Innovation and harm reduction

Balancing the need for rapid product innovation with the need for robust product science

Clive Bates

Counterfactual Consulting

CORESTA Science Day

9th June 2022

I. Fundamentals

II. Innovation and markets

III. The weirdness of harm

What purpose does innovation serve?

1. Smoking cessation aid?

2. Harm reduction product?

3. Recreational drug?

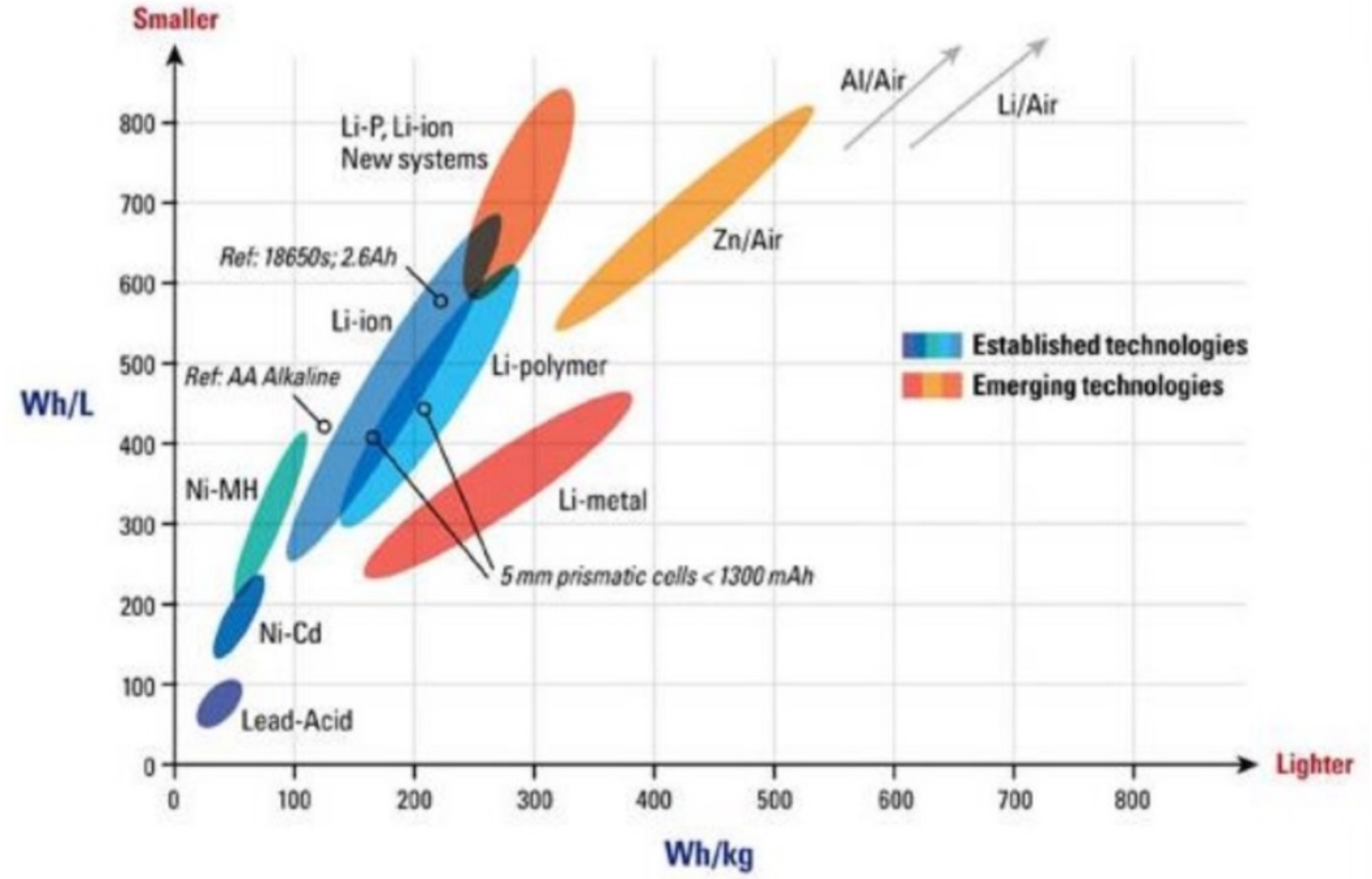
Recreational drug

The platforms for a recreational drug

	Pure nicotine based	Tobacco based
Heated aerosol	Vaping products 	Heated tobacco products “Heat-not-burn” 
Unheated	Oral nicotine products  Items are not shown to scale	Smokeless tobacco 

