//PULZE & ID: THE SCIENTIFIC STORY SO FAR...



→ INTRODUCTION

Science has demonstrated that nicotine, while addictive and not risk-free, isn't the primary cause of smoking-related disease. Rather, the combusting (burning) of tobacco creates smoke containing thousands of chemicals – many of which are harmful. These are then inhaled by adult smokers.

The best course of action adult smokers can take to improve their health is not to use any tobacco or nicotine product. However, millions of people enjoy consuming nicotine and are either uninterested or unwilling to take this step.

Next Generation Products (NGP) including heated tobacco (HT) allow adult smokers to consume nicotine, free from tobacco combustion and the generation of smoke. For this crucial reason, they have the potential to be substantially less harmful than smoking combustible cigarettes.

> TOBACCO HARM REDUCION



TOBACCO HARM REDUCTION AND THE HEATED TOBACCO OPPORTUNITY

Transitioning those adult smokers, who would otherwise continue to smoke, to high-quality NGP is the basis of the public health concept of Tobacco Harm Reduction (THR).

The equation below explains that, to make a meaningful contribution to THR - and public health scientifically substantiated NGP must be both less harmful than cigarettes and used by a significant number of adult smokers instead of cigarettes.

This concept underpins our ambitions for our own proprietary HT system.

HARM REDUCED NEXT GENERATION PRODUCT

ADULT SMOKER ACCEPTANCE PRODUCT CHARACTERISATION SCIENCE

BIOLOGICAL SCIENCE

PERCEPTION 6 BEHAVIOURAL

→ INTRODUCING PULZE & ID

We believe the premise of HT is simple and its role in THR compelling.

All HT products operate on the same basic principle. A stick containing a portion of reconstituted tobacco is inserted into the device and heated in a controlled manner, but *never burnt*. This produces an inhalable aerosol containing nicotine and flavour aromas from the tobacco.

As HT products eliminate the need to burn tobacco, and don't generate smoke, research shows the aerosols they produce contain fewer and substantially lower levels of harmful chemicals compared to cigarettes.

It's for this reason we believe HT products offer an attractive, potentially harm reduced alternative to continued cigarette smoking and, therefore, public health.

Our HT product comprises of the Pulze device and iD tobacco consumable. Here's a breakdown of the system.



ID TOBACCO CONSUMABLE (STICK)

1. RECONSTITUTED TOBACCO

Wrapped in aluminium foil, ensuring D sticks can't be misused and moked like combustible cigarettes.

2. BORE FILTER

Creates a pressure change, allowing nicotine and flavour aromas to mix for a more satisfying user experience.

3. VENTILATED SPACER

Cardboard tube which cools the aerosol with ambient air. It also adds structure to the iD stick.

4. MOUTHPIECE FILTER

Acts as a mouthpiece for users. There are three filters, including triple bore and a 'crushball', which can be squeezed to release a flavour.



SMART PUFF SENSOR TECHNOLOGY™

Provides a consistent user experience by monitoring the number of puffs users take, and adapting device performance accordingly. It also lets users know when the end of a session is approaching, activating the 'Extra Time' mode if available.

BATTERY

1340 mAh, allowing up to 20 consecutive sessions (iD sticks) between charges.

LED INTERFACE

Shows current battery status and heating mode.

ON-THE-GO CLEANING TOOL

D sticks may leave some tobacco residue on the rod, or in the heater cavity. As well as this discreet in-built cool, Pulze also comes with a larger version when more comprehensive cleaning is required. •

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RUBBER CAP

Seals device while not in use.



CERAMIC HEATING ROD

Directly pierces the tobacco in iD sticks, heating them to a defined temperature. Pulze has two heating modes: Standard, which heats at 345°C for a more intense experience, and Eco, which heats at 315°C for a more discreet taste experience.

POWER BUTTON ON/OFF

Also used to switch between Standard and Eco heating modes, as well as activate the safety lock.

POWER LED INDICATOR



PULZE HEATS, NOT BURNS

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PUBLIC HEALTH ADVOCACY TIMELINE

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\rightarrow PULZE HEATS, NOT **BURNS, TOBACCO**

As mentioned previously, the Pulze device operates by heating iD sticks to a defined temperature, either 345°C or 315°C. Both temperatures are, by design, significantly lower than the 900°C at the burning tip of a cigarette.

