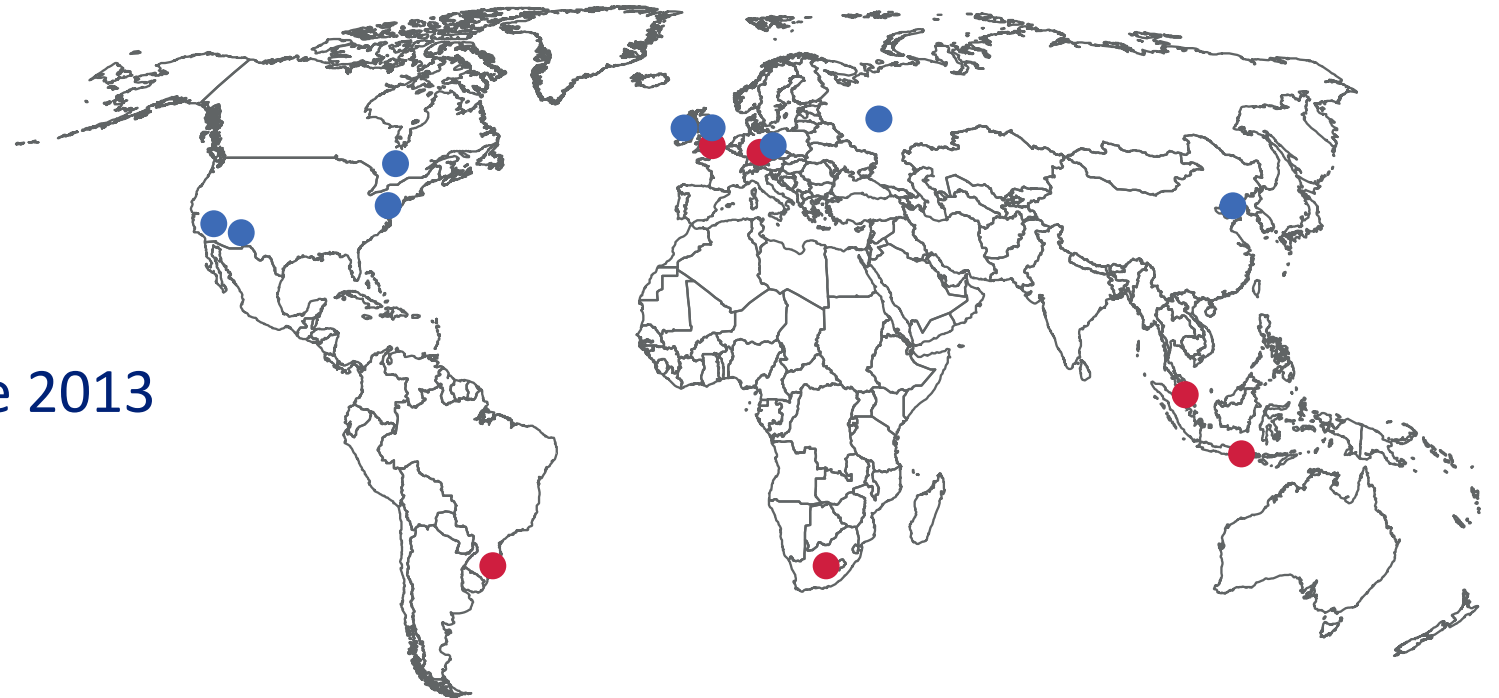


# Agenda

- Insight into BAT R&D
  - Evolution of next generation products across the risk spectrum
  - Multidisciplinary approach to demonstrate the reduced risk potential of next generation products
  - Source of emission toxicants and data on e-cigarettes
  - Bridging data between product variants: A new requirement in the fast paced world of next generation products
- 

# R&D at British American Tobacco

- Global R&D reach
- 1200 scientists and technologists
- > 50 scientific disciplines
- £0.5Bn R&D expenditure since 2013
- 2010–15, over 3000 patents filed, over 1800 granted