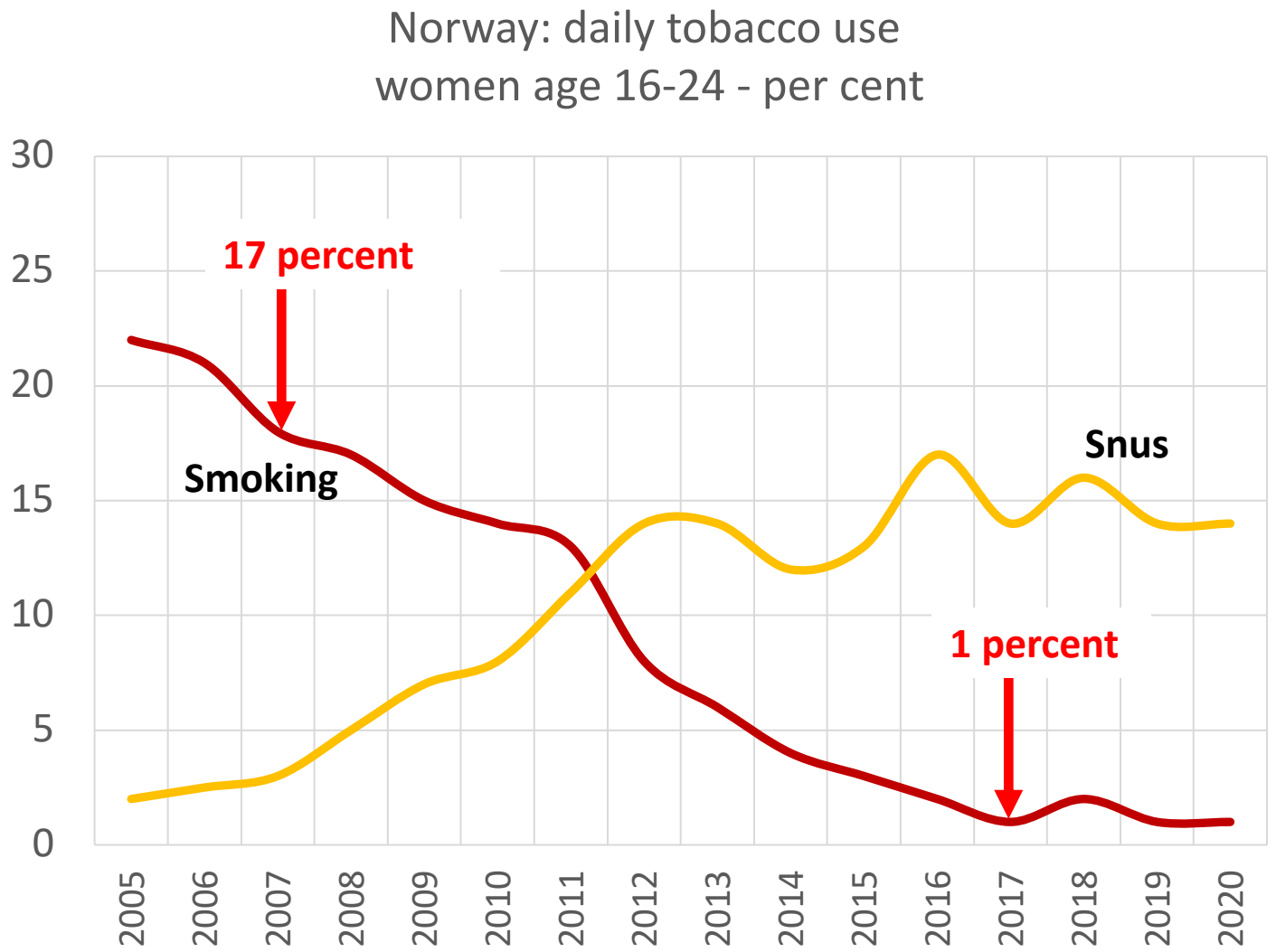
Fundamental technology driver

Battery Energy Density

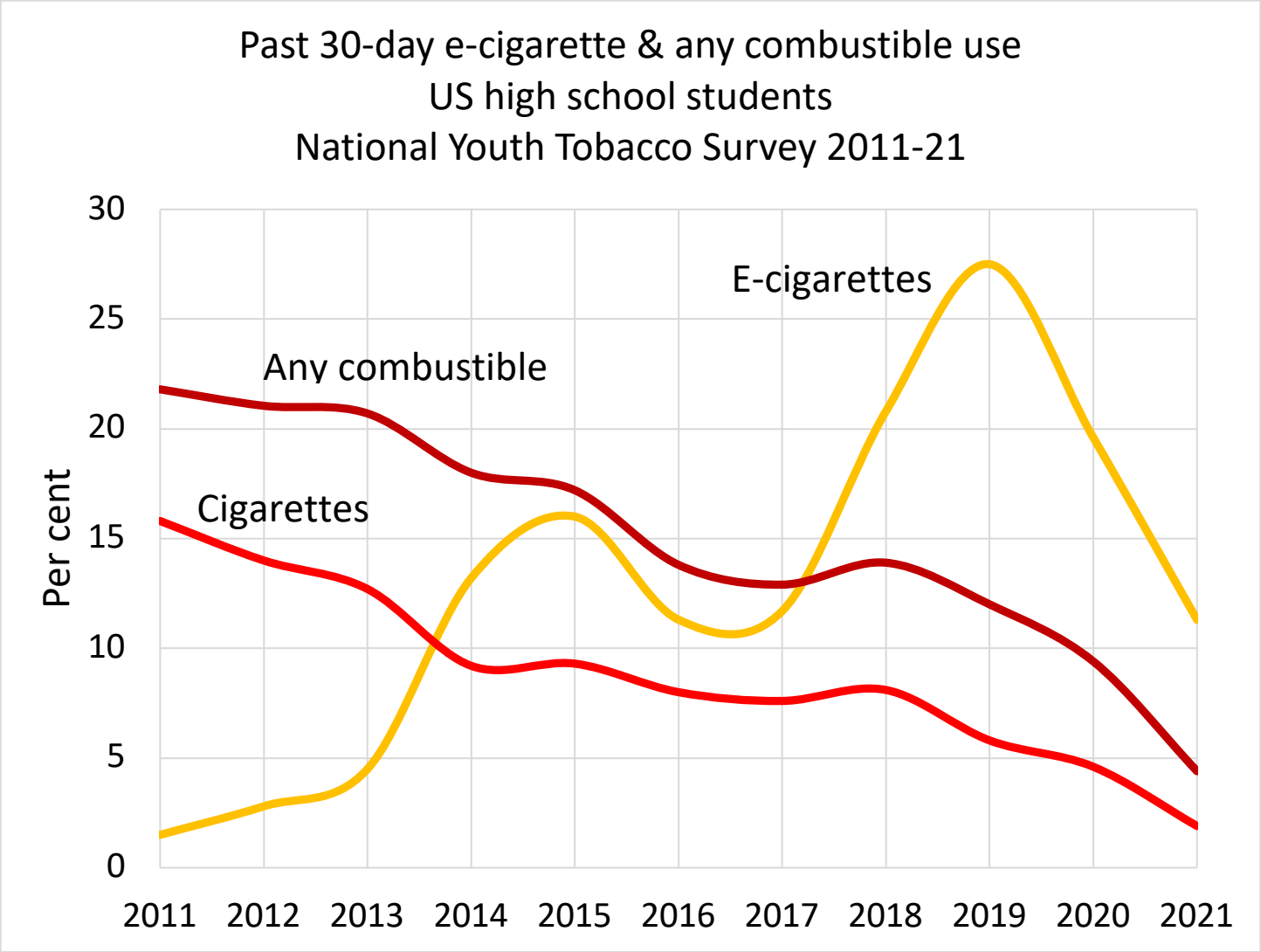



NUON

Norwegian young women – it's over for smoking



US high school students - it's over for smoking



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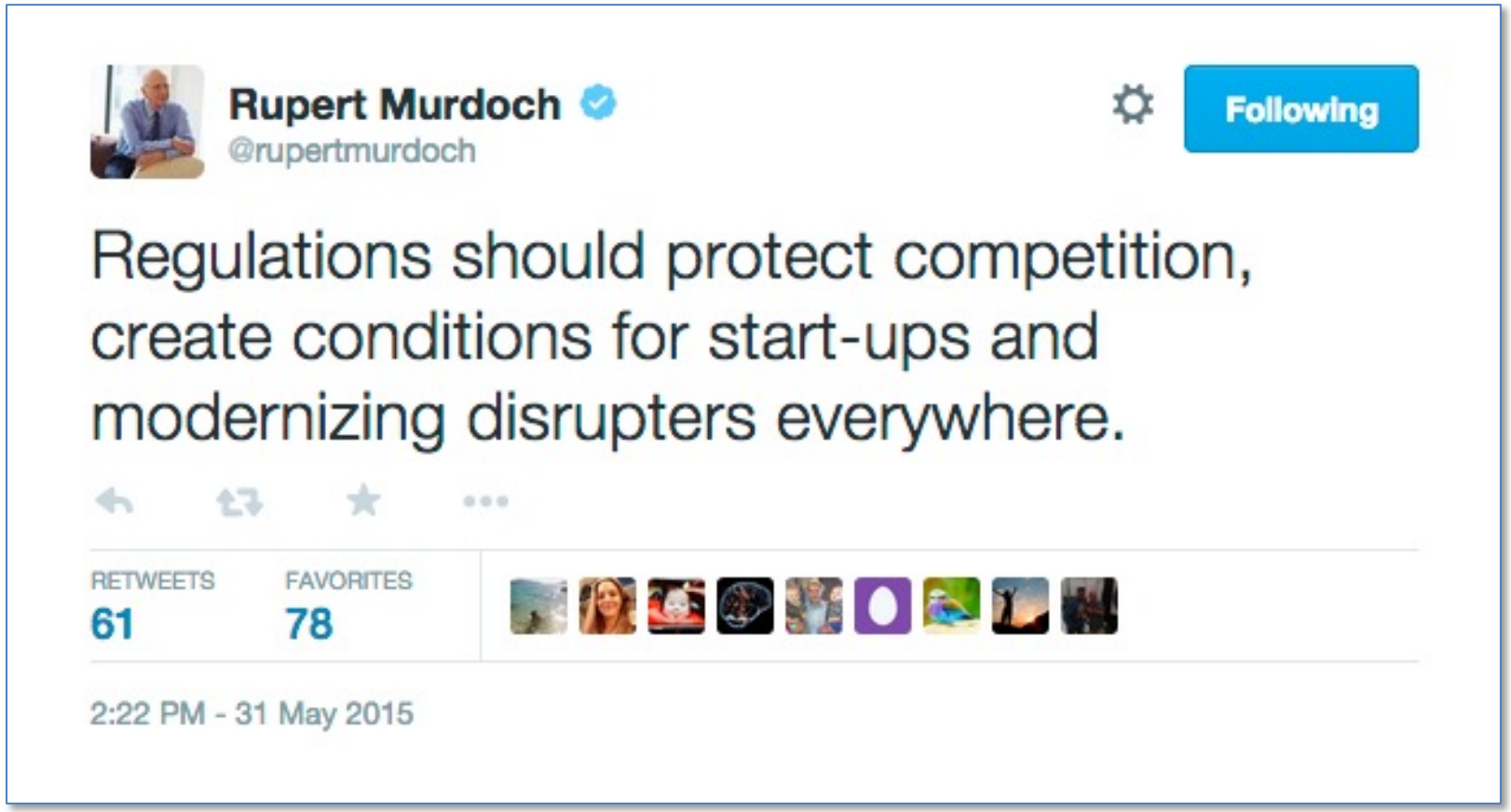
