

SUMMARY OF THE SCIENTIFIC EVIDENCE ON E-CIGARETTES

Comment Submitted in Response to FDA Regarding Proposed Rule Deeming Tobacco Products to be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products

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We are submitting two recent reviews of the scientific evidence on the marketing, behavioral, and health effects of e-cigarettes for the FDA's consideration:.

- Grana R, Benowitz N, Glantz SA. Background Paper on E-cigarettes (Electronic Nicotine Delivery Systems): Prepared for the 7th Meeting of the WHO Study Group on Tobacco Product Regulation. December 2013.
- Grana R, Benowitz N, Glantz SA. E-cigarettes: A Scientific Review. *Circulation* 2014;129:1972-86.

The first of these reviews was prepared for a meeting of the World Health Organization's Study Group on Tobacco Product Regulation (WHO TOBREG) committee and delivered in early December 2013. It contains a detailed discussion of all the available literature that presented data (as opposed to commentaries and opinion pieces) as of November 2013.

The second, a peer reviewed literature review published in *Circulation*, summarizes the information in the report to WHO and adds several important new papers that were published after the report was completed.

These reviews present and discuss many peer reviewed publications that are not included in the draft rule, probably because they were published after the rule was submitted for clearance to the Office of Management and Budget.

While the literature on e-cigarettes is continuing to develop, as demonstrated in these two publications, there is already a more-than-adequate scientific evidence base to support FDA regulation of e-cigarettes to protect the public health.

- E-cigarettes are evolving rapidly and being marketed like cigarettes were in the 1950s and 1960s
 - Marketing is back on television and radio
 - Aggressive placement in convenience stores (next to candy) and in other stores (next to medications)
- Youth are rapidly adopting e-cigarettes
 - E-cigarettes contain candy flavors (e.g., cherry, chocolate, turkish delight)
 - High levels of dual use
 - Youth who use e-cigarettes are heavier (not lighter) smokers
 - Youth who use e-cigarettes are much less likely to have stopped smoking (OR 0.1-0.2)
 - The temporal and causal relationships between e-cigarette use and youth smoking have not been determined
- E-cigarettes have not been proven to help adults quit smoking
 - Longitudinal population studies show that e-cigarette use is associated with a lower odds of quitting (pooled OR=0.61; 95% CI: 0.50 - 0.75).
 - The randomized trial comparing e-cigarettes to nicotine patch shows that in the context of low level behavioral support, the quit rate for those using e-cigarettes is low and similar to those using a nicotine patch
- There is a high level of dual use of e-cigarettes and conventional cigarettes among adults
- The hope that e-cigarettes will reduce harm by delivering "clean" nicotine will not be realized in continuing dual users
 - Continuing to smoke any conventional cigarettes confers essentially the full cardiovascular risk
 - Cancer risk may only be modestly affected because smoking duration is more important than intensity
- E-cigarettes deliver lower levels of toxins than conventional cigarettes, but they still deliver some toxins
- E-cigarettes pollute the air less than conventional cigarettes, but they pollute the air
 - They do not just emit "harmless water vapor"
- People passively exposed to e-cigarettes aerosol absorb nicotine (measured as cotinine), with one study showing levels comparable to passive smokers
- There is little research on direct health effects
 - One study shows short-term pulmonary effects
 - Evidence of cytotoxicity in animal and human *in vitro* test systems
- While the original e-cigarette companies were competing with conventional cigarette companies, all the major cigarette companies are now in the e-cigarette business
- E-cigarette companies are using the same political and public relations strategies as cigarette companies (most notably organizing users, similar to how the cigarette companies organized smokers)
- E-cigarette policy making in many countries is dominated by assumptions about their use (utility as a smoking cessation aid or for harm reduction) that are not supported by the evidence available to date

At minimum, the FDA should:

- Apply the same restrictions on e-cigarette advertising and promotion as apply to conventional cigarettes
- Ban the use of characterizing flavors in e-cigarettes
- Prohibit claims that e-cigarettes are effective smoking cessation aids until such time as there is convincing scientific evidence that such claims are true for e-cigarettes as they are actually used in the general population.
- Regulate e-cigarettes to set standards for product performance in order to minimize risks to users and bystanders
- Require childproofing of e-cigarette devices and refill solutions to prevent accidental pediatric poisoning.
- Regulations regarding e-cigarettes need to take into account the fact that, unlike conventional cigarettes and other tobacco products and medicinal nicotine replacement therapies, e-cigarettes can be altered by users to change the nicotine delivery and be used to deliver other drugs

We are also submitting, by reference, all papers and other materials cited in the report to WHO and *Circulation* paper that are being submitted with this comment.