



# Smoking and Non-Communicable Diseases in Hong Kong

Current Status and the Way Forward

Prof. David Khayat

Former Head of Medical Oncology at the Pitié-Salpêtrière in Paris  
Former President of the National Cancer Institute in France  
Harm Reduction Consultant to PMI

# Agenda

- Smoking and Non-Communicable Diseases in Hong Kong
- Causes of Cancer in China
- The need for alternatives to smoking
- How does cigarette smoke cause cancer?
- How much can alternatives reduce the risks of smoking?
- What evidence exists and how credible is the science?
- Emerging Regulatory Trends"

# Smoking and Non-Communicable Diseases in Hong Kong

# The Burden of Non-Communicable Diseases (NCDs)

## Global Burden of NCDs

NCDs such as Cardiovascular, Respiratory Disease and Cancer caused:

- > 39 Mio deaths globally in 2016 (70% of all deaths)
- ~ 9 Mio cancer deaths in 2016

## NCD Burden in Hong Kong

NCDs such as Cardiovascular, Respiratory Disease and Cancer caused:

- >25 K deaths in Hong Kong in 2016 (55% of all deaths)
- ~ 14 K cancer deaths in 2016

Numbers are based on public statistics for HK

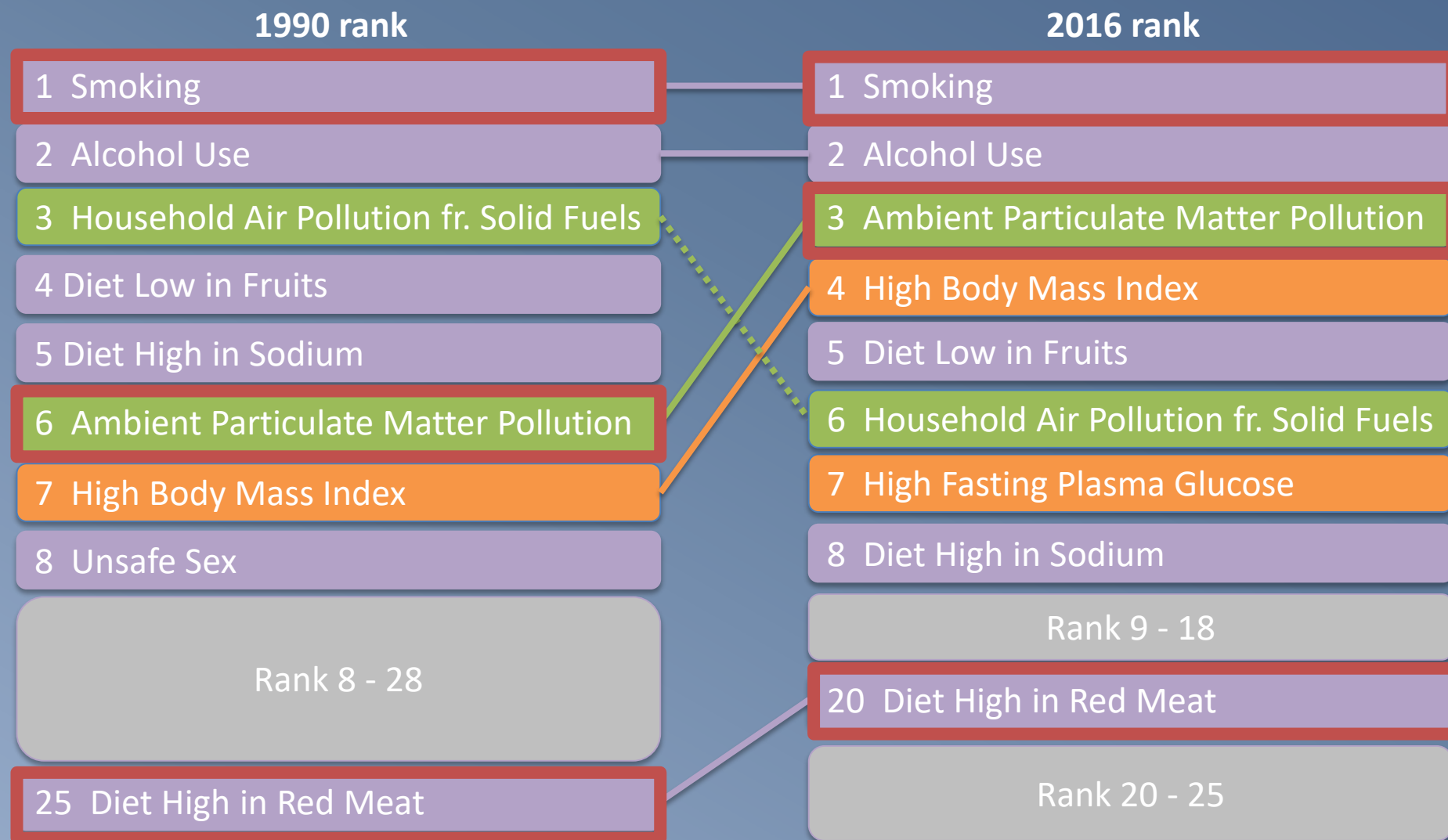
Source: Hong Kong's Center for Health Protection – Summary Report: TOWARDS 2025 Strategy and Action Plan to Prevent and Control Non-communicable Diseases in Hong Kong (May 2018).

[https://www.chp.gov.hk/files/pdf/saptowards2025\\_summaryreport\\_en.pdf](https://www.chp.gov.hk/files/pdf/saptowards2025_summaryreport_en.pdf) Summary Report

# Causes of Cancer in China

# Risk Factors for Cancer in China

China, All Ages, Both Sexes, Deaths per 100,000



Numbers are based on public statistics for China



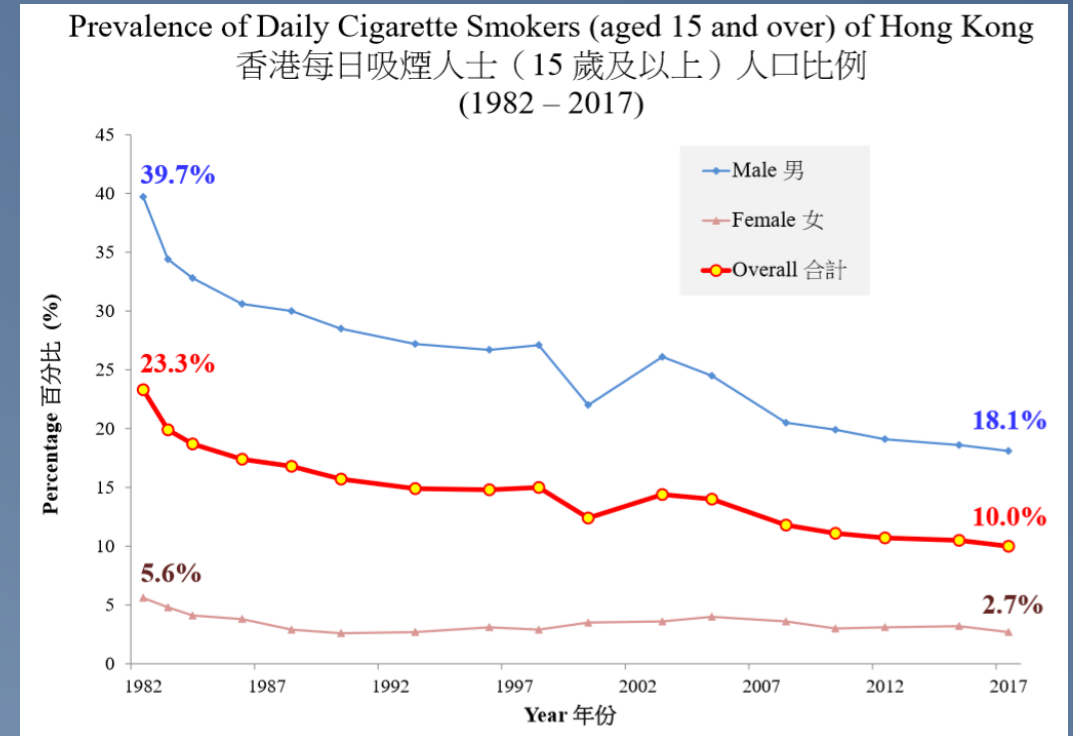
# Overview of HK Accomplishments in Tackling Tobacco Use as a Risk Factor for NCDs

	WHO recommended interventions	Local situation
Best buys	Increase excise taxes and prices on tobacco products	Yellow
	Implement plain/standardised packaging and/or large graphic health warnings on all tobacco products	Green
	Enact and enforce comprehensive bans on tobacco advertising, promotion and sponsorship	Green
	Eliminate exposure to second-hand tobacco smoke in all indoor workplaces, public places, public transport	Green
	Implement effective mass media campaigns that educate the public about the harms of smoking/tobacco use and second-hand smoke	Green
Effective interventions	Provide cost-covered, effective and population-wide support (including brief advice, toll-free quit line services) for tobacco cessation services to all those who want to quit	Green
Other recommended interventions	Implement measures to minimise illicit trade in tobacco products	Green
	Ban cross-border advertising, including using modern means of communication	Yellow
	Provide mobile phone based tobacco cessation services	Green

Numbers are based on public statistics for HK

# People continue to smoke

- Worldwide it is estimated that more than **1 billion people** will continue to smoke in the foreseeable future.<sup>1</sup>
- About 10.0% (615,000 daily cigarette smokers) of the population (18.1% males and 2.7% females) continue to use tobacco each day in Hong Kong in 2017.<sup>2</sup>
- More than 6,826 death are attributable to tobacco-caused diseases every year in Hong Kong.<sup>3</sup>



SOURCE: The Government of Hong Kong Special Administrative Region – “Government survey reveals reduction in smoking” Press Release March 2018  
([http://gia.info.gov.hk/general/201803/22/P2018032200255\\_280462\\_1\\_1521699863718.pdf](http://gia.info.gov.hk/general/201803/22/P2018032200255_280462_1_1521699863718.pdf))

<sup>1</sup> <http://www.who.int/tobacco/publications/surveillance/reportontrendstobaccosmoking/en/index4.html>

<sup>2</sup> <https://www.censtatd.gov.hk/hkstat/sub/sp140.jsp?productCode=B11302013> Zahra, A; Cheong, HK; Park, JH; Burden of Disease Attributable to Smoking in Korea, Asia

<sup>3</sup> Jing Chen, Sarah McGhee, Tai Hing Lam; Economic Costs Attributable to Smoking in Hong Kong in 2011: A Possible Increase From 1998, *Nicotine & Tobacco Research*, , ntx254, 8

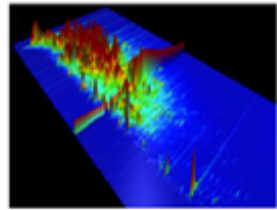
<https://doi.org/10.1093/ntr/ntx254>



# The need for alternatives to smoking

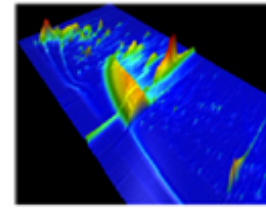
# Categories of Alternative Products and the Risk Continuum

FDA acknowledges the risk continuum to truly protect public health<sup>a</sup>



CIGARETTES

Position confirmed through epidemiology<sup>b</sup>

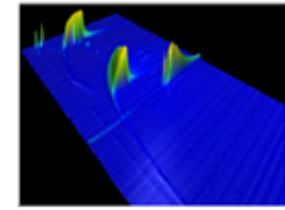


HNB

Position to be confirmed\*

Snus

Position confirmed through epidemiology<sup>b</sup>



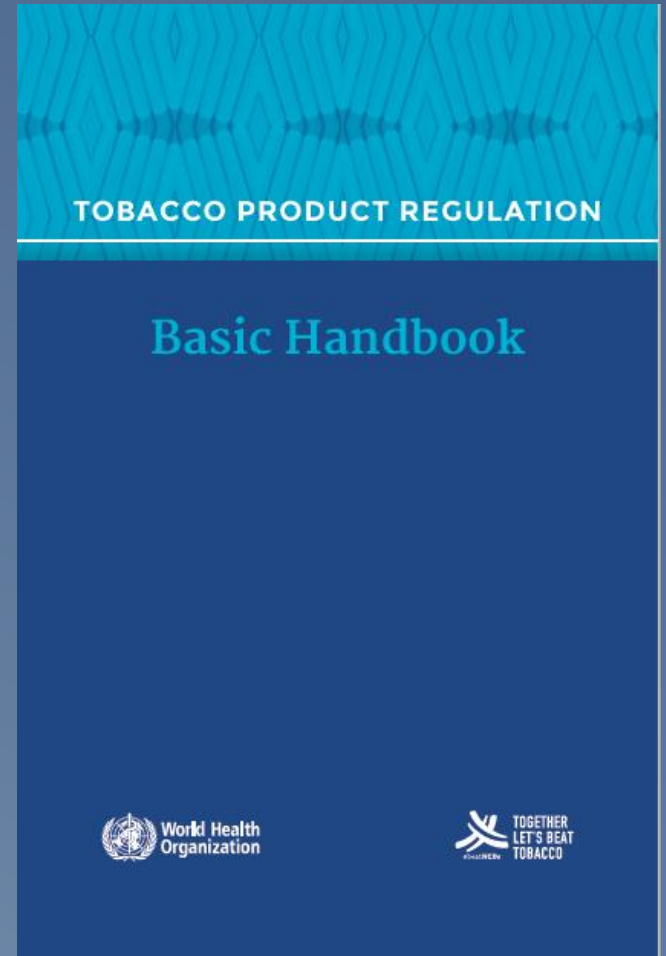
Vapour

Position proposed By Public Health Authorities\*

a. Gottlieb & Zeller (2017) *NEJM* DOI: 10.1056/NEJMp1707409  
b. Doll & Hill (1954) *BMJ* 1954: 1451-1455  
c. Fearon et al 2017 Poster 113 GFN Conference <http://bit.ly/2xRPVvD>  
d. Lee (2013) *Harm Reduct J* 10: 36, doi: 10.1186/1477-7517-10-36  
e. PHE Report 2015 [bit.ly/11yp57N](http://bit.ly/11yp57N); RCP Report 2016 <http://bit.ly/244lizV>; CRUK 2016 <http://bit.ly/2yVZlq0>

