**Transnational tobacco companies and new nicotine delivery systems (NNDs): A new phase in tobacco industry globalization**

**ABSTRACT**

While the public health community has focused on the harm reduction potential of new nicotine delivery systems (NNDs) and, conversely, their potential for impeding overall efforts to prevent and reduce tobacco use, limited analysis has been conducted on the role of leading transnational tobacco companies (TTCs) in this rapidly growing market. Following aborted efforts during the 1980s and 1990s to develop reduced risk products, TTCs have heavily invested in selected NNDs products since 2010 via acquisitions and internal research and development. This paper catalogues and analyzes the patterns of investment in NNDs by leading TTCs over time, and identifies differences in the companies' approaches to NNDs product acquisition and development in specific markets globally. This analysis raises important questions regarding the companies' intent, which appear to be to sustain, rather than replace, cigarette sales, and increase their influence and credibility with respect to NND policy and regulation. We identify the need for greater public health vigilance and research to understand and respond to the increasingly significant role of NNDs in TTCs’ global business strategies, to ensure that NNDs advance, rather than hinder, tobacco control efforts.

**INTRODUCTION**

New Nicotine Delivery systems (NNDs) are a rapidly growing market which include two principle categories. First, *electronic cigarettes (e-cigarettes)* heat a liquid solution usually containing nicotine (nicotine-free liquids also available) to produce an aerosol to be inhaled by users. There are different types of devices within the e-cigarette category including ‘cigalikes’, which closely resemble conventional cigarettes, and larger tank-based devices which can be customized or modified by users (often called ‘mods’).[[1]](#endnote-2) Second, the *heat-not-burn (HNB)* category heats tobacco leaf contained in disposable, cigarette-shaped plugs which are then inserted into a device to produce an aerosol to be inhaled by users. The total value of the global market for both categories of NNDS devices is still only 1-2% of combustible cigarettes (US$12.3 billion versus US$683 billion in 2016).[[2]](#endnote-3) However, the NNDs market is growing at a much faster rate, expected to rise to US$34 billion by 2021.[[3]](#endnote-4) HNB devices are described as especially “poised for explosive global growth”.[[4]](#endnote-5)

Public health debates about NNDs to date focus on their potential effectiveness in harm reduction versus their impacts on smoking initiation and relapse.[[5]](#endnote-6),[[6]](#endnote-7) Others have emphasised their potential to aid smoking cessation alongside robust claims about their relative safety.[[7]](#endnote-8) While available studies suggest nicotine aerosol is less toxic than cigarette smoke, concerns remain about the possible long-term health effects of NNDs products.[[8]](#endnote-9) Critics argue that the current lack of evidence on their long-term safety requires governments and health authorities to exercise caution in promoting their use, and regulatory frameworks which balance potential health benefits and as yet unknown harms.[[9]](#endnote-10) In addition, there is growing evidence that NNDs products are being used in addition to, rather than instead of, combustible cigarettes by many smokers; this “dual use” weakens claims of NNDs ‘harm reduction’ potential, given that reduced levels of smoking still confer significant health risks.[[10]](#endnote-11) To the extent that NNDs deter quit attempts, these products may prolong smoking and the associated health harms.5,[[11]](#endnote-12) Moreover, there is a growing body of evidence that NNDS products may attract new nicotine users, acting as a gateway to combustible cigarette use, particularly among youth.[[12]](#endnote-13) The similarities between combustible cigarettes and some NNDs devices (i.e. cigalikes), in terms of product appearance, packaging and marketing, raise concerns that hard-won tobacco control measures such as standardized packaging, public smoking bans and point of sale advertising may be undermined, in addition to concerns regarding the close mimicking of smoking behaviour in some NNDs products as potentially renormalizing smoking.[[13]](#endnote-14) The public health community has been deeply divided on these debates, between a precautionary approach to regulating NNDs and rapid and widespread use.

Alongside the public health community, leading transnational tobacco companies (TTCs) have also been active in research and policy debates about NNDs. This includes the creation by Philip Morris International of the Foundation for a Smoke-Free World.[[14]](#endnote-15) To date, however, there has been limited analysis of the substantial investments by TTCs in the rapidly growing NNDs market. To better understand the context for contemporary debates about the health risks and benefits from NNDs products, and the relevance of tobacco industry involvement in such debates, this article addresses two gaps in the current literature. First, we document patterns of investment by major TTCs in NNDs. Today, 84% of the world’s cigarette manufacturing (excluding the closed Chinese market controlled by state-owned Chinese National Tobacco Corporation) is dominated by four TTCs: British American Tobacco (BAT), PMI, Japan Tobacco International (JTI) and Imperial Tobacco.[[15]](#endnote-16) We analyse investments by these companies in NNDS over time, from 2010 to 2018, by company/products acquired, products developed and by target market. In addition, we include Reynolds, which was acquired by BAT in 2017, and Altria, the company which controls Philip Morris brands in the US. While a separate legal entity, close association exists between Philip Morris’ global and US-based businesses and the brand they market. As such, an analysis of PMI’s global investment in NNDS products which ignored the vital US market would be incomplete and so the term TTC should be read as including Altria in the context of this article.

Second, the article begins to address the limited analysis to date of the role of NNDs products within TTCs’ global business strategies. Previous research has found that TTC investments in NNDs products in European markets have been “driven by regulatory threats and health concerns, both likely to impact cigarette sales negatively, and the potential to create a new form of tobacco use among those no longer interested in taking up smoking. Young people were a key target.”[[16]](#endnote-17) TTC investments in e-cigarettes have been documented in the Tobacco Tactics website to 2016.[[17]](#endnote-18) As the first systematic analysis of TTC investments in NNDs, this paper locates the observed investment patterns (focused on cigalike and HNB devices) within the context of substantial global restructuring and consolidation within the tobacco industry since the 1990s. It has been argued elsewhere that these changes have been prompted by trends within the industry, notably declining smoking rates and stronger regulation in traditional markets, and by broader changes associated with economic globalization.[[18]](#endnote-19) This article builds on these insights to consider the extent to which TTC investments in NNDs can be explained by tobacco industry globalization, and identify areas of further research concerning tobacco control.

