PMI SCIENCE
PHILIP MORRIS INTERNATIONAL

INVESTIGATOR-INITIATED STUDIES (IIS) IN NON-PHARMA INDUSTRIES

Conny Johansson
Philip Morris International R&D, Neuchâtel, Switzerland

Medical Affairs Strategic Summit East
April 26th 2017, Parsippany, NJ, US

INTRODUCTION TO PHILIP MORRIS INTERNATIONAL

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WHO WE ARE

Our Goal and Strategies

Our goal is to design a smoke-free future

Our core strategies are:

SMOKE-FREE

Develop, market, and sell smoke-free alternatives, and switch our adult smokers to these alternatives, as quickly as possible around the world

TRANSITION

Transition our resources from cigarettes to smoke-free alternatives

REGULATION

Propose regulatory policies that encourage the replacement of cigarettes by smoke-free alternatives

THE EXTERNAL PERCEPTION

Bloomberg

In Marlboro Country, a Big-Money Race for the New Smoke

"Philip Morris has demonstrated time and time again in the past its introduction of new products has led to more smokers," says Matt Myers, president of the Campaign for Tobacco-Free Kids, a leading U.S. anti-smoking group. "Given their history, no one should ever trust what a tobacco company says it intends to do."

https://www.bloomberg.com/news/articles/2016-10-24/in-marlboro-country-a-big-money-race-for-the-new-smoke

CREATING A SMOKE-FREE FUTURE

Science and Innovation

Our vision is to offer smokers a **better choice**

How are we making this vision a reality?

The answer is that we are **developing and testing products** that deliver nicotine **without the harmful smoke** of cigarettes – yet that consumers will find satisfying. Since 2008, we've invested over USD 3 billion, employing over 400 world-class scientists, engineers, and technicians.

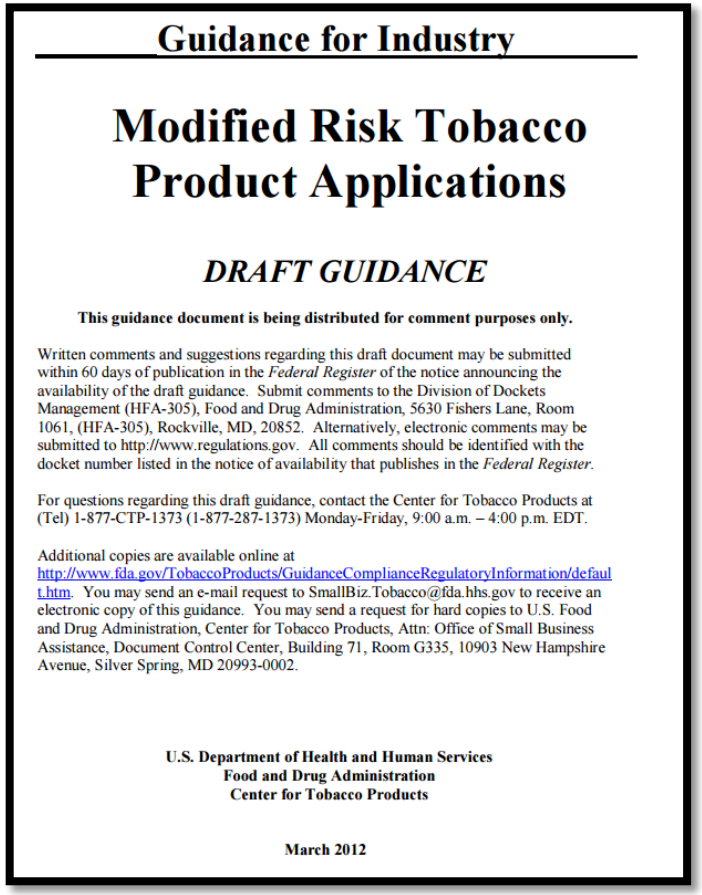
We're already making these new products available. **Over a million consumers have switched** to the first of our smoke-free products.

What is an RRP?

Reduced-Risk Products ("RRPs") is the term we use to refer to products that present, are likely to present, or have the potential to **present less risk of harm to smokers who switch to these products versus continued smoking**.

We have a range of RRPs in various stages of development, scientific assessment and commercialization.

Because **our RRPs do not burn tobacco, they produce far lower quantities of harmful and potentially harmful compounds than found in cigarette smoke.**



Guidance for Industry

Modified Risk Tobacco Product Applications

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Written comments and suggestions regarding this draft document may be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Alternatively, electronic comments may be submitted to http://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft guidance, contact the Center for Tobacco Products at (Tel) 1-877-CTP-1373 (1-877-287-1373) Monday-Friday, 9:00 a.m. – 4:00 p.m. EDT.

Additional copies are available online at http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/default.htm. You may send an e-mail request to SmallBiz.Tobacco@fda.hhs.gov to receive an electronic copy of this guidance. You may send a request for hard copies to U.S. Food and Drug Administration, Center for Tobacco Products, Attn: Office of Small Business Assistance, Document Control Center, Building 71, Room G335, 10903 New Hampshire Avenue, Silver Spring, MD 20993-0002.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Tobacco Products

March 2012

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https://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM297751.pdf

PMI RRP PLATFORMS

"It is primarily the toxins and carcinogens in tobacco smoke – not the nicotine – that cause illness and death."

