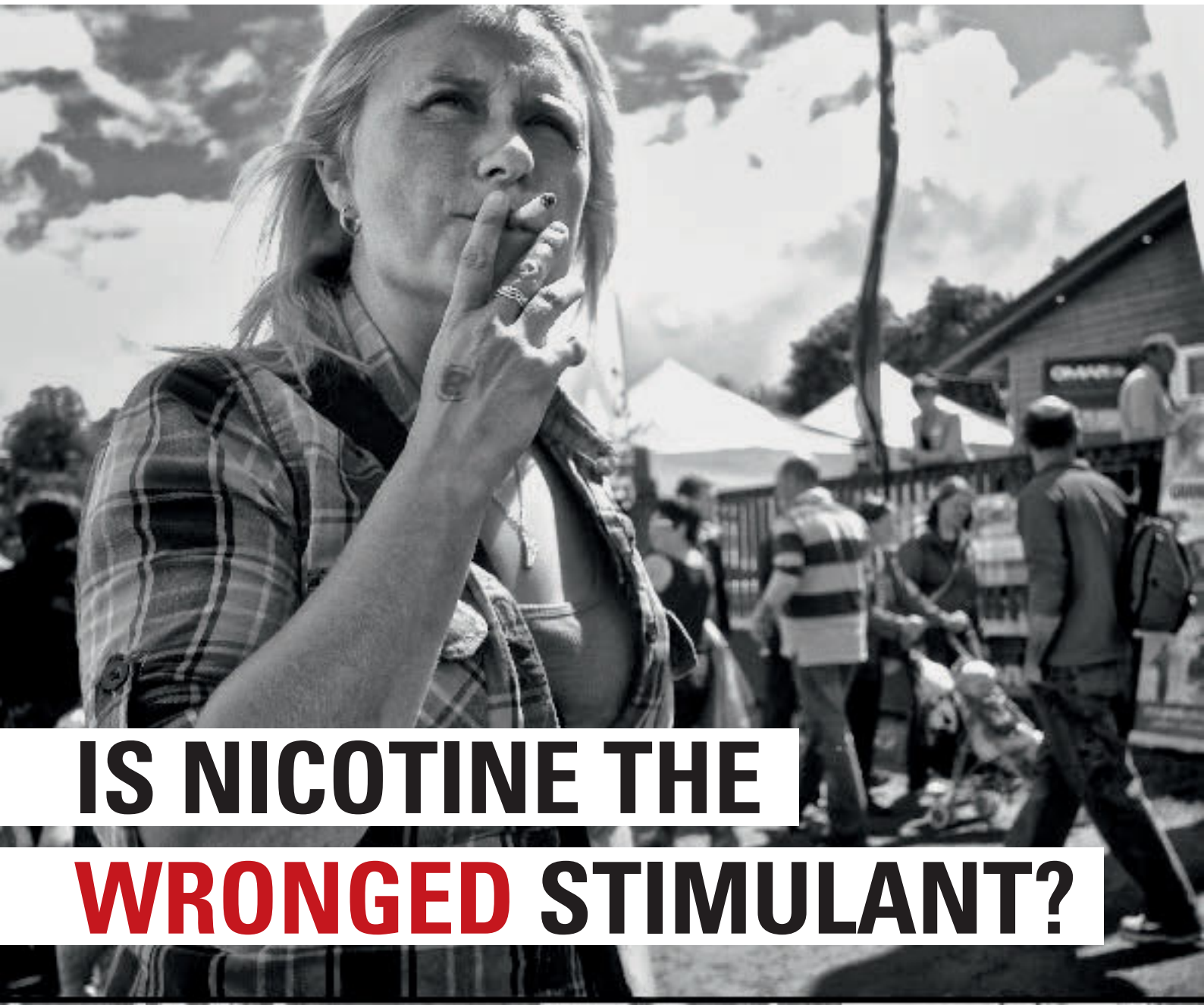


IS NICOTINE THE WRONGED STIMULANT?

The FDA could be heading down the wrong path by **naming and shaming nicotine**. For one, the agency's strategy would embrace high nicotine-delivery tobacco products which could appeal to former smokers. At the very least, new science will be needed, writes Dr John Lauterbach.