In other words, Pulze doesn't burn the tobacco in an iD stick. This is the fundamental concept behind the THR potential of HT, and something we've been able to measure and demonstrate through three specific tests. They arrived at the following conclusions:

1. PULZE DOESN'T REACH **TEMPERATURES HIGH ENOUGH TO CAUSE COMBUSTION**

As the adjacent image and temperature profiling graph overleaf indicate, the maximum temperature the Pulze device operates at is 345°C. This isn't high enough for tobacco combustion (burning) to occur, but is sufficient to release nicotine and flavour aromas from the iD tobacco consumable.

FIND OUT MORE ..



345°C // MAXIMUM RÓD HEATER TEMPERATURE

→ ID STICK TOBACCO **TEMPERATURE PROFILING**

The graph illustrates that, after switching on the Pulze device, the temperature of the tobacco in the iD stick begins to increase. The 'spikes' in the temperature occur because of users' puffing. The data also demonstrate the tobacco reaches a maximum of 240°C in Pulze's 'hottest' (Standard) mode, allowing nicotine and aromas to be released into the aerosol.



We've demonstrated the Pulze device only heats the iD stick tobacco to a maximum of 240°C, but what exactly is combustion and how do we confirm its absence?

As heat is applied to a fuel source a chemical reaction takes place. This creates new by-products while also consuming the fuel. This is true for all stages of thermal decomposition - including evaporation (turning

a liquid into vapour), torrefaction (a thermochemical process in the absence of oxygen) and pyrolysis (the thermal decomposition of a compound). These processes all occur at lower temperatures than visible combustion.

When combustion itself occurs. the fuel (tobacco) is depleted at an even faster rate because it reacts with oxygen - causing a high energy

GRAPH DENOTES TEMPERATURE OF TOBACCO ACCORDING TO DISTANCE FROM HEATER ROD SURFACE

OMM

0.5MM



reaction, releasing heat and light while also impacting mass.

Using this knowledge, we employed thermogravimetric analysis (TGA) to determine the temperature at which the tobacco and paper wrap used in an iD tobacco consumable would begin to combust.

The test itself involved situating an iD stick's tobacco and paper wrap in different atmospheric conditions

and measuring its mass while slowly increasing the temperature. The graph below compares the results.



SAMPLE TEMPERATURE (°C)

→ TGA SUBSTANTIATING PULZE & ID'S LACK **OF COMBUSTION AT MAXIMUM OPERATING** TEMPERATURE (STANDARD MODE, 345°C)

As the graph indicates, deviation in mass at >400°C indicates the point of oxidation (the process by which a chemical substance changes because it starts to react with oxygen) and the beginning of tobacco combustion.

The Pulze device doesn't cause combustion of the iD tobacco consumable - or any ensuing smoke - because it simply doesn't reach temperatures anywhere near 400°C, let alone the 900°C recorded at the burning tip of a cigarette.

The nicotine-containing aerosol the device generates from the tobacco must therefore be the result of evaporation, torrefaction and some low-temperature pyrolysis - but not combustion.

2. RESEARCH SHOWS PULZE & **ID'S AEROSOL DEMONSTRATES** A SIGNIFICANT REDUCTION IN **COMBUSTION MARKERS**





Combustion is the name of the chemical products, termed gaseous oxides. Examples include carbon (NOx); these are always produced tobacco, burns. As these gases result from combustion. we term them

As the chart shows, when we compare Pulze & iD's aerosol to cigarette smoke, we see a significant reduction in combustion markers. This suggests while some elements of thermal decomposition are occurring during the heating process, combustion itself clearly isn't taking place.

This is important considering the adverse effects of potential carbon monoxide (CO) toxicity from tobacco PRODUCT RACTERISA SCIENCE

PULZE HEATS, NOT BURNS

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SCIENCE

3. VISUALLY, A CIGARETTE AND AN ID STICK LOOK VERY DIFFERENT AFTER USE

As a cigarette's fuel (the tobacco) combusts, it produces ash and smoke - leaving a small, charred butt behind. As iD sticks *don't* combust, they undergo little to no reduction in size as the illustration below suggests.

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In fact, their only visible degradation is a slight discolouration. They appear 'toasted', like a roasted coffee bean.

Having clearly demonstrated the absence of combustion. our scientists are ready to proceed Pulze & iD through our rigorous scientific assessment framework to further determine their THR potential.

