Will FDA harm health, destroy businesses, and protect the cigarette industry through regulatory overkill? A preview.

This blog gives my take on how to think about the FDA's decisions (some taken, some forthcoming) on approving or denying thousands of "pre-market tobacco applications" (PMTAs) to allow vaping products to remain on the US market. FDA must make decisions no later than 9th September 2021, following legal action brought against the agency. FDA's Director of the Center for Tobacco Products, Mitchel Zeller, provides the background in a February 2021 blog.

There's a lot to be written on this, but I will settle for 16 observations and questions that will shape my take on FDA's announcements.

1. Will the FDA lay waste to much of the US vaping industry?

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There will be a lot of commentary this week on the US FDA’s decisions on vaping products and the related fate of the businesses that make them. It is important to keep in perspective what is really happening here, so I have put down some views to help frame the discussion following the announcements, which have to be made on or before 9th September.

Based on its guidance, statements and decisions so far, it looks like FDA is just about to wipe out most of the vaping industry that isn’t owned by large corporate entities – that means most businesses and most products will go, with a residual industry of big players selling a few high-volume commoditised products in a narrow range of flavours (menthol and tobacco most likely) and strength combinations. However, there is another, countervailing, pressure: FDA has to keep the viability and credibility of its nicotine strategy intact. It cannot do that if it destroys the most promising harm-reduction pathway from smoking to vaping. At this point, therefore, we can only speculate and look for underlying drivers.

Nevertheless, many small to medium businesses are at existential risk: they are overwhelmingly good businesses selling health-improving products to willing

adults improving their own health and wellbeing, on their own initiative, and at their own expense. If they are sacrificed, it will be for bureaucratic, legalistic and political reasons rather than for public health, ethical or economic reasons. There will still be a vaping industry, but it will likely be very different and, in my view, unlikely to be better for public health. But we shall see.

2. Is the PMTA mainly a test of scale?

Under its interpretation of the Tobacco Control Act (2009), FDA requires manufacturers to undergo an extremely burdensome process to justify that each of its vaping products is "appropriate for the protection of public health" – many companies have hundreds or thousands of product varieties. FDA has provided only a *maximal* account of what might be needed to do this in its guidance [overview][final guidance], not what would be *sufficient*, so companies do not generally know how much is enough. Instead, they will inevitably ask, how much can we afford?

There is a fixed or minimum cost associated with the testing and evidence gathering for each product required to meet FDA's standards (and companies have to guess what will suffice), so it will only be economically viable for products with an actual or expected turnover capable of absorbing this cost. Estimates run from hundreds of thousands to millions of dollars for these costs. In court filings in 2019, the Vapor Technology Association provided a cost estimate:

> *85. […] First, preparing a PMTA is an extremely costly and time-consuming endeavor, with estimated costs for only five e-liquid flavors running between $2.5 million and $3.5 million. Costs for only HPHC 29 testing, stability testing, and environmental assessments for one unique e-liquid product are over $300,000 (without consideration of the many other elements of a PMTA described in greater detail below). For only 10 unique e-liquid products, a company would spend $1,629,470 on these 3 components. For 50 unique e-liquid products, the cost would be in excess of $7 million, and for 100 unique e-liquid products, the cost would be more than $14 million on these three components alone. These actual costs are exponentially greater than the $300,000 to $500,000 total PMTA cost per product that FDA estimated in its Regulatory Impact Analysis.*

Even allowing for some pessimism on the part of a trade association, these are massive burdens for a small business loaded onto each individual product. Some estimates are even worse. One professional analytics company estimated PMTA costs of $8.7 to $11.2 million flat costs and $597,000 per flavour [link].

FDA itself was far too sanguine about these costs in its 2016 Regulatory Impact Analysis and grossly underestimated them – and this was in 2016, years before FDA actually specified the requirements in final guidance published in 2019.

FDA estimates	E-liquids	Devices
First application	$131,643	$466,563
Subsequent applications	$117,486	$192,654

Source: from FDA Final Regulatory Impact Analysis 2016 Docket No. FDA-2014-N-0189 10 May 2016.

The PMTA cost assumed by FDA is a weighted average and assumes each PMTA will include several products (on average, 11 liquids and 6 devices). Had FDA used realistic compliance costs, it is likely that the 2016 Deeming Rule that brought vaping into the Tobacco Control Act would not have passed through scrutiny during the nine-stage rulemaking process by the regulatory watchdogs at the WhiteHouse (OMB and OIRA).

The emerging 'marketing denial orders' (MDOs), FDA's term for a rejection, will mainly result from businesses that cannot meet these costs because they do not sell enough of each of their products to bear the costs of meeting the evidential threshold. They have tried to make a case for their products based on what they can do, but many will not do it to the FDA's satisfaction. A high regulatory cost burden per product simply wipes out all the products with insufficient sales to justify spending the money to meet FDA's expectations – it doesn't matter how good they are for public health in real life.

Other companies may have exited without applying. The investors and owners of these businesses will have seen this process as too risky and success as too uncertain to justify the expense on a bet against arbitrary regulation and uncertain outcomes. FDA's specification of PMTA requirements was open-ended, there was little concrete guidance on success criteria, not much insight into how FDA would evaluate these cases, and nothing on how FDA would ensure

consistency across its evaluators, between companies and products, and over time.