● BAT Sites

● Collaborators

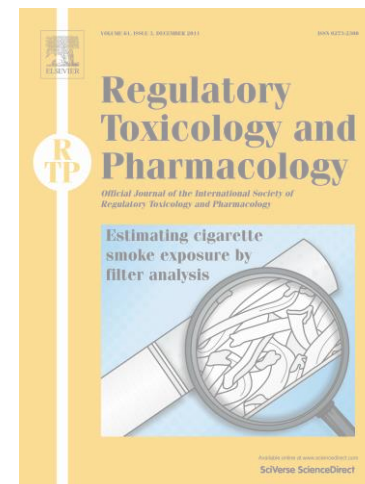
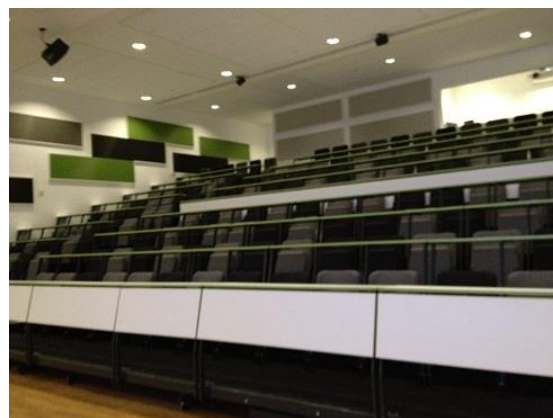
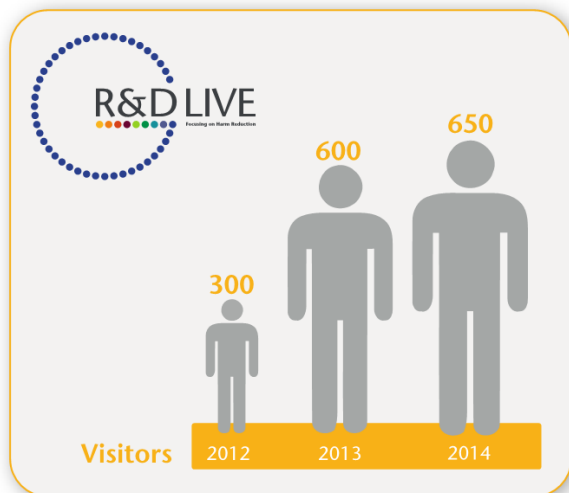
# An open approach to R&D

## Visitors

## Conferences

## Publications

## Social Media



Over 1500 visitors to our R&D Live Centre at Global R&D since 2011


Presentation of data at global scientific & regulatory conferences and hosting of conferences on site

Over 180 publications since 2008

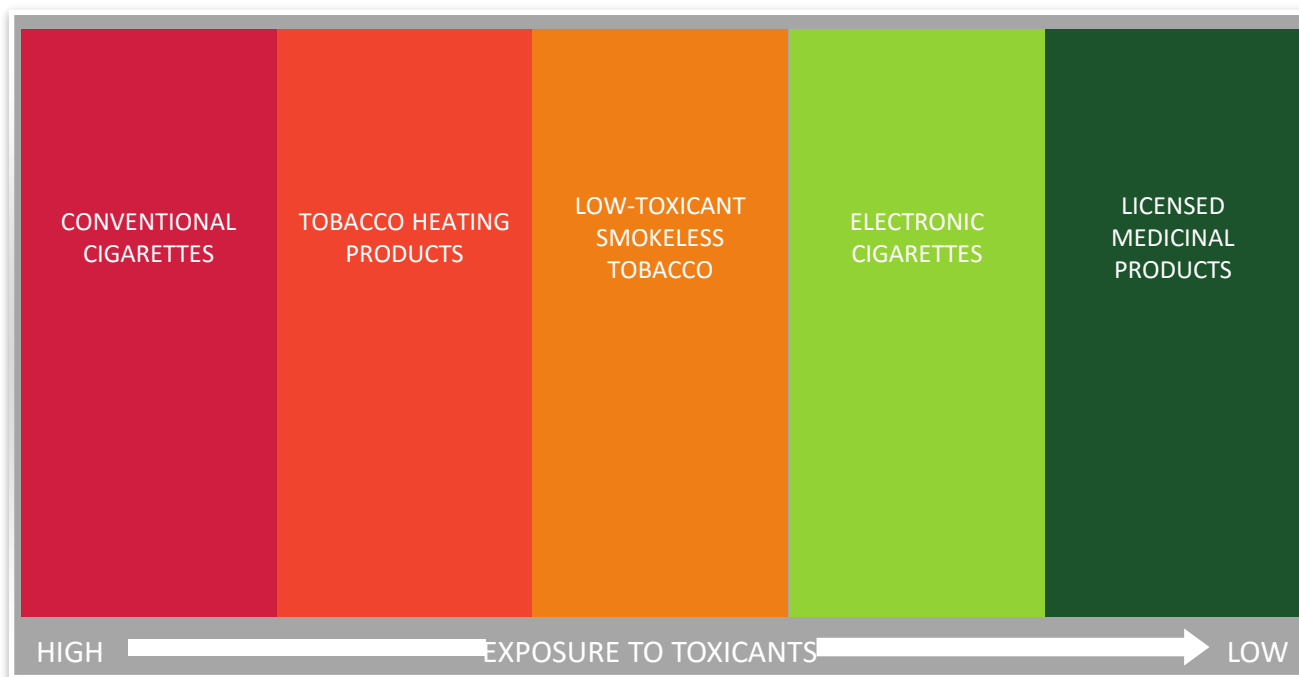
Website dedicated to science



# Agenda

- Insight into BAT R&D
  - Evolution of next generation products across the risk spectrum
  - Multidisciplinary approach to demonstrate the reduced risk potential of next generation products
  - Source of emission toxicants and data on e-cigarettes
  - Bridging data between product variants: A new requirement in the fast paced world of next generation products
- 