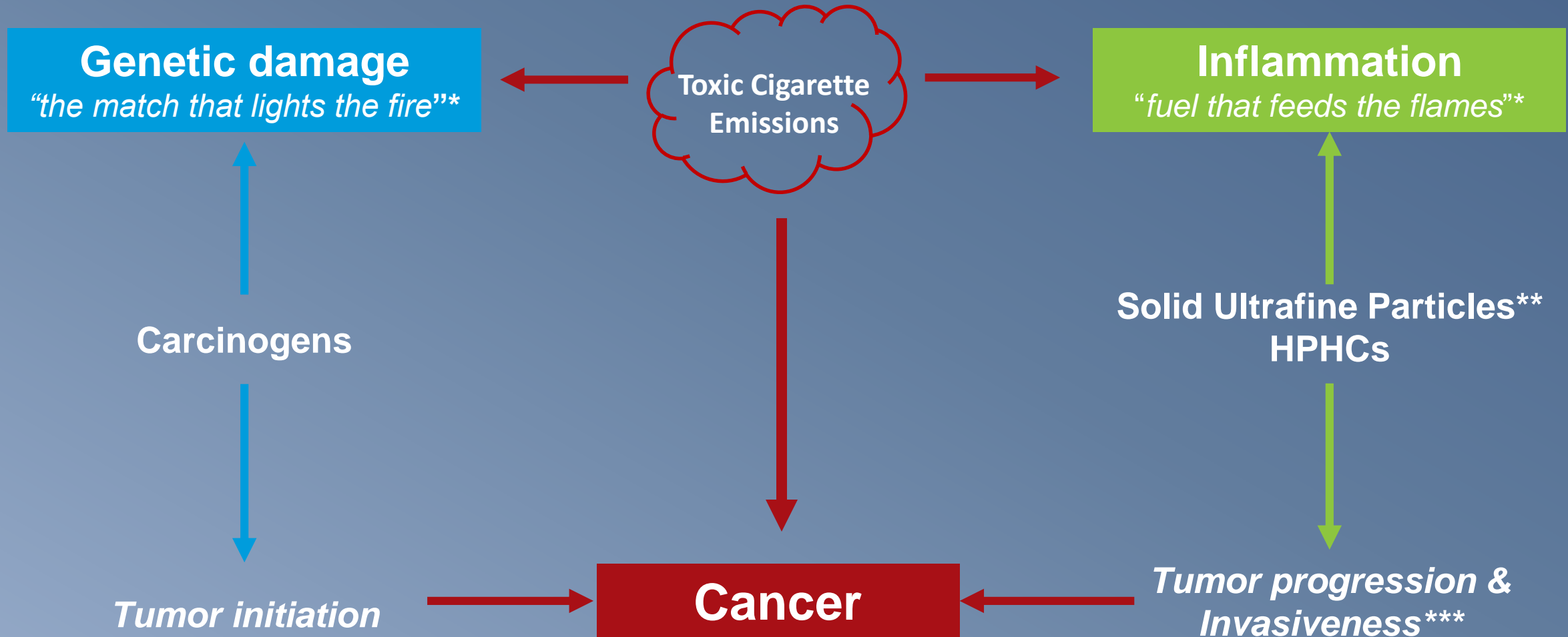
\*Clinical data suggests reduced exposure<sup>c</sup>  
\*UK public health suggests reduced risk<sup>d</sup>

*... For the purposes of developing a regulatory approach, it may prove useful initially to distinguish new products according to their relative degree of difference from traditional combusted or non-combusted tobacco products ...*



**How does cigarette smoke cause cancer?**

# How Cigarette Smoke Causes Cancer?



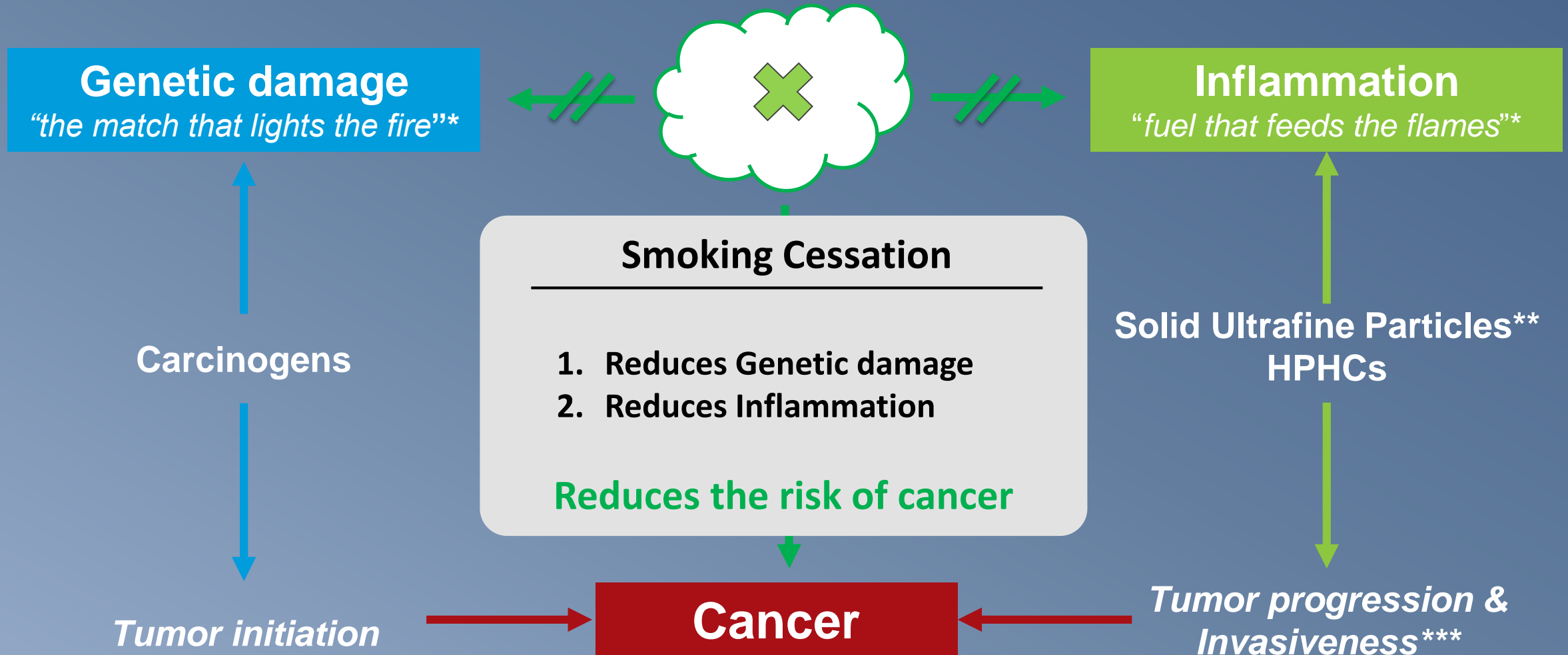
\* Balkwill F and Mantovani A. Inflammation and cancer: back to Virchow? *Lancet*, 2001, 357:539–45.

\*\* You *et al.* Nanoparticulate carbon black in cigarette smoke induces DNA cleavage and Th17-mediated emphysema. *eLife* 2015; 4:e09623

\*\*\* Rothwell *et al.* Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials. *Lancet* 2011; **377**:31–41.



# How Smoking Cessation Decreases Cancer Risk

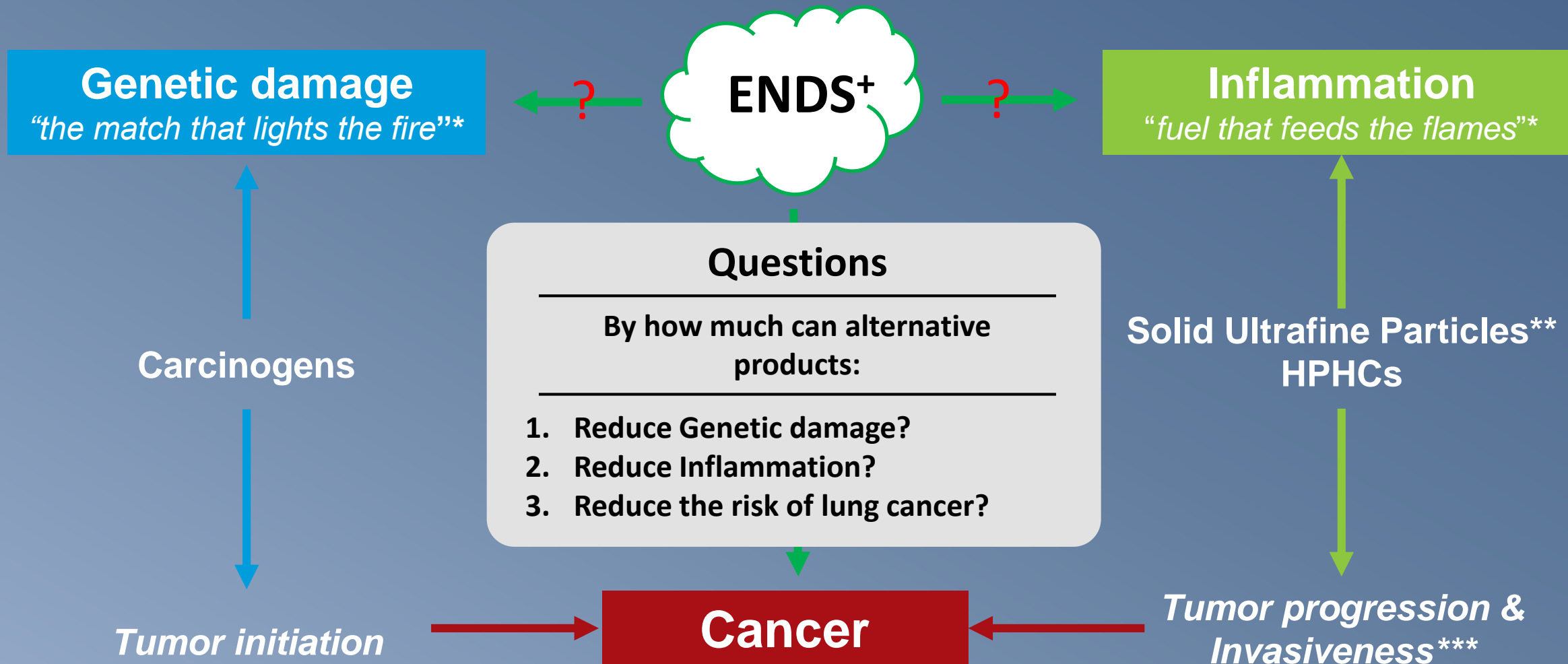


\* Balkwill F and Mantovani A. Inflammation and cancer: back to Virchow? *Lancet*, 2001, 357:539–45.

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# How Much Can ENDS Reduce Cancer Risk?