PRODUCT CHARACTERISATION SCIENCE

RESEARCH SHOWS PULZE & ID'S AEROSOL HAS A SIMPLER CHEMICAL COMPOSITION THAN CIGARETTE SMOKE AND CONTAINS FEWER AND SUBSTANTIALLY LOWER LEVELS OF HARMFUL CHEMICALS

By capturing and comparing Pulze & iD's aerosol with combustible cigarette smoke in our laboratories, we learned the former has a much simpler chemical composition compared to the latter. As the illustration shows, Pulze & iD's aerosol contains only 36 chemicals.

Tobacco smoke contains over 7,000 chemicals, around 100 of which are classified by public health experts as causes or potential causes of smoking-related disease. Importantly, none of the chemicals in Pulze & iD's aerosol were not also found in tobacco smoke.



→ CHEMICAL COMPARISON BETWEEN PUZLE & ID AEROSOL AND CIGARETTE SMOKE

APPROX.

PULZE & **ID AEROSOL:** CHEMICALS





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Our analysis shows Pulze & iD's aerosol also contains significantly lower levels of the harmful chemicals which are present compared to cigarette smoke.

To demonstrate this, our scientists measured the levels of 40 chemicals known to be harmful or potentially harmful constituents in combustible cigarette smoke.

These include nine specific toxicants proposed for mandated reduction in combustible cigarette smoke by the World Health Organization's (WHO) Study Group on Tobacco Product Regulation - known collectively as the TobReg9. As the graph overleaf illustrates, our laboratory studies demonstrated an average 96% reduction in harmful chemicals assessed – including those of public health interest – compared to levels found in cigarette smoke.

Finally, Pulze & iD's aerosol possesses a markedly different chemical composition compared to cigarette smoke. This is reflected in the Total Particulate Matter (TPM) captured by a Cambridge filter pad (below).



→ PULZE & ID AEROSOL % COMPARED TO CIGARETTE SMOKE -OUR STUDIES SHOW AN AVERAGE 96% REDUCTION IN HARMFUL CHEMICALS



NOT QUANTIFIABLE

Ethylene oxid. Propylene oxid. Acrylonitrili. Vinyl acetat. Methane, nitro Methane, nitro Methane, nitro Resorcino Phenco Phe PULZE HEATS, NOT BURNS

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> YSTANDER XPOSURE

PUBLIC HEALTH ADVOCACY TIMELINE

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SIGNIFICANT REDUCTIONS IN HARMFUL CHEMICALS IN PULZE & ID'S AEROSOL TRANSLATE TO MARKEDLY REDUCED IN-VITRO CELL TOXICITY

The next stage of Pulze & iD's scientific substantiation involves using recognised regulatory methods to assess Pulze & iD in our laboratories. This included the aerosol's impact on cell viability and/or growth rates, as well as the possibility of causing DNA mutation

or genetic damage to cells.

In addition, a series of cutting-edge, cell-based laboratory studies (known as in-vitro: Latin for 'within the glass' e.g. test tubes or vessels) were also conducted, focusing on pulmonary and cardiovascular endpoints.

As the graphics below illustrate, substantial reductions in invitro toxicological responses to Pulze & iD's aerosol compared to combustible cigarette smoke were observed across all tests.

CARDIOVASCULAR ENDPOINT (CARDIO QUICKPREDICT[™]): **95% REDUCTION COMPARED** TO CIGARETTE

This assay explores the impact of product samples on human-derived stem cells to investigate their relative cardiotoxity potential.



MECHANISTIC TOXICOLOGY ENDPOINT (2D LUNG TISSUE **HIGH CONTENT SCREENING):** 95% REDUCTION COMPARED TO CIGARETTE

This assay combines automated imaging and quantitative data analysis to provide rich systems biology information, detecting cellular events in human cell lines in response to test materials.

MECHANISTIC TOXICOLOGY ENDPOINT (CILIA BEAT ASSAY): 97% REDUCTION COMPARED TO CIGARETTE

This assay evaluates the impact of product samples on the cilia - mobile hair-like structures that line human airways and assist lung function- by focusing on any impact on normal cilia beat activity.

CYTOTOXICITY: 97% REDUCTION COMPARED TO CIGARETTE

Cytotoxicity is considered a potential step in several chronic disease processes associated with smoking - including cancer, cardiovascular disease and emphysema.

MUTAGENICITY: 91% REDUCTION COMPARED TO CIGARETTE

The Ames test uses bacteria strains to assess whether a test article can cause changes to the genetic material (mutagenicity). This event can cause cellular dysfunction and potentially lead to cancer susceptibility.