# BAT is investing in a range of products across the risk spectrum



# E-cigarettes have evolved rapidly



2013

2016

Disposable

Rechargeable  
(cig-alike)

Tank  
Modular

Rechargeable  
(non-cig-like)

Full  
(large-size)  
Modular


Compact  
Modular

Development of eliquids





# Agenda

- Insight into BAT R&D
  - Evolution of next generation products across the risk spectrum
  - **Multidisciplinary approach to demonstrate the reduced risk potential of next generation products**
  - Source of emission toxicants and data on e-cigarettes
  - Bridging data between product variants: A new requirement in the fast paced world of next generation products
- 

# Consumer safety testing of e-cigarettes

## *What do we need to know?*

### Stewardship of e-cigarette flavours

S. Costigan and C. Meredith

*Regul Toxicol Pharmacol*

72: 361–369, 2015

## eLiquid

What's in the liquid?

## Device

What's the device made of?

Does it conform to electrical safety?

## Product

What's in the vapour?

How stable is the product over time?

How is it used?

# Assessing the potential for reduced risk

*Multi-platform testing to assess impact on individual and population risk*

Population risk reduction

Individual risk reduction

Toxicant exposure reduction

Stewardship science

Purpose

10) Post-market surveillance

9) Consumer perception study

8) Biomarker of effect study

7) Systems Science

6) *In vitro* models of disease

5) Exposure and pharmacokinetic studies

4) Computational toxicology

3) *In vitro* regulatory toxicology

2) Chemical and physical characterisation


1) Product design stability

Type of study





# Agenda

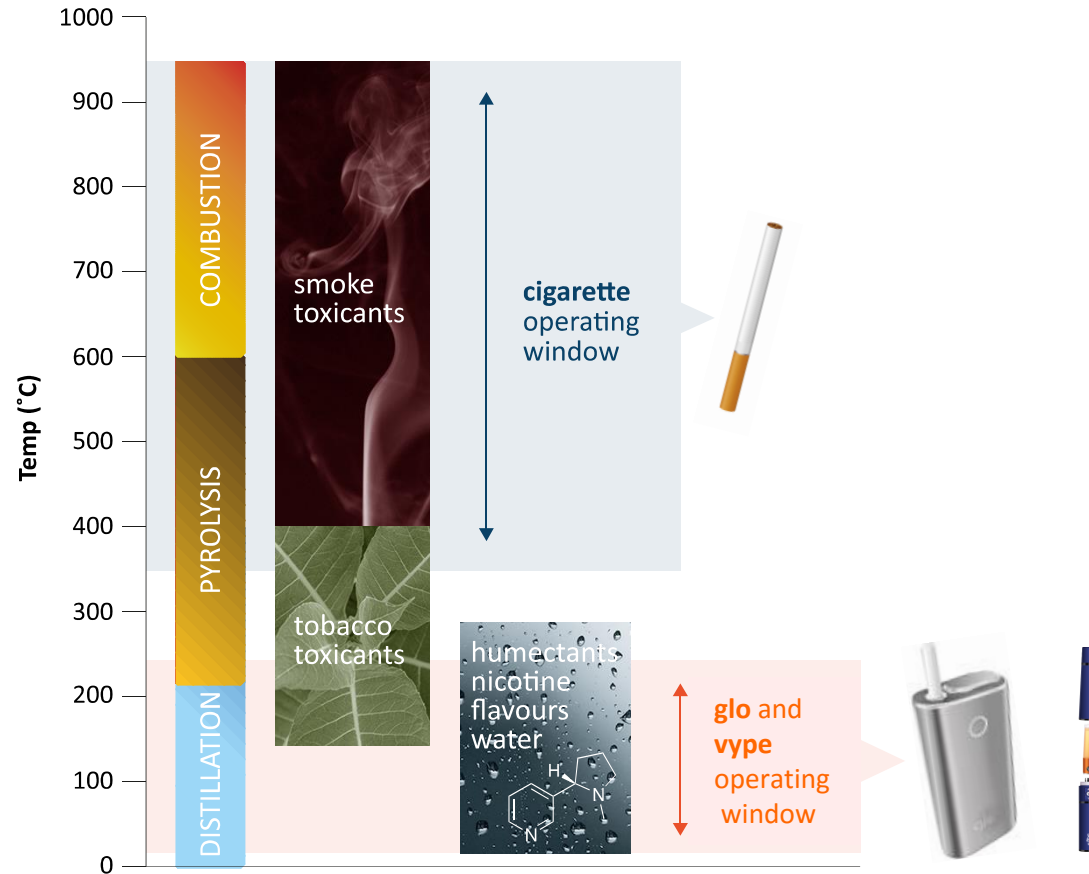
- Insight into BAT R&D
  - Evolution of next generation products across the risk spectrum
  - Multidisciplinary approach to demonstrate the reduced risk potential of next generation products
  - Source of emission toxicants and data on e-cigarettes
  - Bridging data between product variants: A new requirement in the fast paced world of next generation products
- 