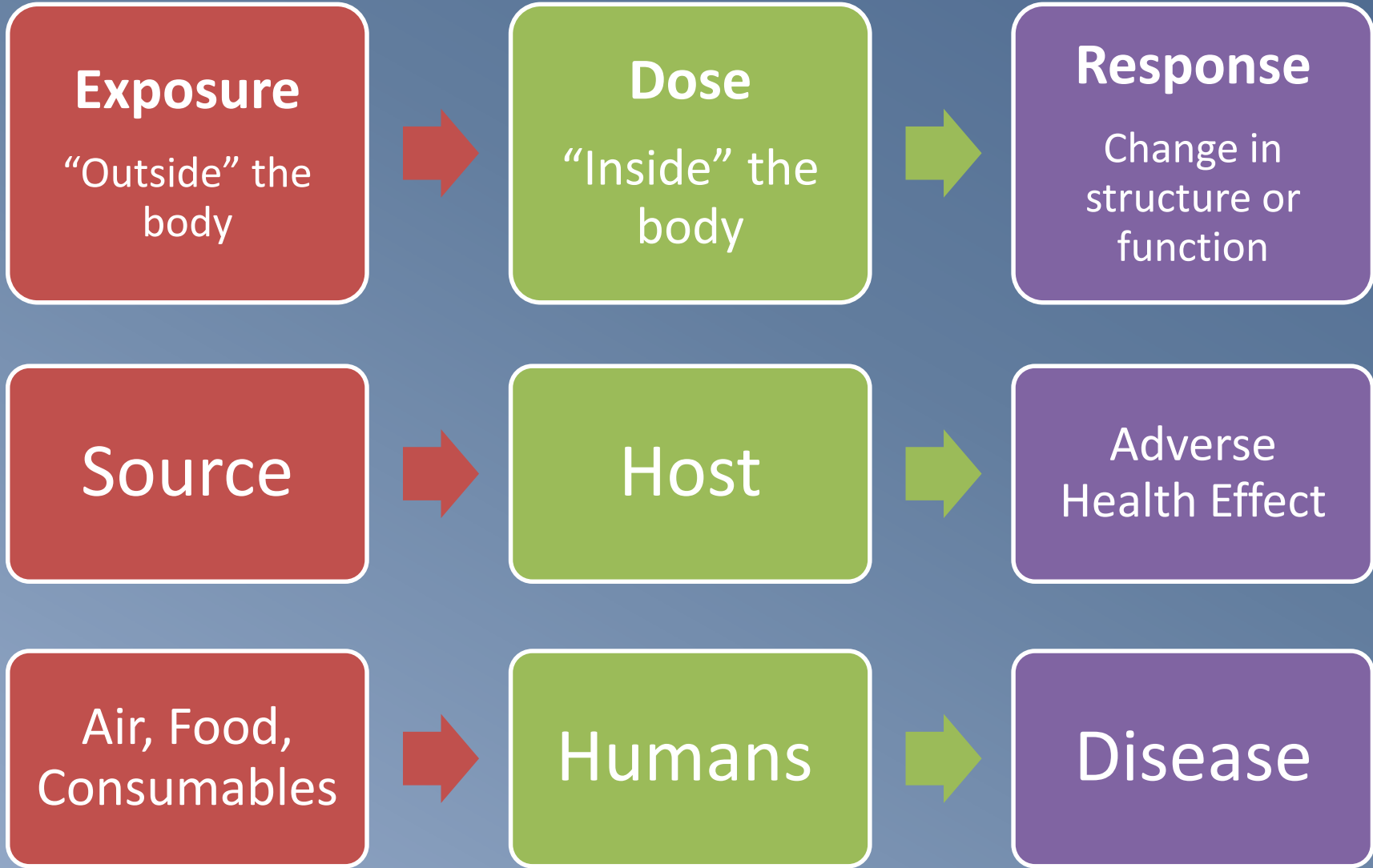
\* Balkwill F and Mantovani A. Inflammation and cancer: back to Virchow? *Lancet*, 2001, 357:539–45.

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**How much can these alternatives  
reduce the risks associated with  
smoking?**

# Dose Response



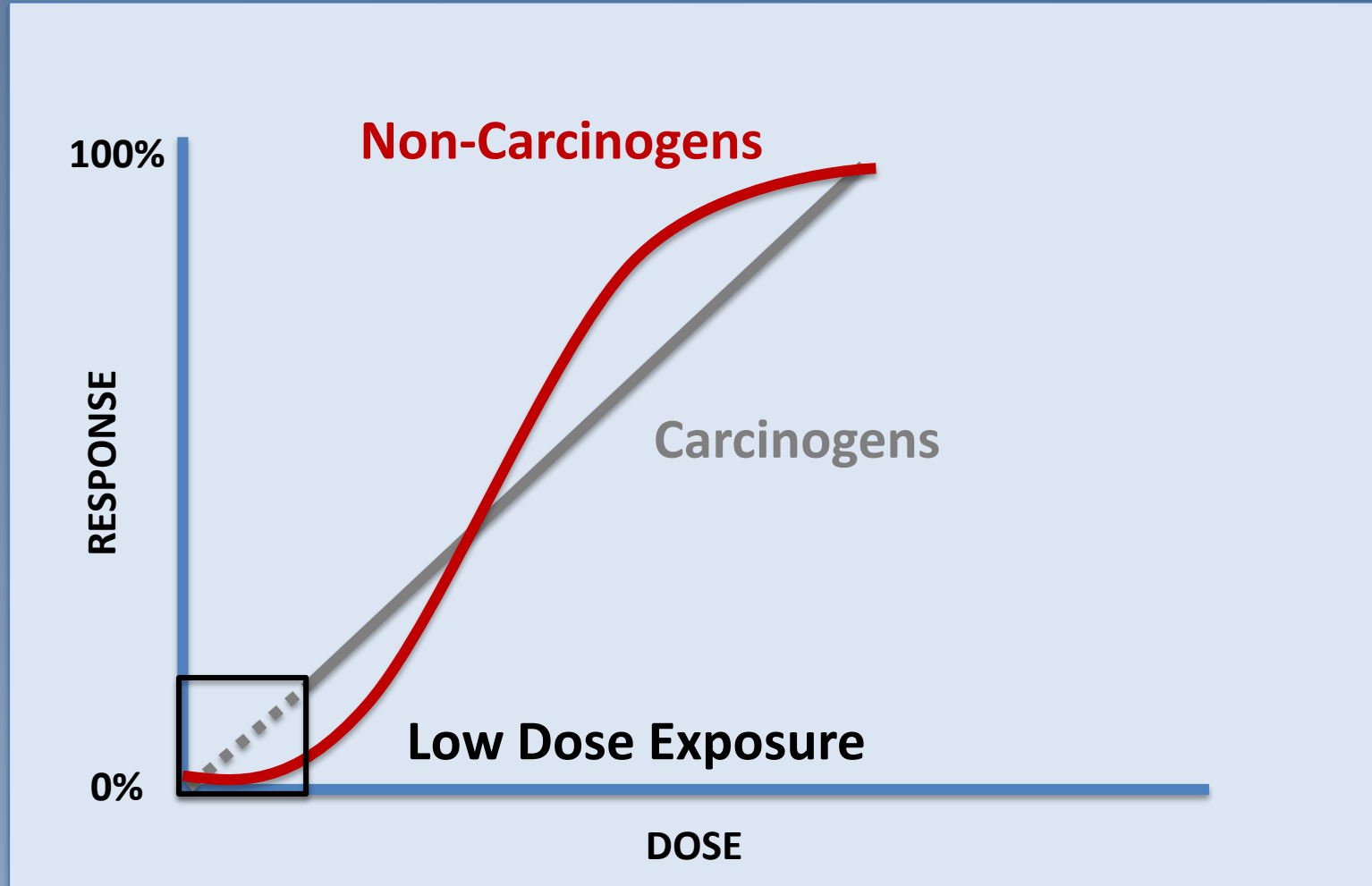
# Dose Response

*“What is there that is not poison? All things are poison and nothing is without poison. Solely the dose determines that a thing is not a poison.”*

*Paracelsus*



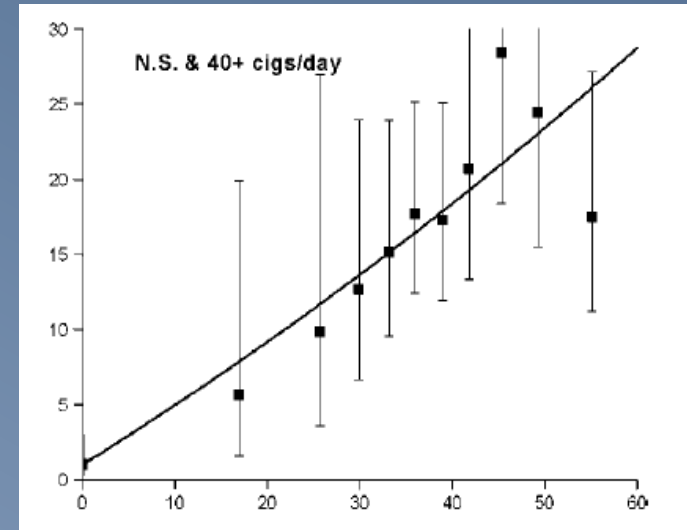
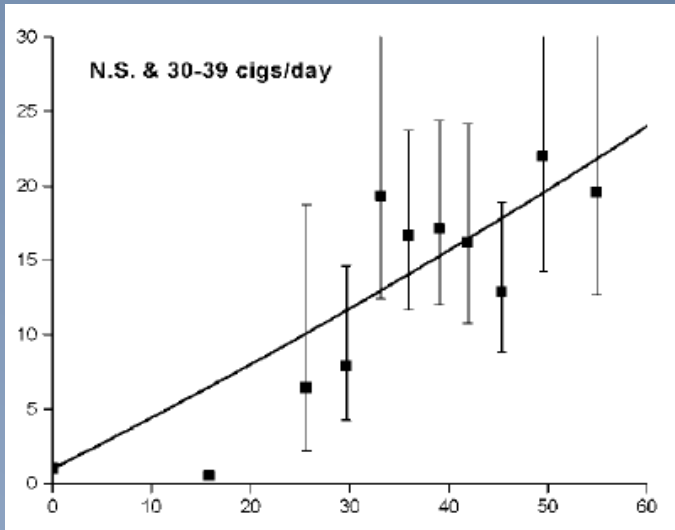
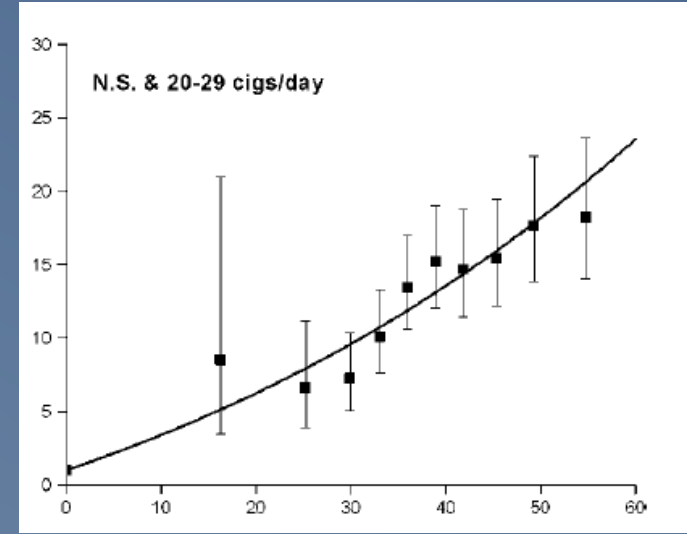
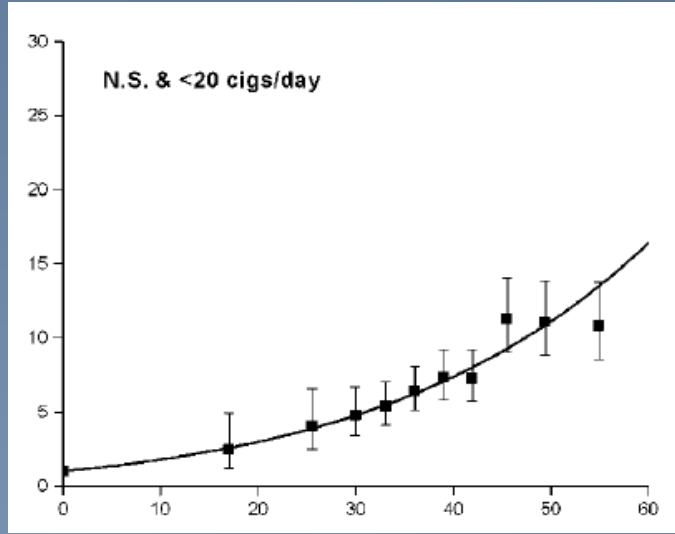
# Types of Dose Response



The schematic presented here illustrates that the lower the dose, the more reduced is the response and therefore the risk associated with the response

# Smoking: Lung Cancer

Odd Ratio



Years of Cigarette Smoking

# Carcinogens in Cigarette Smoke



- Tobacco smoke contains more than 6,000 chemicals, as well as solid ultrafine particles.<sup>1</sup>
- 93 of them have been listed by the FDA as Harmful and Potentially Harmful Constituents (HPHCs).<sup>2</sup>
- The majority are classified as carcinogens or potential carcinogens.<sup>2</sup>

<sup>1</sup> Rodgman A, Perfetti TA. The chemical components of tobacco and tobacco smoke 2nd ed: CRC Press, Taylor & Francis Inc (United States); 2013.