**BACKGROUND**

The first commercially available e-cigarettes came to market in the US and UK around 2006.[[19]](#endnote-20) Rapid expansion of the cigalike market in the US, largely from imports and small independent companies, was prompted in 2010 by the overturning by a Federal District Court of a 2009 US Food and Drug Administration (FDA) decision to regulate e-cigarettes as therapeutic devices rather than tobacco products, which removed the FDA’s block on e-cigarette imports.[[20]](#endnote-21) In 2011, the FDA issued regulation (followed by a “deeming rule” in 2016) allowing it to regulate all e-cigarettes and HNB devices as tobacco products, thereby restricting producers’ ability to make reduced-risk claims or to sell products without FDA permission (see, for example, the Modified Risk Tobacco Product [MRTP] claim that PMI submitted in 2016 for *IQOS*)*.*[[21]](#endnote-22),[[22]](#endnote-23) Despite the substantial TTC investment in research and development (R&D) on reduced risk products from the 1960s, their investment in NNDs remained limited until the late 2000s.

Previous analyses of internal tobacco industry documents revealed longstanding efforts to develop reduced harm products.[[23]](#endnote-24) Industry investment in “a safer cigarette” began as early as 1960, with patents for “non-combustible cigarettes” and “nicotine inhalers,” closely resembling modern devices, registered in 1979.[[24]](#endnote-25) Documents leaked in 2018 from PMI acknowledge that TTC investment in NNDs products was driven by an awareness of the need to “establish the legitimacy of tobacco companies to be a part of the regulatory debate on RRPs [reduced risk products]”[[25]](#endnote-26) and thus to position the industry as being part of the solution to smoking harms by offering alternative tobacco and nicotine products as part of a wider attempt to reframe tobacco cessation debates in terms of harm reduction.[[26]](#endnote-27)

The industry’s development of purportedly reduced harm products, however, was halted by concerns from TTC industry management about their liability under personal injury lawsuits in the US. If less harmful products were developed and marketed, this would contradict decades of industry denial of the health harms from smoking.[[27]](#endnote-28) In September 1999, the US Department of Justice began a US$280 billion legal action under the Racketeer Influenced and Organized Crime Act, to hold major US cigarette companies liable for their decision not to develop less hazardous products despite collective knowledge of the health risks posed by their products. [[28]](#endnote-29) The case was supported by many tobacco control organizations including Action on Smoking and Health and the Imperial Cancer Research Fund which found that, although TTCs had the knowledge, resources, and technology to sell alternative cigarette products, such products were kept in the “bottom drawer” for decades. This case prompted an admission by Philip Morris regarding the “overwhelming medical and scientific consensus" that smoking causes lung cancer, emphysema, and heart disease, marking what former US Food and Drug Administration (FDA) David Kessler called “a new stage for regulation and legislation.”[[29]](#endnote-30) These findings were further supported by the leaked internal documents from PM noted above.25

**METHODS**

We undertook a narrative review of scholarly and grey literature, using PubMed. The JSTOR database was then searched to capture social science publications which may fall outside the remit of PubMed. Additional searches were undertaken using Google Scholar, to identify further publications on TTC engagement with NNDs. The search terms used in the databases were “vap\*”, “e-cigarette”, “heat-not-burn”, “next generation product”, “alternative tobacco product”, “reduced risk products” and “ENDS”. We used the same keywords to search industry-related publications (*Tobacco Reporter*, *Tobacco Journal International, Tobacco Today, Tobacco Tactics)* and specialist business news sources (*Vaping Post, Bloomberg, Business Insider and Reuters*). Euromonitor International reports on the e-cigarette market were also examined. Searches were undertaken from January 2017-May 2018 for articles published after 2010.

We then searched the global websites of four TTCs (BAT, Imperial, PMI, JTI) plus Altria for information on their investments in the NNDS market. We excluded the Chinese National Tobacco Corporation (CNTC) given the little evidence of its investment in NNDs. Given the timeframe of our analysis, from 2010-2018, we searched for additional information on Lorillard (merged with Reynolds American in 2015) and Reynolds American (merged fully with BAT in 2017 when BAT purchased the remaining 58% share in Reynolds not previously controlled). Internal tobacco industry documents, currently available from the Truth Tobacco Documents Library, were not examined given the limited data they offer on events since 2010. We included a small number of studies using contemporary tobacco industry documents published by Reuters and situated our research in relation to previous studies of tobacco industry documents that examined relevant aspects of TTC strategy such as the development of ‘reduced risk’ products.[[30]](#endnote-31)

We collated information from these sources into a dataset (see Tables 1 and 2) to identify patterns of investment by each TTC from 2010 to 2018, identifying the specific products marketed by each company; product type (e.g. e-cigarette or HNB devices); if products were developed internally (via R&D) or obtained through company acquisitions; and their target markets and demographics. Together, these two tables identify the specific ways in which TTCs have entered the NNDs market as well as highlighting differences in TTCs’ approaches to NNDs, both globally and in particular target markets.

To analyze the role of NNDs products within TTCs’ global business strategies, we were guided by the heuristic framework set out by Lee and Eckhardt.15 This focuses on three key questions: (a) what are the primary factors behind industry/company globalization; (b) what are the specific globalization strategies pursued by the industry/company; and (c) to what extent has the industry as a whole, or specific companies, globalized to date? Our dataset helped to address the second and third questions, namely the importance of NNDs company and product acquisition to the globalization strategies of leading tobacco companies; and the extent to which this has been achieved to date. This analysis was triangulated with market analyses and public statements by tobacco companies, in relation to these investments, to identify stated strategies behind TTCs entering the global NNDs market.

**RESULTS**

**Patterns of investment in NNDs by TTCs over time**

Since the late 2000s, leading TTCs have pursued two main strategies in the NNDs sector: acquiring local companies producing specific types of NNDs products (Table 1), and developing and marketing their own NNDs products (Table 2). Table 1 shows that TTCs initially engaged with NNDs through acquisition of e-cigarette manufacturers. In the late 2000s, there were multiple independent manufacturers supplying a rapidly growing demand in the US, where there were more than 460 brands on the market in 2014.[[31]](#endnote-32) By 2012, TTCs began to buy leading manufacturers in the US and UK markets, notably Blu cigs, Logical Technology and Dragonite. These acquisitions particularly focused on cigalike products rather than tank-system and other recently emerging e-cigarette devices (e.g. *Juul*).