- NICE Public Health Guidance: Tobacco: Harm Reduction Approaches to Smoking (2013)

TABLE 1—ESTABLISHED LIST OF THE CHEMICALS AND CHEMICAL COMPOUNDS IDENTIFIED BY FDA AS HARMFUL AND POTENTIALLY HARMFUL CONSTITUENTS IN TOBACCO PRODUCTS AND TOBACCO SMOKE

Constituent	Carcinogen (CA), respiratory toxicant (RT), cardiovascular toxicant (CT), reproductive or developmental toxicant (RDT), addictive (AD)
Acetaldehyde	CA, RT, AD
Acetamide	CA
Acetone	RT
Acrolein	RT, CT
Acrylamide	CA
Acrylonitrile	CA, RT
Aflatoxin B1	CA

	P1 - THS	P2
Heat-Not-Burn		
E-vapor	P3	P4 (Mesh)
		

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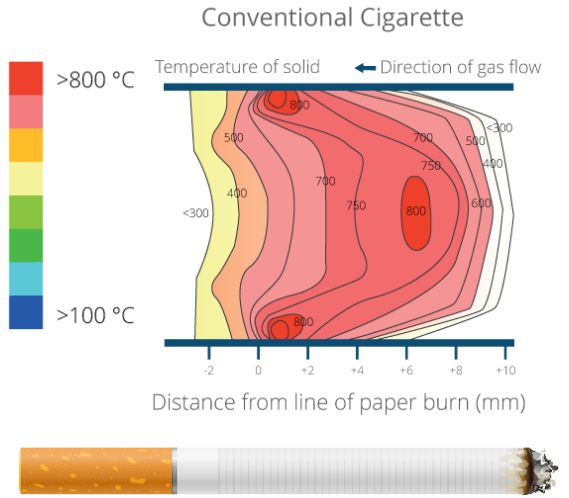
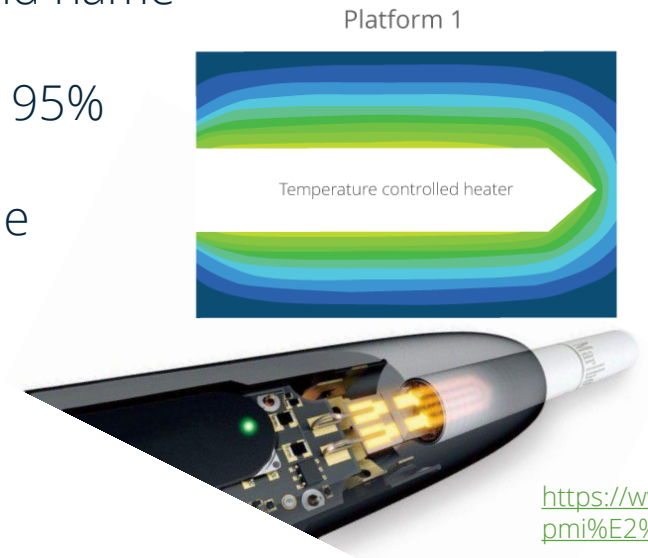
https://www.nice.org.uk/guidance/ph45/
https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM297981.pdf

PMI RRP PLATFORMS – THS*



Collection of smoke on Cambridge pad

- Commercialized in various markets under the IQOS brand name
- Heats tobacco without combustion
- Levels of HPHCs formation reduced on average by 90 to 95% compared to the smoke of a 3R4F cigarette
- Preserves elements of taste, sensory experience, nicotine delivery, and ritual of conventional cigarettes



Collection of aerosol on Cambridge pad

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https://www.pmiscience.com/news/absence-combustion-pmi%E2%80%99s-heated-tobacco-product-platform-1

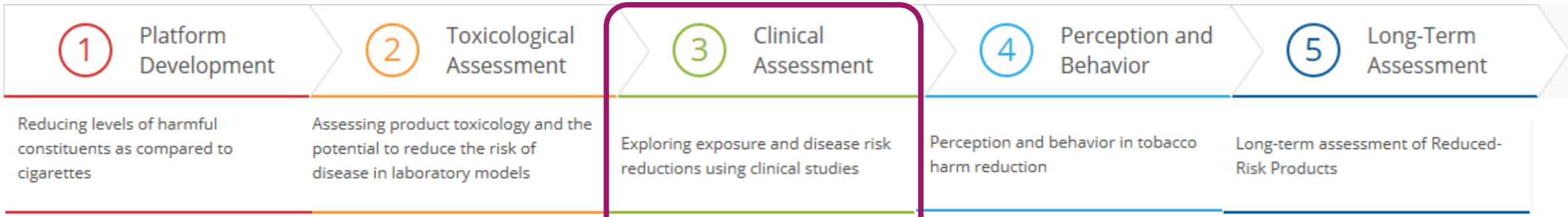
SCIENCE AND INNOVATION

Assessing Risk Reduction

Conducting a **rigorous step-by-step assessment** program

Our goal is to develop a portfolio of less harmful alternative products to continued cigarette smoking. In fact, our aim is that these products, which we call reduced-risk products (RRPs)*, will replace cigarettes.