<sup>2</sup> Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act; <https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm297828.pdf>

# Understanding Cancer Potency of Carcinogens\*

Carcinogens		Tobacco Smoke (n=309)	Heat-Not-Burn (n=44)	E-Cigarettes (n=44)	Nicotine Inhaler (n=1)
Compound	IARC Class	Mean Concentration (µg/mL)	% Reduction*	% Reduction*	% Reduction*
Acrylonitrile	2B	4.59×10 <sup>-2</sup>	99.4% ↓	NR	99.8% ↓
1,3 - Butadiene	1	1.83×10 <sup>-1</sup>	99.8% ↓	NR	99.9% ↓

BDL: Below detection limit; NR: Not reported

\* compared to Tobacco Smoke

\* Based on :Stephens WE; Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke; Tobacco Control Published Online First: 04 August 2017. doi: 10.1136/tobaccocontrol-2017-053808

# Understanding Cancer Potency of Carcinogens\*

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1,3 - Butadiene	1	$1.83 \times 10^{-1}$	99.8% ↓	NR	99.9% ↓
Acetaldehyde	2B	$2.55 \times 10^{-0}$	86.9% ↓	99.8% ↓	NR
Formaldehyde	1	$1.54 \times 10^{-1}$	93.1% ↓	94.8% ↓	NR
Cadmium	1	$1.99 \times 10^{-4}$	BDL ↓	94.9% ↓	99.5% ↓
TSNA - NNN	1	$4.63 \times 10^{-4}$	94.5% ↓	99.96% ↓	BDL ↓
TSNA - NNK	1	$2.88 \times 10^{-4}$	94.3% ↓	99.7% ↓	BDL ↓
Mean Life Time Cancer Risk*		1	0.024 ↓	0.004 ↓	0.0004 ↓

BDL: Below detection limit; NR: Not reported

\* compared to Tobacco Smoke

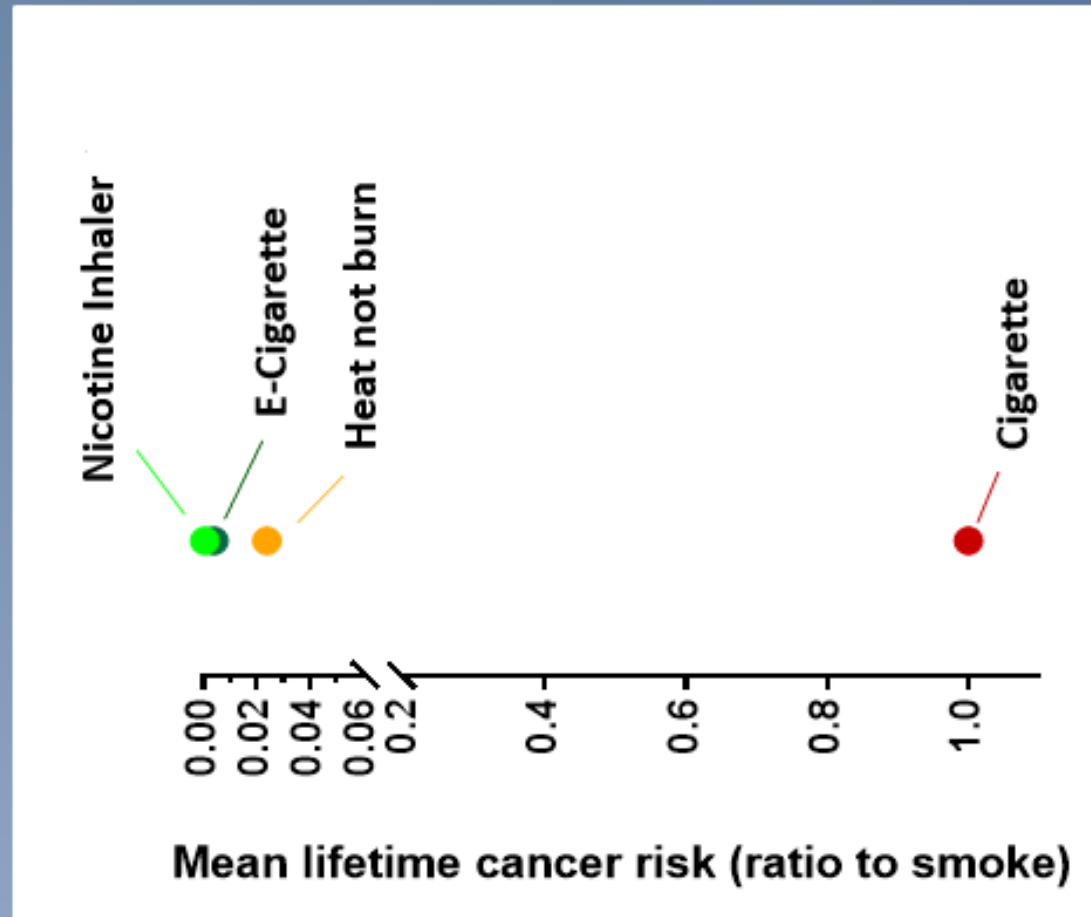
\* Based on :Stephens WE; Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke; 23

Tobacco Control Published Online First: 04 August 2017. doi: 10.1136/tobaccocontrol-2017-053808



# Cancer Potency of Carcinogens of Nicotine and Tobacco Containing Products

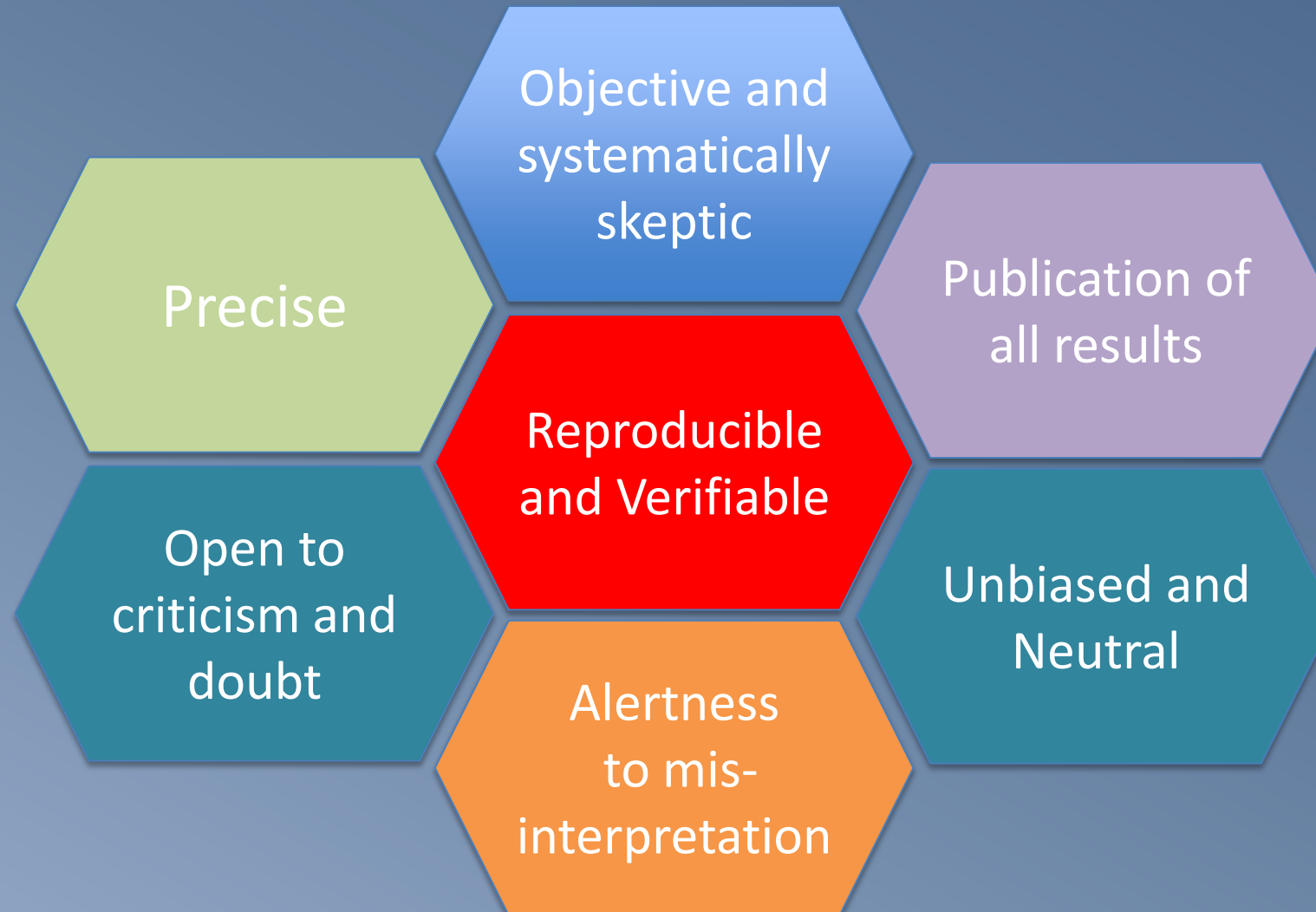
*(Adapted from Stephens, 2017)*



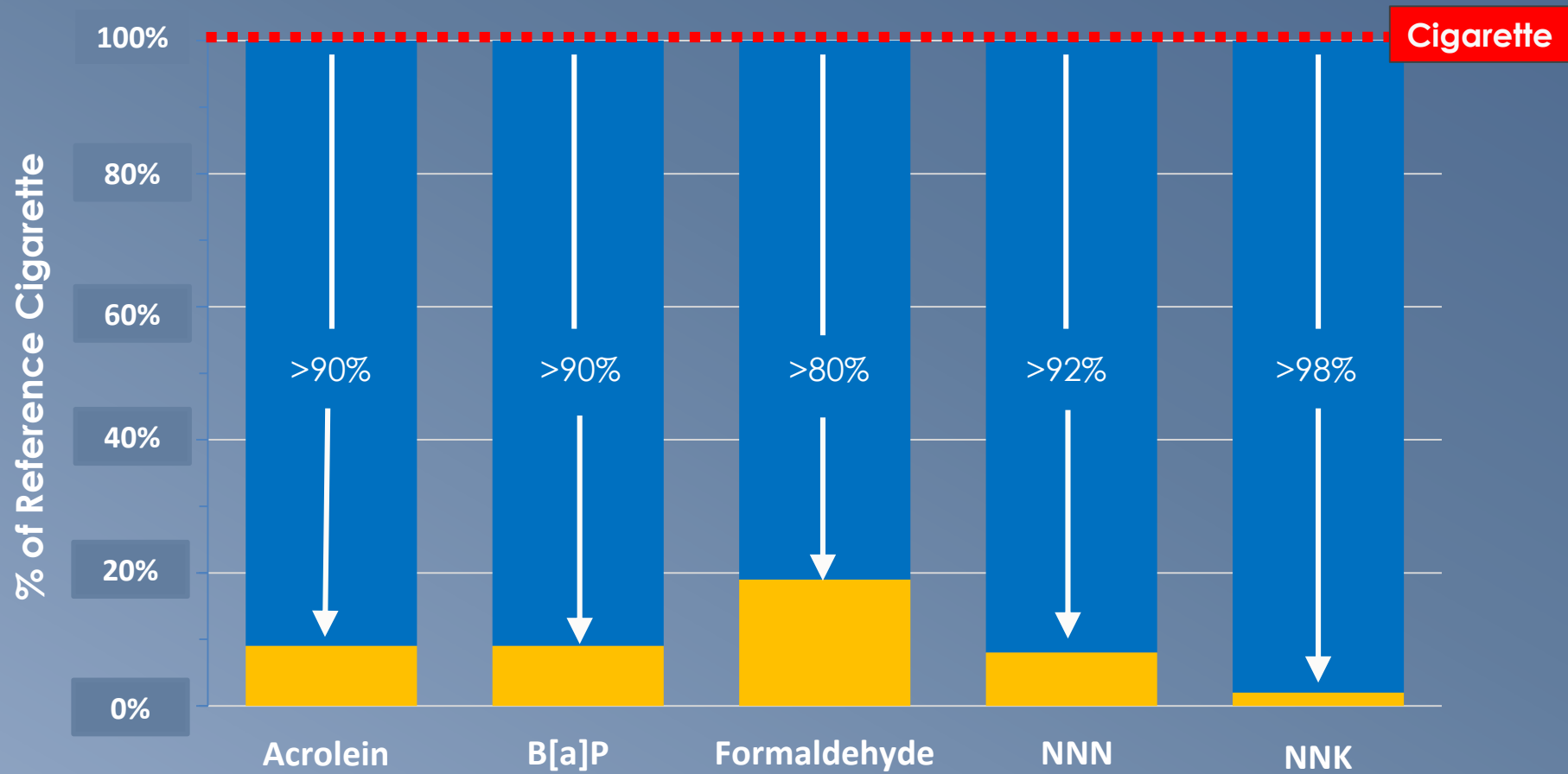
**What evidence exists and how credible  
is the science?**

# What evidence exists and how credible is the science?

The main characteristics of sound & credible science:



# FDA Independent Study on IQOS Emissions



Source: FDA Briefing Book for TPSAC, Page 12 as accessed at <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM593109.pdf>

Note:

- Intense Health Canada's Smoking Regime;
- Comparison on a per-stick basis; Excludes Nicotine, Glycerin and Total Particulate Matter

# Summary on Available Evidence



Public Health  
England

*“The available evidence suggests that heated tobacco products may be considerably less harmful than tobacco cigarettes and more harmful than e-cigarettes”*

*“It has been previously estimated that [electronic cigarettes] are around 95% safer than smoking. This appears to remain a reasonable estimate.”*



*“...new product innovations could make a lot of sense and help people transfer off cigarettes”*



*“The concentration levels of hazardous compounds in the mainstream smoke of IQOS are much lower than those in conventional combustion cigarettes...”*



*“The herein confirmed reductions of relevant toxicants by about 80-99% are substantial, leading to the relevant question of putatively reduced health risks.*

Sources: Public Health England, Evidence review of e-cigarettes and heated tobacco products 2018, 6 February 2018; FDA: Scott Gottlieb, Commissioner Food & Drug Administration; National Institute of Public Health, Bekki et al., Comparison of Chemicals in Mainstream Smoke in Heat-not-burn Tobacco and Combustion Cigarettes, September 2017

BfR: Mallock et al., (German Federal Risk Assessment Institute (BfR)), Levels of selected analytes in the emissions of “heat not burn” tobacco products that are relevant to assess human health risks, Archives of Toxicology, 5 May 2018



# Emerging Smoke-Free Regulatory Trends



*“...**new product innovations** could make a lot of sense and **help people transfer off cigarettes**”*

*- Scott Gottlieb, Commissioner Food & Drug Administration*



Public Health  
England

*“help people to quit smoking by **permitting innovative technologies that minimise the risk of harm**” / “maximise the availability of safer alternatives to smoking”*



*“**heat-not-burn, snus, moist snuff, dissolvable and inhaled nicotine may be significantly safer than cigarettes.**”*