TTCs invested in NNDs companies that offered competitive advantages and the ability to control the development of the market through patent rights, retail distribution networks, and ancillary products (e.g. vaping liquid). For example, Imperial (through its subsidiary Fontem Ventures) acquired Dragonite International in 2013 and its many patents, and launched legal action the following year in the US claiming patent infringement against eleven leading e-cigarette manufacturers, many of which by then had been bought by other TTCs. Importantly, this legal action made market access more difficult for small independent companies. The ambiguities surrounding the ownership of patent rights over different cigalike products coincided with major investments by Reynolds American (*Vuse*), BAT (*Vype, e-Voke*), Altria (*MarkTen*), Imperial (*Jai*) and PMI (*MESH*). By 2015 the e-cigarettes market had undergone significant consolidation due to TTC acquisition of cigalike manufacturers, as well as mergers and acquisitions among leading tobacco companies themselves (e.g. Reynolds American-Lorillard, BAT-Reynolds American).

[INSERT TABLE 1 HERE]

From 2012, TTCs also began to launch internally developed NNDs products to compete in what had become a booming market, including the development of HNB products. Table 2 shows that, unlike e-cigarettes, there were no independent manufacturers of heat-not-burn devices.Market research on cigalikes found that, while the devices mimicked the look and use of combustible cigarettes, many consumers reported dissatisfaction with their use (e.g. lack of “throat hit” delivered by combustible but not most e-cigarettes).4 The movement into the HNB market was accompanied by investments into different types of e-cigarettes, such as the BAT Pebble. To date, PMI and BAT have led the HNB market, with KT&G entering the Asian market in 2017 with the product *lil*.

[INSERT TABLE 2 HERE]

**Comparing the global business approaches of transnational tobacco companies**

All leading TTCs have invested in NNDs, but with differences in approach.

First, BAT (2010) and Imperial (2013) are the only leading tobacco companies that have sought to develop and gain licences for medicalised nicotine inhalation devices (*Voke*/e-*Voke* and *Puritane* respectively) to assist with smoking cessation. *Voke* is a nicotine inhalation device which does not use electronic heating technology and is thus not strictly speaking an NNDs product. However, it formed an important part of a BAT’s range of new nicotine delivery devices at a key stage in the development of the sector and TTC strategy, and is thus included in the analysis here. At the time of *Voke’s* development, it appeared that medicalization may be the principle regulatory approach taken by governments and an important strategy adopted by TTCs.[[32]](#endnote-33) However, both regulation and TTC product development have subsequently developed in this way. Moves to obtain medically licensed products were, in part, a response to attempts by the US Food and Drug Administration (FDA) to regulate NNDs in 2010 as medical devices under the auspices of the Family Smoking and Prevention Act.21 Similarly, the UK Medicines and Healthcare Products Regulatory Authority (MHRA) announced in 2013 that it would also regulate e-cigarettes as medical devices.[[33]](#endnote-34) Following legal challenges, the FDA announced in April 2011 that e-cigarettes would be regulated as tobacco products, although more stringent regulatory regulations as drugs or drug delivery devices would apply to any products marketed as smoking cessation tools or advertising other health benefits; at this time, no NNDs products have been approved for this purpose.21 The European Union Tobacco Products Directive in 2014 adopted a ‘dual approach’ which allows non-licenced NNDs devices to be brought to market, appear to have removed the incentive for TTCs to seek medical licences. PMI’s 2016 FDA application to market *IQOS*, as a “modified risk tobacco product”, eschewing medical regulation,reflects this broader shift by leading TTCs away from medical licensing.22

Second, some companies have invested exclusively in e-cigarettes (Imperial, JTI, and Altria), while PMI and BAT have invested in both e-cigarettes and HNB devices. The diversification in terms of the specific type of NNDs product each TTC has invested in has also been reflected in their approach to acquisitions versus internal product development. JTI has entered the NNDs market exclusively through acquisition of existing companies (Zandera, Ploom, Logic) as has Imperial (with the exception of its *Jai* e-cigarette). In contrast, PMI has made only two acquisitions (*Solaris*, *NicoCigs*), instead investing heavily in R&D to create its own NNDs products (*IQOS*, *MESH*, *STEEM*, and *TEEPS*). Altria has made one major acquisition (Green Smoke) and developed one brand internally (*MarkTen)*, with both marketed through its subsidiary NuMark. Meanwhile, BAT has taken the most diversified approach to its product portfolio, acquiring products (*Voke, CHIC, Vuse*) and developing others internally (*Vype, e-Voke, iFuse, glo*).

**Targeting of specific countries and markets**

All leading TTCs sought to gain an initial foothold in the US and UK as fast growing NNDs markets. By 2015, the companies widened their sights to other traditional tobacco markets, notably Canada, Asia (Japan and Korea) and Europe. Reynolds American had marketed earlier HNB devices *Premier* and *Eclipse* during the mid-1990s, although efforts to relaunch *Eclipse* as *Revo* in 2015 proved unsuccessful.26 Reynolds did have success marketing a subsequent e-cigarette product, *Vuse,* in the US vaping market, which was subsequently acquired by BAT in 2017 when it took over Reynolds. Thus BAT has been able to add this leading brand to its NNDs portfolio, alongside its *Vype* e-cigarette offered in the UK, Italy, France, Poland, and Germany, with expansion planned in Colombia, the Philippines, Guatemala, Kuwait, and Bahrain.[[34]](#endnote-35) With an existing presence in 200 markets worldwide for combustible tobacco products, BAT describes itself as “now a truly global company in the Next Generation Products category”.[[35]](#endnote-36) The globalization of NNDS is also reflected in PMI’s close cooperation with Altria to sell the latter’s e-cigarette *MarkTen* as *Solaris* outside the US. In the HNB category, PMI launched IQOS in specific cities and at duty free outlets, and have exceeded their projected targets to reach 37 markets by the end of 2017.[[36]](#endnote-37)

