VAPOR TRIALS

The booming e-cigarette trade has thrown down the gauntlet to the tobacco industry. Yet if the new, safer smokes are classed as a medicine, the battle could be over before it even begins.

By **Clive Bates**

The World Health Organisation estimates that on current trends one billion people will die prematurely from diseases arising from smoking tobacco. For every death there is also a burden of illness, poor health and wellbeing and various impacts on non-users through passive smoking.

The tobacco business is a powerful, stable oligopoly striding the globe. The six largest firms had revenues of $350 billion and profits of £35 billion (2010). However, the basic product of this industry, six trillion cigarettes annually, has not changed that much in 50 years. But that is all about to change.

If smoking is so harmful, why do people do it? It's an often-denied fact, but nicotine, like any drug, provides functional benefits to the user. In fact is a 'good drug' in many respects: it provides a calming of mood, relief from anxiety and it can improve concentration and cognitive abilities. It is thought to provide relief to some psychotic symptoms. It is also widely understood to be 'addictive' for some users, as characterised by withdrawal symptoms and the early morning imperative to smoke.

Drugs do not become addictive unless they provide rewards – and nicotine definitely does. Nicotine use is fuelled by behavioural ritual and its association with cues and particular moments that punctuate the day. Nicotine has other 'positive' characteristics for the user: it does not cause intoxication, because users control their intake and start to feel nauseous if they take too much. The development of tolerance and need for ever greater doses is limited.

Nicotine itself is wrongly maligned as the dangerous agent in tobacco, yet it isn't really harmful at all. Nicotine is relatively benign, with a risk profile analogous to caffeine. It is often said that people 'smoke for the nicotine but die from the smoke'. And this is right: it is the mix of smouldering particles of tobacco and the hot toxic gases and vapours drawn deeply into the lungs that does the damage.

E-cigarettes have the potential to create a decisive change in the trade-offs facing smokers. They allow the user to retain the benefits of nicotine use, and provide much more effective delivery than nicotine replacement therapy (NRT) products. They mimic closely the behavioural aspects of smoking. They remove practically all the long and short term health and other negative impacts, and cost less. They have negligible impact on surrounding people. Moreover, they allow a user to move away from the dangers of smoke inhalation without suffering cravings and withdrawal, and with no great personal effort.

It is this dramatic change in the choices now facing smokers that make e-cigarettes a disruptive technology. The investment bank Goldman Sachs regards e-cigarettes as one of eight significantly disruptive technologies, and a leading analyst at Wells Fargo Securities, Bonnie Herzog, is forecasting that e-cigarettes will overtake cigarette use in the United States with a decade. If that happened and became a global trend it would be a wrenching disruption of the cigarette-based business model of the tobacco industry, and it would make dramatic inroads into avoiding the one billion deaths forecast by WHO on current trends.

But are e-cigarettes safe? No-one is claiming they are 100 per cent safe – very little is. But a common-sense consideration of what is in them and how they work should tell us they will be very much safer than cigarettes themselves. They contain three main ingredients: nicotine, flavouring and an excipient to create vapour when heated, typically pharmaceutical-grade propylene glycol or glycerol.

The ingredients are vaporised at relatively low temperature rather than burnt, so there are no new products of combustion. By contrast, tobacco is a complex organic material with toxic substances formed during growing,

curing and then as products of combustion. The physics and chemistry of e-cigarettes mean that it is common sense that they will be much lower risk. This is backed by studies showing many tobacco toxins are not present at detectable levels. The few that are present, are at levels many times lower than in cigarette smoke. It is possible that prolonged exposure will cause irritation or that some flavourings might be harmful, but the total risk is likely to be around 99 per cent lower than smoking. Obviously, we can't know the long term effects until the long term has passed, but everything about the products suggests it is far less harmful.

Some health activists claim that e-cigarettes are unregulated. While it is true that at present there are no specific regulations covering e-cigarettes, it is not true that they are unregulated. They fall within the scope of 17 European directives, regulations and decisions that apply to all products. These cover general safety obligations, pan-European safety and defect notification, electrical safety, packaging and labelling of hazardous substances, weights and measures and fair commercial practices. Together these could be purposefully applied and enforced to remove defective or unsafe products from the market, apply a range of safeguards and to prevent false or misleading claims.