*- Nicky Wagner, Associate Health Minister*

**Growing number of countries are recognizing the benefit of novel smoke-free products**



# Facts & Evidence of Smoke-Free Products

PMI's Evidence on IQOS related to Cancer

Dr Gizelle Baker

Director of Scientific Engagement

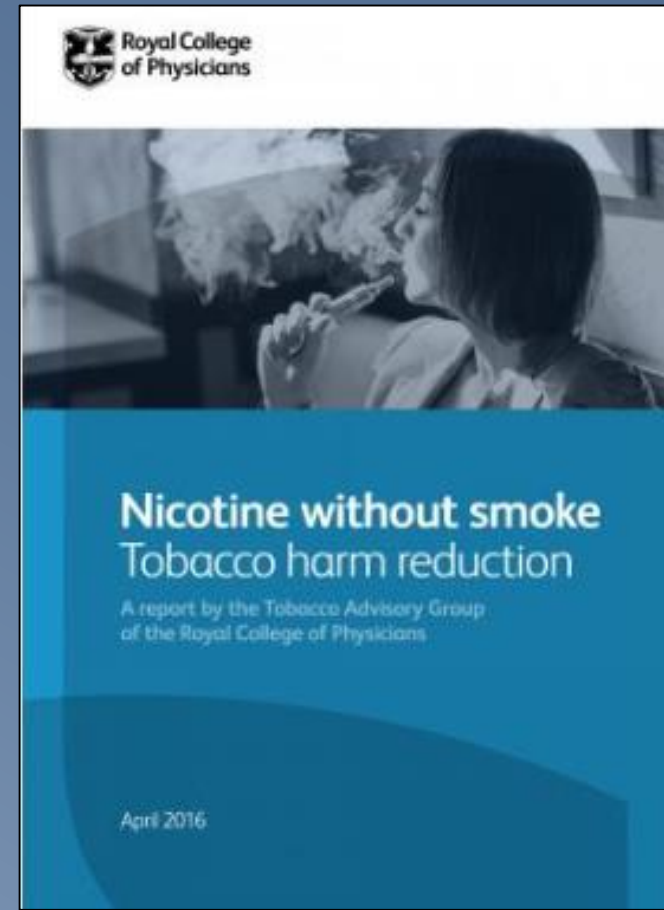
# Agenda

- Concept behind Heat-not-Burn Products
- Totality of Evidence on IQOS to date
- Can switching to IQOS reduce genetic damage, inflammation?
- Independent Studies available on IQOS?

# What is an Ideal Harm Reduction Product

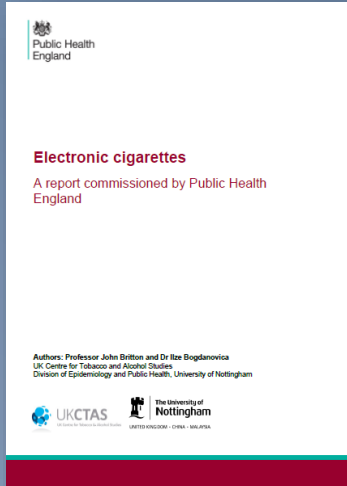
“The ideal harm-reduction device should therefore **deliver nicotine in a manner as similar as possible to cigarettes**, while at the same time maximising palatability and nicotine delivery to approximate the experience of cigarette smoking more closely.”

*(Royal College of Physicians 2016)*





# Nicotine is Not the Primary Cause of Smoking-Related Diseases....



***May 2014, Public Health England:***

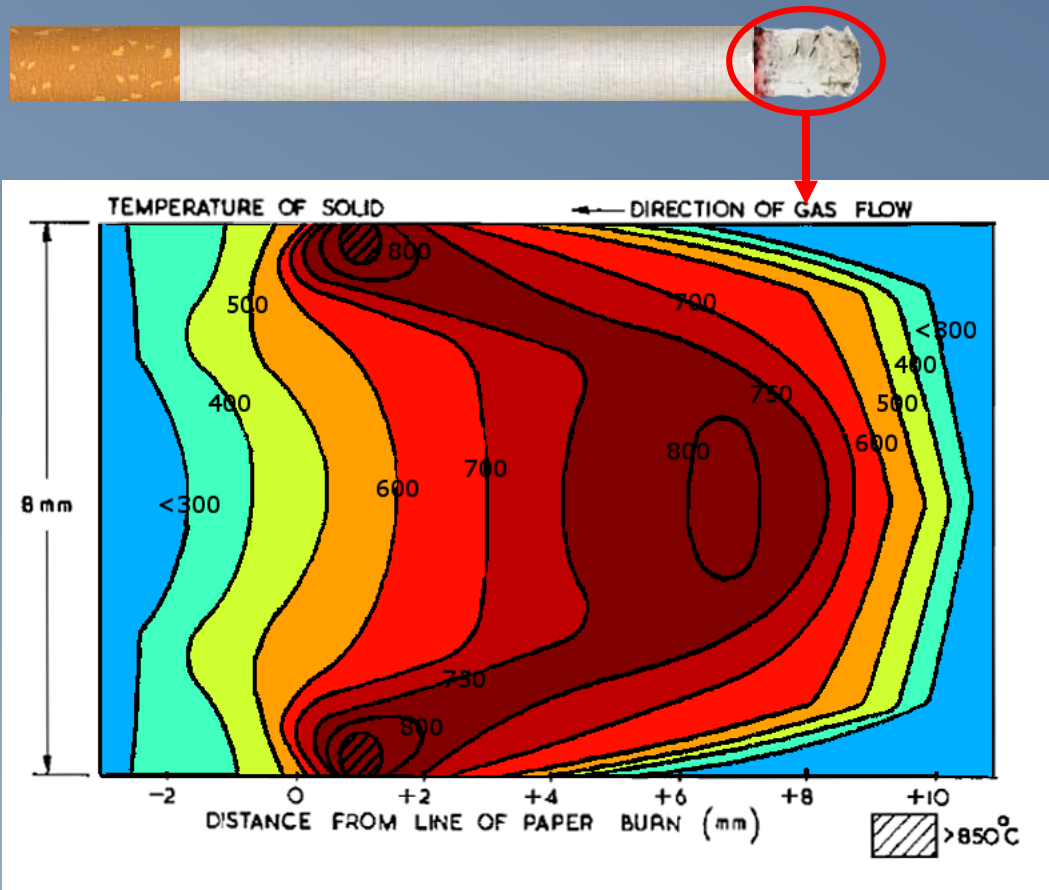
**“[...] Nicotine does not cause serious adverse health effects** such as acute cardiac events, coronary heart disease or cerebrovascular disease, and is **not carcinogenic**. The doses of nicotine delivered by electronic cigarettes are therefore extremely unlikely to cause significant short or long-term adverse events.[...]”

***July 2017, FDA Commissioner Dr. Scott Gottlieb:***

**“[...] nicotine in itself is not responsible** for the cancer, the lung disease and heart disease that kill hundreds of thousands Americans every year. [...] it is the **other chemical compounds** in tobacco and in the **smoke created by setting the tobacco on fire** that directly cause illness and death.”



# Primary cause of smoking-related diseases ...



Baker R. R., 1975, Temperature variation within a cigarette combustion coal during the smoking cycle, High Temp. Sci., 7, 236 – 247). Coloration by PMI.

- Cigarette smoke is a complex mixture of **more than 6000 chemicals**
- Several of these chemicals are harmful and have been classified as **likely causes of smoking related diseases**
- The temperature at the **burning tip > 600 °C**
- When air is drawn through the cigarette (during a puff) the temperature **rises > 800 °C**
- The heat released breaks down tobacco components generating smoke and ash



# Absence of combustion fundamental to product developments

PMI developed several lines of evidence to establish lack of combustion



Heated below 400C



No self-sustaining heat



Oxygen-free operation

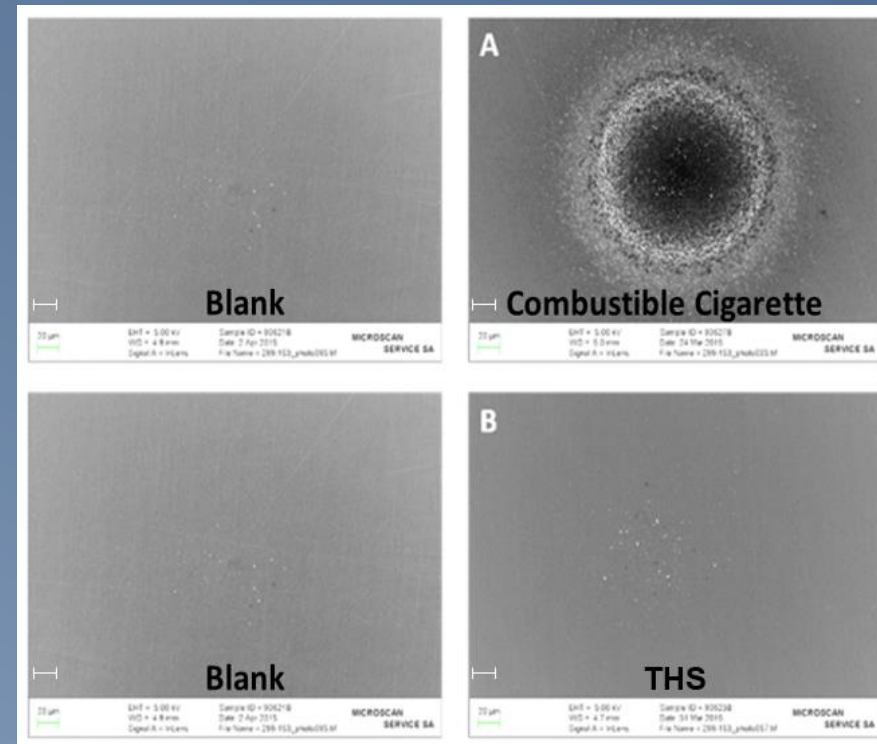


No ash



No solid particles (fig 1)

Fig 1: no solid particles in IQOS aerosol



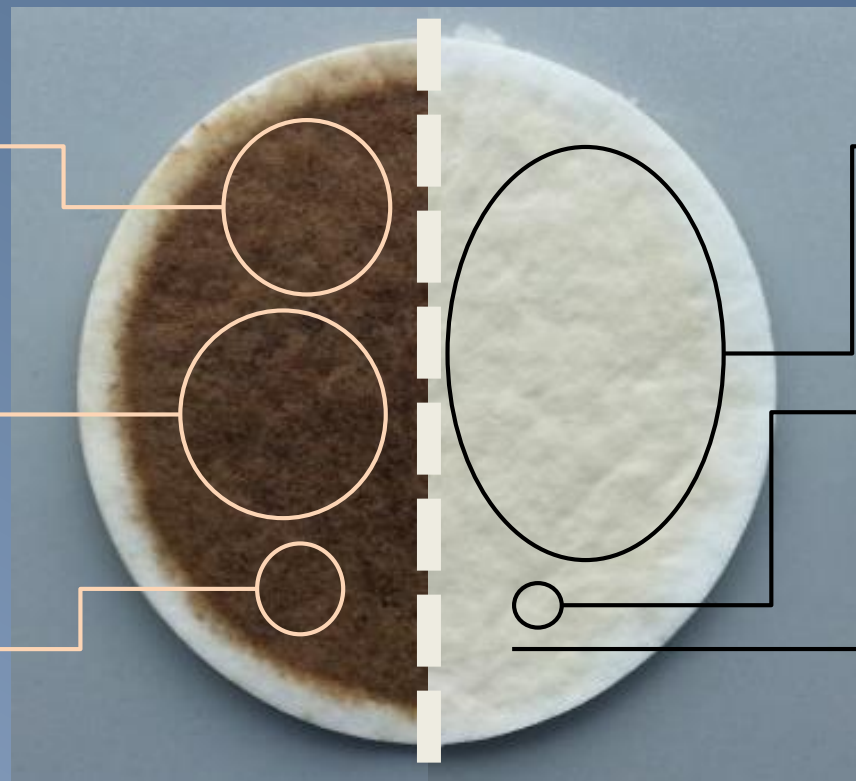
# Smoke is Different from Tobacco Vapor (Aerosol)



Water and glycerin form **50%** of smoke mass

Toxicants

Contains **~0.5 trillion** Carbon-based solid particles



Water and glycerin form **90%** of aerosol mass

Levels of Toxicants reduced by **>90%**

**No** Carbon-based solid particles



Smoke and aerosol were collected on a Cambridge filter pad using Health Canada Intense smoking regime

