Hidden in plain sight: how vaping manufacturers exploit legislative loopholes

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In this issue of the *MJA*, Jenkins and colleagues report their chemical analysis of nine e-cigarette products purchased in Australia in November 2023.[1] The products were variously labelled as containing a "nicotine alternative" or providing a "nicotine-like experience, without the nicotine". Using gas chromatography–mass spectrometry, magnetic resonance spectroscopy, and high resolution mass spectrometry, the authors identified and fully characterised the nicotine alternative as 6-methylnicotine.

Identifying 6-methylnicotine in products purchased in Australia is worrying for several reasons. Importantly, while 6-methylnicotine has been known for more than half a century,[2] very little is known about its pharmacokinetics or potential toxicity. Jenkins and colleagues refer to two studies which indicate that 6-methylnicotine could be more potent and elicit greater cytotoxic effects in an immortalised cell line than nicotine.[3,4] One study, sponsored by an e-liquid manufacturer, found that 6-methylnicotine exposure led to more differential gene expression than exposure to nicotine.[3] These findings are concerning, as immortalised cells are typically more robust than primary cells in their response to inhaled insults;[5] harmful effects could be more severe in e-cigarette users. Conversely, a recent (unpublished) study concluded that 6-methylnicotine "exhibits comparable toxicological behavior to (*S*)-nicotine with no mutagenic or genotoxic activity and limited cytotoxicity",[6] despite the authors finding that 6-methylnicotine (2.5 or 5 mg/mL) reduced the cellular viability of cell lines to a considerably greater degree than nicotine at the same concentrations. The bottom line is that there are effectively no unbiased data on the potential toxic effects of 6-methylnicotine derived from a realistic biological model, or in human studies. A great deal more research is needed.

Another problem regarding 6-methylnicotine is its potency compared with nicotine. A patent[7] notes that racemised 6-methylnicotine "has strong satisfaction and throat-hitting feel" at 1 mg/mL and "better sensory experience" than nicotine at 3 mg/mL. This suggests that users unfamiliar with the difference could inadvertently dilute concentrated 6-methylnicotine as they would nicotine solution, increasing the "risk of accidental exposure to high concentrations of a compound with unknown health effects", as suggested by Jenkins and colleagues.[1] The fact that one of the samples they tested contained 104 mg/mL 6-methylnicotine provides evidence for this possibility. The confusing, misleading, and inaccurate labelling reported by Jenkins and colleagues was also reported in a recent United States study.[8]

6-Methylnicotine is structurally similar to nicotine (having a single additional methyl group), but the manufacturers of e-cigarette products containing it claim it will not be detected by standard nicotine test procedures. For example, the manufacturers of "Metatine", a trademarked 6-methylnicotine product for use in vape products and identified in at least one product in Australia, state on their website that Metatine "does not fall under the regulatory purview of the FDA's Center for Tobacco Products", and "is not subject to FDA tobacco requirements".[9] This is despite the Food and Drug Administration (FDA) recently redefining "tobacco products" to include synthetic nicotine,[10] and means that 6-methylnicotine-containing products are not required to obtain FDA pre-marketing authorisation before being sold in vapes in the United States. This use of "non-nicotine tobacco alkaloids or other synthetic nicotine analogs" has been identified by the World Health Organization as one way manufacturers could bypass nicotine regulations.[11]

A similar loophole could be exploited in Australia, where the Therapeutic Goods Standard for Nicotine Vaping Product (TGO 110) simply defines nicotine as "nicotine in salt or base form".[12] While this scheduling established a therapeutic pathway for vaping products as smoking cessation aids, the vaping industry has capitalised on a regulatory loophole that allows the retail sale of purportedly nicotine-free vaping products. The result is a thriving market of nicotine-containing vapes mislabelled as not containing nicotine, sold on street corners, in convenience stores, and in petrol stations, and targeting children and young people with their bright packaging and child-alluring flavours. New Australian laws, effective since 1 July 2024, have closed this loophole, requiring all vapes to be sold in pharmacies, effectively ending retail sales of any vaping product (regardless of nicotine content). These regulations also place some limits on what chemicals a "therapeutic vaping substance" can include, a different approach to the shortlist of banned ingredients specified by TGO 110. While enforcing the previous regulations required testing to detect the presence of nicotine — using procedures unlikely to find "nicotine-alternatives" — the new laws include minimum quality standards that will stop synthetic nicotine analogues being used. The findings by Jenkins and colleagues[1] have implications for Therapeutic Goods Administration procedures when testing for nicotine and related substances in vaping products.

Competing interests: We are both affiliated with the Australian Council on Smoking and Health, an anti-smoking/anti-vaping advocacy organisation; Laura Hunter is chief executive and Alexander Larcombe is a member.

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