In addition to the rapid expansion of NNDs in the US and UK, our findings show that NNDs have also been introduced in markets with much weaker tobacco control regimes and limited or no regulation of NNDS devices. Japan has emerged as an important NNDs market for TTCs, with the launch of JTI’s *Ploom* and *Logic* brands, BAT’s *iGlo* and PMI’s *IQOS*. This is in part due to weak regulation, including the permitted selling of e-cigarettes to minors.[[37]](#endnote-38) Israel was selected as a test market for Altria’s *Green Smoke*. In March 2017, the Health Minister decided to allow unrestricted import, marketing and tax exemption of vaping devices.[[38]](#endnote-39)

**DISCUSSION**

This paper catalogues how leading TTCs have actively entered, and quickly come to dominate, certain product categories within the NNDs market through investments from 2010 to 2018. In the e-cigarette sector, TTCs focused on acquiring independent ‘cigalike’ manufacturers, thereby gaining intellectual property, market share and distribution networks. This was supplemented by the internal development of additional branded e-cigarettes. Through this strategy, TTCs have come to dominate the global ‘cigalike’ sector, but have not entered the market for modifiable or tank-based e-cigarettes. The paper also identifies the more recent, yet also significant, investment in HNB products particularly by PMI and BAT, which enjoy a strong competitive advantage in this sector. Our findings show that specific products are targeted at different national markets and certain populations within them. Follow up research is needed to better understand the brand identities of specific NNDs products, the way in which they are positioned and targeted across (i.e. in different countries) and within markets (i.e. different sub-populations and demographics).

These findings raise important implications for current debates on how to regulate NNDs in ways that support tobacco control. TTCs operate on a global scale, developing products which are promoted and sold in markets worldwide, and benefiting from differences in regulatory regimes across jurisdictions. We suggest that surveillance of these NNDs investments should be situated within ongoing changes in the tobacco industry, including increased concentration of ownership, product diversification, and global expansion into new markets.15 Study of company-level NNDs strategies are needed to support the development of effective regulatory action nationally and globally. Furthermore, this research raises important questions concerning TTC intentions in entering the NNDs market. There is little evidence to support claims that tobacco companies are “getting out of the cigarette industry”.14 TTCs investing in NNDs continue to aggressively market conventional cigarettes and challenge all attempts to regulate these further and reduce smoking.[[39]](#endnote-40) These findings suggest that NNDs may be serving an important strategic role in the globalization of the tobacco industry, not as a reduced harm alternative to combustible tobacco products, but as a key means of supporting their core tobacco businesses.

Moreover, our findings suggest that TTCs may be using investments in NNDs to position themselves as legitimate stakeholders in research and policy debates, premised on claims of their intent to reduce harm.29 PMI’s Foundation for a Smoke-Free World (created after the development of IQOS), for example, seeks to influence research and policy debates “[t]hrough the support of Centers of Excellence for science-based tobacco control research at academic centers around the world” as well as planning “to develop private-public partnerships”.14 TTCs’ attempts to rebrand themselves as nicotine technology companies through investments in NNDs would offer a way for a discredited industry to re-engage scholars and policy makers, and ultimately influence the regulatory environment. In this sense, current investments in NNDs may represent the latest iteration of longstanding tobacco industry strategies to muddy the waters in policy debates, distract attention from effective tobacco control measures, and gain access to policy processes and decision makers through the development and promotion of allegedly reduced harm products.30

Finally, the findings raise important questions about the effective implementation of the Framework Convention on Tobacco Control (FCTC).[[40]](#endnote-41) TTC investments in NNDs suggest that the FCTC should be extended to cover the regulation of all tobacco-derived products, including NNDs. This would avoid country-by-country regulation which has enabled the “divide and conquer” tactics of TTCs used for combustible cigarettes in the past.25 Perhaps of greatest importance for the future of global tobacco control is the potential for NNDs to be used by TTCs to undermine Article 5.3 of the FCTC, which obliges governments to ward against attempts by the tobacco industry interference in health policy. An extension of the FCTC to include NNDS would prevent leading TTCs from re-entering research and policy debates as NNDs manufacturers while still maintaining their profits from cigarettes.

**CONCLUSION**

This paper analyses patterns of investment by leading TTCs in NNDs, comparing approaches between companies and across target markets worldwide. It identifies how TTCs have positioned themselves as dominant players in the ‘cigalike’ and HNB product categories. Given the well-documented history of TTCs’ use of product innovation and investment in ‘reduced harm’ products to stymie regulation and engage policy makers, these latest developments call for governments to regulate NNDs in ways which support existing tobacco control regimes and to treat TTCs with great caution in the guise as NNDs producers. The highly adaptive political strategies of TTCs calls for vigilance by public health actors, while additional research is needed to document the ongoing development of TTCs’ investments in NNDs and to investigate the synergies which exist between their market and political strategies and between their NNDs and traditional tobacco products.

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**REFERENCES**

1. Bauld, L., Angus, K., & Ford, A. (2016). Electronic Cigarette Marketing: Current Research and Policy. [↑](#endnote-ref-2)
2. Euromonitor. *Global Tobacco: Key Findings Part II: Vapour Products*. October 2017. [↑](#endnote-ref-3)
3. Euromonitor. *What the 2017 Edition Tobacco Data is Telling Us*. June 26, 2017. <http://blog.euromonitor.com/2017/06/latest-research-tobacco-2017-edition-data.html>. Accessed November 2, 2017. [↑](#endnote-ref-4)
4. # Caputi T, Leas E, Dredze M, Cohen J, Ayers J. They’re heating up: Internet search query trends reveal significant public interest in heat-not-burn tobacco products. *PLoS One.* 2017;12(10):e0185735.