# Scientific Assessment

## Studies

**18** Non-Clinical Studies

**10** Clinical Studies

## Publications

**30+** on IQOS assessment

**150+** on assessment methods and verification

# Totally of Evidence on IQOS



Toxic Cigarette Emissions



Reduced Emissions

Reduced Exposure

Reduced Adverse Health Effects

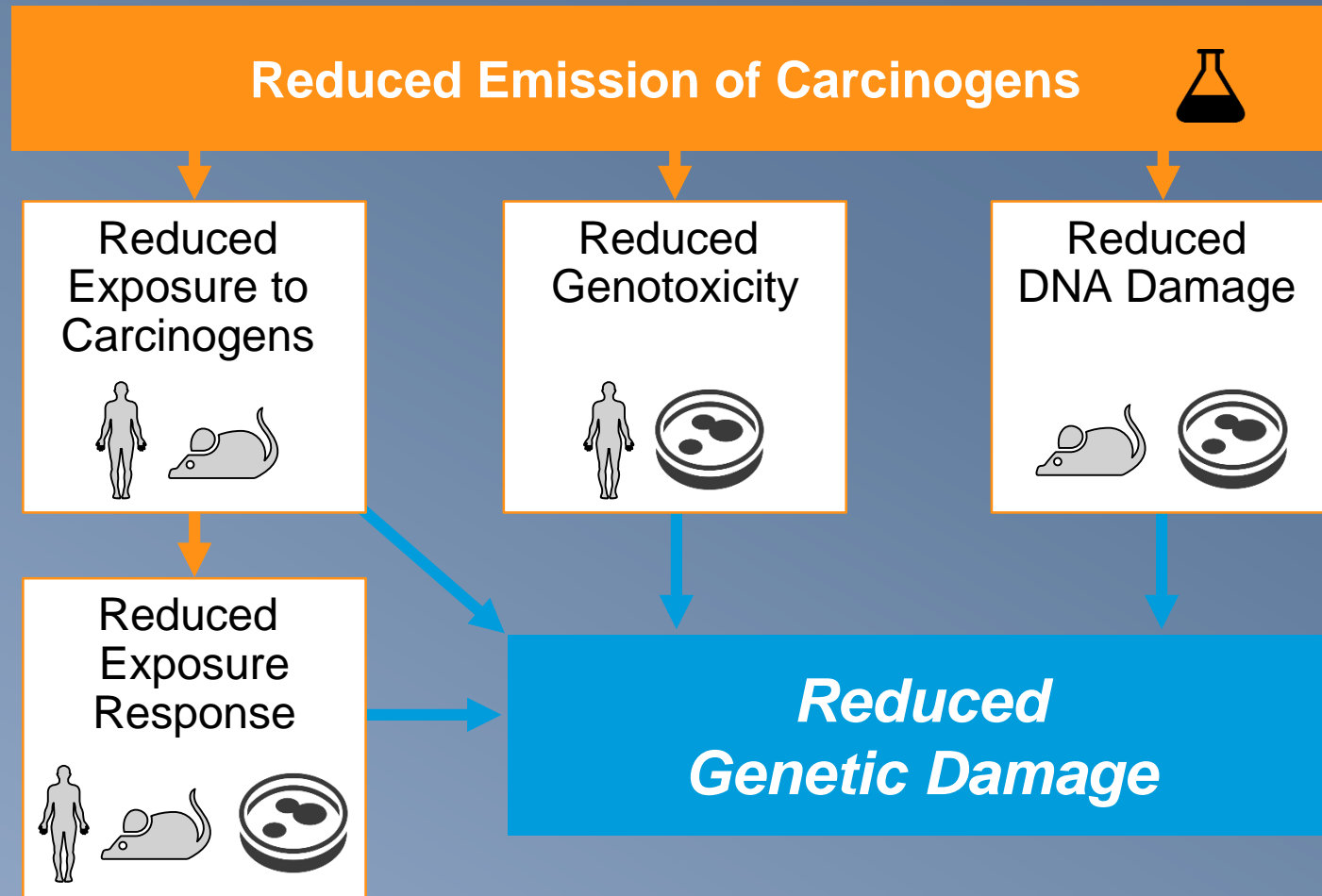


PMI

18 Non-Clinical Studies and 10 Clinical Studies

# Genetic Damage is Reduced by IQOS

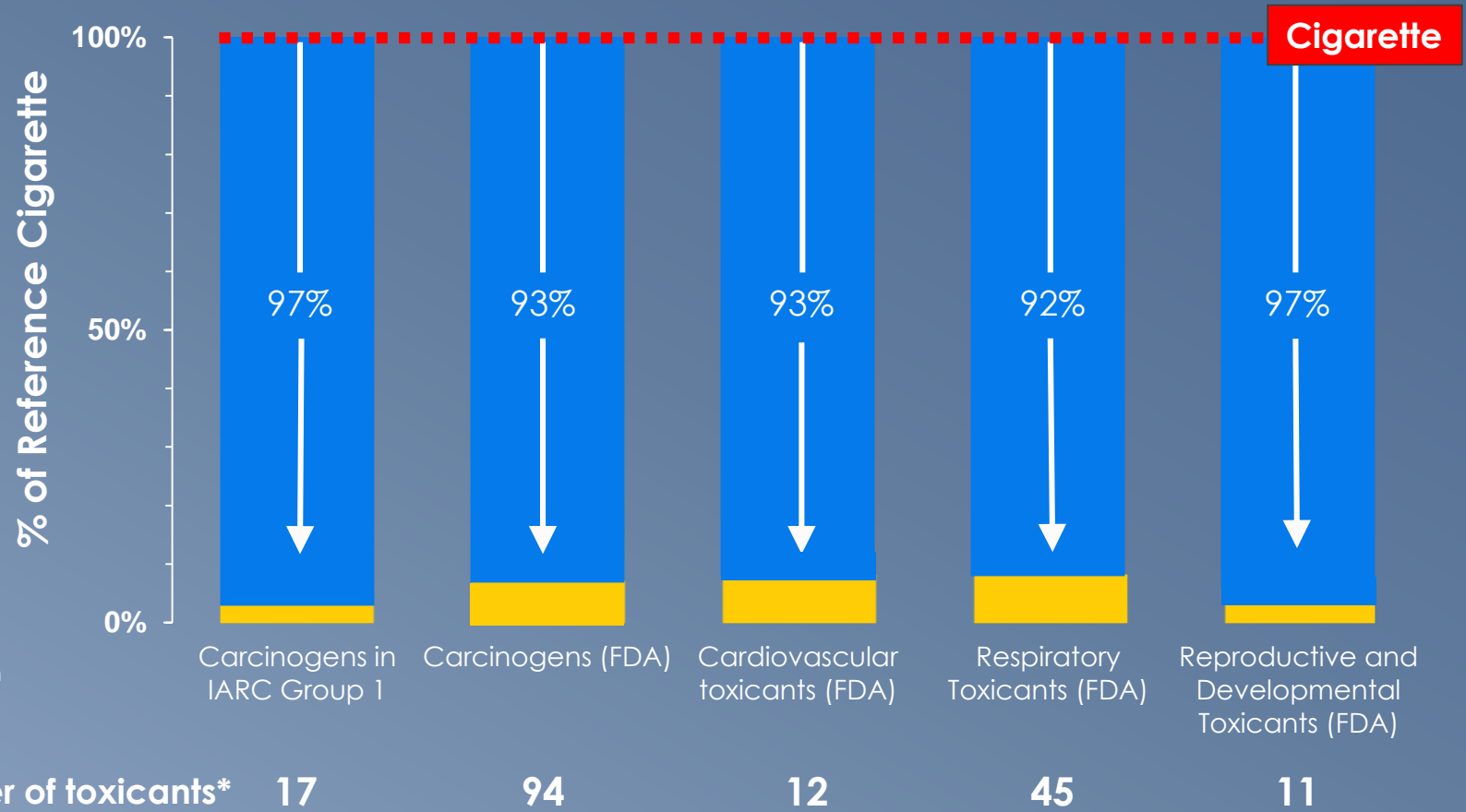
Evidence from  
IQOS Assessment



# Reduced Formation: by Disease Category

Average reductions in the formation of harmful or potentially harmful constituents for *THS* compared to levels measured in smoke from the 3R4F reference cigarette by disease category\*

- Note:
- Intense Health Canada's Smoking Regime;
  - Comparison on a per-stick basis; Excludes Nicotine, Glycerin and Total Particulate Matter



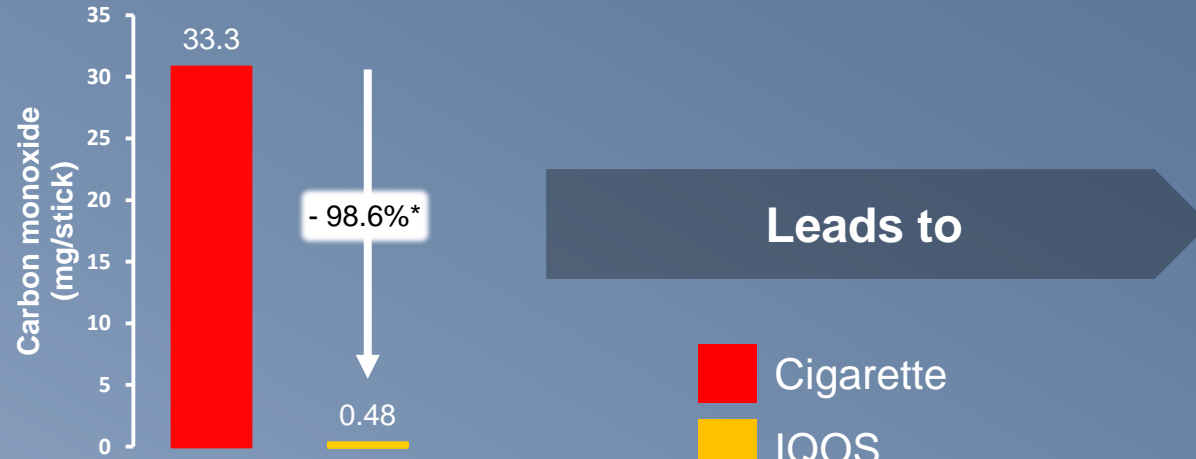
\* Analysis contains all compounds included in the FDA-93 list of HPHCs. Number of toxicants analyzed can be more than 93 because we considered individual compounds as FDA-93 groups some compounds per classes or isomers



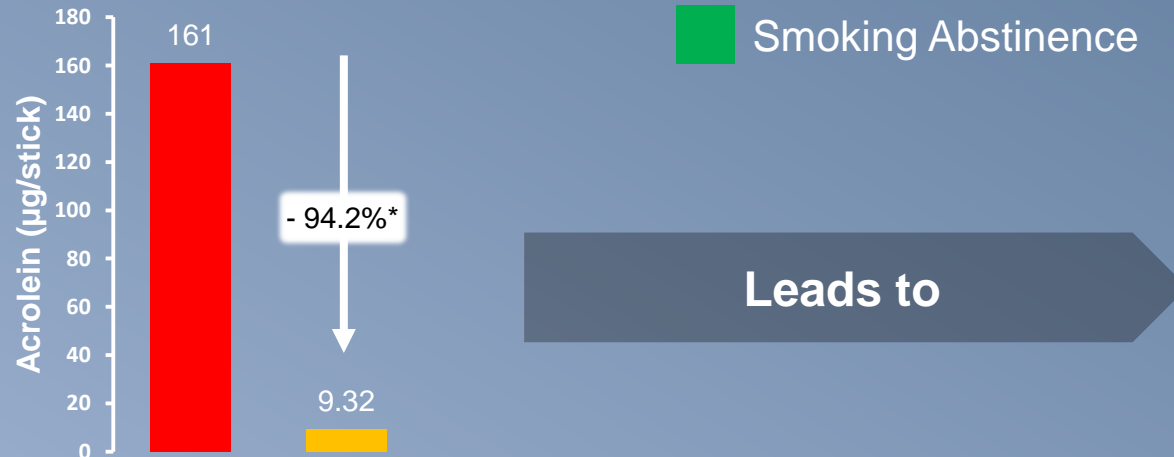
# Changes in Exposure to HPHCs with IQOS Use

Reduced Exposure in Healthy Adult Smokers

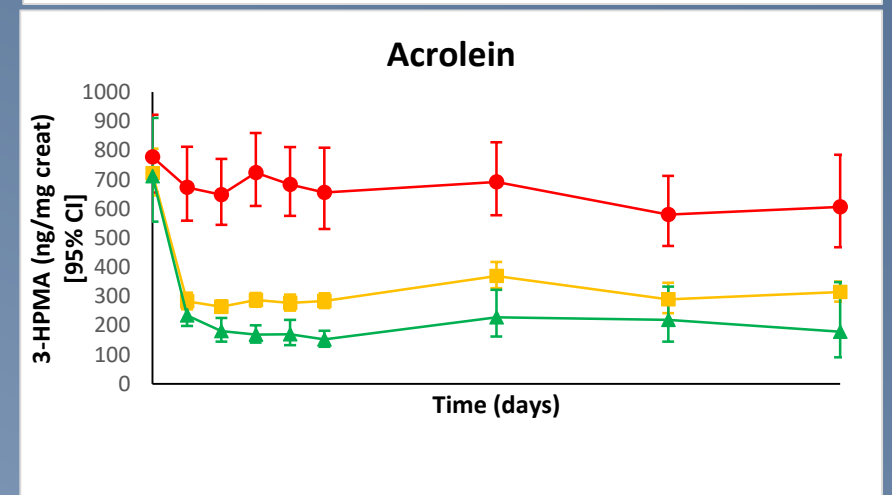
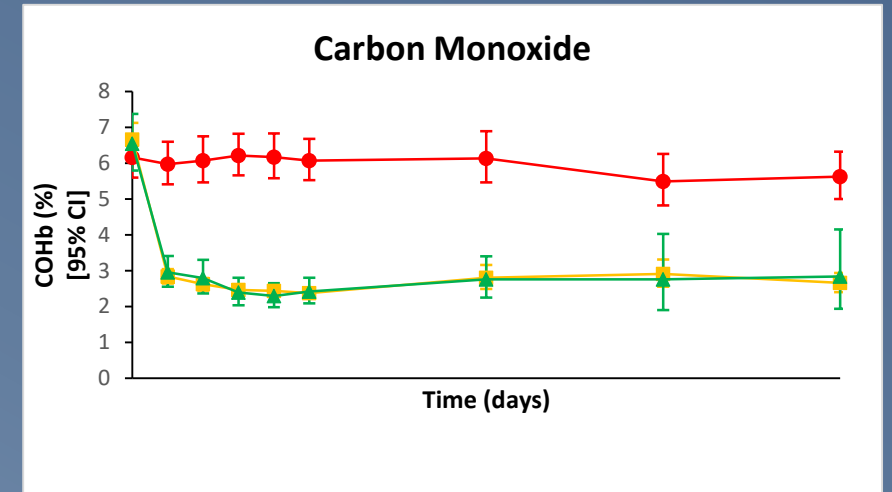
HPHCs are Drastically Reduced in IQOS Aerosol