What purpose does innovation serve?

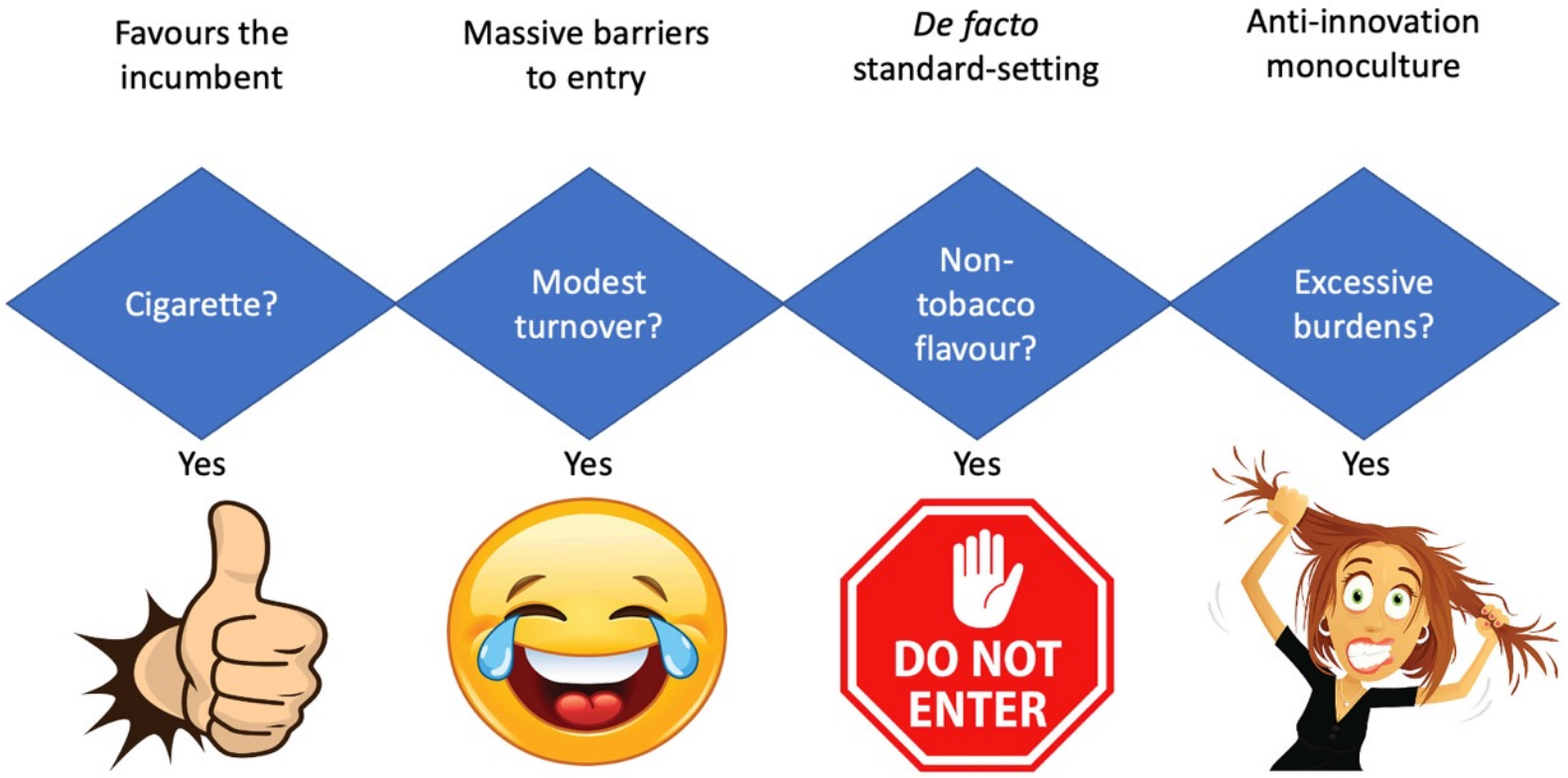

Rupert Murdoch
@rupertmurdoch
Following
Regulations should protect competition, create conditions for start-ups and modernizing disrupters everywhere.
RETWEETS
61
FAVORITES
78
2:22 PM - 31 May 2015