# TOXICANTS CAUSE HARM (NOT NICOTINE)

What is the source of toxicants in NGPs

	Cigarettes	THP	Vapour
Approximate number of compounds found in aerosol	>6,500	100-1000	10-100
Toxicants from burning tobacco	Yes	Trace	No tobacco
Toxicants transferred from tobacco	Yes	Yes	No tobacco
Other potential sources of toxicants	Combustion / pyrolysis of cigarette paper	-Thermal degradation of PG/VG & flavours -Leachables from device materials	-thermal degradation of PG/VG & flavours -Leachables from device materials

# NGPs deliver a different aerosol to cigarette smoke<sup>a</sup>



- Cigarettes burn tobacco at around 900°C<sup>b</sup>
- glo heats tobacco up to a maximum of 240°C<sup>c</sup>
- Vype heats liquids at around 250°C

<sup>a</sup>These qualities do not necessarily mean this product produces less adverse health effects than other tobacco products; <sup>b</sup>RR Baker, (2006) *Progress in Energy and Combustion Science*, 32 (4), 373; <sup>c</sup>Method adapted from: Forster *et al*, (2015) *Chemistry Central Journal*, 9, 20

# There is a growing consensus on e-cigarettes harm reduction potential



Public Health  
England

---

Kevin Fenton, Public Health  
Director of Health and Wellbeing:  
“The wider body of evidence  
consistently finds that e-cigarettes  
are less harmful than smoking”

*E-cigarettes: an evidence update*  
“The current best estimate is that  
e-cigarettes are around 95% less  
harmful than smoking”



Royal College  
of Physicians

---



*Nicotine without smoke:  
tobacco harm reduction*  
“Promote e-cigarettes  
widely as substitute for  
smoking” says new RCP  
report

ash briefing  
action on smoking and health

---

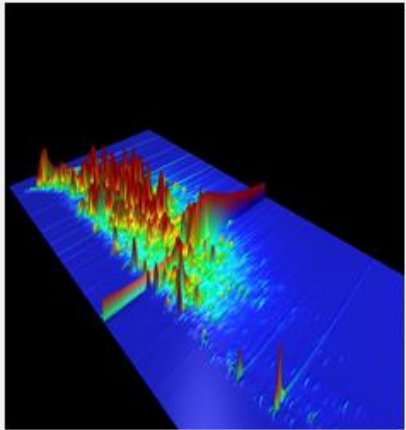
*Electronic cigarettes (also  
known as vapourisers)*  
“Compared to tobacco  
products, electronic  
cigarettes are significantly  
safer”

# Products assessed in this study to compare e-cigarette aerosol with cigarette smoke

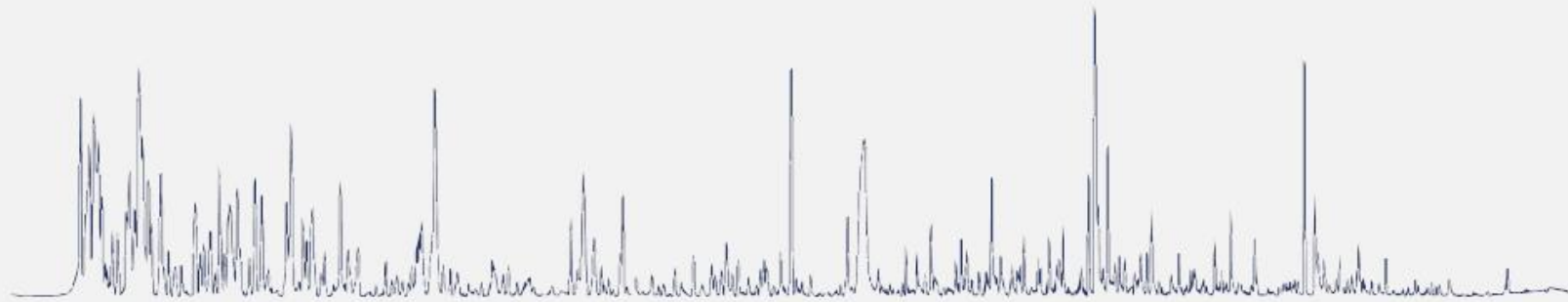
	Visual	Description	Aerosol generation
Reference cigarette		US blend (3R4F) reference cigarette from the University of Kentucky, US	Combustion and pyrolysis of tobacco
Vype e-Pen		A closed system vaping device	Heating of a tobacco-free, flavoured nicotine solution