PMI'S APPROACH TO RISK ASSESSMENT



- Less smell, No ash
- Reduced formation of HPHCs
- No negative impact on indoor air quality

Reduced toxicity

Reduced exposure to measured HPHCs

Appeals to current legal age smokers and *not to* non-smokers and former smokers

Reduced disease risk

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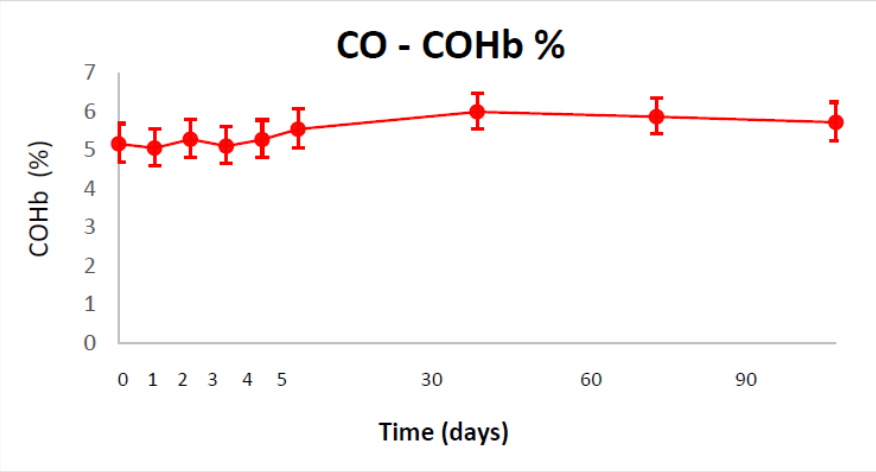
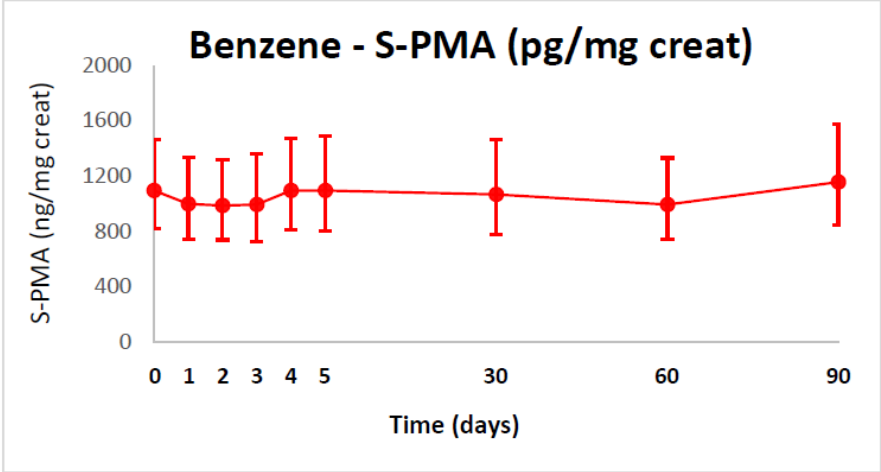
http://dx.doi.org/10.1016/j.yrtph.2016.07.006
https://www.pmiscience.com/our-scientific-approach/learn-more