Authorisation systems present major barriers to innovation

- Authorisation regime

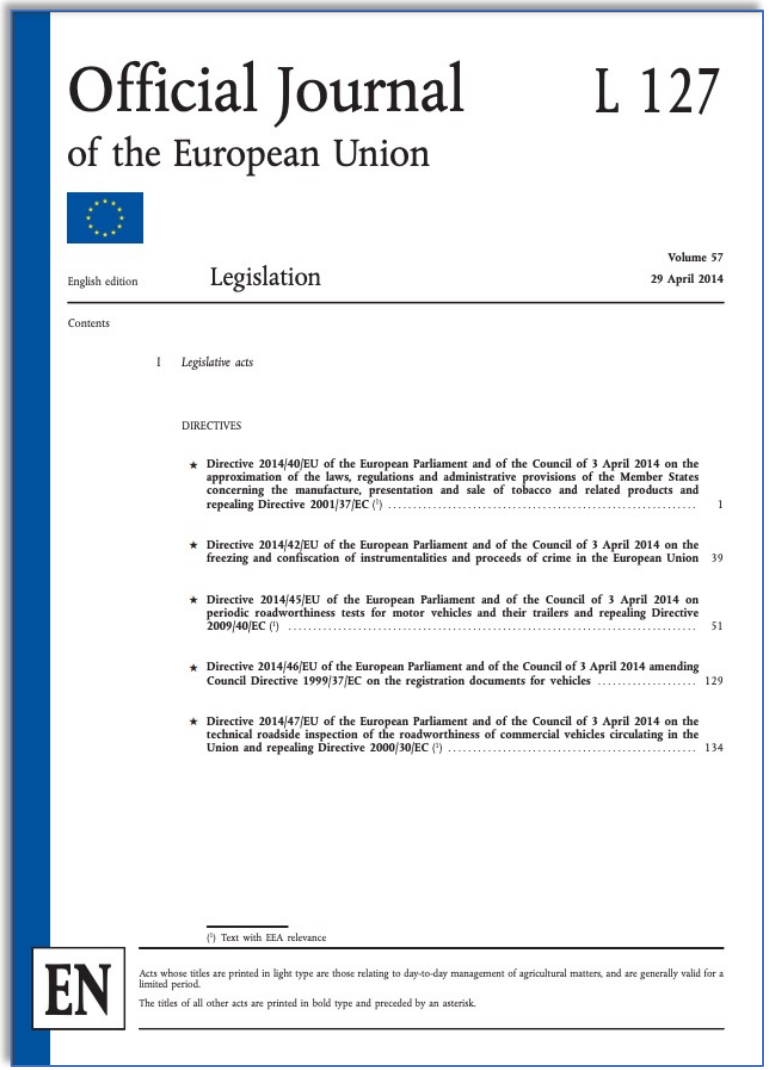
The FDA authorisation system (PMTA)

- Authorisation regime



Standards can be both constraining and a driver of innovation

- Authorisation regime
- Standards



Official Journal of the European Union

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English edition — Legislation — Volume 57, 29 April 2014

Contents

I *Legislative acts*

DIRECTIVES

★ **Directive 2014/40/EU of the European Parliament and of the Council of 3 April 2014 on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco and related products and repealing Directive 2001/37/EC** [1] 1

★ **Directive 2014/42/EU of the European Parliament and of the Council of 3 April 2014 on the freezing and confiscation of instrumentalities and proceeds of crime in the European Union** 39

★ **Directive 2014/45/EU of the European Parliament and of the Council of 3 April 2014 on periodic roadworthiness tests for motor vehicles and their trailers and repealing Directive 2009/40/EC** [1] 51

★ **Directive 2014/46/EU of the European Parliament and of the Council of 3 April 2014 amending Council Directive 1999/37/EC on the registration documents for vehicles** 129

★ **Directive 2014/47/EU of the European Parliament and of the Council of 3 April 2014 on the technical roadside inspection of the roadworthiness of commercial vehicles circulating in the Union and repealing Directive 2000/30/EC** [1] 134

[1] Text with EEA relevance

EN

Acts whose titles are printed in light type are those relating to day-to-day management of agricultural matters, and are generally valid for a limited period.

The titles of all other acts are printed in bold type and preceded by an asterisk.

- Notification – ingredients, toxicology, pharmacology, production process
- Technical design restrictions and requirements
- Leaflet, packaging and warning
- Advertising, promotion, sponsorship
- Cross border sales
- Disclosure commercial data
- Market surveillance
- Public disclosure of commercial data
- Surveillance for adverse effects

Standards allow innovation within known (arbitrary?) boundaries

- Authorisation regime
- Standards

Max e-liquid = 20mg/ml (~2%)

"This concentration allows for a delivery of nicotine that is comparable to the permitted dose of nicotine derived from a standard cigarette during the time needed to smoke such a cigarette."

Source: TPD 20(3)(b) TPD recital 38

- Authorisation regime
- Standards
- Scientific burdens

United States: compliance focus

FEDERAL REGISTER
The Daily Journal of the United States Government

Rule

Premarket Tobacco Product Applications and Recordkeeping Requirements

A Rule by the Food and Drug Administration on 10/05/2021

PUBLISHED DOCUMENT

AGENCY:

Food and Drug Administration, HHS.

ACTION:

Final rule.

SUMMARY:

The Food and Drug Administration (FDA, the Agency, us, or we) is issuing a final rule that sets forth requirements for premarket tobacco product applications (PMTAs) and requires manufacturers to maintain records establishing that their tobacco products are legally marketed. The rule will help ensure that PMTAs contain sufficient information for FDA to determine whether a marketing granted order should be issued for a new tobacco product. The rule codifies the general procedures FDA will follow when evaluating PMTAs and creates postmarket reporting requirements for applicants that receive marketing granted orders. The rule also requires tobacco product manufacturers to keep records establishing that their tobacco products are legally marketed, such as documents showing that a tobacco product is not required to undergo premarket review or has received premarket authorization.