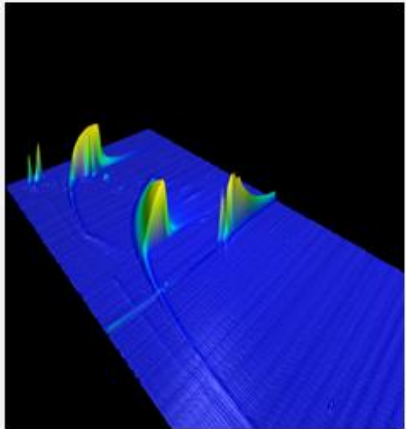
# Complexity of cigarette smoke compared with e-cigarette aerosol\*



Cigarette smoke



1. Wright *et al* (2016) *J of Chromatography*, in press



E-cigarette aerosol

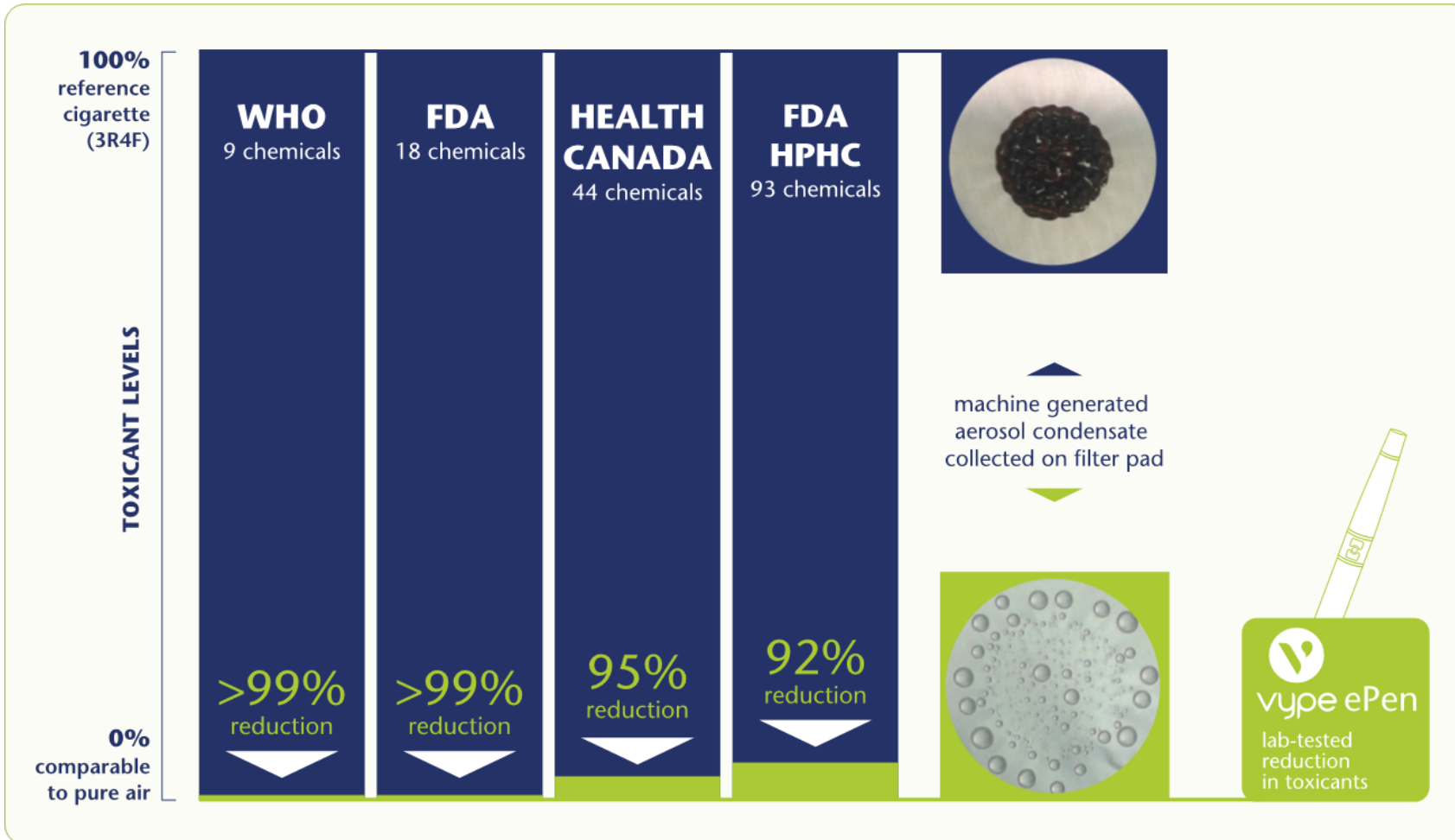


ePen produces a simpler aerosol comprised of fewer compounds than cigarette smoke