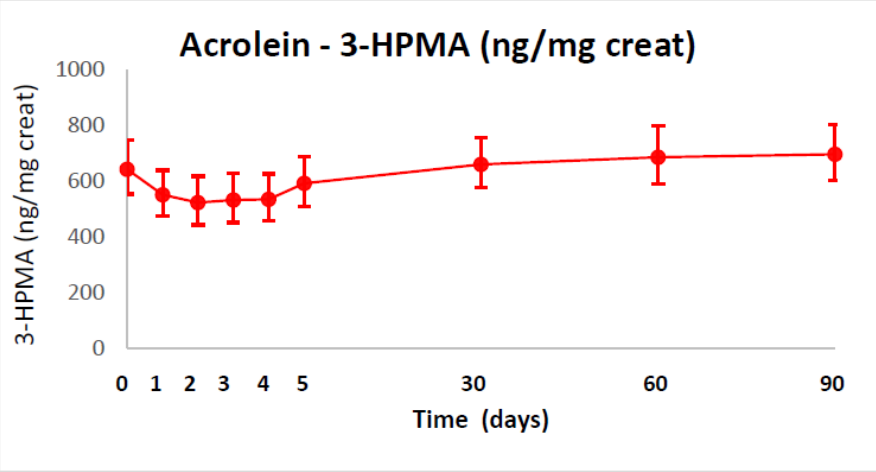
RESULTS TO DATE – REDUCED EXPOSURE

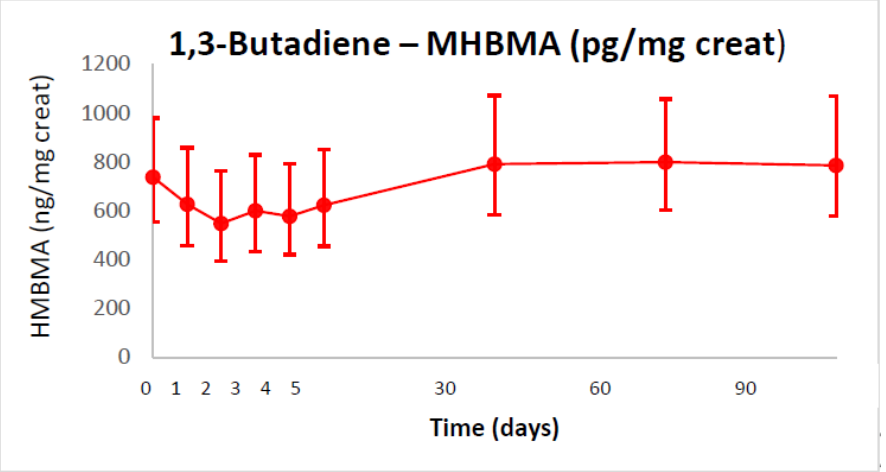
"Reduced Exposure Study Using THS 2.2 Menthol With 5 Days in a Confinement Setting and 85 Days in an Ambulatory Setting"

CC









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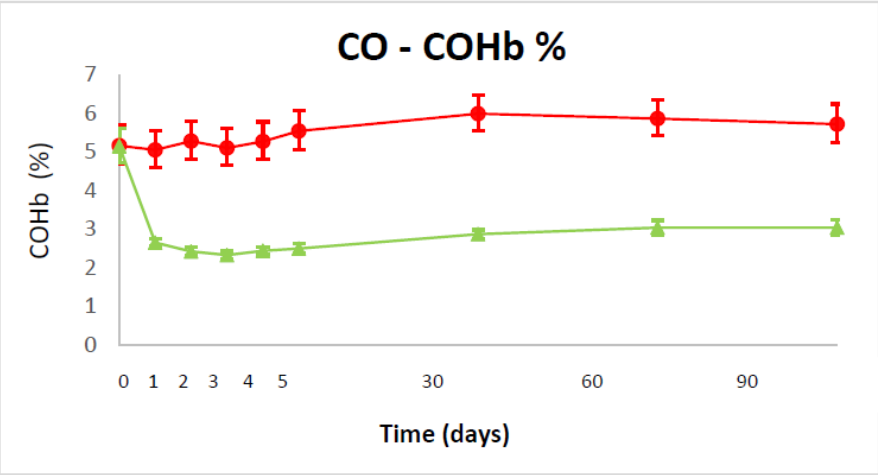
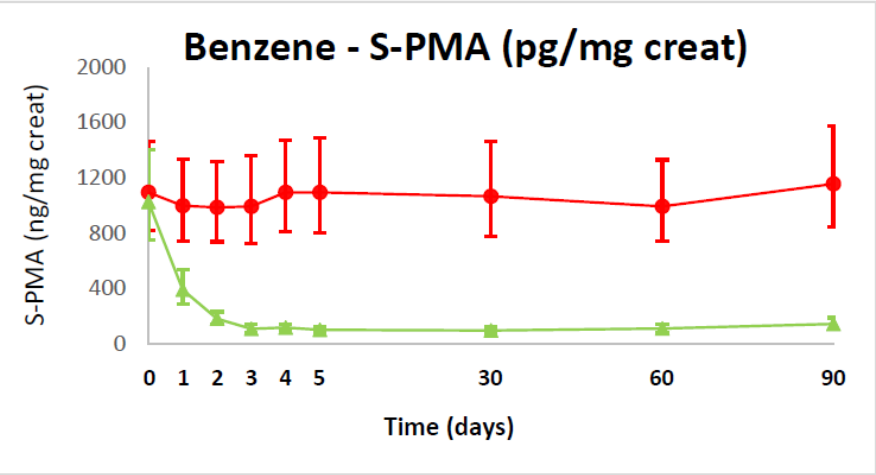
https://clinicaltrials.gov/ct2/show/NCT01970995