- Cigarette
- IQOS
- Smoking Abstinence



Exposure is Significantly Reduced After Switching to IQOS

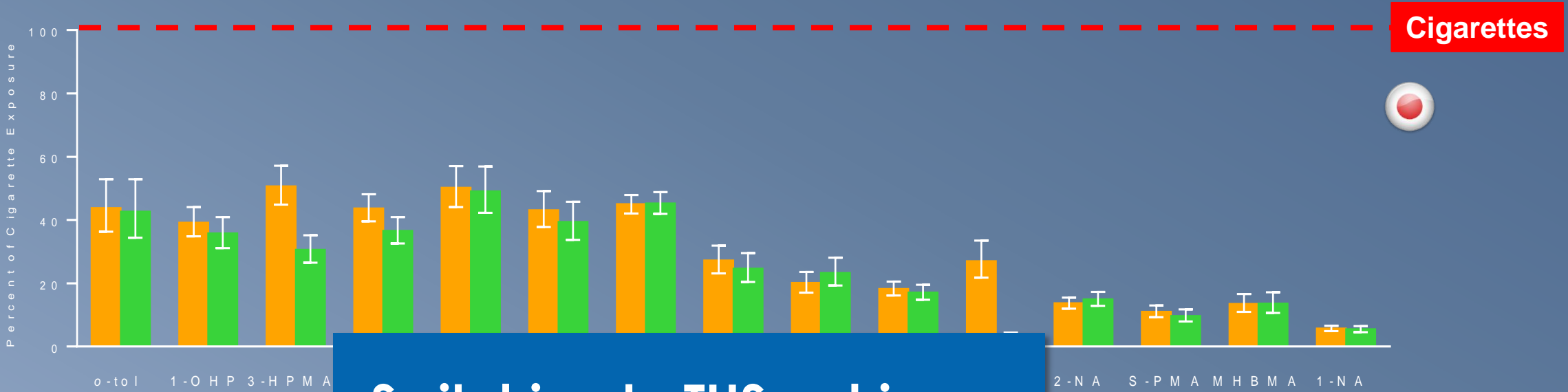


\* On equivalent nicotine basis

# Reduced Exposure

## Reduced Exposure in Healthy Adult Smokers

■ IQOS
 ■ Smoking Abstinence



**Switching to THS achieves almost 95% of the reduction achieved by smoking abstinence**

# Reduced Exposure Response

	Disease	Patho-mechanism	Directional Change	Statistically Significant
HDL-C	Cardiovascular Disease	Lipid Metabolism	⬆️	✓
COHb	Cardiovascular Disease	Acute Cardio-Vascular Effects	⬇️	✓
sICAM-1	Cardiovascular Disease	Endothelial Function	⬇️	Borderline
11-DTX-B2	Cardiovascular Disease	Clotting	⬇️	
8-epi-PGF2α	All Diseases	Oxidative Stress	⬇️	Borderline
WBC Count	All Diseases	Inflammation	⬇️	✓
FEV1 %pred	Respiratory Disease	Lung Function	⬇️	✓
Total NNAL	Cancer	Genotoxicity	⬇️	✓

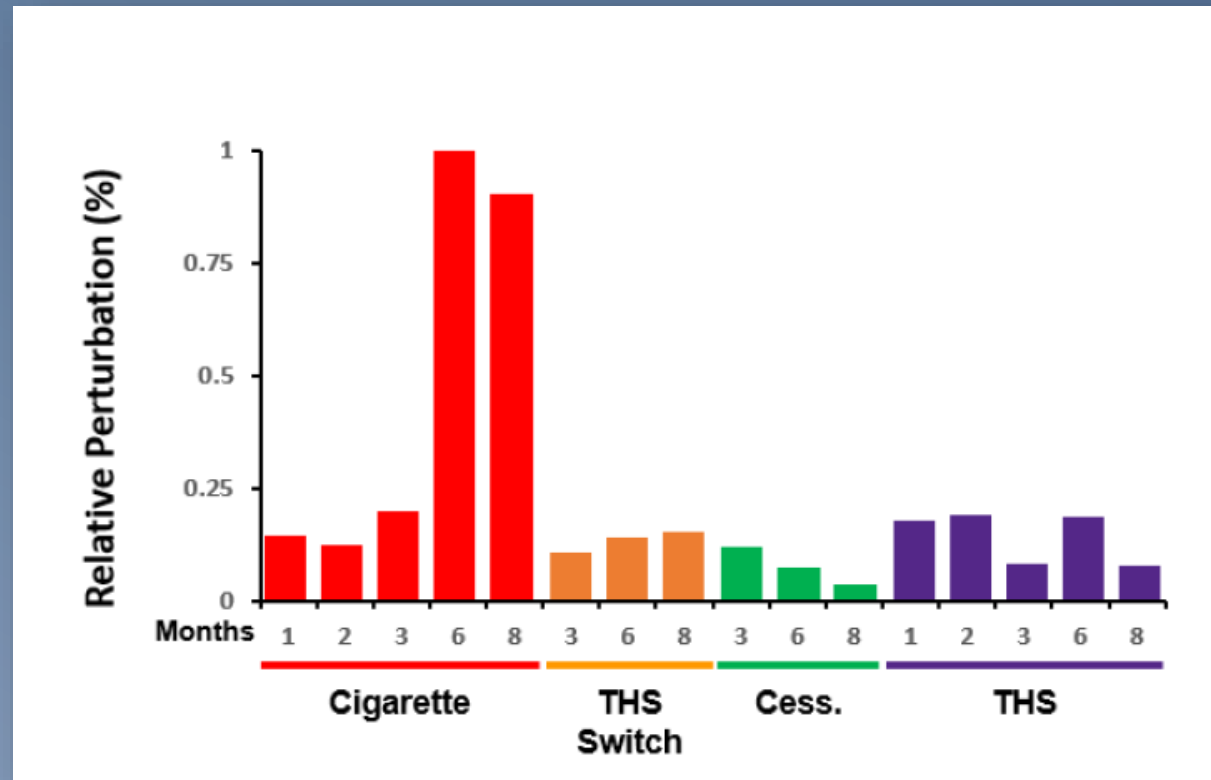
## Conclusions

All clinical risk endpoints shift in the same direction as smoking cessation.

Five of eight clinical risk endpoints statistically significant different vs. continued smoking

- Statistical significance defined as  $p \leq 0.0156$  (using a Hailperin Ruger adjustment for multiplicity)
- Borderline is defined as  $0.0156 < p\text{-value} < 0.05$
- Green arrows indicated that the direction of the change is the same as cessation [www.primscience.com](http://www.primscience.com)

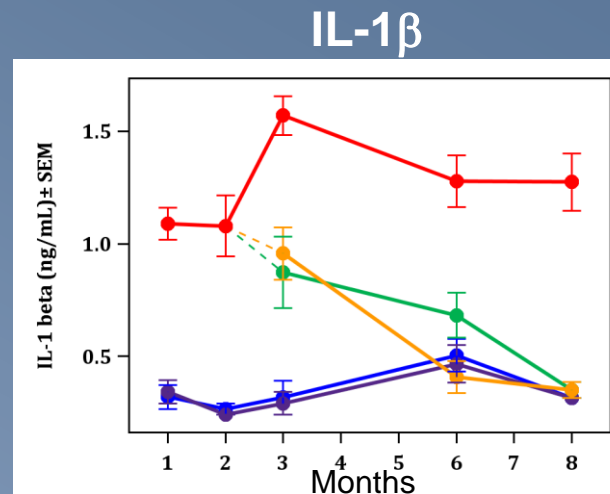
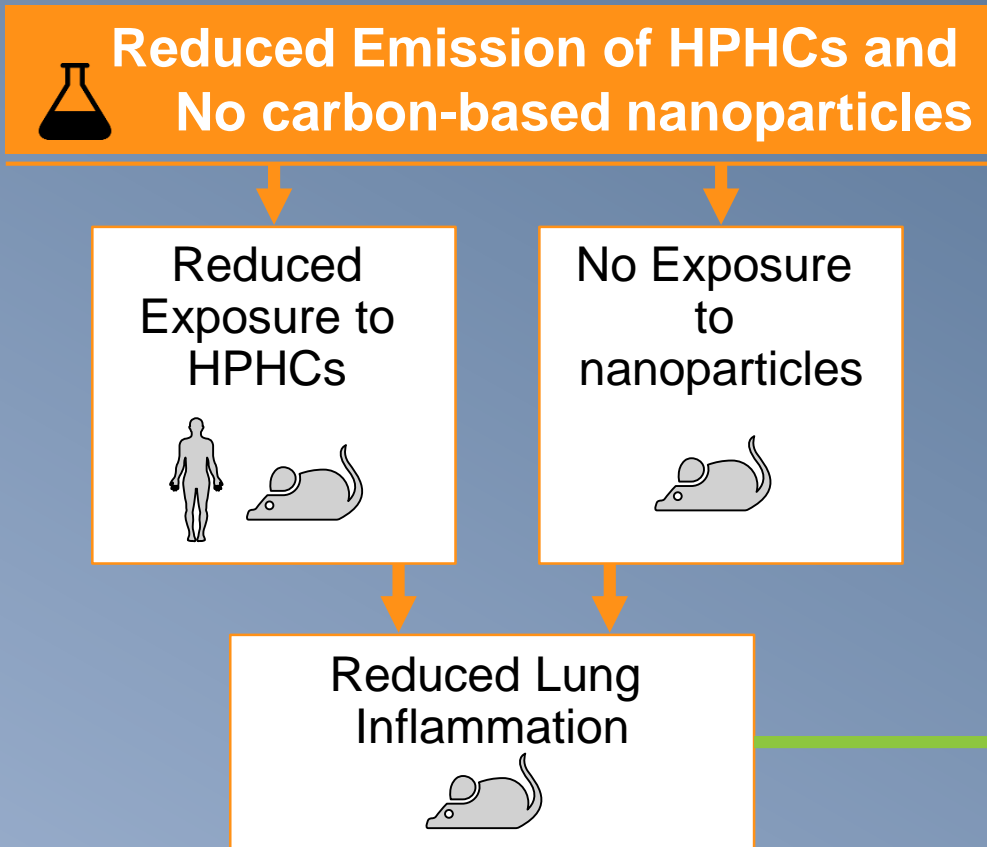
# Genetic Damage is Reduced by IQOS



Perturbations of the DNA damage response network or the nasal epithelium in the Apoe<sup>-/-</sup> Switching Study (Phillips et al. 2016)

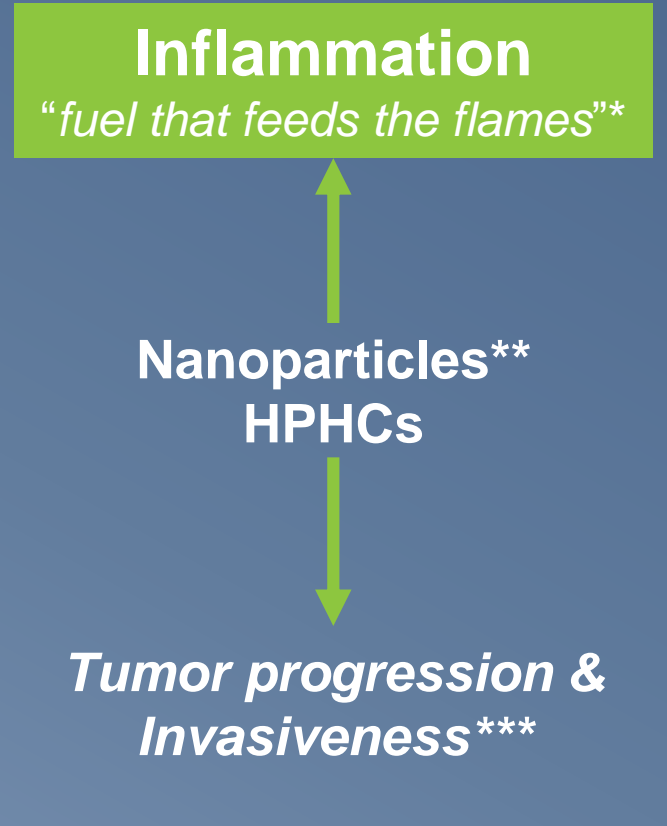
# Inflammation is Reduced by IQOS

## Evidence from IQOS Assessment



**Reduced Inflammation**

## Does Switching to IQOS Reduce Inflammation?



\* Balkwill F and Mantovani A. Inflammation and cancer: back to Virchow? *Lancet*, 2001, 357:539–45.