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

# CHEMICAL CHARACTERISATION

## Reduced levels of toxicants\*



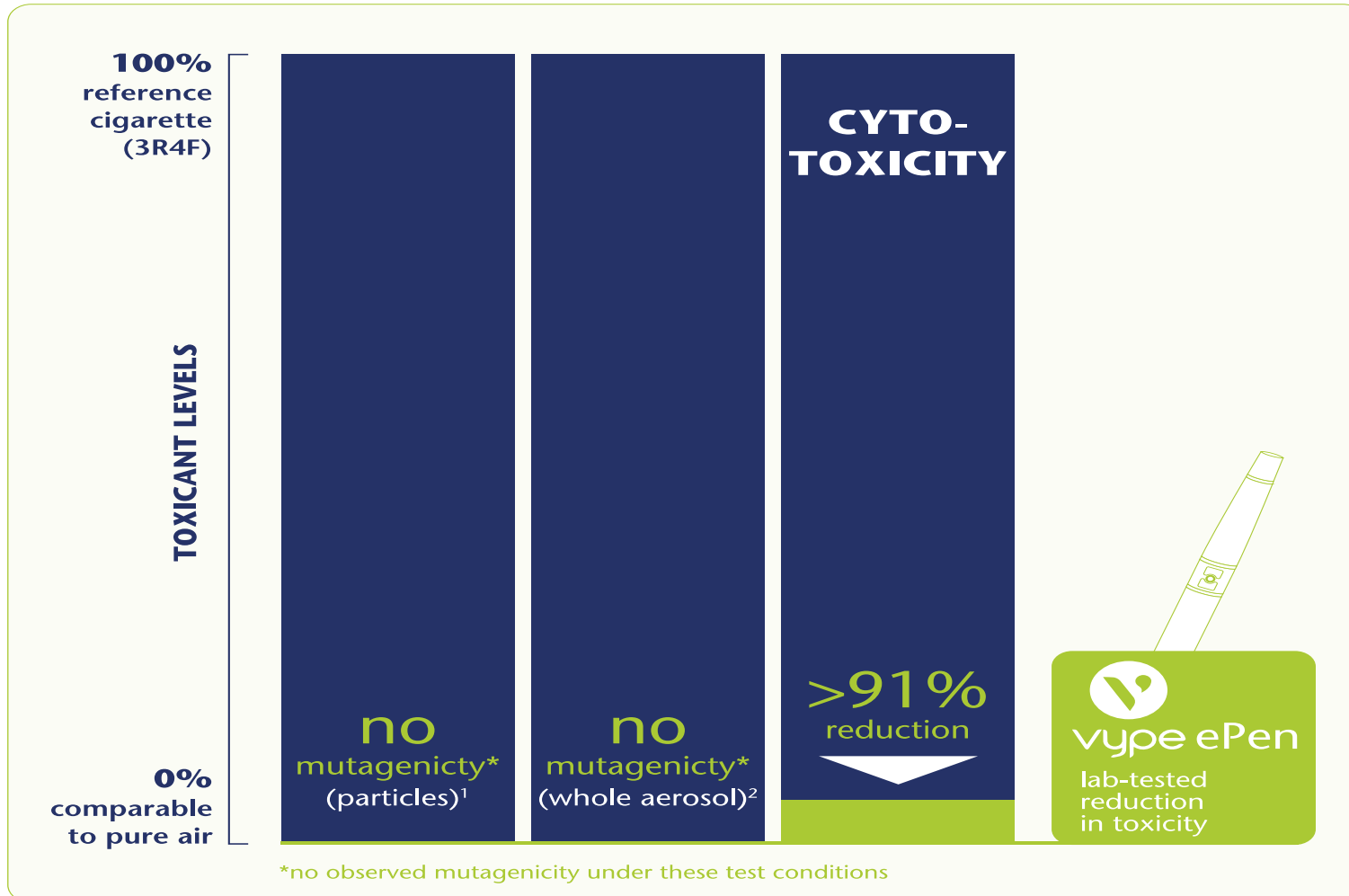
1. McAdam *et al* (2016) Chem Res Tox, in press (doi: 10.021/acs.chemrestox.6b00188)

Substantial reductions in toxicant levels observed versus cigarettes for all regulatory lists under these test conditions