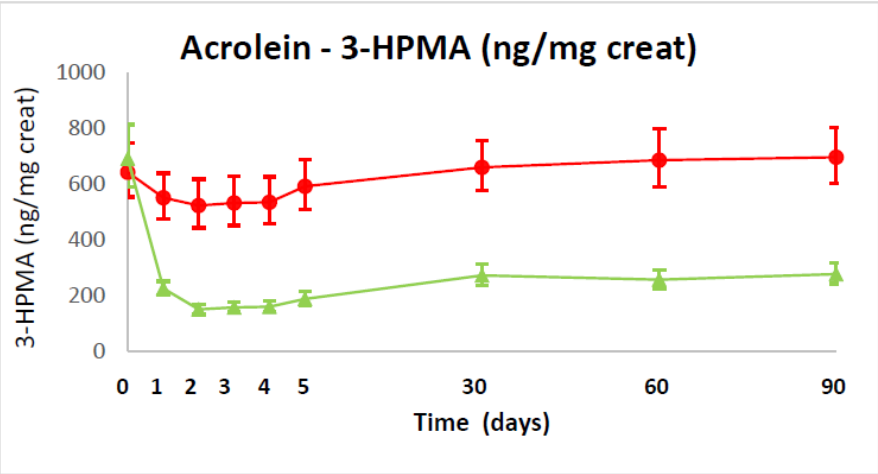
RESULTS TO DATE – REDUCED EXPOSURE

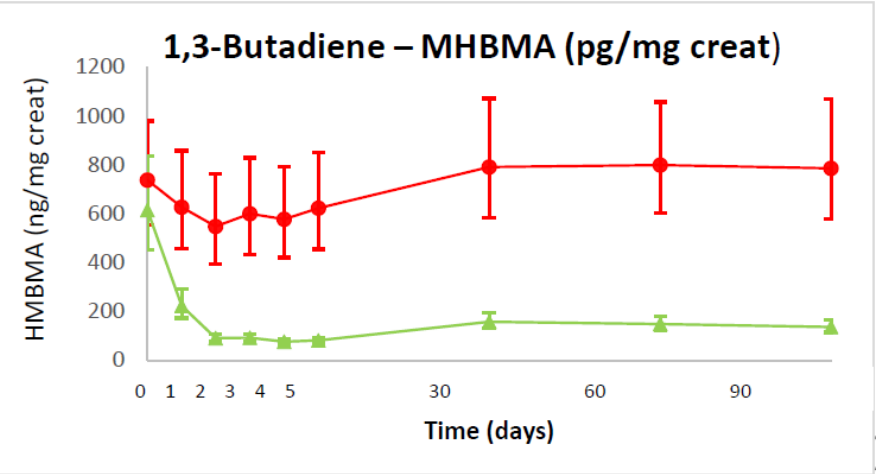
"Reduced Exposure Study Using THS 2.2 Menthol With 5 Days in a Confinement Setting and 85 Days in an Ambulatory Setting"

CC SA









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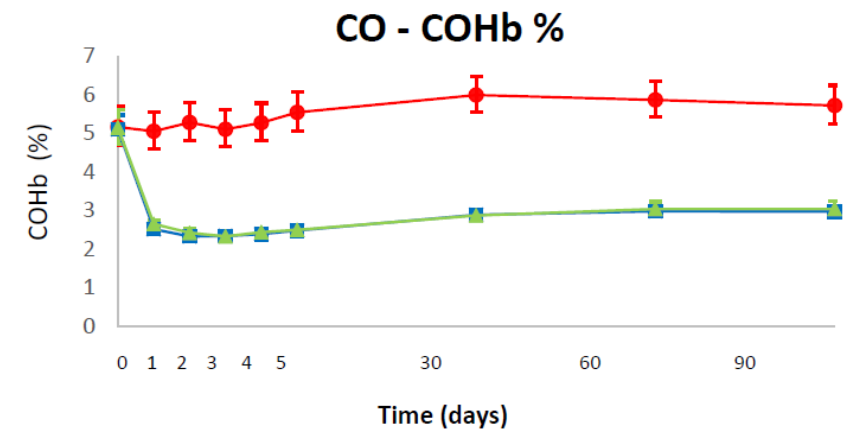
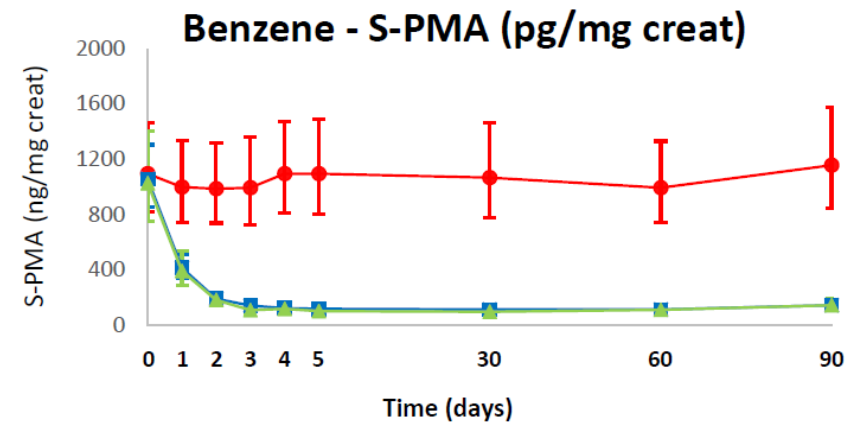
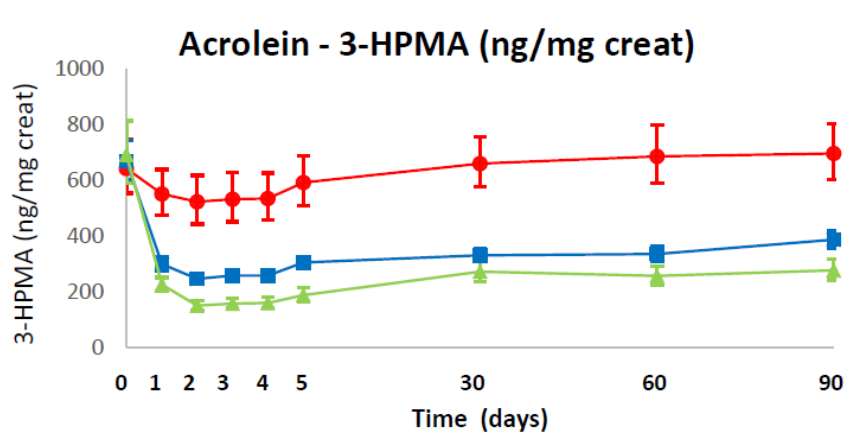
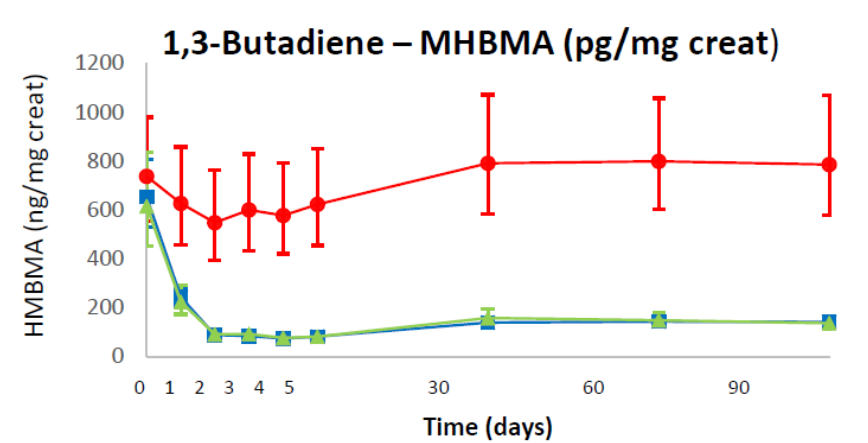
THS2.2 CC SA