3. Will human consequences of a market shake-out be severe?

For some idea of why a precipitous decline in the products available might not be "appropriate for the protection of public health"… Mitch Zeller, the Director of FDA's Center for Tobacco Products and effectively the lead regulator for vaping explained this in court proceedings:

> *"[…] mass market exit of such products would limit the availability of a potentially less harmful alternative for adult smokers seeking to transition or stay away from combustible tobacco products. Dramatically and precipitously reducing availability of these products could present a serious risk that adults, especially former smokers, who currently use ENDS products and are addicted to nicotine would migrate to combustible tobacco products, even if particular ENDS products ultimately receive marketing authorization and return to the market later.*
>
> *Declaration of Mitchell Zeller, Director of the Center for Tobacco Products to the US District Court for the District of Maryland Case 8:18-cv-00883-PWG Doc 120-1, para 15. June 12, 2019.*

Zeller's comments here are correct, along with much else he says in this filing. They refer to the effect of a court decision that would have had a precipitous impact on the products available. These effects will happen to *some degree* if there is a dramatic reconfiguration and concentration of the market, and their extent will depend on the scale of the disruption.

4. Will good businesses be destroyed?

Hundreds of businesses have tried in good faith to meet FDA's demands, but many will have come up short – how many remains uncertain. These businesses will be penalised twice. First, the loss of market access and future income from FDA's denial, and second, the sunk cost in time and money of trying. This will break many companies, and they will go out of business. Other businesses will

have withdrawn from or never entered the process to contain their losses. The scale of the market is hard to gauge, but this is one estimate of the commerce at risk:

> *Analysis by consultants John Dunham & Company found that in 2018, the US e-cigarette industry created $24.46 billion in economic activity, supported 166,007 jobs (direct, indirect and induced) and consisted of 380 liquid manufacturers, 2,012 vape shop manufacturers and 11,469 specialist retail outlets ("vape stores"). See court testimony of John Dunham.*

Small-to-medium vape businesses. We do not yet know what proportion of this industry will fail – essentially, the higher FDA's evidence hurdle, the more severe the barrier to entry and the more the market will contract and concentrate. I should emphasise there is likely to be nothing at all wrong with most of the products. Most would easily pass through the European Union notification regime and access the EU market, where there really are no particular problems. They are likely to have a modest following of dedicated users, the vast majority of whom will be over 21, and who are enjoying their own chosen way to quit smoking. These will be good products and businesses that just cannot meet the FDA's demands, and they will have to exit the nicotine vaping market (go out of business or switch to related products)

Vape shops. The high street presence of tobacco harm reduction is in mortal danger. Without the broad range of flavours, strengths and devices, they do not have much to offer above convenience stores, and their USP is destroyed. Vape shops rely on diversity in the marketplace to provide a specialist offer to their customers. Vape shops do not just provide products, many are also operating a public service business, helping smokers and vapers navigate the market and technologies to find what works for them. There is a considerable danger this will be lost.

Big Vape. I am not opposed to the vaping businesses of the tobacco companies and think they form part of a vital migratory path away from cigarettes and other combustibles. Nor do I have an argument with the larger vaping companies like Juul, Smok and NJOY. these companies have all played a role in helping smokers quit, and their products may be essential in the early stages of transition from smoking when ease of use, convenience and familiarity matter. I hope all these

companies succeed in their PMTAs. My real concern is with the long tail of smaller businesses and highly diverse low-volume product offerings.

Big Vape to Lesser Vape. My concern with the larger companies is threefold: (1) they only submitted narrow product ranges – some didn't even try to get popular flavours approved (rationally) fearing rejection at great cost; (2) FDA will not approve many or any non-traditional flavoured products, limiting the market to tobacco and menthol; (3) FDA will only approve weaker nicotine strengths because of 'abuse liability', fatally weakening the pharmacokinetic profile of some products relative to cigarettes. I hope this is not the case.

5. What could happen to the vaping innovation model?

As well as the adverse effects on vapers (mostly former smokers), potential vapers (current smokers), and thousands of small businesses, there is a danger that this type of regulation forms a barrier to product innovation. The innovation model of the industry could be damaged in three fundamental ways.

- By the cost and time for bringing a new product to market combined with the difficulty of meeting FDA's evidence threshold with products that have not so far been in the market (nearly all current applications are for products that were on sale in 2016).
- The loss of trial and error as a driver of innovation: products are placed on the market, and if consumers like them and buy them, the innovation has been a success. But that is hard to predict and prove in advance. Diversity and low barriers to entry are integral to innovation via this mechanism – and innovation is integral to displacing smoking and meeting public health goals.
- Because of barriers to entry, consumers seeking innovation may turn to illicit or cross-border suppliers and circumvent FDA imposed barriers to innovation. It reduces the incentives to innovate among law-abiding American businesses.

6. Will regulatory barriers to entry favour Big

Tobacco?