   [↑](#endnote-ref-5)
5. National Academies of Sciences, Engineering, and Medicine. Public Health Consequences of E-Cigarettes. Washington DC: The National Academies Press; 2018. [↑](#endnote-ref-6)
6. Warner KE, Mendez D. E-cigarettes: Comparing the Possible Risks of Increasing Smoking Initiation with the Potential Benefits of Increasing Smoking Cessation. Nicotine Tob Res. 2018; pmid:29617887 [↑](#endnote-ref-7)
7. McNeill A, Brose LS, Calder R, Bauld L & Robson D (2018). Evidence review of ecigarettes and heated tobacco products 2018. A report commissioned by Public Health England. London: Public Health England. [↑](#endnote-ref-8)
8. Dutra LM, Glantz SA. E-cigarettes and National Adolescent Cigarette Use: 2004-2014. Pediatrics. 2017 Feb;139(2). pii: e20162450. doi: 10.1542/peds.2016-2450. [↑](#endnote-ref-9)
9. Pearson J, Richardson A, Niaura R, Vallone D, Abrams D. E-Cigarette awareness, use, and harm perceptions in US adults. *American Journal of Public Health.* 2012;102(9):1758-1766. [↑](#endnote-ref-10)
10. McMillen R, Gottlieb M, Shaefer R, Winickoff J, Klein J. Trends in electronic cigarette use among US adults: use is increasing in both smokers and nonsmokers. *Nicotine and Tobacco Research.* 2015;17(10):1195-202. [↑](#endnote-ref-11)
11. Dinakar C, O’Connor G. The Health Effects of E-cigarettes. *New England Journal of Medicine*. 2016; 375:1372-81. [↑](#endnote-ref-12)
12. [↑](#endnote-ref-13)
13. Primack BA, Shensa A, Sidani JE, Hoffman BL, Soneji S, Sargent JD, Hoffman R, Fine MJ. Initiation of Traditional Cigarette Smoking after Electronic Cigarette Use among Tobacco-Naïve U.S. Young Adults. Am J Med. 2017 Nov 17. pii: S0002-9343(17)31185-3. doi: 10.1016/j.amjmed.2017.11.005. McKee, M., Daube, M., & Chapman, S. (2016). E-cigarettes should be regulated. *The Medical journal of Australia*, *204*(9), 331. [↑](#endnote-ref-14)
14. PMI. *Designing a smoke-free future*. Available at: https://www.pmi.com/who-we-are/designing-a-smoke-free-future. Accessed March 25, 2017. [↑](#endnote-ref-15)
15. Lee, K., & Eckhardt, J. (2017). The globalisation strategies of five Asian tobacco companies: An analytical framework. *Global Public Health*, *12*(3), 269-280. [↑](#endnote-ref-16)
16. Peeters S, Gilmore AB. Transnational tobacco company interests in smokeless tobacco in Europe: analysis of internal industry documents and contemporary industry materials. *PLoS Medicine.* 2013;10(9):e1001506. [↑](#endnote-ref-17)
17. Tobacco Tactics. *E-Cigarettes.* Last modified July 5, 2016. Available at: <http://www.tobaccotactics.org/index.php/E-cigarettes>. Accessed November 10, 2017. [↑](#endnote-ref-18)
18. Lee K, Eckhardt J, Holden C. Tobacco industry globalization and global health governance: Towards an interdisciplinary research agenda. *Palgrave Communications.* 2016;2:16037. doi:10.1057/palcomms.2016.37 [↑](#endnote-ref-19)
19. US Centers for Disease Control and Prevention. *E-Cigarette Use Among Youth and Young Adults*. A Report of the Surgeon General. Atlanta, GA, 2016. Available at: <https://www.cdc.gov/tobacco/data_statistics/sgr/e-cigarettes/pdfs/2016_SGR_Chapter_1_non-508.pdf> [↑](#endnote-ref-20)
20. # Wilson D. Judge Orders F.D.A. to Stop Blocking Imports of E-Cigarettes From China. *New York Times.* January 14, 2010.

    [↑](#endnote-ref-21)
21. US Food and Drug Administration. (2011). Regulation of E-cigarettes and other tobacco products. Available at: [www.fda.gov/newsevents/publichealthfocus/ucm252360.htm](http://www.fda.gov/newsevents/publichealthfocus/ucm252360.htm) [↑](#endnote-ref-22)
22. PMI Science. PMI’s applications to the US Food and Drug Administration. Available at: <https://www.pmiscience.com/smoke-free/regulation/fda-mrtpa> Accessed May 18 2018. [↑](#endnote-ref-23)
23. Glantz, S. A., Bero, L. A., Slade, J., Barnes, D. E., & Hanauer, P. (Eds.). (1998). *The cigarette papers*. Univ of California Press. [↑](#endnote-ref-24)
24. Dutra L, Grana R, Glantz S. Philip Morris research on precursors to the modern e-cigarette since 1990. *Tobacco Control.* 2016. doi: 10.1136/tobaccocontrol-2016-053406 [↑](#endnote-ref-25)
25. PMI Foundation. 2014. 10 year corporate affairs objectives and strategies. Available at: <https://www.documentcloud.org/documents/4333395-10-Year-Corporate-Affairs-Objectives-and.html> Accessed May 18 2018. [↑](#endnote-ref-26)
26. McDaniel PA, Smith EA, Malone RE. Philip Morris's Project Sunrise: weakening tobacco control by working with it. Tob Control. 2006 Jun;15(3):215-23. [↑](#endnote-ref-27)
27. Cummings K, Brown A, Douglas C. Consumer acceptable risk: how cigarette companies have responded to accusations that their products are defective. *Tobacco Control*. 2016;15(S4):iv84-iv89. [↑](#endnote-ref-28)
28. Milberger S, Davis RM, Douglas CE, et al. Tobacco manufacturer’s defence against plaintiffs’ claims of cancer causation: throwing mud at the wall and hoping some of it will stick. *Tobacco Control.* 2016;15(S4):iv17-iv26. [↑](#endnote-ref-29)
29. Anon. Tobacco Giant Admits Health Risk. *BBC News*, October 13, 1999. Available at: <http://news.bbc.co.uk/2/hi/health/473630.stm>. Accessed November 13, 2017. [↑](#endnote-ref-30)
30. Bansal, P., Lasseter, T., Wilson, D., Wilson, T., Miyazaki, A. & Kalra, A. How Philip Morris is selling regulators on its hot new smoking device. *Reuters*. December 21 2017. Available at: <https://www.reuters.com/investigates/special-report/tobacco-iqos-marketing/> Accessed May 18 2018 [↑](#endnote-ref-31)
31. Zhu SH, Sun J, Bonnevie E, Cummins S, Garnst A, Yin L, Lee M. Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. *Tobacco Control* 2014;23(Suppl.3): iii3-iii9. [↑](#endnote-ref-32)
32. ## Hawkins, B & McKenzie, R. 2018. Tobacco industry investment in electronic nicotine delivery devices: an evolving strategy. Tobacco Control. BMJ Blogs. Available at:

    <https://blogs.bmj.com/tc/2018/05/03/tobacco-industry-investment-in-electronic-nicotine-delivery-devices-an-evolving-strategy/> Accessed on June 2, 2018. [↑](#endnote-ref-33)
33. Gornall J. Electronic cigarettes: medical device or consumer product. *BMJ*. 2012;345: e6417. [↑](#endnote-ref-34)
34. Vype. *Vype*. Available at: <https://www.govype.com/> Accessed March 29, 2017 [↑](#endnote-ref-35)
35. BAT. *Our Next Generation Products business*. 2017. Available at: <http://www.bat.com/group/sites/uk__9d9kcy.nsf/vwPagesWebLive/DOA89DQ4>. Accessed November 11, 2017. [↑](#endnote-ref-36)
36. Philip Morris International. *Sustainability Report 2017.* 2017. Available at: [https://www.pmi.com/docs/default-source/pmi-sustainability/pmi-sustainability-report-2017.pdf Accessed September 4](https://www.pmi.com/docs/default-source/pmi-sustainability/pmi-sustainability-report-2017.pdf%20Accessed%20September%204), 2018. [↑](#endnote-ref-37)
37. Yui M. Big tobacco wants to turn Japan’s smokers into vapers. *Bloomberg*. August 28 2016. Available at: <https://www.bloomberg.com/news/articles/2016-08-28/no-smoke-nicotine-hits-heat-up-japan-s-moribund-tobacco-market> Accessed March 25, 2017 [↑](#endnote-ref-38)
38. Linder-Ganz R. (2017). Israel’s huge gift to Philip Morris. *Haaretz*. March 22 2017. Available at: <http://www.haaretz.com/science-and-health/1.778773?v=E2F040F760B4E118A64848FB99132338> Accessed March 25, 2017 [↑](#endnote-ref-39)
39. Hawkins, B., Holden, C., Eckhardt, J., & Lee, K. (2018). Reassessing policy paradigms: A comparison of the global tobacco and alcohol industries. *Global public health*, *13*(1), 1-19. [↑](#endnote-ref-40)
40. Framework Convention on Tobacco Control. 2018. WHO. Available at: <http://www.who.int/fctc/cop/about/en/> Accessed June 2, 2018.

    **Table 1. NNDs-related acquisitions by leading tobacco companies**

    |  |  |  |  |  |
    | --- | --- | --- | --- | --- |
    | **TOBACCO COMPANY** | **YEAR** | **PRODUCT/**  **COMPANY ACQUIRED** | **TARGET MARKET** | **NOTES** |
    | **Lorillard** | 2012 | Blu e-cigs (e-cigarette company) | US | Lorillard purchases e-cigarette company Blu e-cigs for US$154 million. Company becomes one of three companies selling to US national market. |
    | 2013 | Skycig (e-cigarette company) | UK | Lorillard purchases Skycig for US$48.5 million (additional US$48.5 million in 2016 depending on financial performance benchmarks) as leading premium brand in the UK. |
    | **Imperial** **Tobacco** | 2012 | Fontem Ventures (e-cigarette company) | Netherlands | Imperial creates subsidiary “to acquire, manage, operate, encumber and dispose of property, including patents and other intellectual property” related to e-cigarettes. |
    | 2013 | Dragonite International (e-cigarette company) | US, UK | Subsidiary Fontem Ventures acquires portfolio of global patents for e-cigarettes from healthcare and pharmaceutical company Dragonite International for US$75 million. Co-founder Hon Lik joins Fontem Ventures. |
    | 2014 | *Puritane* (e-cigarette product) | UK | Subsidiary Fontem Ventures rebrands Dragonite brand *Ruyan* as *Puritane* and markets as behind-the-counter healthcare product to aid cessation. Application submitted for MHRA approval as a medical device. |
    | 2014 | Fontem Ventures | US | Subsidiary launches legal case against 11 US vaping companies/brands for patent infringement (based on Dragonite patents) including NJOY, Blu e-cigs, Nicoventures and Logic Technology. |
    | 2015 | blu e-cigs (e-cigarette company) | US | Imperial Tobacco buys blu e-cigs from Reynolds (after purchasing Lorillard) for US$7.1 billion. Imperial Tobacco markets *Blu* as a “lifestyle brand” consumer product and safer alternative to smoking. |
    |  | 2016 | Fontem Ventures | US | Subsidiary reaches legal settlement with 11 US e-cigarette companies in the form of non-exclusive royalty-bearing license. |
    | 2017 | Von Erl Gmbh (e-cigarette company) | Austria | Imperial acquires e-cigarette manufacturing company for undisclosed amount. |
    | 2017 | Nerudia | UK | Imperial acquires e-juice manufacturing company for undisclosed amount. |
    | **British American Tobacco** | 2010 | *Voke* (e-cigarette brand) | UK | Start-up Nicoventures acquires license to manufacture, market and brand rights, and intellectual property for *Voke* from Kind Consumer. |
    | 2012 | CN Creative (e-cigarette company) and *Intellicig* brand | UK | BAT acquires company and its products |
    | 2013 | CN Creative (e-cigarette company) | UK | BAT merges company with BAT subsidiary Nicoventures. |
    | 2014 | *Voke* (e-cigarette product) | UK | Nicoventures gains approval from MHRA for *Voke* as a medicinal product to aid smoking cessation and reduce harm. *Voke* is an inhaler but, rather than heat or batteries (electronic), it uses “a pressurised system that atomises a nicotine formulation into fine droplets, capable of lung absorption.” |
    | 2015 | CHIC Group (e-cigarette company) | Poland | BAT acquires company and gains control of 70% of Polish market. CHIC produces Polish brands such as *VOLISH*, *P1*, *Provog*, *LiQueen* and *Aromativ*, and distributes Chinese brands *Joyetech* and *Kangertech*. BAT strengthens retail networks and R&D capabilities in continental Europe. |
    | 2016 | *Vuse* (e-cigarette product) | US | BAT acquires *VUSE* brand through merger with Reynolds American. *Vuse* launched in 2014 by RJ Reynolds Vapor Company as one of three brands sold in US national market. |
    | 2016 | Ten Motives (e-cigarette company) | UK | BAT acquires company for undisclosed sum to expand retail networks through grocery and convenience stores. |
    | 2017 | Kind Consumer and Nicovations (e-cigarette companies) | UK | Nicovations (formerly Nicoventures) terminates development and distribution agreement, and reverts rights and intellectual property, to Kind Consumer on the grounds that *Voke* failed to be launched by December 2016 due to manufacturing challenges. |
    | **Philip Morris International** | 2011 | Jed Rose (Duke University) | US | PMI acquires patent for nicotine inhaler (e-cigarette). |
    | 2013 | *Solaris* (e-cigarette product) | Israel, Spain | PMI obtains exclusive rights from Altria to PMI to market *MarkTen* products outside the US market under rebranded name. |
    | 2014 | Nicocigs (e-cigarette company), along with *Nicolite, Nicocig* and *Vivid* products | UK | PMI acquires company,, which held 27% of UK market, for undisclosed sum. |
    | 2017 | *STEEM* (e-cigarette product) | TBD | Development and market test of technology acquired from Jed Rose in 2011. Device creates chemical reaction between nicotine liquid and organic acid to produces nicotine-salt vapour. |
    | **Altria** | 2014 | Green Smoke (e-cigarette company) | US, Israel | Subsidiary Nu Mark acquires Green Smoke (founded in 2008) for US$110 million (and US$20 million in incentive payments). |
    | 2017 | Avail Vapor (e-cigarette retailer) | US | Altria acquires one of largest US vaping product retailers (e-cigarettes, e-juice). |
    | **Japan Tobacco International** | 2011 | Ploom (e-cigarette company) | US | JTI buys minority stake in company. Ploom technology vaporizes pods of loose leaf tobacco. |
    | 2014 | Zandera (e-cigarette company) and *E-Lites* product | UK | JTI acquires Zandera (founded in 2009) for undisclosed sum. |
    | 2015 | *Model Two* and pods (e-cigarette product) and *Ploom* trademark | US | JTI acquires product line and brand name for undisclosed amount from Ploom. |
    | 2015 | Ploom (e-cigarette company) | Japan | Ploom buys back minority stake from JTI and changes its name to Pax Labs. |
    | 2015 | Logic Technology Development (e-cigarette company) | US | JTI acquires company (founded in 2010) for undisclosed sum. Logic Technology was leading US independent e-cigarette company. |
    | 2017 | *Ploom Tech* (e-cigarette product) | Japan, Switzerland | JTI launches *Ploom Tech* brand as a “hybrid technology to create a tobacco-enriched vapor, by heating a non-nicotine liquid, which passes through a capsule containing granulated tobacco”. |