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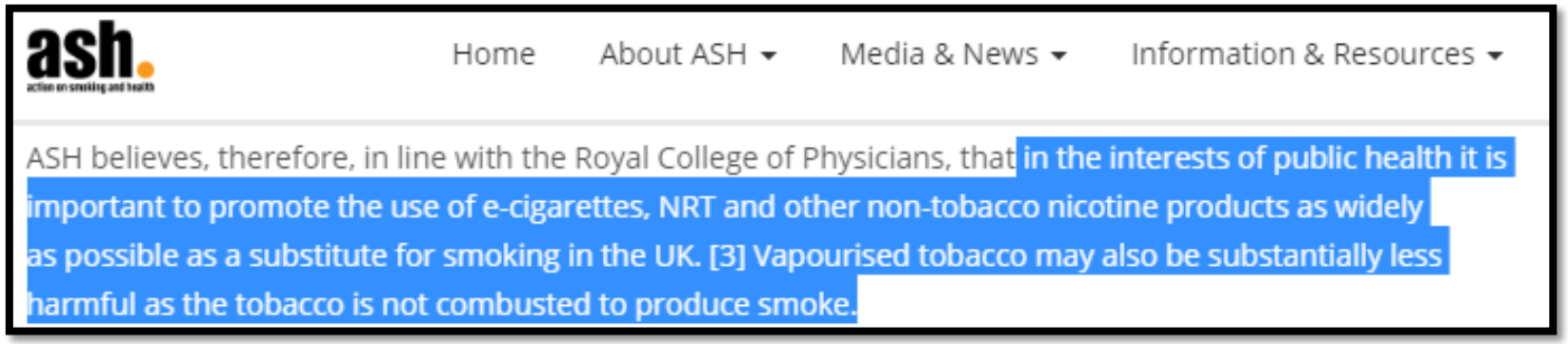
THE EXTERNAL PERCEPTION



ASH therefore believes that unless and until independent evidence shows that IQOS and similar products are substantially less harmful than smoking then these products should be regulated in the same way as other tobacco products.

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http://ash.org.uk/media-and-news/press-releases-media-and-news/ash-reaction-to-new-philip-morris-iqos-heat-not-burn-product/

INVESTIGATOR-INITIATED STUDIES (IIS) AT PHILIP MORRIS INTERNATIONAL

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IIS – WHY ARE WE DOING IT?

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IIS – WHAT IS IT?

An Investigator Initiated Study (IIS) is a research effort in which the investigator:

- Independently initiate, design, execute and publish the research with corresponding raw data
- Acts as study sponsor and assumes all legal & regulatory responsibilities

PMI supports IIS in the form of:

- Material Support
  (RRP product and equipment)
- Financial Support
  (fair market value for study procedures)
- Technical Support
  (access to critical PMI technology)

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IIS – WHAT IS IT?