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

# IN VITRO REGULATORY TOXICOLOGY

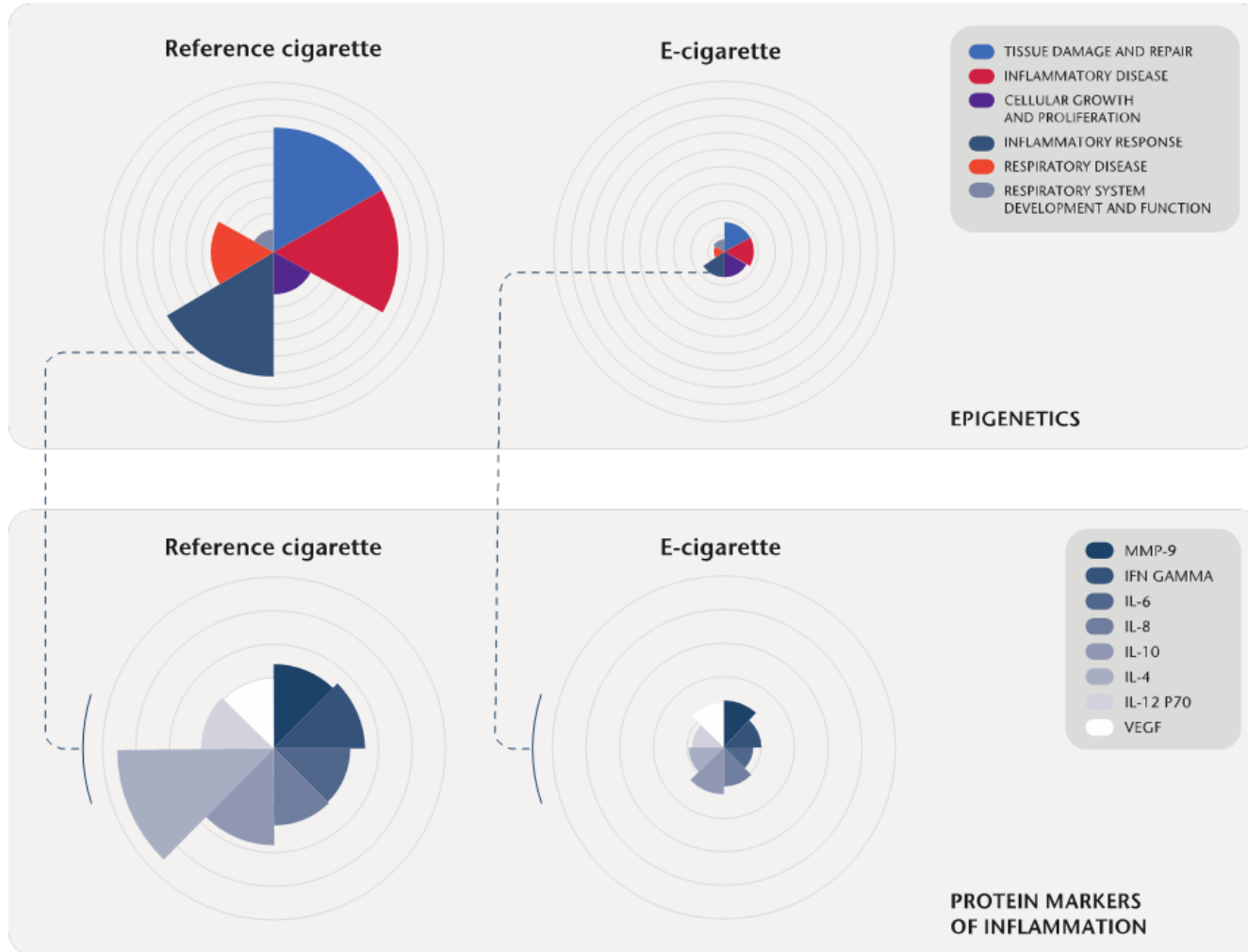
## Reduced toxicity\*



1. Thorne *et al* (2016) *Mutation Research – Genetic Toxicology and Environmental Mutagenesis*, in press
2. Azzopardi *et al* (2016) *Toxicology Mechanisms and Methods*, Vol. 26 , Iss. 6, 477-491, 2016

Reductions in aerosol toxicant reductions lead to reductions in lab based toxicological tests

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



Markers of disease and function after exposure to emissions from a reference cigarette and an e-cigarette.

1. Banerjee *et al* (2016) *Applied in vitro toxicology*, in press


Systems science allows us to assess multiple disease end points in lab based models

ePen has greatly reduced responses to disease relevant tests in lab based models

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




# Agenda

- Insight into BAT R&D
  - Evolution of next generation products across the risk spectrum
  - Multidisciplinary approach to demonstrate the reduced risk potential of next generation products
  - Source of emission toxicants and data on e-cigarettes
  - Bridging data between product variants: A new requirement in the fast paced world of next generation products
- 