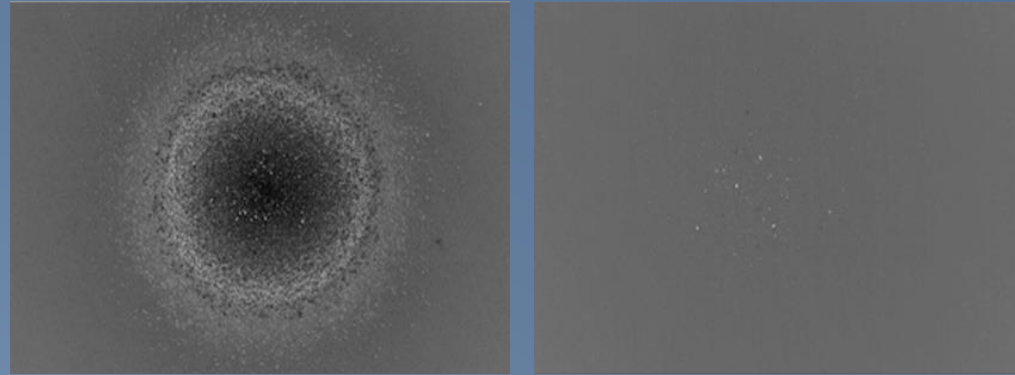
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# Nanoparticles Deposit in the Lung

## Cigarette Smoke

Carbon-based nanoparticles  
 $6 \times 10^{11}$  particles  $\approx 0.7$  mg\*

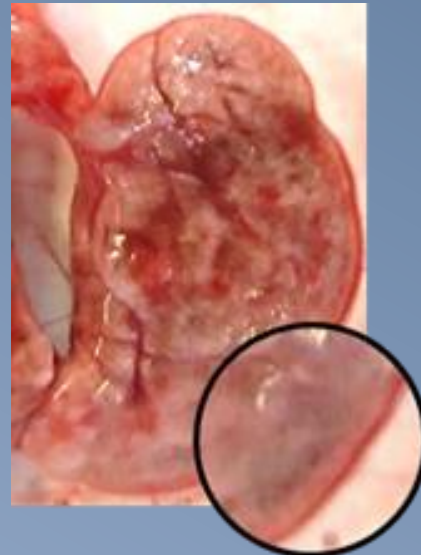


## IQOS Aerosol

No solid particles

## Lung Deposition after 6 months

Cigarette smoke  
(600 mg/m<sup>3</sup> TPM)



Corresponding  
concentration of  
IQOS aerosol





# Totally of Evidence on IQOS



Pharmacokinetics

5-day confinement reduced exposure

90-day ambulatory reduced exposure

Impact on Bystanders IQOS exposure

Exposure response 6 + 6 months Smoking Cessation Response

A/J Mouse Study

Nicotine absorption similar to cigarette

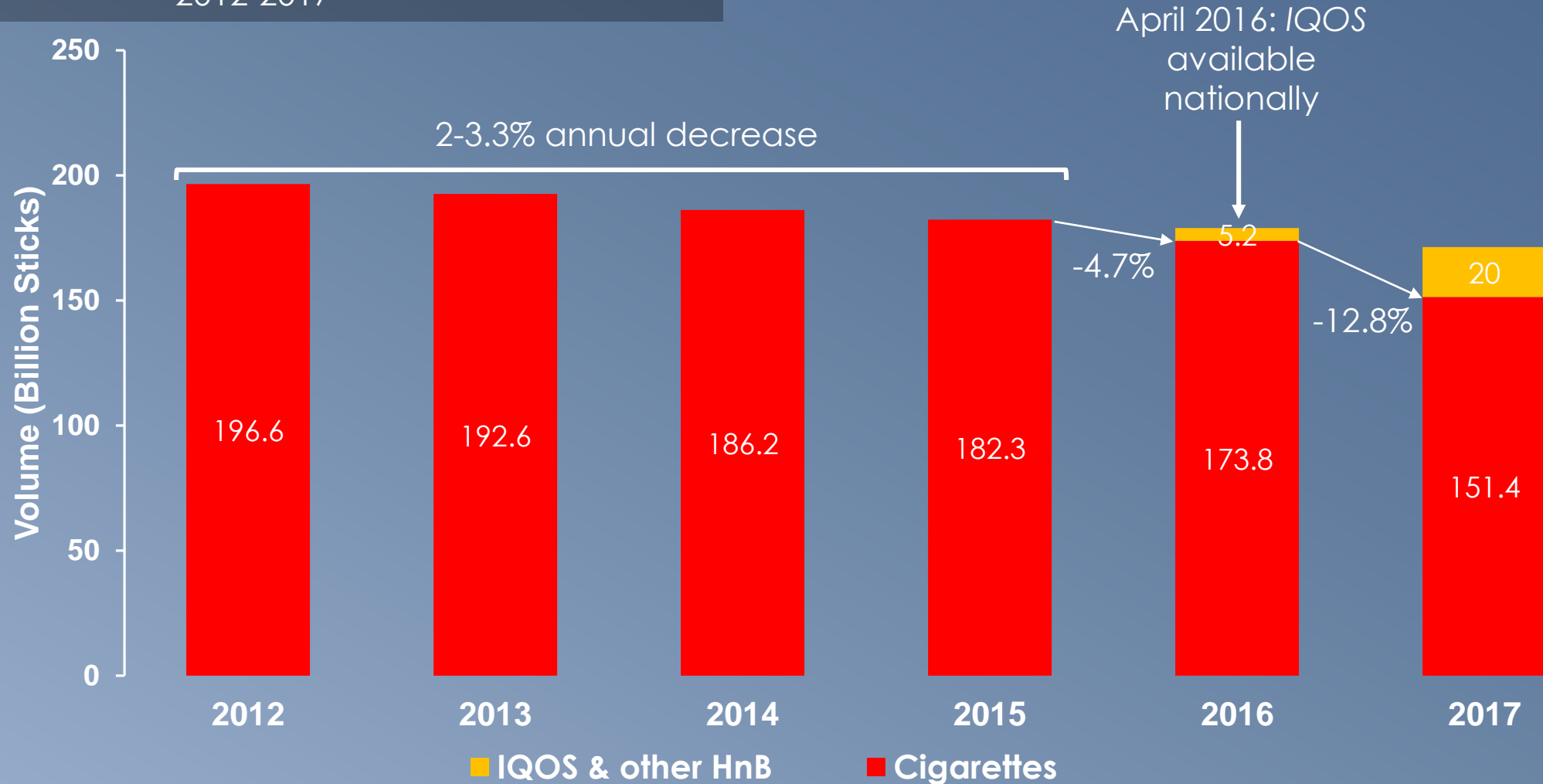
Exposure to toxicants is reduced  
No carbon based solid particles  
Exposure to nicotine is similar  
No negative effect to bystanders

Reduced exposure leads to positive biological changes  
Incidence of Lung Tumors (A/J Mouse model) is significantly reduced

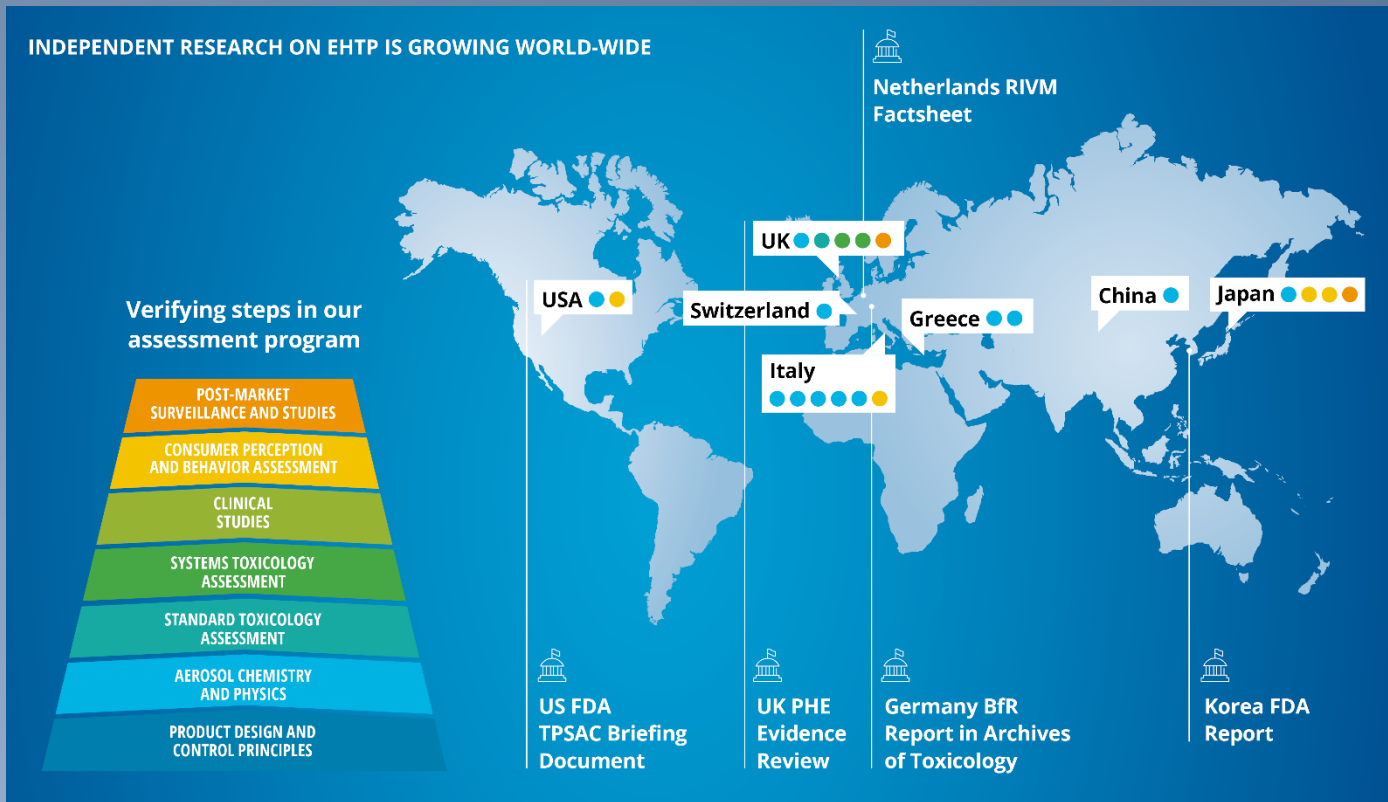
# Post-Market Decline in Cigarette Sales

## Japan Total Industry Volume (Including IQOS)

2012-2017



# Independent research on IQOS



## Five Government Reports

&

## Over 20 independent research publications

Independent research generally confirms: *IQOS* produces significantly lower levels of harmful chemicals compared to cigarettes

See our Scientific Update on Smoke-Free Products Issue 5 focusing on Independent Research

# Highlighted Government Reports



**Federal Institute for Risk Assessment (BfR)** (Germany - 2018) – in line with our results:

*“The herein confirmed reductions of relevant toxicants by about 80-99% are substantial”*



**Food and Drug Administration Briefing Document** (FDA, US – 2018) - in line with our results:

*“The independent testing performed by STL [FDA’s Southeast Tobacco Laboratory] confirmed the lower levels of selected [harmful and potentially harmful compounds] HPHCs in the aerosol from the HeatSticks compared to mainstream cigarette smoke.”*



**Public Health England** (UK – 2018) – in line with our results:

*“Compared with cigarette smoke, heated tobacco products are likely to expose users and bystanders to lower levels of particulate matter and harmful and potentially harmful compounds. The extent of the reduction found varies between studies.”*



**National Institute for Public Health and the Environment (RIVM)** (Netherlands – 2018)  
in line with our results:

*“The use of heatsticks with the IQOS is harmful to health, but probably less harmful than smoking tobacco cigarettes.”*



**Report by Korean Food and Drug Administration** (Korea – 2018) – conclusions not in line with the results:

KFDA results confirm significant reductions of HPHCs in heated tobacco products compared to cigarettes, but omit to discuss them.

# Highlighted Independent Peer-reviewed Research



## Department of Environmental Health, Japan (J UOEH 2017)

A member of the WHO Tobacco Laboratory Network

*“The concentrations of nicotine in tobacco fillers and the mainstream smoke of iQOS were almost the same as those of conventional combustion cigarettes, while the concentration of TSNAs was one fifth and CO was one hundredth of those of conventional combustion cigarettes.”*



## Researchers at University of St. Andrews, Scotland, UK (Tobacco Control, 2017)

*“Mean lifetime risks decline in the sequence: combustible cigarettes >> heat-not-burn >> e-cigarettes (normal power) ≥ nicotine inhaler.”*



## Researchers at the IRCCS Foundation National Cancer Institute in Milan, Italy (Aerosol Science and Technology, 2017)

*“Overall, our results indicate that iQOS devices, while having substantially lower emissions of most toxic compounds compared to CC [combustible cigarettes], are still not risk-free.”*



## Leading e-cigarette researchers at Onassis Cardiac Surgery Center, Greece (Addiction, 2018)

*“The IQOS heated tobacco product emits substantially lower levels of carbonyls than a commercial tobacco cigarette (Marlboro Red) but higher levels than a Nautilus Mini e-cigarette.”*



# What We Know Today

- IQOS is not risk free and is addictive and the best choice is to quit
- Smokers carry a time-dependent relative risk of disease based on their smoking history when they quit or switch to IQOS
- IQOS is a much better choice for smokers than to continue smoking cigarettes
  
- We all share the responsibility to provide accurate information based on sound science
- Consumers have the right to receive accurate and non-misleading information to make an informed, better choice for their health

*This Scientific Update is issued for the purpose of publishing and disseminating scientific information and not for advertising or marketing purposes regarding tobacco or nicotine-containing products. The content of this Scientific Update is not and should not be regarded as an offer to sell, or a solicitation of an offer to buy, any product of PMI or its affiliates. The content on this Scientific Update is also not and should not be regarded as a promise, warranty, characterization or guarantee regarding any product of PMI or its affiliates.*





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