Written evidence submitted by Dr. Graham F. Cope (ECG0013)

Executive Summary

- Nicotine is a neurotoxin
- Nicotine affects non-nervous cell types, such as immune cells and other organ cells
- Chronic nicotine intake from electronic cigarettes can have harmful effects
- Warnings should be given to certain groups who are considering using electronic cigarettes

I am a medical toxicologist specialising in smoking-related diseases and the author of a text book on the subject (1). I believe that the toxic nature of nicotine is not sufficiently highlighted or understood when describing the effects of electronic cigarettes.

1. Electronic cigarettes (EC) are without doubt less harmful than conventional combustible cigarettes. They do not emit the cancer-causing chemicals such as polyaromatic hydrocarbons and the levels of inflammation-inducing substances such as free radicals are much less and they do not produce the oxygen-starving chemical carbon monoxide (1). However, they are a source of atomised nicotine supplied at high temperatures in a mixture of water vapour and organic flavourings.

2. The effects of nicotine from EC are difficult to separate from those effects from combustible cigarettes as the vast majority of EC users are current or previous users of cigarettes. Nevertheless nicotine is a neurotoxin which has powerful effects on the nervous system, usually via nicotinic receptors of the autonomic nervous system. In the brain this causes arousal and increased information processing, which smokers and users of EC find beneficial (1). But nicotine disrupts the neurotransmitters in the brain, such as dopamine and serotonin and may influence mood disorders, such as depression, anxiety and schizophrenia (2), which are more prevalent in smokers than non-smokers (3). There is also growing evidence from animal models indicating that nicotine intake during pregnancy is responsible for detrimental effects on fetal brain development, including auditory processing defects and behavioural deficits in later life (4).

4. While the intake of EC vapour is less damaging to the lungs and delicate pulmonary tissues there is evidence that this vapour can change the cell structure leading to lung remodelling (5). Also chronic obstructive pulmonary disease (COPD) is common in smokers and one reason is that nicotine modifies the action of the delicate hair-like structures on the bronchi called cilia. This prevents mucus expulsion causing ‘pooling’ in the lungs which is a source of respiratory infections (6). While nicotine is not carcinogenic it has been shown to promote lung cancer cell proliferation, invasion and migration (7) and reduces the efficacy of anti-cancer treatment (8).

5. Nicotinic receptors on the surface of many immune cells modify their activity (9). This immunomodulation is partially responsible for the increase in respiratory diseases, such as tuberculosis, influenza and HIV in smokers (10). This is believed to be due to impaired immunological eradication of the pathogen (11). Nicotine-induced immunomodulation is also responsible for poorer wound healing (12), for example in the oral cavity, with detrimental changes to periodontal soft tissues (13) and to bone resulting in dental implant failure (14). There is also increasing the risk of infections after general surgery, specifically that involving skin flaps (15) or plastic or orthopaedic procedures (15).

6. Smoking increases the risk of cardiovascular disease. Nicotine plays an important role in this by reducing the heart muscle cell or myocardium activity and interferes with the nervous supply to the heart so reducing the action of the heart (17). Nicotine also modifies the atheromatous plaques that occlude the arteries in the heart so increasing the risk of a heart attack (18).

7. Other immunological effects have been found in relation to rheumatoid arthritis whereby nicotine has been shown to affect the immune cells such that they increase the inflammation related to rheumatoid arthritis. The study recommended against the use of nicotine-containing products, including e-cigarettes, in individuals with or at risk of developing this disease (Lee).
As well as detrimental changes to fetal development nicotine intake has been shown to adversely affect reproductive hormone levels by having anti-oestrogen effects and increasing the ratio of androgens to estrogens throughout life (20). This can reduce the chances of fertilisation and possibly adversely affect IVF treatment (21).

9. RECOMMENDATIONS
EC could be offered as an alternative to nicotine replacement therapy as a means of quitting smoking. But the long term effects of the inhalation of nicotine and flavourings have yet to be established. There is abundant and growing evidence that nicotine can influence the central nervous system and the development of fetal brains, with other possible adverse effects during pregnancy. Non-neuronal effects of nicotine have adverse influence the immune system, with effects on post-operative recovery, encouraging growth of cancerous tumours and increasing the likelihood of and impaired treatment of infectious diseases.

10. Therefore my recommendation is that EC should not be used during pregnancy, after surgical operations, in those with diagnosed heart disease and cancer, and in patients with serious respiratory infections.

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REFERENCES