Those who have been following the debates surrounding nicotine for many years may have recognised the title of this article as being similar to the title of Chapter 6 of the book 'Virtually safe cigarettes: Reviving an opportunity once tragically rejected'. Authored by Dr Gio B. Gori and published in 2000 by IOS Press, the book was written before the advent of the e-vapor category and the recent reintroduction of heat-not-burn products (remember that Premier and Eclipse were heat-not-burn) such as the IQOS by Phillip Morris International (PMI) and competitive products sold in some European countries and Japan.

PMI's IQOS device, the consumables for which are sold as HeatSticks and Heets, have drawn fire from critics claiming that the aerosols they produce still contain many of the same toxicants as in regular cigarette smoke[1] and should not be permitted in the

The US Food and Drug Administration announced in July that the agency will rehaul its philosophy on tobacco and insist upon reduced nicotine levels in cigarettes. No further details had been made public as this issue of TJI went to print.

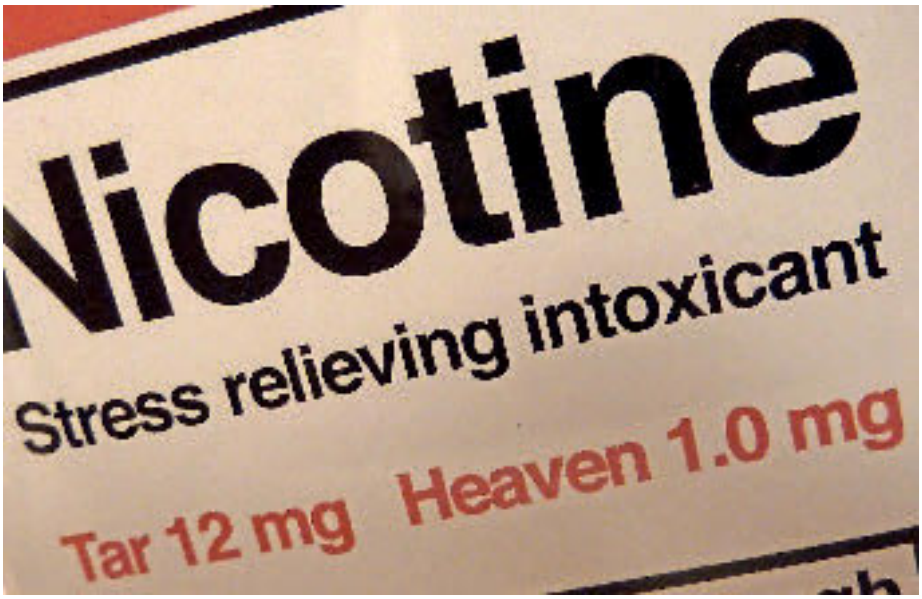
USA as they are not a safe alternative to cigarettes. This is a claim that has also been made against some e-vapor products. However, the extensive toxicological research and human biomonitoring studies done by PMI and published in peer-reviewed journal articles should minimise critique based solely on smoke chemistry. Essentially, these products are the high-nicotine, low-tar, low-other-toxic-component products that were postulated as being less toxic back in 1979.[2]

TOO CLOSE TO CIGARETTES?

Since the IQOS products deliver about the same amount of nicotine with similar pharmacokinetics to conventional cigarettes[3] it is likely that they would be popular with current smokers, former smokers, and even non-smokers who may have tried a few cigarettes and never became regular smokers because of the health risks associated with smoking. If that is indeed the case for potential users of the IQOS in the USA, it could be grounds for the US Food and Drug Administration (FDA) to issue a 'No Marketing Authorisation' letter, in response to the PMTA [pre-market review of a new tobacco product] that PMI submitted to the FDA last December. In the most recent instance where PMTAs were approved (eight brand-styles of Swedish Match NA snus), the FDA noted "It is anticipated that the marketing of the proposed products, as described in the PMTAs, [presents] a low likelihood of nonuser uptake of these products, decreased or delayed cessation, or other significant shifts in user demographics".[4] According to a commentary on the Forbes Magazine website, PMI and its US marketer, Altria, have high hopes for the IQOS products in the US market.[5]
The same fate could befall e-vapor products, especially those whose nicotine pharmacokinetics are close to those of conventional cigarettes.