The Goal

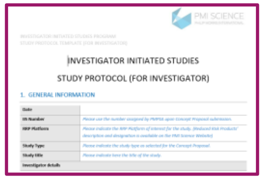
Promote and support external RRP research that **independently advances** and **verifies** PMI science

IIS- HOW

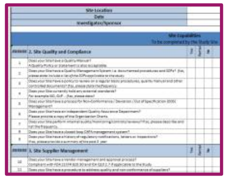
	Investigator Interest	Concept	Protocol	Execution
Process	Investigator Interest	Concept → IISC	Protocol → IISC	Execution
Governance – Ext	Guidelines	Terms & Conditions	Terms & Conditions	Contractual Agreement
Governance – Int		IIS SOP & Governance WKI		
Governance – Int		Concept Stage WKI	Protocol Stage WKI	Execution Stage WKI
Documents		Concept Template	Protocol Template; Evaluation Form	IIS Agreement; Status Reports; Publication

Concept Template

Protocol Template



Evaluation Form



IIS Agreement

Status Reports

Publication

Oversight by IIS Committee (IISC)

Cross-functional body overseeing the Investigator Initiated Studies program

Responsible for cross-functional evaluation review of all investigator initiated studies

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IIS SCOPE

Aerosol Chemistry	**Reduced Formation** *(of HPHCs)* e.g. Mainstream, Sidestream, Environmental Air, Indoor Quality Air e.g. Development and validation of new methods
Standard Toxicology	**Reduced Toxicity** e.g. Standard Tox: Ames, Neutral Red Uptake, Mouse Lymphoma e.g. Development and validation of new assays or biomarkers *NB: *In vivo studies subject to internal review where 3Rs apply*
Systems Toxicology	**Reduced Risk in Lab Models** e.g. Independent network verification
Clinical	**Reduced Exposure or Reduced Risk** e.g. Development & validation of new biomarkers of Exposure or Risk e.g. Short & long term health benefits which may lead to reduced risk
Perception & Behavioral	**Perception and Behavioral Assessment** e.g. population impact, observational, new assessment tools
Post-market Surveillance	**Post Launch** e.g. Prevalence, safety surveillance, new assessment tools

Must Include PMI's Developed & *Commercialized RRP Platforms in the Applicable Market*

IIS PROPOSAL EVALUATION

IIS Program Lead → Check

Subject Matter Expert → Scoring

IIS Committee → Confirmation and decision

- ✓ Study in scope
- ✓ No Conflict of Interest

Concept

- **Scientific strength** Advancing/validating
- **Scientific credibility** Investigator's qualifications and expertise
- **Scientific impact** Type of study
- **Compliance with regulatory framework & testing guidelines**
- **Type of support requested** Financial vs material

Protocol

- **Scientific capability** Resources capabilities, network
- **Scientific rigor** Correctly designed, sample size
- **Quality standards** QMS, data integrity

IIS STUDY INDEPENDENCE

- Individual IIS proposals are unsolicited (Submitted via PMI Science website IIS Portal)
- PMI does not influence the study conduct or outcome (Final study design is with Investigator/Sponsor)
- PMI support shall be Fair Market Value (and limited to activities directly related to the study)
- PMI has no operational oversight or access to data (Investigator/Sponsor owns data)
- PMI will not review any manuscripts (Informed after journal manuscript acceptance)