The advantages in a regulatory system like this are all with the large corporate entities selling a few high-volume products. These companies also have financial and technical capabilities to make the applications and understand the demands of the FDA. They are also more likely to have ready access to third parties (labs, trial organisers, document managers, etc.) essential for making PMTA applications that meet the FDA's standards.

A new oligopoly? The tobacco companies also have a further advantage… they have fat cash flows from the lucrative cigarette business that can cross-subsidise the costs of making PMTA applications for vaping products while competitors bleed out. The exclusive US vaping companies will have to draw on cash or call on investors as the market gets much tougher for them on multiple fronts. Tobacco companies can play a longer game, expecting to be the beneficiaries of an abrupt contraction and concentration of the market driven by regulation. My concern is that, through regulatory barriers to entry, FDA will grant the tobacco companies and perhaps a few large vape-only companies like Juul and NJOY a brand new anti-competitive oligopoly in the vaping sector.

A double win for Big Tobacco? So for Big Tobacco, high regulatory barriers to entry provide a win on two fronts. First, regulation is protecting the cigarette oligopoly from disruptive competition from vaping products that the tobacco companies do not control. Second, regulation enables them to dominate the remains of the vaping market, extending Big Tobacco's oligopoly grip on the nicotine market.

7. Could FDA have done it differently?

Yes, that is at least an open question. There is not a binary choice between the FDA's interpretation of the Act and going *laissez-faire* and having no regulation at all – the trick is to make regulation 'proportionate'.

There is a range of options for meeting the Appropriate for the Protection of Public Health standard and complying with the Tobacco Control Act that could have been far less onerous. In July 2019, Iowa's Attorney General, supported by a panel of experts, wrote to the then Secretary of Health and Human Services Alex Azar to set out the problem and propose options to reduce burdens. These are

elaborated at 4.3 in the letter and briefing from AG Miller warning HHS, FDA and Congress of a crisis about to befall the industry should the barriers to entry be too high. These are the proposed options to reduce burdens:

- *FDA could resolve many aspects of its public health test at the level of the whole e-cigarette category.*
- *FDA should concentrate its limited scientific resources on products that contain novel technologies or present unusual risks*
- *FDA could severely limit the use of costly and time-consuming human subject studies*
- *FDA could establish a system of standards for conventional vaping products*
- *FDA could rely more heavily on post-market surveillance and corrective action*
- *FDA could develop a streamlined process for authorizing incremental improvements in vaping products*
- *FDA should publish its own guidance to reviewers*

The statute itself (section 910) does not specify the exacting requirements that FDA has actually set out in its guidance. It requires the Secretary to determine that these products are appropriate for the protection of public health, taking into account changes in patterns of tobacco use. This is the relevant text:

> *For purposes of this section, the finding as to whether the marketing of a tobacco product for which an application has been submitted is appropriate for the protection of the public health shall be determined with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product, and taking into account–*
>
> *A. the increased or decreased likelihood that existing users of tobacco products will stop using such products; and*
> *B. the increased or decreased likelihood that those who do not use tobacco products will start using such products.*

If we start from the fact that the individual risk is much lower, a finding that is inescapable, it is almost impossible to fail this test without there being some sort of gateway effect from vaping to smoking, which there is not. In addition, impacts

on population behavioural pathways are impossible to determine in advance (which model predicted the rise of Juul from 2016?). So some of these demands can only be realistically met through post-market surveillance.

8. Surely vape companies must prove "appropriate for the protection of public health"?

There is no dispute about this: the FDA has to apply the 'appropriate for the protection of public health" (APPH) test. It is written in the law. But what standard of "proof" should be demanded is a matter of degree. A modern regulator doesn't usually seek absolute certainty as this leads to paralysis, but calibrates the demands for evidence and controls to reflect a number of risk-based factors:

- What is known about these products in general (vaping products have been extensively studied and are reasonably well characterised)
- The novelty of the product under consideration (most of the products are in a small number of subcategories with mostly common characteristics)
- The risk of allowing a product approval and it proving harmful (the risks are so far minor, but if new evidence emerges, corrections can be made and products withdrawn)
- The risk of denying a product approval and the potential benefits being lost (the risk of extra smoking is a major and immediate risk)
- The ability to reverse a decision and to correct subsequently (there is high potential for post-market correction, implying that more could be done through post-market surveillance)

This philosophy is known as "risk-based regulation". Below is a summary of the concept by the World Bank (and more here)…

> *Risk-Based Regulation (RBR) achieves public policy objectives by targeting activities that pose the highest risk to the public well-being, and in turn lowers burdens for a variety of lower-risk sectors and firms. Lowering burdens improves compliance and allows firms to benefit from a more level playing field. By directing government resources towards the highest-risk areas, risk-based approaches also make the most of limited public resources. Well-functioning RBR systems further improve accountability by enhancing transparency and predictability of requirements in given sectors and as applied to different firms.*

The Tobacco Control Act, as interpreted by FDA, is basically doing the opposite of this. It imposes minor burdens on the nicotine market incumbent, cigarettes. It is a concept familiar to most regulators and is a practical implementation of the precautionary principle, recognising that a regulator can do harm by being excessively zealous or pedantic. See this paper on the abuse of the precautionary principle in Australia's regulatory regime:

> Morphett K, Hall W, Gartner C. The Misuse of the Precautionary Principle in Justifying Australia's Ban on the Sale of Nicotine Vaping Products. *Nicotine Tob Res* 2020; [link]

Is the APPH test appropriate? The second problem is more fundamental (i.e. it conflicts with the basic premise of the Act). Why should a legal recreational stimulant drug (nicotine) need to be "appropriate for the protection of public health"? We don't ask that of beer, wine, spirits, coffee or caffeinated colas. No one sees that as a prerequisite for recreational cannabis. Harm reduction is a transient rationale while nicotine use through smoking is prominent. The long-term challenge for the nicotine market is to make the drug nicotine available in an acceptably safe way, as with beer regulation (see Section 10 below). That does not mean completely safe. It means within the normal societal appetite for recreational risk. But this is a matter for Congress, not FDA, and there is no sign at all that Congress is capable of enacting rational regulation in this area or along these lines.

9. FDA implies it will place impossible demands on smaller applicants

In one of its first marketing denial orders, the FDA hinted at the size of its evidential hurdle. See: *FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health* 26 August 2021 (here).

FDA denies multiple product variants (55,000 to be precise) from three companies.

> *The products from JD Nova Group LLC, Great American Vapes, and Vapor Salon subject to this action are non-tobacco-flavored ENDS and they include flavors such as Apple Crumble, Dr. Cola and Cinnamon Toast Cereal.*

FDA provides advice on what it needs, and these companies did not provide:

> *Based on existing scientific evidence and the agency's experience conducting premarket reviews, the evidence of benefits to adult smokers for such products would likely be in the form of a randomized controlled trial or longitudinal cohort study, although the agency does not foreclose the possibility that other types of evidence could be adequate if sufficiently robust and reliable. Because this evidence was absent in these applications, the FDA is issuing MDOs. (emphasis added)*

These decisions are predictable, given what FDA has been saying since 2016. But it is still worth stepping back and looking at the remarkable uselessness of the PMTA system.

The problem for the manufacturers is showing the effect these products have at a *population* level, even though they are small firms with limited product lines that will make no detectable difference at the population level. They simply cannot provide the RCTs or longitudinal cohort studies to show a population benefit for adults *at the individual product level*.

*Think about what this means…*Imagine trying to set up an RCT for one company's *Apple Crumble* flavour? Firstly, the cost of doing it would be almost certainly prohibitive given the likely sales. But where would you find the volunteers willing to try this flavour and this manufacturer and no other for 6 months or a year? What would it actually tell you – especially if the investigator randomises subjects to the Apple Crumble arm who don't like Apple Crumble flavour and wouldn't buy it if they had the choice, which they do in real life. On the slightest inspection, the idea of a longitudinal cohort study is just as ridiculous: where would you find a cohort of exclusive Apple Crumble users who didn't try anything else and maintained their unswerving loyalty to this specific Apple Crumble brand for long enough for the cohort study to provide reliable product-specific data. Then repeat all this for dozens or possibly thousands of flavour, strength, excipient mixes.

Obviously, it is not possible for a small company with a range of brands with a few users and a few tens of thousands in turnover.

10. Why can't it be like beer?

My ideal shape for the vaping market would be similar to the US beer market, which has a few large mass-market players, and a long tail of diverse regional and local breweries, microbreweries and brew-pubs – see Brewers Association National Statistics.

Type of brewery (2020)	Number
Regional Craft Breweries	220
Microbreweries	1,854
Taprooms	3,471
Brewpubs	3,219
Large/Non-Craft	120
Total U.S. Breweries	8,884

Imagine if the only beer you could find legally in the US was made by a few super-brewers with sales over $1 billion (AB Inbev, Molson Coors, Carlsberg, Heineken etc)? In the analogy, that is where we may be heading with vaping. The big difference is that it's not just dull industrial beer; vaping *helps people quit smoking*.

Beer is used by millions of American teenagers (alcohol used by high school students (9-12 grade) = 12 million or 29% (data), uses quirky branding, and alcohol can be very harmful in many ways, notably to young people through road and other accidents, violence, abuse, vulnerability. Yet somehow the beer industry has a regulatory regime that allows for high participation, low barriers to entry and considerable diversity. No one asks a new craft brewer to prove its latest concoction is "appropriate for the protection of public health". It's beer, FFS!

FDA does not have the authority to regulate nicotine in this way, and it would require new legislation from Congress to do this. But regulation of alcoholic beverages appears to be more rational and proportionate, despite vaping having much lower risks to health, safety and wellbeing.

11. The evidence at the category level is compelling

While it is impossible for most companies to provide RCTs or cohort data for each *product*, there is compelling positive evidence at the level of the *category* – and this should condition the context in which FDA makes determinations for smaller companies.

There is good RCT data, synthesised by the Cochrane Review, showing that vaping, in general, is effective for smoking cessation and more effective than FDA-blessed nicotine replacement therapy (NRT). There is also good data showing population benefits at the level of the overall category, much of this is summarised in a recent our submission to Health Canada [Summary / Full PDF] on its proposed flavour ban. Here are a few sources that would provide a base suggesting vaping is appropriate for the protection of public health:

- Jackson SE, Kotz D, West R, Brown J. Moderators of real-world effectiveness of smoking cessation aids: a population study. *Addiction* [Internet] 2019 [cited 2020 Dec 3];114(9):1627–1638. [link]
- Kotz D, Brown J, West R. "Real-world" effectiveness of smoking cessation treatments: A population study. *Addiction* 2014;109(3):491–499. [link]
- Beard E, West R, Michie S, Brown J. Association of prevalence of electronic cigarette use with smoking cessation and cigarette consumption in England: a time–series analysis between 2006 and 2017. *Addiction* 2020];115(5):961–974. [link]
- Zhu S-H, Zhuang Y-L, Wong S, Cummins SE, Tedeschi GJ. E-cigarette use and associated changes in population smoking cessation: evidence from US current population surveys. *BMJ*. 2017;358:j3262. [link]
- Levy DT, Yuan Z, Luo Y, Abrams DB. The relationship of e-cigarette use to cigarette quit attempts and cessation: Insights from a large, nationally representative U.S. Survey. *Nicotine Tob Res* 2018; [link]
- Beard E, West R, Michie S, Brown J. Association between electronic cigarette use and changes in quit attempts, success of quit attempts, use of smoking cessation pharmacotherapy, and use of stop smoking services in England: time series analysis of population trends. *BMJ* [Internet] 2016 [cited 2020 Dec 3];354:i4645. [link]
- Levy DT, Borland R, Lindblom EN, et al. Potential deaths averted in USA by replacing cigarettes with e-cigarettes. *Tob Control* [Internet] 2018 [cited 2020 Dec 5];27(1):18–25. [link]
- Mendez D, Warner KE. A Magic Bullet? The Potential Impact of E-Cigarettes on the Toll of Cigarette Smoking. *Nicotine Tob Res* 2020; [link]

There is enough here to be confident that vaping products *in general*, at least those chosen by consumers, will be appropriate for the protection of public health. FDA should have taken this evidence base as a starting point and looked for reasons why specific products might diverge from the norm.

12. The unspoken problem of cigarettes – FDA

does not apply the public health standard to itself

In contrast to vapes, cigarettes almost have a free pass. Thousands of cigarette products currently on the US market were 'grandfathered' (admitted to the market without scrutiny – see TCA s910a) under the terms of the Tobacco Control Act then kept in place by the relatively light touch substantial equivalence test.

The public health test of evidence does not have to be (and obviously cannot be) met by the dominant recreational nicotine product in the US market, cigarettes (other than the reduced nicotine products, which FDA authorised in 2019, a mystifying decision). But it forms a major barrier for the entrant challenging the incumbent.

The presence of cigarettes in the recreational nicotine market is the most important reason why FDA is not actually regulating for public health. If it denies a product based on an inadequately stuffed folder of evidence for a vaping product, then the users do not necessarily stop what they were doing and do something virtuous instead. They will have a range of behavioural responses. Some users may relapse to smoking, end their transition via dual-use, reckon that FDA must believe these products are dangerous – with the result that *smoking will increase*. Smoking doesn't have to increase by much for FDA to have done more harm than good – a prospect it was reluctant to contemplate in its regulatory impact analysis for the 2016 Deeming Rule, even though there are many plausible ways vaping regulation could lead to more smoking. The Royal College of Physicians provided a useful summary paragraph in 2016:

> *However, if [a risk-averse, precautionary] approach also makes e-cigarettes less easily accessible, less palatable or acceptable, more expensive, less consumer friendly or pharmacologically less effective, or inhibits innovation and development of new and improved products, then it causes harm by perpetuating smoking. Getting this balance right is difficult.*
>
> *Royal College of Physicians. Nicotine without smoke: tobacco harm reduction. London: RCP; 2016. [link] (Section 12.10 page 187)*

The problem is that FDA's method is indifferent to the consequences of its rejections – the burden of proof is placed solely on the applicant. FDA is not

using a risk-based regulatory philosophy to ensure it isn't actually making things worse for public health "by perpetuating smoking". It does not have to check if its own regulatory philosophy, interpretations of the law, and determinations are "appropriate for the protection of public health" and do not, in fact, cause harm. Suppose it had to comply with this hypothetical edited population health test:

> *For purposes of this section, the finding as to whether the ~~marketing~~ regulation of a tobacco product for which an application has been ~~submitted~~ rejected is appropriate for the protection of the public health shall be determined with respect to the risks and benefits to the population as a whole, including potential users and nonusers denied use of the tobacco product, and taking into account–*
>
> *A. the increased or decreased likelihood that existing users of tobacco products will stop using such products; and*
> *B. the increased or decreased likelihood that those who do not use tobacco products will start using such products.*

We could only know if FDA was really regulating for public health if it applied a standard like this to its own decisions, thus making a symmetrical assessment of the risks of denial and the risks of authorisation. But it doesn't have to do this under the law, and it doesn't do it.

13. What about the children? Being sceptical about the youth vaping epidemic

Isn't this all about protecting kids and the youth vaping epidemic? FDA frames the problem that it is trying to address as youth vaping. In its recent press release: *FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health* 26 August 2021 (here). FDA asserted its regulatory challenge as follows:

> *Flavored ENDS products are extremely popular among youth, with over 80 percent of e-cigarette users between ages 12 through 17 using one of these products. Companies who want to continue to market their flavored ENDS products must have robust and reliable evidence showing that their products'*

> *potential benefit for adult smokers outweighs the significant known risk to youth," said Mitch Zeller, J.D., director of the FDA's Center for Tobacco Products.*

There are important elements missing from this framing of the problem of adolescent uptake of vaping being the detriment which must be outweighed by benefits to adults.

First, ignoring the beneficial public health effects of vaping for adolescents

It continues the pattern of the FDA being unresponsive to the idea that vaping may be an "off-ramp" for adolescent smoking – a diversion from a more harmful to a much less harmful pattern of nicotine use. Former FDA Commissioner, Scott Gottlieb laid out this doctrine in a speech in 2018. It is highly unethical in my view.

> *No child should use any tobacco product. We've seen cigarette use decline among kids, while e-cig use has grown sharply. This is happening even as overall rates of tobacco use among kids has declined, according to recent data.*
>
> *This is still not acceptable, even if the trends are moving in a more positive direction of reduced overall use of tobacco products. Even if kids are using ENDS instead of cigarettes — and that migration in part accounts for the decline in youth cigarette use — that's still not an acceptable trade.*
>
> *Parents who see their children using e-cigs and say, "well at least my child isn't smoking," should take no comfort.*
>
> *No child should be using any tobacco product.*
>
> *Scott Gottlieb, FDA's Nicotine and Tobacco Regulation and the Key Role of Regulatory Science, 18 June 2018 [link] (emphasis added)*

Yet this seems to be exactly what is happening – there is an increasing body of research suggesting that vaping is displacing smoking and diverting adolescents away from smoking. For example:

- Selya AS, Foxon F. Trends in electronic cigarette use and conventional smoking: quantifying a possible 'diversion' effect among US adolescents. *Addiction* 2021;add.15385. [access]

- Sokol N, Feldman J. High school seniors who used e-cigarettes may have otherwise been cigarette smokers: evidence from Monitoring the Future (United States, 2009-2018). *Nicotine Tob Res* [Internet] 2021 [access]
- Levy DT, Warner KE, Cummings KM, et al. Examining the relationship of vaping to smoking initiation among US youth and young adults: a reality check. *Tob Control* 2019;28(6):629–635. [access]

Second, ignoring the fact that the most frequent vapers are likely to have been or would become smokers

For public health purposes, it is essential to segment the population of teenage vapers according to how frequent their vaping is (i.e. whether it is potentially problematic or frivolous and experimental) and by what these young people would be doing if they were not vaping – i.e. would they be smoking? Independent analysis of the US data suggests that the "youth vaping epidemic" has characteristics that are very different to those promoted by campaigners trying to pressure FDA into more prohibitive approaches.

> *Conclusions: Vaping increased among US youth in 2018 over 2017. The increases are characterized by patterns of low past-30-day vaping frequency and high poly-product use, and a low prevalence of vaping among more frequent but tobacco naïve vapers.*
> *Glasser AM, Johnson AL, Niaura RS, Abrams DB, Pearson JL. Youth Vaping and Tobacco Use in Context in the United States: Results From the 2018 National Youth Tobacco Survey. Nicotine Tob Res, 2021 [link]*

> *Conclusions: While use of e-cigarettes in US high-school students increased sharply between 2017 and 2019, frequent use and signs of e-cigarette dependence remained rare in students who had only ever used e-cigarettes and never any other tobacco product*
> *Jarvis M, Jackson S, West R, Brown J. Epidemic of youth nicotine addiction? What does the National Youth Tobacco Survey 2017-2019 reveal about high school e-cigarette use in the USA? Qeios 2020 [link]*

In 2019, the "youth vaping epidemic" reached its peak, with 27.5% of high school students using e-cigarettes in the past 30 days (2019 survey). It has since fallen back to 19.6% (2020). But look at how that 27.5% breaks down when segmented by frequency of use and prior tobacco use.

Percentage of all high schools students	No prior tobacco use	Any prior tobacco use

Frequent use (20-30 days per month)	1.4%	8.1%
Infrequent (≤ 19 days per month)	7.4%	10.7%
Total	27.5%	
Based on data from NYTS 2019: extract here (with thanks to Martin Jarvis) and analysis here.		

The table shows that most adolescent vaping in the US is infrequent and is of relatively minor public health concern (certainly compared to smoking, drugs, drinking, STDs, violence etc). Among the frequent users, most were former smokers or would-be smokers – and for them, *vaping may be beneficial*. This analysis of patterns of vaping is consistent with vaping being a diversion from smoking for the teenagers most at risk. FDA simply asserts that youth vaping provides its rationale for imposing impossibly heavy evidence burdens on small companies, but a hard look at the numbers with higher resolution weakens any justification for excessive regulatory burdens.

Third, young people have interests in adult smoking cessation

In its public statements, FDA has drawn a distinction between the interests of adults and adolescents. In practice, it is not possible to divide these populations and their respective interests so neatly for tobacco policy purposes.

- Parental smoking and adult role-modelling are important risk factors and predictors for youth smoking initiation. By modelling a different, far less harmful behaviour, adult vaping and associated smoking cessation is likely to have a beneficial effect on youth smoking initiation and prevalence.
- The loss of a parent or close relative to smoking-related disease is a significant detriment to most young people. Likewise, adult ill-health imposes costs on the family in terms of lost economic activity and increased caring responsibilities. Harm reduction for adults has collateral benefits for a whole family, including its younger members.
- Adolescents grow into adults, and today's youth have an interest, not necessarily acknowledged, in having better options for their future. The serious harms of tobacco or nicotine use are not instantaneous and mainly develop over many decades of use. They are an outcome of the pattern of

tobacco use over the life course – almost all of the premature mortality risk of smoking is avoided by stopping smoking by age 35. So, opportunities to stop smoking in the first two decades of adult life are especially valuable, and benefits continue through life.

- Reducing adult smoking reduces young persons' exposure to secondhand smoke.

The overarching public health goal should be to reduce smoking in both *adults and adolescents,* and vaping assists in both. More on this: The US Youth Vaping Epidemic: Really?

14. Is FDA managing risks to itself, not to the public?

Any regulator faces pressure from interest groups, the media, politicians to deliver their preferred outcomes – this is normal politics, but it can deeply distort rational and objective decision-making. FDA has faced intense pressure orchestrated through many organisations from a $160 million advocacy campaign launched by Bloomberg Philanthropies in 2019 with the personal support of its billionaire proprietor, Michael Bloomberg. This is a campaign: Protect kids; Fight Flavored E-cigarettes, in which Mr Bloomberg and his grantees determined that flavoured e-cigarettes could not be appropriate for the protection of public health. But they did this without ever examining the evidence, without giving adequate weight to the risks to adults and without ever recognising (or understanding) that vaping may benefit the at-risk youth population. For example, a prohibitionist activist group lavishly funded by Bloomberg Philanthropies demands its preferred outcome whatever the results of FDA's scientific review.

> Campaign for Tobacco-Free Kids, As E-Cigarette Makers Face Critical September 9 Deadline, Leading Health Groups Urge FDA Not to Allow Sale of Any Flavored Products, August 10, 2020. [link]

$160m buys a lot of advocacy and lobbying, even in Washington DC. It has nourished a broad coalition of 'partners' in health organisations with an abundance of dollars and coordination. This can generate advocacy devoted to influencing a scientific assessment, not a political goal established by funders and activists.

> *Juul fueled the youth e-cigarette epidemic and is still the #1 brand among youth. @FDATobacco must take them off the market—and the same goes for other flavored, high nicotine e-cigarettes.https://t.co/v7buALp7vj*
>
> *— Campaign for Tobacco-Free Kids (@TobaccoFreeKids) August 31, 2021*

This campaign deserves far greater media scrutiny than it has received so far. The media response has been often unedifying, with some newspapers going all in with the false premise that underpins the moral panic that drives this. See: The US media is losing its mind over vaping and Juul – the questions a credible journalist should ask.

It is not unusual or unexpected to find bureaucracies give priority to managing the risks to themselves at the expense of managing risks to the public – a condition sometimes known as asymmetric loss aversion. The most secure way to avoid criticism and blame is to be obsessively pedantic and maximalist about the interpretation of the law. That way, the blame for any adverse consequences to public health can be attributed to the law using the "letter of the law" defence. The greater the political pressure, the more defensively pedantic a regulator is likely to become to consolidate their legal and bureaucratic defences. How far that has afflicted FDA remains to be seen.

In contrast, acting pragmatically and interpreting the statute in a way that is proportionate and does actually support public health – as advocated above – is fraught with litigation risks from well-funded activists and their political coalition.

15. Letters to FDA calling for a more risk-proportionate approach

The FDA has received thousands of solicited and unsolicited representations, setting out better ways to address this regulatory challenge. I have mostly worked with a group of American experts and academics convened by the Attorney General of Iowa, Tom Miller. Here are some of our communications:

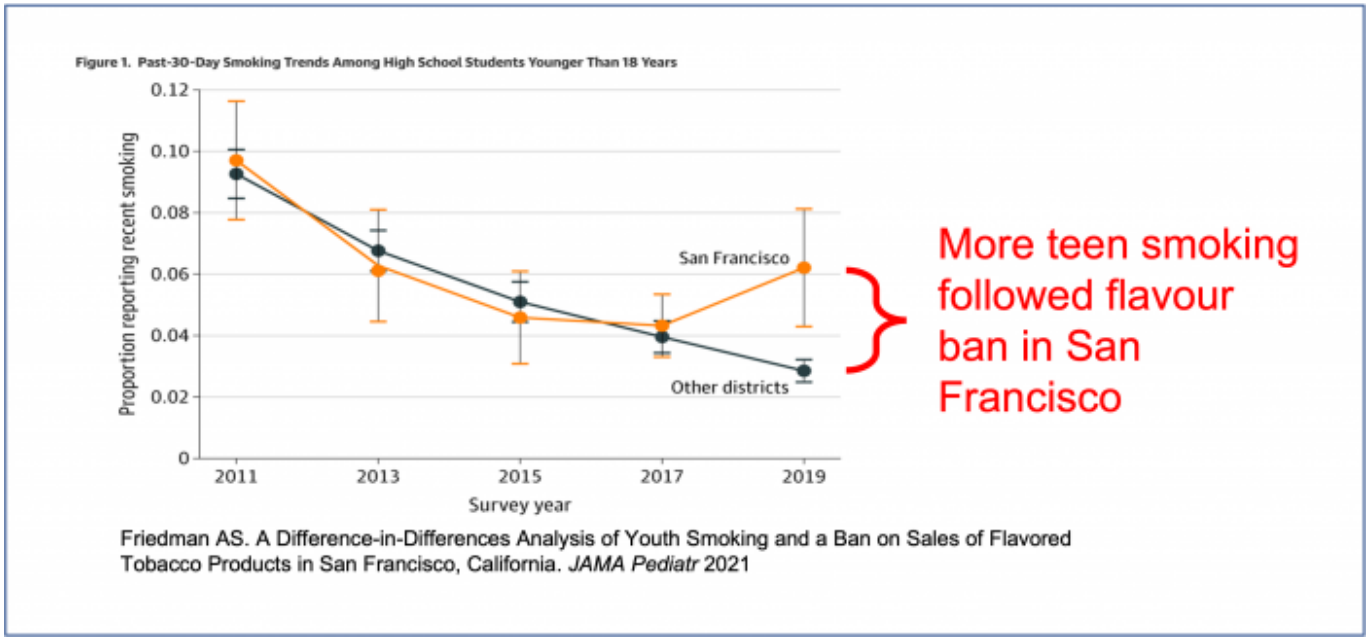
- October 2019. Letter from Attorney General of Iowa, Tom Miller, Clive Bates and Lindsay Lewis of the Progressive Policy Institute to OMB: Follow-up to a meeting on vaping and tobacco policy – a crisis in 2020.

- July 2019. Letter and briefing from Iowa Attorney general, Tom Miller and 12 others to US Health and Human Services Secretary., Alex Azar II Letter and briefing: Regulation of vaping products – a crisis in 2020
- November 2018. Letter from Iowa Attorney General Miller and six others to Scott Gottlieb, FDA. Re: Youth tobacco and nicotine use – proportionate and responsible reaction Letter to set out issues with youth vaping and to caution against over-reaction
- July 2018. From Iowa Attorney General Tom Miller, response to FDA advanced notice of proposed rulemaking (ANPRM) Regulation of Flavors in Tobacco Products
- December 2017. Letter and briefing from Iowa Attorney General and four others on vape flavours and why a more rigorous approach to evaluating harms and benefits is required in the form of ten questions needed to interrogate the issue.

16. Where next? The responses of producers and consumers

Tobacco control activists, regulators and politicians are overly prone to what I call the *compliance fallacy*. This is the idea that a law or regulatory determination can be implemented, and then people will modify their behaviour in the ways envisaged by the regulators or sponsors of the measure. The faintest acquaintance with history will confirm that this is rarely the case, at least unless there is broad consent for the measure among those affected. A regulation is a perturbation of a market, causing consumers and producers to modify their behaviour and to enter or exit the market. It is not an iron rule that governs responses to its restrictions.

FDA should be aware of this because its clampdown on flavoured pod products led to the rapid rise of Puff Bar and disposable devices. The underlying demand will express itself somehow. Following the flavour ban in San Francisco, teen smoking rose sharply compared to other districts (See Friedman A. 2021),



Possible reactions to contraction and concentration of the market by FDA determinations will really depend on what is left and at what price. But likely responses will include:

- Reconfiguration of patterns of tobacco use within the existing legal choices. Users of products rejected by the FDA might turn to products authorised by FDA, giving a payday to the larger companies but allowing users to continue with products that are not their first choice. Some may switch to other products like pouches or snus. Others may return to smoking, not switch or vary their pattern of dual-use to favour cigarettes.
- Development of workarounds. A broad ban on finished flavoured products would likely see a rise in flavours and flavoured e-liquids trading in informal markets, with small scale producers turning out liquids using food flavourings. Flavourings might be marketed as food or drink additives or for aromatherapy.
- Illicit trade. Some manufacturers or importers may ignore FDA's determinations and continue to sell, moving online sales offshore, or consumers will find ways to import for personal use. There is already a thriving illicit market in cannabis vapes, and those suppliers are likely to expand their offerings to meet gaps in popular product options. It may also widen their contact with the public lead to increased uptake of cannabis and other substances available illicitly. The extent of the black market will be a function of how far the residual legal market fails to meet consumer demand and preferences.

- Suppliers turning to ‘tobacco-free nicotine’ (TFN) to continue with existing products. TFN is synthesised in a laboratory and not derived from tobacco. That means so that it would fall outside FDA’s tobacco product jurisdiction. It is more expensive (2.5x pharma grade nicotine), but the cost of nicotine is not an especially large part of the total sale price. Its price may rise if initially in short supply but might ultimately fall if demand increases and now supply becomes available. It is likely to attract a regulatory counter-attack from FDA or states.

Please let me have views on what you think will happen and how consumers and producers will respond.