GENOTOXICITY: 90% REDUCTION COMPARED TO CIGARETTE

The in-vitro Micronucleus (IVM) assay detects damage to the structure of cellular DNA (genotoxicity) following test article exposure. Genotoxicity has been mechanistically linked with the formation of cancer.

FIND OUT MORE.



CIGARETTE SMOKE



CONTROL

HEATED

ARETT

CARDIOVASCULAR ENDPOINT (SCRATCH WOUND ASSAY): **98% REDUCTION COMPARED** TO CIGARETTE

This assay evaluates the impact of product samples on human endothelial cells (the single layer-thick cells that line all human blood vessels) which are essential for healthy cardio-vascular function.

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PULZE & ID DELIVER NICOTINE EFFICIENTLY TO THE BLOOD OF ADULT SMOKERS AND REDUCE DESIRE TO SMOKE*

After demonstrating substantial reduction in the numbers and levels of harmful chemicals in Pulze & iD's aerosol – and subsequent reductions in in-vitro toxicity - compared to combustible cigarettes, our scientific assessment proceeded into the clinical assessment phase using 24 adult smoker volunteers.

This research was intended to assess and understand:

- Pulze & iD's short-term safety and tolerability profile.
- Whether the product delivers nicotine efficiently to subjects' bloodstreams.
- Whether using Pulze & iD reduces subjects' desire to smoke.

The results were very promising, with the data indicating Pulze & iD has a favourable short-term safety and tolerability profile under the conditions of study, with no serious adverse events (SAE) recorded.

The system also delivers nicotine efficiently to the blood of adult smokers, while not exceeding that of a combustible cigarette - as the graph below demonstrates.

While the speed of nicotine absorption from Pulze & iD is comparable to combustible cigarettes, the peak nicotine level (known as Cmax) and overall nicotine exposures (referred to as Area under Curve, or AUC) are lower. This indicates the system has the potential to possess a lower abuse liability compared to combustible cigarettes, with a low potential for increased addictiveness compared to cigarettes when using the product as a smoking alternative.

Meanwhile, the comparable nicotine uptake and exposure

→ CLINICAL STUDY QUALITATIVE DATA DEMONSTRATE PULZE & ID REDUCE SUBJECTS' DESIRE TO SMOKE







between tobacco and menthol iD consumables demonstrates menthol doesn't facilitate inhalation or greater uptake of nicotine.

As the graph below illustrates, Pulze & iD reduce subjects' desire to smoke - potentially helping many adult smokers in their transitional THR journeys.



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→ PERCEPTION & BEHAVIOURAL SCIENCE

PULZE & ID ARE CORRECTLY UNDERSTOOD BY ADULT SMOKERS TO POSSESS TOBACCO HARM REDUCTION POTENTIAL, WHILE NOT BEING RISK FREE

While our research to-date demonstrates Pulze & iD represent a compelling potentially harm reduced alternative to continued tobacco smoking, we recognised it was also crucial adult smokers understood the HT category and HT products offer a potentially harm reduced alternative to continued combustible cigarettes smoking whilst not being risk-free.

We were also keen to understand any other motivations behind adult smokers' interest in the HT category.

To explore this we conducted a comprehensive survey in Italy, Germany and Greece to explore intentions to use and risk perceptions of Pulze & iD. Over 4,500 adults - including current smokers, HT users, vapers, former and nonsmokers - took part.

The key findings are detailed below and overleaf.



ADULT SMOKERS WOULD PRIMARILY **USE THE SYSTEM TO REDUCE OR REPLACE COMBUSTIBLE CIGARETTES**

 \rightarrow

WOULD USE IT TO EITHER COMPLETELY OR PARTIALLY REPLACE COMBUSTIBLE CIGARETTES

ENCOURAGINGLY.

CURRENT ADULT **SMOKERS SHOW** HIGH INTEREST AND **INTENTION TO USE** PULZE & ID



IN RELATION TO SPECIFIC SMOKING RELATED DISEASES, 97% OF **RESPONDENTS THOUGHT PULZE & ID** CARRIED SOME LEVEL OF RISK.

..........

SO, WHILE ADULT SMOKERS UNDERSTAND PULZE & ID MAY HAVE THE POTENTIAL TO BE LESS LIKELY TO CAUSE SOME OF THESE SPECIFIC SMOKING-RELATED HARMS, THEY ALSO CORRECTLY RECOGNISE THE SYSTEM ISN'T COMPLETELY RISK-FREE.