A QUESTION OF CONVENIENCE

The availability of products such as the IQOS heat-not-burn device on the US market would lessen the impact of the FDA's plan to mandate a reduction in the nicotine content of commercial cigarettes to levels that would minimise the addictive nature of cigarette smoking. Lessen may be the appropriate word as both e-vapor products and heat-not-burn products do not have the convenience of cigarettes. One of the biggest factors in reducing the convenience of these products is that they tie users to a source of power. In that way, they are like cell phones. Without power to recharge the batteries, the devices are useless. Cigarettes, in comparison, are a ▶



stand-alone product that needs little more than a light. This is not a superfluous argument as week-long power outages were common following recent hurricanes that struck the US. Meanwhile, some stores selling cigarettes operated as normal. Moreover, is it not hard to imagine a private party where everyone is using e-cigs and/or heat-not-burn products while they sip their cocktails? Equally difficult to imagine is a group of construction workers taking a 'heat-not-burn break' on the building site.

THE NEED FOR NEW SCIENCE

Even if we discount such arguments, there are numerous scientific, societal, political and economic issues that would need to be resolved before implementation of mandated nicotine reductions. Some of these were discussed in my last TJI column (TJI August-September) and have also been published in various media. Perhaps one of the better summaries was given in a recent editorial in Tobacco Control, titled 'FDA's new plan to reduce the nicotine in cigarettes to sub-addictive levels could be a game-changer'.[6] In the article, Robert Proctor, the author and noted critic of the tobacco industry, appears to make the assumption that cigarette manufacture, distribution, and sales are concentrated under the control of the major cigarette manufacturers and could, therefore, easily be regulated by the FDA. This is not the case in the USA. There are numerous small businesses involved in the production and supply chain, not to mention distribution. Companies involved range from the small tobacco product manufacturers all the way down to local c-store owners and thousands like them across the country, all of which depend heavily on cigarette sales to stay in business. The potential of such businesses, and tobacco farmers, to lobby the US Congress to curtail the FDA's nicotine plans should not be underestimated.

Proctor mentions but then dismisses the notions of significant contraband cigarettes entering the market, and/or a shift to other forms of combustible tobacco. We could easily see a return to pipe smoking, although that might raise the spectre of sexual discrimination, as few women smoked pipes even when pipe smoking was at the height of its popularity. The creativity of cigarette smokers should also not be under estimated. With plenty of nicotine around in the forms of pipe tobacco, smokeless tobacco, and, nowadays, e-liquids, we could easily see some smokers adding nicotine back into their nicotine-reduced cigarettes, much as tobacco flavourists add their new creations for casings and top flavours to uncased, unflavoured cigarettes made specifically for such studies.

Proctor fails to mention the need for studies to determine the toxicity of the smoke from cigarettes with non-addictive levels of nicotine in the tobacco. In particular, toxicity not determined by the conventional *in vitro* and *in vivo* assays used in the past, but toxicity determined by the latest techniques used for evaluating the IQOS, including human clinical studies.

Clearly, such extensive studies are needed because of the large numbers of smokers that would be exposed to novel cigarettes under the FDA's plan – 'novel' because of the extremely low, non-addictive levels of nicotine in the tobacco of each cigarette. The FDA would be hard-pressed to argue against the need for such studies.

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Dr Lauterbach is a diplomate of the American Board of Toxicology. He is a leading expert in the chemistry and toxicology of tobacco products and tobacco smoke. He is author or co-author of over a dozen journal articles and more than sixty presentations on tobacco-related scientific matters. In April 2010, he was appointed to the Food and Drug Administration's Tobacco Products Scientific Advisory Committee.

1 Auer et al. Heat-not-burn tobacco cigarettes: Smoke by any other name. JAMA Intern Med. 2017 Jul 1;177(7):1050–1052; see also the following editorial by Dr Michell Katz on page 1052
2 Banbury report; 3. Proceedings of a meeting held at the Banbury Center, Cold Spring Harbor. NY, Oct. 14–16,1979; available at: http://industrydocuments.library.ucsf.edu/tobacco/docs/jfhv0184
3 Brossard et al. Nicotine pharmacokinetic profiles of the tobacco heating system 2.2, cigarettes and nicotine gum in Japanese smokers. Regul Toxicol Pharmacol. 2017 Oct;89:193–199 open access available at www.sciencedirect.com/science/article/pii/S0273230017302283?via%3Dihub
4 available at www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/ucm472108.htm
5 see www.forbes.com/sites/greatspeculations/2016/12/30/fda-approval-for-iqos-to-be-a-game-changer-for-altria/#555388811a36
6 Proctor RN. Tobacco Control. 2016 Sep;26(5):487–488