DOCUMENT DETAILS

Printed version: PDF

Publication Date: 10/05/2021

Agencies: Food and Drug Administration

Dates: This rule is effective November 4, 2021.

Effective Date: 11/04/2021

Document Type: Rule

Document Citation: 86 FR 55300

Page: 55300-55439 (140 pages)

CFR: 21 CFR 1100, 21 CFR 1107, 21 CFR 1114

Agency/Docket Number:

- Authorisation regime
- Standards
- Scientific burdens

100 metres

- Authorisation regime
- Standards
- Scientific burdens

How much science is enough science?

Advertising – communication and trust

- Authorisation regime
- Standards
- Scientific burdens
- Marketing freedoms

Control advertising themes and placement

- Authorisation regime
- Standards
- Scientific burdens
- Marketing freedoms

- ✓ Don’t be socially irresponsible
- ✓ Don’t target or feature children
- ✓ Don’t confuse e-cigarettes with tobacco products
- ✓ Don’t make health or safety claims
- ✓ Don’t make smoking cessation claims
- ✓ Don’t mislead about product ingredients
- ✓ Don’t mislead about where products may be use

EU Tobacco Products Directive

- Authorisation regime
- Standards
- Scientific burdens
- Marketing freedoms
- Claims

Manufacturers must not suggest:

"that a particular tobacco product is less harmful than others or aims to reduce the effect of some harmful components of smoke"

Source: TPD 13(1)(b) applied to vaping products via 20(4)(b)(ii)

US FDA MRTP (Swedish Match)

- Authorisation regime
- Standards
- Scientific burdens
- Marketing freedoms
- Claims

10 June 2014

Initial submission

> 5 years

22 Oct 2019

MRTP order

No tobacco product is safe, but this product presents substantially lower risks to health than cigarettes

Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis

WARNING: This product is not a safe alternative to cigarettes

Canada - abandoned

- Authorisation regime
- Standards
- Scientific burdens
- Marketing freedoms
- Claims

Health Canada vaping comms (Proposed, not implemented)

1. If you are a smoker, switching completely to vaping is a much less harmful option.
2. While vaping products emit toxic substances, the amount is significantly lower than in tobacco smoke.
3. By switching completely to vaping products, smokers are exposed to a small fraction of the 7,000 chemicals found in tobacco smoke.
4. Switching completely from combustible tobacco cigarettes to e-cigarettes significantly reduces users' exposure to numerous toxic and cancer-causing substances.
5. Completely replacing your cigarette with a vaping product will significantly reduce your exposure to numerous toxic and cancer-causing substances.
6. Switching completely from smoking to e-cigarettes will reduce harms to your health.
7. Completely replacing your cigarette with an e-cigarette will reduce harms to your health.

- Authorisation regime
- Standards
- Scientific burdens
- Marketing freedoms
- Claims
- Tax regime

- Authorisation regime
- Standards
- Scientific burdens
- Marketing freedoms
- Claims
- Tax regime
- Attitude

Philip Morris International “cigarette sales can end”

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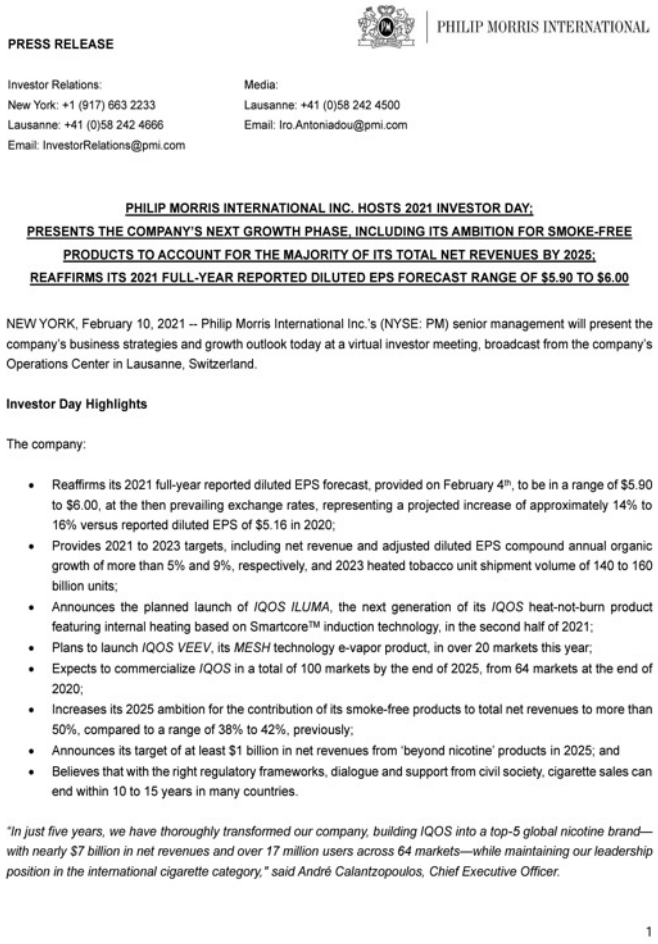

PHILIP MORRIS INTERNATIONAL

PRESS RELEASE

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PHILIP MORRIS INTERNATIONAL INC. HOSTS 2021 INVESTOR DAY;
PRESENTS THE COMPANY'S NEXT GROWTH PHASE, INCLUDING ITS AMBITION FOR SMOKE-FREE PRODUCTS TO ACCOUNT FOR THE MAJORITY OF ITS TOTAL NET REVENUES BY 2025;
REAFFIRMS ITS 2021 FULL-YEAR REPORTED DILUTED EPS FORECAST RANGE OF $5.90 TO $6.00

NEW YORK, February 10, 2021 -- Philip Morris International Inc.'s (NYSE: PM) senior management will present the company's business strategies and growth outlook today at a virtual investor meeting, broadcast from the company's Operations Center in Lausanne, Switzerland.

Investor Day Highlights

The company:

- Reaffirms its 2021 full-year reported diluted EPS forecast, provided on February 4th, to be in a range of $5.90 to $6.00, at the then prevailing exchange rates, representing a projected increase of approximately 14% to 16% versus reported diluted EPS of $5.16 in 2020;
- Provides 2021 to 2023 targets, including net revenue and adjusted diluted EPS compound annual organic growth of more than 5% and 9%, respectively, and 2023 heated tobacco unit shipment volume of 140 to 160 billion units;
- Announces the planned launch of *IQOS ILUMA*, the next generation of its *IQOS* heat-not-burn product featuring internal heating based on Smartcore™ induction technology, in the second half of 2021;
- Plans to launch *IQOS VEEV*, its *MESH* technology e-vapor product, in over 20 markets this year;
- Expects to commercialize *IQOS* in a total of 100 markets by the end of 2025, from 64 markets at the end of 2020;
- Increases its 2025 ambition for the contribution of its smoke-free products to total net revenues to more than 50%, compared to a range of 38% to 42%, previously;
- Announces its target of at least $1 billion in net revenues from 'beyond nicotine' products in 2025; and
- Believes that with the right regulatory frameworks, dialogue and support from civil society, cigarette sales can end within 10 to 15 years in many countries.

"In just five years, we have thoroughly transformed our company, building IQOS into a top-5 global nicotine brand—with nearly $7 billion in net revenues and over 17 million users across 64 markets—while maintaining our leadership position in the international cigarette category," said André Calantzopoulos, Chief Executive Officer.

Philip Morris International “cigarette sales can end”

- Authorisation regime
- Standards
- Scientific burdens
- Marketing freedoms
- Claims
- Tax regime
- Attitude

The company … believes that with the right regulatory frameworks, dialogue and support from civil society, cigarette sales can end within 10 to 15 years in many countries.

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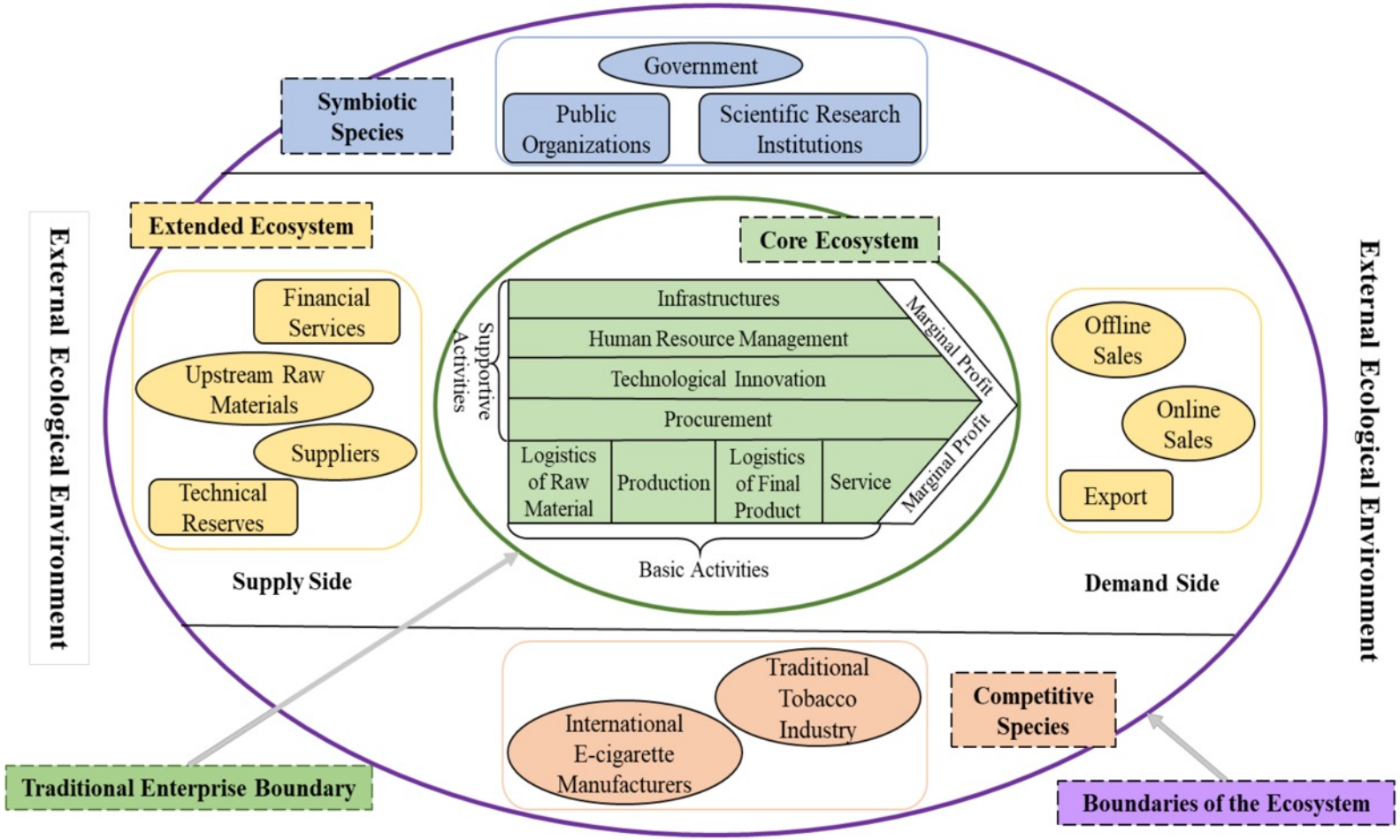
1

The Shenzhen vape innovation ecosystem

Shenzhen, China: consumer focus



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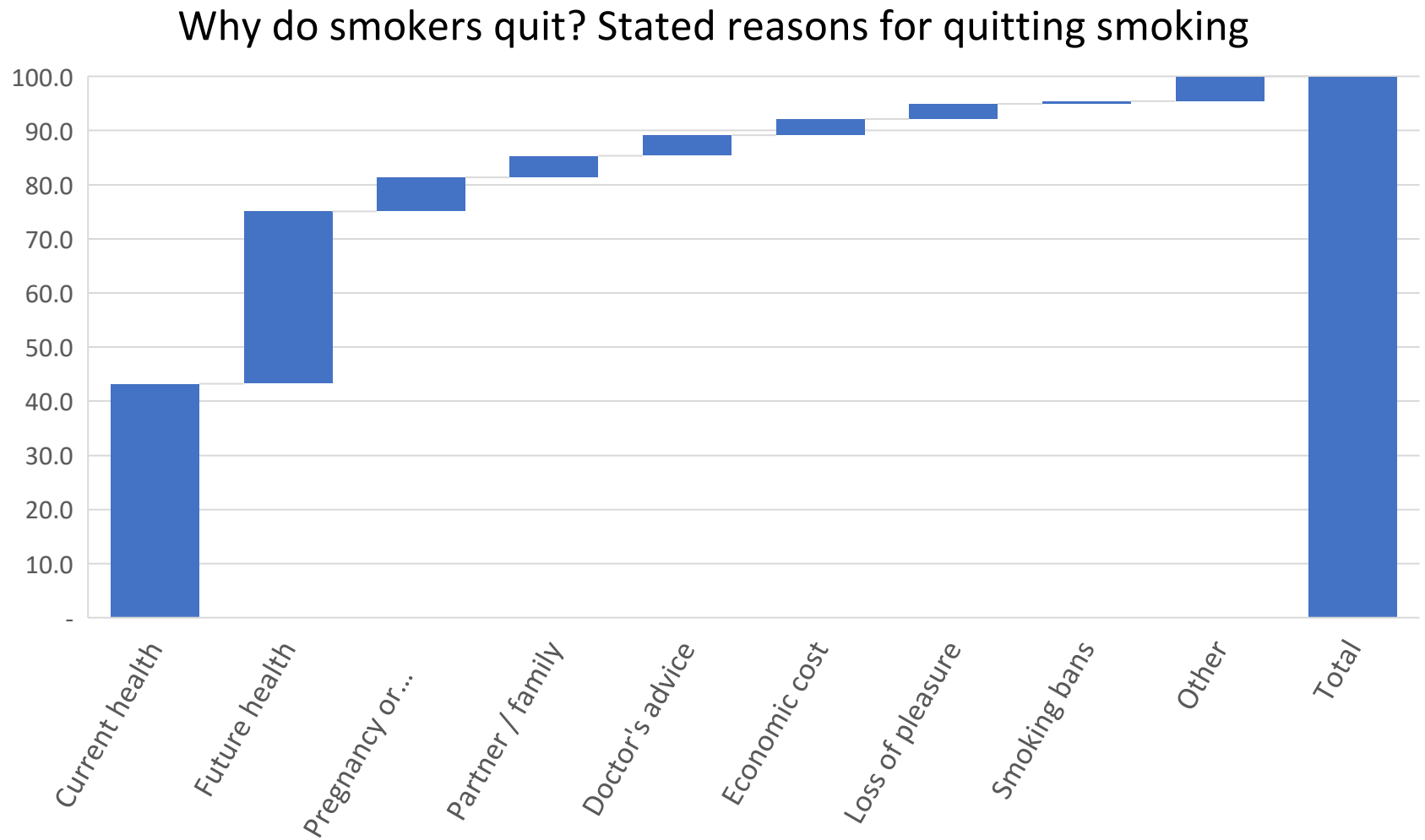
Why is there so much controversy about harm reduction?

1. Without harm, the tobacco control profession loses its purpose

2. Without harm, the deterrent to nicotine use falls away



Gallus S, Muttarak R, Franchi M, et al. Why do smokers quit? *Eur J Cancer Prev* 2013;22(1):96–101.

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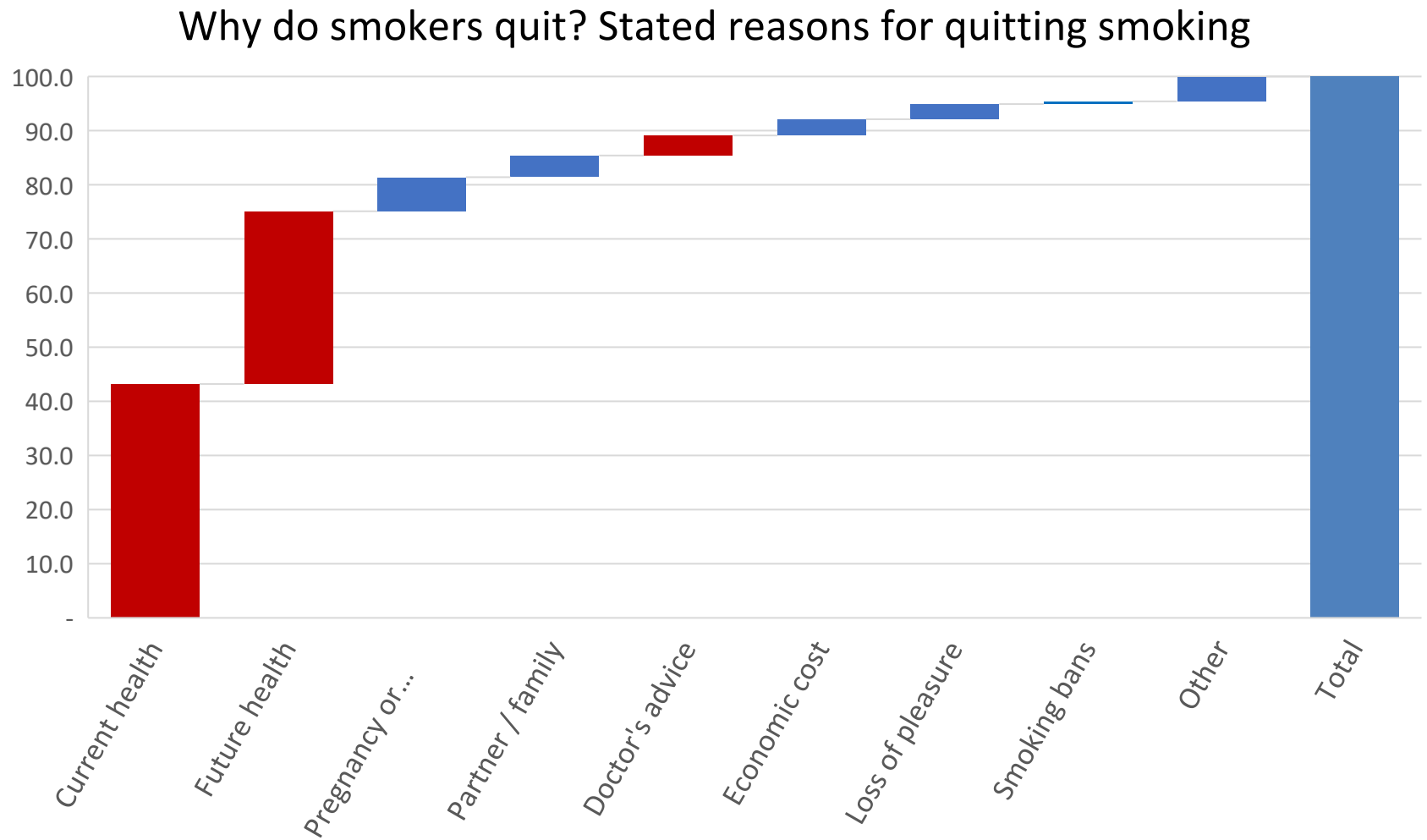

Gallus S, Muttarak R, Franchi M, et al. Why do smokers quit? *Eur J Cancer Prev* 2013;22(1):96–101.