IIS STUDY TRANSPARENCY

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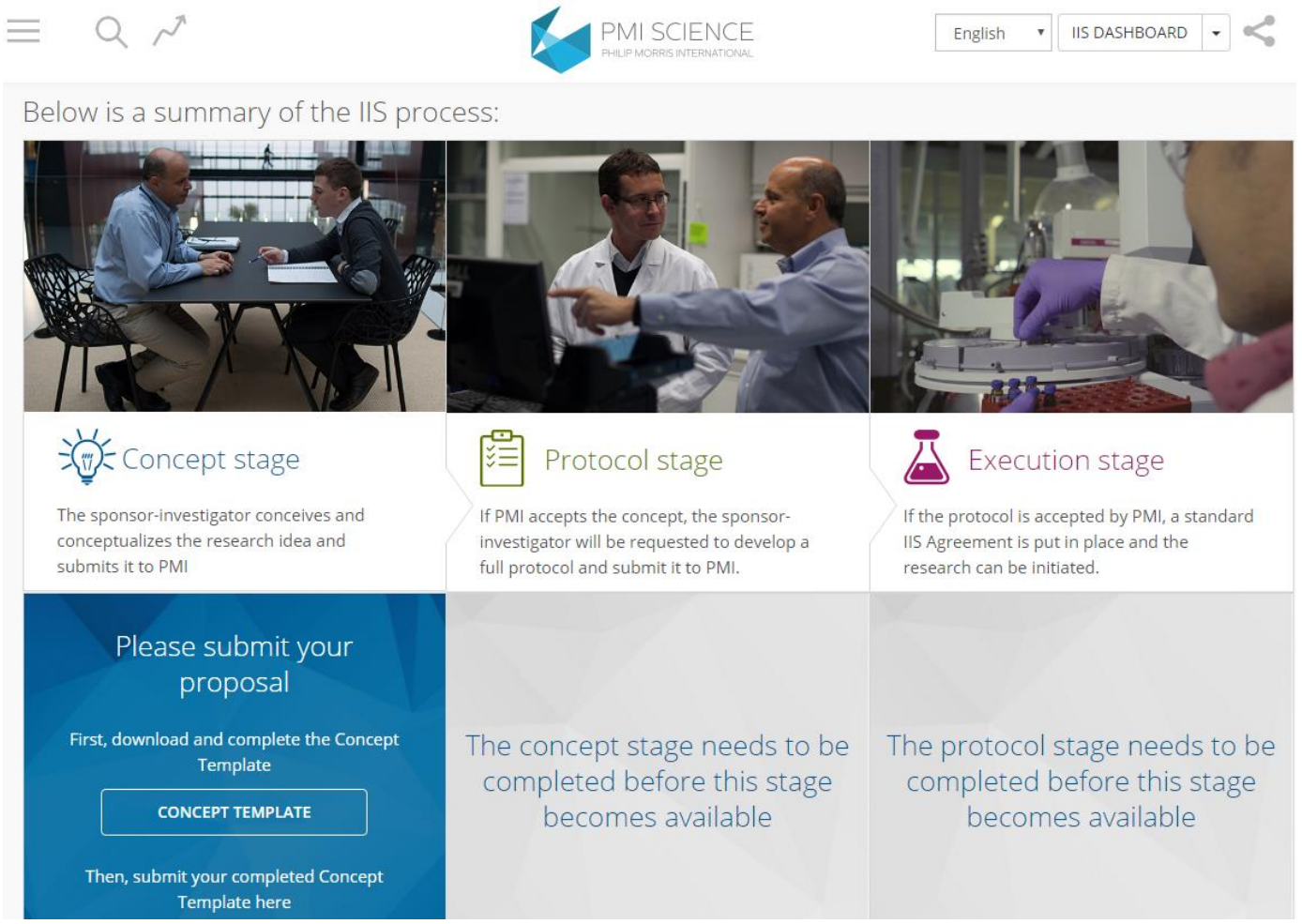
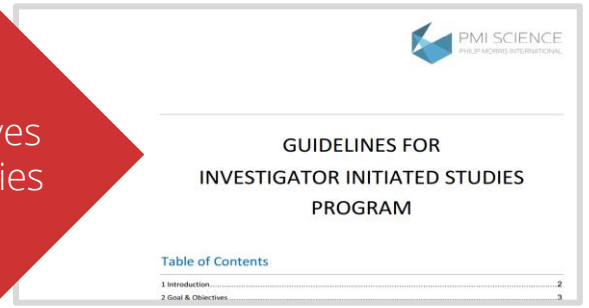
IIS STARTING POINT: WEBSITE

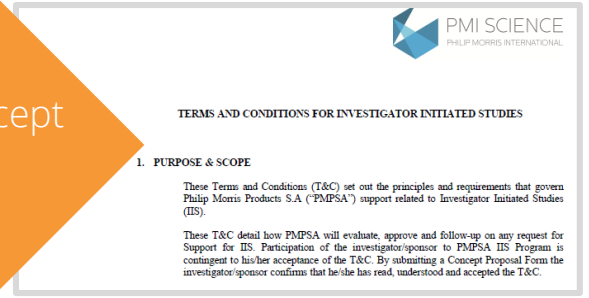
Starting Point



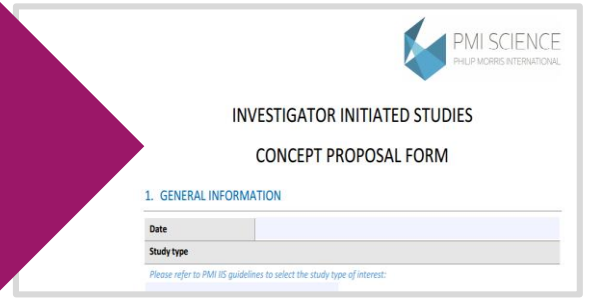
Explains the objectives & roles/responsibilities



Accepted when concept is submitted



Concept Template



SIMILARITIES & DIFFERENCES TO PHARMA

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SIMILARITIES TO PHARMA

Similar objectives and strategies

Objective:
Independently advance and verify science on company's products

Strategy:
Independent investigator initiated studies brings credible verification and innovation

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DIFFERENCES TO PHARMA

PMI	Pharma 
Funding	
• Often sole supporter & funding source • Often monetary & product	• Often several supporters & funding sources • Often product/placebo • Sometimes financial support
Scope	
• From basic chemistry to social sciences	• Mostly clinical • Sometimes pre-clinical
Product	
• Completely novel & unique product • Investigators relatively naïve to product characteristics • Placebo typically not used	• Often relatively similar products • Investigators often experts in the field and products • Placebo often used

DIFFERENCES TO PHARMA

PMI	Pharma 
Regulations	
• Consumer Product: EC/IRB • No Sunshine act • High level of regulatory variability between jurisdictions	• Medicinal Product: EC/IRB, IND • Sunshine act • Reasonable level of regulatory alignment between jurisdictions
Industry Stigma	
• Significantly limits number of investigators	• May limit number of investigators

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CONCLUSIONS

PMI is transitioning to a smoke free future with RRPs

External verification is important to increase external credibility, verify and advance PMI science

Independence and transparency are fundamental to the PMI IIS Program

The PMI IIS program is similar to pharma IIS programs, despite some differences

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Check out PMI Science

Check out sbvIMPROVER

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Thank You! – Questions?