    Source: See List of Supplemental Data Sources

    **Table 2. NNDs product development by leading tobacco companies**

    |  |  |  |  |  |
    | --- | --- | --- | --- | --- |
    | **TOBACCO COMPANY** | **YEAR** | **PRODUCT** | **TARGET MARKET** | **NOTES** |
    | **Imperial Tobacco** | 2015 | *Jai* (e-cigarette product) | France, Italy | Vaping product developed and marketed as consumer product alternative to smoking to be sold by tobacconists. |
    | **British American Tobacco** | 2011 | Nicoventures (e-cigarette company) | UK | BAT start-up standalone company formed to “focus exclusively on the development and commercialisation of innovative regulatory approved nicotine products.” |
    | 2013 | *Vype* (e-cigarette product) | UK | Launch of vaping product with varying products such as eBox, eTank and ePen. BAT becomes first TTC to launch a vaping product in the UK. |
    | 2015 | Nicovations (e-cigarette company) | UK | Nicoventures split into two arms - Nicovations (for licensed nicotine products) and another arm. |
    | 2015 | *e-Voke* (e-cigarette product) | UK | Nicovations receives licence from MRHA to market *e-Voke* as smoking cession aid, the first e-cigarette to be licensed as a medical product. The electronic-based product is distinct from the non-electronic *Voke*. |
    | 2015 | *iFUSE* (heat-not-burn product) | Romania | Launch of BAT’s first heat-not-burn product |
    | 2016 | *Vype Pebble* | UK, Italy | Launch of “mod” e-cigarette at opening of new *Vype* branded store in Milan, Italy |
    | 2016 | *glo* (heat-not-burn product) using *NeoStiks* (heat-not-burn sticks) | Japan, Canada, Switzerland | Launch of product to compete with PMI’s iQOS product. *NeoStiks* available in 3 flavors (Bright Tobacco, Intensely Fresh (menthol), Fresh Mix (mint). |
    | 2017 | *glo* (heat-not-burn product) | South Korea | Launched by BAT Korea into domestic market. |
    | 2017 | Nicovations | UK | Nicoventures trades under name of Nicovations. |
    | **Philip Morris International** | 2015 | *iQOS* (heat-not-burn product) using *HEETS/HeatSticks* (heat-not-burn sticks) | UK, Japan, US, Canada, Switzerland, South Korea, | Launch of the world’s first heat-not-burn product. Thirty-seven city roll out by end of 2017. *HEETS/Heatsticks* available in 3 flavors (Amber, Yellow, Turquoise). |
    | 2016 | MESH (e-cigarette product) | UK | Development and test launch of “next generation e-vapor product platform” |
    | 2017 | TEEPS (heat-not-burn product) | TBD | Development and test market of heat-not-burn product using carbon heat-source as “alternative heat source” to heat tobacco plug. |
    | **Altria** | 2012 | NuMark (e-cigarette company) | US | Altria creates subsidiary to develop and market e-cigarettes. |
    |  | 2014 | *MarkTen* vaping product | US | Subsidiary launches *MarkTen* as one of three vaping products sold in US national market. Device manufactured in China and e-liquid produced by US affiliate. |
    | **RJ Reynolds** | 1996 | *Eclipse* (e-cigarette product) | US | *Eclipse* still sold upon request to wholesalers and retailers. |
    | 2012 | RJ Reynolds Vapor Company | US | RJ Reynolds creates subsidiary to develop and market vaping devices. |
    | 2013 | *Vuse* (vaping device product) | US | Test marketing and launch of disposable vaping device. |
    |  | 2014 | *Eclipse* (heat-not-burn product) | US | RJ Reynolds discontinues production. |
    |  | 2015 | *Revo* (heat-not-burn product) | US | RJ Reynolds rebrands and relaunches *Eclipse* as *Revo* but deemed unsuccessful. |