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PULZE DOESN'T APPEAL TO NON-SMOKERS I.E. NON-USERS OF EITHER **TOBACCO OR NICOTINE PRODUCTS**

While it's encouraging adult smokers find Pulze & iD appealing as a potential replacement for combustible cigarettes, it's also equally crucial to survey nonsmokers to ensure the system doesn't appeal to them. Usage by unintended audiences (i.e. non-smokers and those under the legal smoking age) would potentially seriously impact Pulze & iD's THR potential.

OF ADULTS WHO DON'T USE TOBACCO OR NICOTINE PRODUCTS SAID THEY WOULDN'T USE PULZE



→ PULZE AND BYSTANDER EXPOSURE FROM EXHALED AEROSOL

PULZE & ID USE DOESN'T NEGATIVELY IMPACT INDOOR AIR QUALITY, UNLIKE CIGARETTE SMOKING

As a result of Pulze's low temperature heating of the tobacco in iD sticks, we've already scientifically demonstrated the ensuing aerosol is very different to combustible cigarette smoke in terms of its chemical composition.

After conducting further studies focusing on exhaled aerosol, we learned Pulze & iD generates a mist that's distinct from cigarette smoke. As the graphics below illustrate, it's far less dense than cigarette smoke, consisting of 75-85% water. Exhaled Pulze & iD aerosol droplets evaporate quickly – disappearing around 10 seconds after a puff. In contrast, the particles from burning tobacco are much more stable than their HT equivalents, taking between 30-45 minutes to dissipate.

Another advantage of HT is there are no 'side-stream' emissions to impact air quality or disturb bystanders (these emissions form part of the ambient smoke often referred to as 'second-hand' smoke). Why? Unlike a combustible cigarette there's no constantly burning tip. In fact, our research suggests Pulze & iD use has *no* negative impact on indoor air quality.

However, users should always comply with any rules around indoor usage and be courteous towards bystanders.

75-85%

WATER

PULZE

PULZE AEROSOL CONSISTS OF











NO SIDE-STREAM EMISSIONS

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OUBLIC HEALTH ADVOCACY TIMELINE

→ HEATED **TOBACCO:** A **HISTORY OF HARM REDUCTION PUBLIC** HEALTH ADVOCACY

As the comprehensive evidencebase substantiating the HT category builds, so does the number of endorsements from public health bodies, many of whom are increasingly recognising HT's dramatic harm reduction potential.

The timeline to the right summarises the major milestones to date.

Hopefully, as the scientific weightof-evidence - and subsequent regulatory and public health advocacy - continues to grow, ever more adult smokers will choose to leave combustible cigarettes behind and transition to products like Pulze & iD.

This will provide the HT category with the exciting opportunity to fulfil its potential and make an important positive contribution to public health.

FIND OUT MORE.





OCTOBER 2020



JULY 2020





JULY 2020





APRIL 2020



2018



NOVEMBER 2018



AUGUST 2018





JUNE 2018

MAY 2018



Netherlands



MAY 2018





FEBRUARY 2018



DECEMBER 2017



NOVEMBER 2017

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CLINICAL SCIENCE

→ CONCLUSIONS: PULZE LOOKS PROMISING FOR TOBACCO HARM REDUCTION

Our Pulze & iD research to-date is extremely encouraging, with high-quality data generated across our scientific assessment framework. So far, our research has demonstrated:

- Pulze heats, not burns, the tobacco in iD.
- The system's aerosol has a simpler chemical composition compared to cigarette smoke and contains substantially fewer chemicals.
- Significant reductions in harmful chemicals in Pulze & iD's aerosol translate to markedly reduced invitro cell toxicity.
- Pulze & iD deliver nicotine efficiently to the blood of adult smokers, and test subjects report reduced desire to smoke.
- The system is correctly understood by adult smokers to possess THR potential, while not being risk free.
- Pulze & iD use doesn't negatively impact indoor air quality, unlike cigarette smoking.

Future studies include further clinical trials, as well as investigating the real-world usage of Pulze & iD by assessing the system's impact on the smoking behaviours of those adult smokers with no current intention to quit.

As we continue to conduct more research, the weight-of-evidence demonstrating the system's potential to make a meaningful contribution to tobacco harm reduction grows further.

Please stay up-to-date with our latest HT findings via the following channels:





