FDA spreads confusion about nicotine and smoking

written by Clive Bates | 23 December 2021

In one of its most ill-judged moves to date, the US Food and Drug Administration has today granted 22nd Century Group the right to market its VLN King and VLN Menthol King combusted, filtered cigarettes as modified risk tobacco products.

It has done this because these products are reduced in nicotine and, FDA concludes, anyone who is willing to smoke them will experience lower exposures to *nicotine*. But we have known for a long time that "people smoke for the nicotine but die from the tar" (Mike Russell). This is a product that reduces the nicotine but keeps the tar. What could possibly go wrong?

What has been announced?

The MRTP (Modified Risk Tobacco Product) is the authorisation process for allowing companies to make marketing claims about reduced risk. The claims have to be assessed by FDA as "appropriate for the promotion of public health"

under Section 911 of the US Tobacco Control Act.

Here is the announcement press notice: *FDA Authorizes Marketing of Tobacco Products that Help Reduce Exposure to and Consumption of Nicotine for Smokers Who Use Them*. Here is the formal documentation: VLN King / VLN Menthol King.

This is the risk communication package authorised by FDA.

> *The MRTP allows certain reduced exposure claims regarding nicotine, including:*
>
> *"95% less nicotine."*
>
> *"Helps reduce your nicotine consumption."*
>
> *"…Greatly reduces your nicotine consumption."*
>
> *When using any of the reduced exposure claims in the product label, labeling or advertising, the company must include, "Helps you smoke less." The FDA also recommends that the labeling and advertising include the statement, "Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death."*
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> *FDA announcement 23 Dec 2021 [here] – also see appendix A for further permitted claims.*

Update 18 January 2022. The company has announced that it will be marketing these products from March 2022: 22nd Century Launching the First Reduced Nicotine Cigarette Authorized by the FDA That Helps You Smoke Less. The company is positively gushing about the help it has had from FDA:

> *The FDA decision on VLN® is a major event for public health in the fight to reduce the harm caused by smoking. Not only did 22nd Century receive the MRTP authorization based on its application requests, the FDA proactively added an extra and incredibly valuable claim of "Helps You Smoke Less" mandated on every package to educate the consumer about the product's benefit.*
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> *22nd Century Press release, 18 January 2022.*

The problems with this – a quick thought experiment

If you want a quick route to understanding how bad this is: imagine taking the popular Juul product and modifying it to reduce the nicotine to a negligible level and then (somehow) increasing the toxicity of the aerosol to be equivalent to that of cigarette smoke. Once you have created a new toxic but inadequate substitute for smoking, then it goes on the market with FDA approved claims saying that it will help you cut down on smoking and nicotine use. It couldn't be more ridiculous – a super-toxic low-nicotine Juul would never even be allowed on the market in the first place, let alone blessed by FDA.

The problems with this – more detailed

I think there are four main problems with this:

1. A diversion from better options. The only real value these products have in public health terms is if smokers don't use them because they are so unsatisfying, and switch to something with lower risk (that is the promise of a VLN rule). If they do use them, they are still exposed to thousands of toxins from smoke and no-one would be happy with vaping products that create the toxic exposures created by VLN cigarette products. However, the purpose of the marketing communication is precisely to encourage people to buy these products – that is what 22nd Century exists for. If people want to reduce their *health risks*, then they are far better advised to switch to a non-combustible vaping or heated tobacco products. So for health-conscious smokers, this is a diversion from a strategy that would actually help them. Instead, the authorised claims falsely promote reduced nicotine exposure as a health benefit, though with the sly disclaimer: "*Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death*." What, then, is the point?
2. Not marketed for smoking cessation. This is not being marketed as a smoking cessation strategy. FDA and 22nd Century are not saying "*use these as part of your journey to smoking abstinence*". The claims relate to reduced exposures to nicotine arising from ongoing smoking, not a smoking cessation strategy. The 22nd Century products have not been

evaluated by FDA as a smoking cessation strategy either for the PMTA or MRTP. I can't think of anyone in public health that would suggest switching to these products to quit smoking – rather than tying Rx meds, NRT, or a non-combustible alternative to smoking (see *What is the use case*? below). FDA's justification for the MRTP rests on the idea that people will use these products indefinitely, but just smoke less – and there will be some benefits from that.

3. Misunderstands nicotine use. It's almost as if FDA has no idea about smoking as a nicotine-seeking behaviour and the struggles that users would have with switching to these products (see rampant non-compliance in trials of VLNC cigs – see Benowitz et al. 2015). So where is the caution to smokers about the negative effects (withdrawal, craving) on them of reduced nicotine? Where is the consumer protection caution that "*these products may not be as satisfying as your normal brand*". It implies that the drop in nicotine exposure just somehow happens as a result of using the product with no other impact on the user.
4. Making nicotine the problem. These claims strongly imply that nicotine is the problematic agent that needs to be cut out as far as possible. Yet that is not the case (or a gross over-simplification) and perceptions of nicotine risk are already wildly inaccurate among the public and professionals. Only 21.4% of the US public (HINTS, 2019) disagrees that the nicotine in cigarettes is the substance that causes most of the cancer caused by smoking. How does this help Americans really understand and act accordingly?

What is the use case?

So, here is my question to FDA and to everyone who sees this as a positive development. If you were giving advice to a friend or if you were a health professional advising people who smoke, for what type of consumer and in what situation would you advise trying to use this product, given all the alternatives?

You have the option to advise people to try smoking cessation medications or NRT. You could advise counselling (what counselling services would advise switching to VLN cigarettes?). You could recommend trying some or all of vaping, heated tobacco, snus or nicotine pouches. You could even recommend a period of 'dual use' and gradual transition. But I can think of no circumstances where I

would advise someone to go out and buy a packet of reduced nicotine cigarettes. It is not much different to advising them to just cut down their smoking, a strategy likely to fail.

So what is the use case? When would FDA officials or supporters of this measure advise users to switch to VLN cigarettes? Because that is exactly what they are doing by authorising or supporting these marketing claims. So I tweeted a reply to a prominent supporter of this measure. Still hoping for a reply.

> *Richard, what sort of person in what circumstances would you recommend should switch to using these products, given the alternatives?*
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> *I doubt they will cause smoking to increase because almost no one will use them. They only conceivably work under duress (trials, VLNC rules).*
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> *— Clive Bates (@Clive_Bates) December 24, 2021*

Prediction

In my view, after an initial surge of interest, these products will bomb in the marketplace and 22nd Century will revert to its ongoing strategy of trying to sell these products to smokers under regulatory duress by pressing for a VLN rule (a prohibition on normal nicotine cigarettes).

The inimitable David Sweanor describes it as:

> *Removing the nicotine consumers seek in order to wean them off smoking might actually work for some people. But it looks a lot like an effort to end gun violence by marketing versions that cannot fire bullets. It is hard to imagine a significant number of those interested in either product finding such things to be acceptable options.*
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> *David Sweanor, by email, 23 December 2021*

Does it help secure a 'nicotine standard'?

Some supporters of this new MRTP authorisation see it as progress towards a greater goal: that would be imposing a 'nicotine standard' that requires rather than permits and promotes cigarettes with very low nicotine levels. I disagree with this strategy for many well-rehearsed reasons (see Twenty reasons to be sceptical about rules lowering nicotine levels in cigarettes – and what to do instead). But its only plausible rationale is that it forces people who smoke to either quit smoking or switch to a non-combustible reduced-risk product (in practice, they would also access illicit products). It works only because the VLN products *are not a satisfactory alternative to smoking regular cigarettes*.

That is not what is happening here. FDA's MRTP authorisation stresses the public health value of actually using these products *instead of* regular smoking – not as a means to trigger smoking cessation or switching. It is offering this as a harm reduction strategy in its own right, rather than a device to move users on to a genuine harm reduction approach. 22nd Century will be promoting this product with a view to people using it as an alternative to smoking cessation or genuine harm reduction option. For this reason, it is a distraction from all the better options. This leads to the key challenge for FDA and those backing this authorisation: the use case.

What are MRTPs and PMTAs?

Under the US Tobacco Control Act, a new tobacco product requires a Pre Market Tobacco Application (PMTA). Under this process, FDA has to be satisfied that the product is appropriate for the protection of public health before it can be placed on the market. There are various exceptions for products that were already on the market in 2007 and derivatives of these products. Also, FDA is using enforcement discretion to allow many vaping products to remain on the market while it evaluates their PMTAs.

In contrast, the Modified Risk Tobacco Products (MRTPs) is about *communication*. The MRTP application is the process for making authorised marketing claims about reduced risk. FDA has to determine that such claims are "appropriate for the promotion of public health".

22nd Century received its marketing order in 2019. FDA has so far granted PMTAs for five product sets: UST (Altria) Verve chewable tobacco disks (2021); Reynolds Vuse vaping product (2021); PMI iQOS (2020, 2019); 22nd Century reduced nicotine products (2019); Swedish Match General snus (2015).

The 22nd Century cigarettes are the third product set to receive an MRTP – see Modified Risk Orders – the previous two were PMI's iQOS (2020) and Swedish Match General snus (2019).

Multiple researchers used to support cigarette company claims

Another commentator points out that this is might as well be seen as FDA approving an MRTP to itself.

> *This is best seen as FDA awarding itself an MRTP. The only sales of these products are for research purposes and FDA has spent well over a hundered million dollars on researching these products. FDA has promoted the idea of reduced nicotine cigarettes for years and now it has waved the products through a process that is almost impossibly burdensome for others in record time. Yet the public health case for these products is very weak.*
>
> *Private communicaton.*

One of the quite insidious aspects of FDA granting an MRTP order to the 22nd Century very low-nicotine cigarette (VLNC) is the extent to which FDA/NIH has financially supported the company's application by buying its cigarettes and using independent research organisations and investigators in the United States to provide the evidence to support its case.

Any other tobacco or vape company would need to present extensive trials that it conducted itself and at its own expense, something that would be prohibitively expensive for most companies. But not so for 22nd Century.

The FDA's decision summary explains… the application uses extensive "bridging". Bridging is the use of evidence gathered from a very similar product for use in a commercial application to the FDA.

> *Bridging from SPECTRUM NRC102/103*
> *Much of the evidence reviewed in these MRTPAs is based on studies of SPECTRUM NRC102 (nonmenthol) and NRC103 (menthol) very low nicotine cigarettes (VLNCs). The applicant stated SPECTRUM NRC102 is the same as VLN™ King, and SPECTRUM NRC103 is the same as VLN™ Menthol King. FDA found that the cigarette weight, cigarette length, cigarette diameter, and tipping paper permeability are the same between SPECTRUM and VLN™ cigarettes. SPECTRUM cigarettes and VLN™ cigarettes also share many identical components and materials including tobacco type, tobacco blend, cigarette paper, filter, seam adhesive, and tipping adhesive. The only material difference is that the SPECTRUM tipping paper has a silver line and the name SPECTRUM printed on it, whereas the VLN™ tipping paper does not have any markings. The base tipping paper for both SPECTRUM and VLN™ cigarettes has the same porosity of CU and is produced by the same manufacturer. Thus, FDA finds it appropriate to bridge data from studies of SPECTRUM NRC102/103 (referred to as "VLNCs") to the proposed MRTPs. In this review, the terms VLNC cigarettes and SPECTRUM NRC102/103 are used interchangeably.*
>
> *FDA Decision summary*

Of course, the SPECTRUM cigarette is the product used and paid for in most (all?) of the trials of VLNC so far. For example, the extensive (and impressive) trial by Donny et al 2015 published in the New England Journal of Medicine states

"Investigational cigarettes were obtained from the National Institute on Drug Abuse". As the supplementary material makes clear, these were Spectrum cigarettes. Hatsukami et al 2018, likewise. In fact, all the investigational cigarettes available to US research institutions are SPECTRUM cigarettes sourced from 22nd Century. See:

- NIDA Nicotine Research Cigarettes Drug Supply Program
- NIDA ordering guidelines for nicotine research cigarettes

FDA and NIH have been extraordinarily generous to this company. These public bodies account for almost all of 22nd Century's reduced-nicotine cigarette sales (there is no significant market for these products other than for research purposes). Not only that, through extensive funding of VLNC research, FDA and NIH have paid for the research base for 22nd Century to make a commercial application, via bridging, for a modified risk claim that is specific to the company and its products (it is not a general claim for the VLNC category). This MRTP order allows it to make actual and implied reduced risk claims for ongoing use of this product. These are set out on Page 1 and appendix A of the marketing order

> *We [FDA] authorize marketing of the tobacco products as modified risk tobacco products with reduced exposure claims, including:*
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> *• "95% less Nicotine*
> *• "Helps reduce your nicotine consumption"*
> *• "…greatly reduces your nicotine consumption"*
> *• "VLN™ cigarettes are substantially lower in nicotine content than any other cigarettes currently available to smokers in the United States.VLN™ cigarette contain an average of just 0.27 mg of nicotine."*
> *• "Without exception, VLN™ cigarettes contain at least 95% less nicotine than the top 100 cigarette brands in the United States."*
> *• "22nd Century's VLN™ cigarettes contain an average of 0.27 mg nicotine – -at least 95% less nicotine compared to conventional cigarettes."*
> *• "22nd Century's VLN™ cigarettes feature the same nicotine content as the lowest nicotine style of the Company's SPECTRUM research cigarettes."*
> *• "VLN™ cigarettes contain 0.27 ± 0.1 mg nicotine."*
> *• "As a result of our unique technology and plant breeding expertise, VLN™ tobacco grows with 95% less nicotine than conventional tobacco."*
> *• Graph depicting nicotine levels of VLN™ cigarettes compared to several other*

cigarette brands.

Where any of the reduced exposure claims listed in Appendix A are used in the product label, labeling, or advertising (LLA), under section 911(h)(1) and 911(h)(3)(B), this order requires that the LLA must also include the following condition of use: "Helps you smoke less." Additionally, we recommend that the LLA include the disclaimer: "Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death."

FDA marketing order

As I have already argued in this blog, these claims are a complete muddle of factually true but profoundly misleading nonsense that adversely affects the perception of nicotine and crowds out other, far better, risk mitigation options for smokers for which FDA has not been so generous. It is also quite different to the impact of a VLNC rule. In fact, the application uses a model that allows for VLN and conventional cigarettes to have equal market share (a risible assumption, but clearly not the intention of a VLNC rule either). See if you like the sound of this from the decision summary (p16)…

Additionally, the epidemiology review evaluated the applicant's population model estimating the public health impacts of the proposed MRTPs. The model assumes that the market share of conventional cigarettes (CC) and VLN™ will be equalized at around 25% by year 2050, meaning that approximately 7.1% of CC smokers will initiate VLN™ smoking per year (i.e., if 7.1% of CC smokers switch to VLN™ cigarettes every year until 2050, then at least 25% of smokers will be using VLN™ cigarettes by 2050).

FDA Decision summary

I doubt that another company making a VLNC cigarette would be able to use 'bridging' to the Spectrum product unless they made their product virtually identical, which would be difficult and not even desirable. So all of that research effort is functioning as a direct subsidy for one cigarette company's marketing claims.

My impression is that the researchers in this field believe they have been doing something quite different to providing material for cigarette marketing claims.

That is, they have been trying to assess the impact of a VLNC rule on the market as a whole, not providing free research to a single tobacco company to support official authorisation to make dubious and confusing claims. I must say, I feel uneasy about this. Did these researchers expect to have their work used in this way? Do they agree with FDA's findings based on their work?

I still come back to the basic 'use case' question – for what sort of person in what circumstances would a public health professional recommend someone tries a 22nd Century VLN cigarette, given the available alternatives? Because this is what FDA is doing by allowing an MRTP claim for this product.