## Product bridging

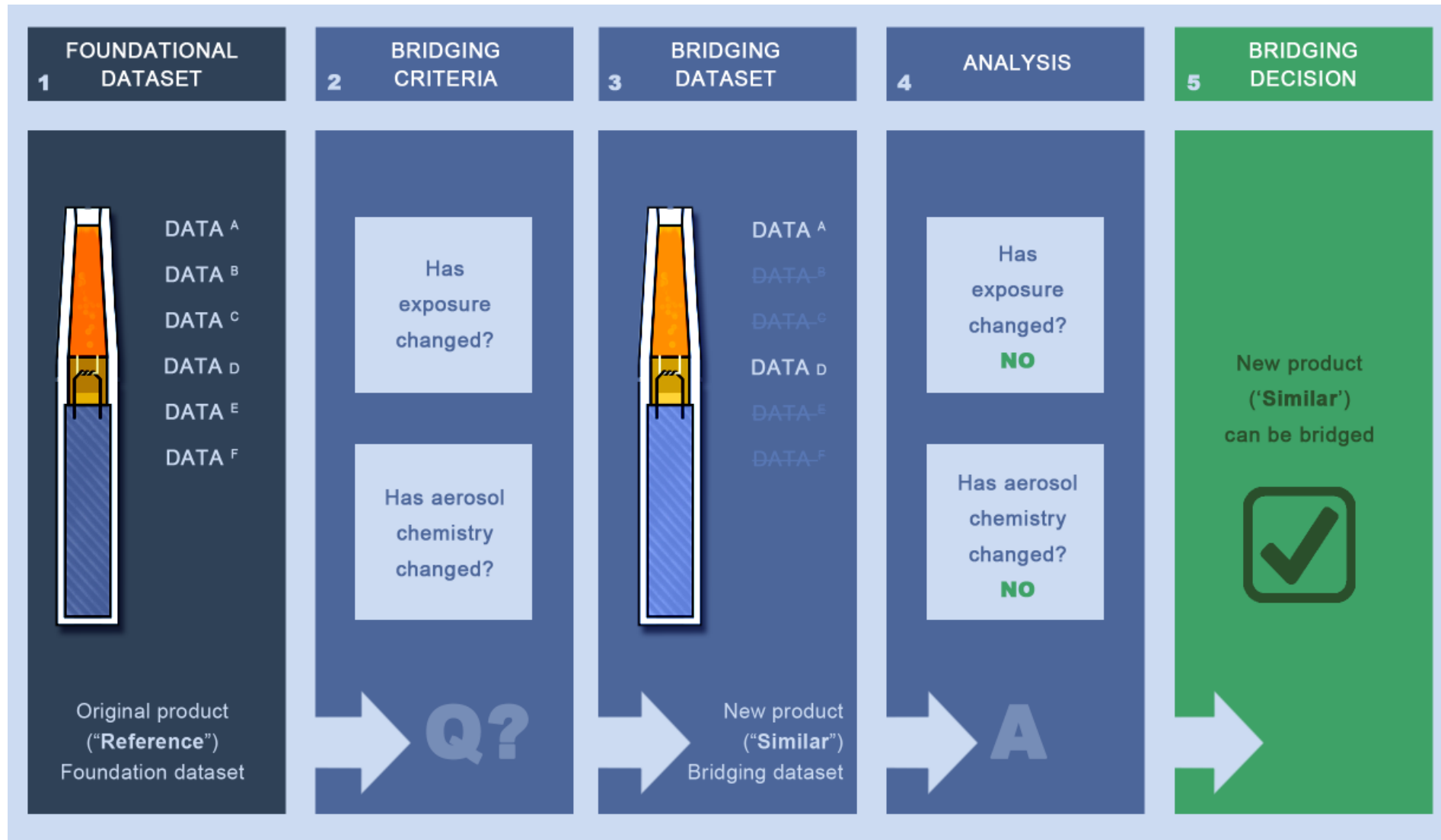
- Next generation product innovation is occurring at a rapid pace
  - Science packages are required for *eg.* safety assessments, regulatory submissions and / or substantiation of risk reduction
  - Conundrum: can we bridge data between product variants in the fast paced world of next generation products?
- 



## Product bridging

- Yes – this is happening today in the world of ‘similar’ and ‘bio-similars’
  - Modified pharma industry approach to bridging could be applied in the nicotine and tobacco product context
  - Foundation datasets on the original product variant (‘reference’) can be added to on a “need” basis to allow bridging to the new variant (‘similar’)
- 

# Proposed principles of product bridging







## SUMMARY

- BAT is active in all categories across the risk spectrum
- Consumer safety framework established and published for e-cigarettes
- Vype ePen assessed versus a reference cigarette in laboratory tests and showed that it has the potential to be a reduced risk product
- A workable framework for bridging data between product variants is required



[bat-science.com](http://bat-science.com)



[@BAT\\_Sci](https://twitter.com/BAT_Sci)

©British American Tobacco (Investments) Limited 2014. All rights reserved. No part of these materials may be reproduced in any form or by any means without the prior written consent of British American Tobacco (Investments) Limited and no responsibility or liability is accepted for any third party reliance on any data contained herein. The data and information used in these materials has been compiled from a number of sources.