3. Harm is integral to the definition of *addiction*

Addiction is defined as a chronic, relapsing disorder characterized by compulsive drug seeking and use despite adverse consequences.
National Institute on Drug Abuse (NIDA)

A compulsive, chronic, physiological or psychological need for a habit-forming substance, behavior, or activity having harmful physical, psychological, or social effects
Meriam Webster Dictionary

Addiction is a complex condition, a brain disease that is manifested by compulsive substance use despite harmful consequence. People with addiction (severe substance use disorder) have an intense focus on using a certain substance(s), such as alcohol or drugs, to the point that it takes over their life.
American Psychiatric Association

A mental disposition towards repeated episodes of abnormally high levels of motivation to engage in a behaviour, acquired as a result of engaging in the behaviour, where the behaviour results in risk or occurrence of serious net harm..
Addiction-O Ontology


NICOTINE = BRAIN POISON

1991 editorial in *The Lancet*

VOL 337: MAY 18, 1991 THE LANCET 1191

EDITORIALS

Nicotine use after the year 2000

Cigarette smoking is now regarded as a form of drug addiction. A landmark in this process was the 1988 report of the US Surgeon General, who concluded that addiction to nicotine resembles addiction to drugs such as heroin, cocaine, and alcohol.[1] What distinguishes nicotine from other widely abused drugs is that its effects are subtle and do not cause socially disruptive intoxication, provoke violence, or impair performance. Yet deaths due to tobacco far outnumber those caused by all other drugs. The central paradox is that, while people smoke for nicotine they die mainly from the tar and other unwanted components in the smoke. Why have governments persisted in allowing the manufacture, extensive advertising, and promotion of such a lethally contaminated drug delivery system as the cigarette, while putting so little pressure on the tobacco industry to develop more purified forms of nicotine delivery?

The pressure for change has come instead from the pharmaceutical industry, driven by the search for more effective aids to smoking cessation. The initial development of nicotine chewing gum has now been followed by other products. Nicotine skin patches maintain stable blood nicotine concentrations over 4–16 h,[2] whereas nicotine vapour inhalers mimic the rapid absorption from cigarette smoking.[3] At least five pharmaceutical companies have skin patches at various stages of testing, and clinical use of such patches is licensed in some countries. Other products undergoing clinical trials include a nasal nicotine spray, nicotine lozenges, and a nicotine vapour puffer.[4] Although these nicotine replacement products are marketed as aids to stopping smoking, with further refinement some may also have potential for long-term use and, if permitted, might eventually replace tobacco on the open market.

If a strategy were adopted to sanction and encourage the use of purified nicotine products as substitutes for smoking, and at the same time impose stringent regulations on permissible constituents of cigarette smoke and progressively lower limits for deliveries of harmful components such as nitrosamines and nitrogen oxides, as well as of tar and carbon monoxide, the virtual elimination of smoking could become a more realistic health promotion target. It could also be achieved more quickly. The question is whether policy-makers will consider such a strategy and whether the antismoking movement would support or oppose it.

Is a new strategy needed? Are existing programmes sufficient? There has been some progress in many countries. In the UK, for example, the prevalence of cigarette smoking has declined steadily from 46% in 1972 to 32% in 1988, an average rate of about 1% per year.[5] But progress worldwide has been swamped by the rapid increase in smoking in developing countries. Progress with tar reduction programmes is likewise slow. The modest aims of the Tar Yield Directive of the EC Council of Health Ministers on Nov 13, 1989, have been hailed as an important measure. The Directive sets a limit for tar yields of 15 mg by the end of 1992, and 12 mg by the end of 1997. Greece has derogation allowing higher yields until 2007. Overall, on the basis of current approaches and policies, there seems little prospect of averting Peto's estimate of 10 million premature deaths throughout the world each year during the next century as a result of tobacco use.[6]

The core of the problem lies in the addictiveness of nicotine. It is nicotine that people cannot easily do without, not tobacco; it is nicotine dependence that slows the progress of existing programmes. As a drug delivery system the modern cigarette is a highly efficient device for getting nicotine to the brain, but by pharmaceutical standards it is also a very "dirty" one, the nicotine being contaminated with nitrosamines and other carcinogens in the tar, as well as with carbon monoxide and other harmful gases. Thus it seems logical to offer either a cleaner product or, better still, an acceptable source of more pure, less contaminated nicotine. The principle is the same as that of the UK low-tar programme,[7,8] albeit a gigantic step—too big it seems for regulatory authorities and health professions in the USA.

In 1988, a major US tobacco company released details of a highly innovative type of cigarette that heats rather than burns tobacco.[9] The smoke particles were virtually tar-free, consisting mainly of water, glycerol, and a small amount of propylene glycol. The nicotine yield was low—0·3 mg. Apart from a carbon monoxide yield of 10·6 mg, amounts of other noxious gases were negligible compared with conventional cigarettes, as was the biological activity in extensive tests.[9,10] In terms of the aims for product modification laid down by the UK Independent Scientific Committee on Smoking and Health,[7] this would seem a near-perfect low-tar cigarette, and there is no doubt that it would be less harmful than most other brands on the market.

Far from welcoming it in the USA, the American

There is no compelling objection to the recreational and even addictive use of nicotine provided it is not shown to be physically, psychologically, or socially harmful to the user or to others.

Nicotine use after the year 2000, *The Lancet,* 1991

Anon. (1991). Nicotine use after the year 2000. In *The Lancet* (Vol. 337, Issue 8751, pp. 1191–1192). Elsevier.

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I. A (legitimate?) recreational drug
II. Innovation is ecological and emergent
III. Harm is political – and in a weird way

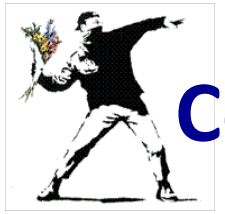
Innovation and its enemies…

"Claims about the promise of new technology are at times greeted with skepticism, vilification or outright opposition—often dominated by slander, innuendo, scare tactics, conspiracy theories and misinformation.

"The assumption that new technologies carry unknown risks guides much of the debate. This is often amplified to levels that overshadow the dangers of known risks."

Juma C. Innovation and Its Enemies: Why People Resist New Technologies. Oxford, New York: Oxford University Press; 2016.

Thankyou!



Counterfactual

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