The European Commission, several governments including the UK, the pharmaceutical industry and many health campaigners want e-cigarettes to be classified and regulated as medicines. This would be done through a revision to the EU directive on the manufacturing, presentation and sale of tobacco products currently under consideration by the European institutions. Article 18 of the proposal would apply the medicines directive 2001/83/EC to e-cigarettes above a very low threshold of nicotine content.

Regulating e-cigarettes as medicines would mean that only products that had been granted a marketing authorisation by a medicines regulator would be allowed on the market. To achieve that, they would have to prove the safety, quality and efficacy of the products to standards determined in medicines regulation. This is an audacious bid for control of the emerging new nicotine market by medicines regulators and their allies in the prohibitionist wing of the health lobby.

There are five main objections to regulating these products as medicines. Firstly, these products are not medicines, they compete with cigarettes. E-cigarettes are not for treating or preventing disease or for any other therapeutic purpose. They are not sold as medicines and the people buying them do not regard themselves as in treatment. They are legal lifestyle drugs like cigarettes, alcohol or caffeinated drinks. Medicines regulation will require pharmacokinetic testing and establishing a system of pharmacovigilance – neither is necessary and neither required of the cigarette manufacturers. There is a further fundamental difference – medicines require prior authorisation to be placed on the market – cigarettes do not. There is no sense at all in allowing regulation to tilt the playing field in favour of cigarettes, providing de facto protection from competition. The likely effect of medicines regulation is legal challenges – there have already been four successful cases – so it doesn't even provide legal certainty.

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Second, it will dramatically limit the choice of products on the market. The UK regulator says that no products currently on the UK market would meet its standards. Yet they have been used by 1.3 millions users, many very satisfied, and there is nothing wrong in practice with these products – they just don't meet arbitrary and unnecessary standards. Many firms produce several hundred flavours and strength combinations. Each would require a lengthy and expensive marketing authorisation process. That simply will not happen. Good products will be banned *de facto* simply because it will not be affordable to go through the licensing process.

Third, regulatory burdens slow innovation. Pharmaceutical innovation involves spending years on drug discovery and then exploiting a patent-protected market for 10-15 years. The innovation model in fast moving consumer goods is very different, more like the short product cycles seen in the personal technology market. Expensive, burdensome and slow authorisation regimes work against this, even if they work for pharmaceuticals.

Fourth, complete reconstruction of the supply chain will be required. Medicines regulation requires that manufacturing and distribution comply with an exacting quality standard known as Good Manufacturing Practice (GMP), which requires pharmaceutical grade facilities, automation, process controls and qualified staff. The existing facilities, many based in China, do not meet these standards and will probably never comply. Nor do they need to – we should recall that the vast majority of recreational nicotine is delivered through toxic smoke at present. There is an acceptable standard between this and pharmaceutical standards. The current companies would have to rebuild their supply chains from scratch. Few have the deep pockets necessary to make the investments and incur financial strain while this overhaul takes place.

And finally, retail access will be limited. This is not so much of a problem in the UK, but in the other major countries in the EU, sales of medicines are restricted to pharmacies or other specialised settings. This not only means users can't access e-cigarettes when and where they want them, but that tobacco retailers will lose revenue as pharmacies gain, creating a negative political lobby against e-cigarettes. Again, it makes no sense to have regulation that makes cigarettes more available than safer alternatives.

The overall effect of medical regulation will not be to raise standards, but to cause an abrupt restructuring that will drive out most of the existing firms. From the users' perspective it will have the effect of banning products they are already using as alternatives to cigarettes. Medicines regulation will force the industry towards a small number of large players, primarily from the tobacco companies, selling a narrow range of more expensive commoditised products in fewer places.

The whole philosophy of tobacco policy is grounded in control – it even goes by the name of 'tobacco control'. The instinct is to control the products that exist and close the door as far as possible to new products. That is an out-dated mind-set. We have products that are many times less harmful than smoking that are good substitutes offering comparable experience. We should be actively encouraging them, not choking them in red tape for no good reason.

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