    Source: See List of Supplemental Data Sources

    **List of Supplemental Data Sources**

    Anon. Altria Acquires Israeli Electronic Cigarettes Company Green Smoke for $110 Million. *Jewish Business News,* February 3, 2014. Available at: <http://jewishbusinessnews.com/2014/02/03/altria-acquires-israeli-electronic-cigarettes-company-green-smoke-for-110-million/> Accessed March 25, 2017.

    Anon. Altria Closes UST Acquisition – What Does This Mean? *Tobacco Today*. January 9 2009. Available at: <http://www.tobaccotoday.info/2009/01/09/altria-closes-ust-acquisition-what-does-this-mean/> Accessed March 25, 2017

    Anon. KT&G Enter the Heat Not Burn Market with the Lil. November 11 2017. Available at: <https://heatnotburn.co.uk/ktg-enter-heat-not-burn-market-lil/> Accessed May 18 2018.

    BAT. *British American Tobacco buys UK based e-cigarette technology company,* December 19, 2012. Available at: <http://www.bat.com/group/sites/UK__9D9KCY.nsf/vwPagesWebLive/DO935CVT> **Accessed March 25, 2017**

    BAT. *British American Tobacco reinforces commitment to next generation products with two announcements*, September 22, 2015. Available at: <http://www.bat.com/group/sites/UK__9D9KCY.nsf/vwPagesWebLive/DOA2LBUA> **Accessed March 25, 2017**

    BAT. *Our next generation products business*. Available at: [http://www.bat.com/group/sites/uk\_\_9d9kcy.nsf/vwPagesWebLive/DOA89DQ4](http://www.bat.com/group/sites/uk__9d9kcy.nsf/vwPagesWebLive/DOA89DQ4R) Accessed March 25, 2017.

    Chambers S. Imperial Brands is Said to Acquire Maker of Vaping Liquids. *Bloomberg*. November 1, 2017. Available at: <https://www.bloomberg.com/news/articles/2017-11-01/imperial-brands-is-said-to-acquire-maker-of-vaping-liquids> Accessed November 6, 2017

    Fontem Ventures. Fontem Ventures Buys Stake in Cosmic Fog Vapors. March 16, 2018. Available at: <http://www.fontemventures.com/news/fontem-ventures-buys-stake-cosmic-fog/> Accessed May 18 2018

    Foundation for a Smoke-free World. Our Vision. Available at: <https://www.smokefreeworld.org/our-vision> Accessed May 18 2018.

    Glantz, S. A., & Forbes, E. R. (1996). *The cigarette papers*(Vol. 17). Berkeley: University of California Press.

    Imperial Brands. Imperial Brands launches new vaping product in the USA. February 1 2018. Available at: <http://www.imperialbrandsplc.com/Media2/Key-announcements/key-announcements/imperial-brands-launches-new-vaping-product-in-usa.html> Accessed May 18 2018

    Imperial Brands. myblu vaping product launched in more markets. April 23 2018. Available at: <http://www.imperialbrandsplc.com/Media2/Key-announcements/key-announcements/myblu-vaping-product-launched-in-more-markets.html> Accessed May 18 2018

    Japan Tobacco. *JT acquires leading e-cigarette brand E-Lites,* November 19, 2014. Available at: <https://www.jti.com/our-views/newsroom/jti-completes-acquisition-e-cigarette-brand-e-lites> Accessed March 25, 2017

    Japan Tobacco. *JTI acquires “Ploom” intellectual property rights from Ploom, Inc*., February 16, 2015. Available at: <https://www.jti.com/our-views/newsroom/jti-acquires-ploom-intellectual-property-rights-ploom-inc> Accessed March 25, 2017

    McDonald J. Big Tobacco company buys into vape shop chain. *Vaping360*. November 3, 2017. Available at: <http://vaping360.com/avail-vapor-altria-investment/> Accessed November 6, 2017

    Nicovations. *Frequently Asked Questions.* Available at: <http://www.nicovations.com/frequently-asked-questions> Accessed May 1, 2017.

    PMI. *Heated Tobacco Products*. Available at: <https://www.pmi.com/science-and-innovation/heated-tobacco-products> Accessed March 25, 2017

    PMI. *Products without tobacco.* Available at: <https://www.pmi.com/science-and-innovation/products-without-tobacco> Accessed March 25, 2017

    PMI Science. PMI’s applications to the US Food and Drug Administration. Available at: <https://www.pmiscience.com/smoke-free/regulation/fda-mrtpa> Accessed May 18 2018.

    Tobacco Atlas. *E-cigarettes, 2015*. Available at: <http://www.tobaccoatlas.org/topic/e-cigarettes/> Accessed March 25, 2017

    Tobacco Products. Accord. Available at: <http://tobaccoproducts.org/index.php/Accord> Accessed June 2, 2018

    Tobacco Tactics. *E-cigarettes*, Last modified July 5, 2016. Available at: <http://www.tobaccotactics.org/index.php/E-cigarettes> Accessed March 25, 2017

    Tobacco Tactics. *Nicoventures,* Last modified June 15, 2016. Available at: <http://www.tobaccotactics.org/index.php/Nicoventures> Accessed March 25, 2017

    US Centers for Disease Control and Prevention. *E-Cigarette Use Among Youth and Young Adults*. A Report of the Surgeon General. Atlanta, GA, 2016. Available at: <https://www.cdc.gov/tobacco/data_statistics/sgr/e-cigarettes/pdfs/2016_SGR_Chapter_1_non-508.pdf> [↑](#endnote-ref-41)