

FDA's Proposed Exception for Premium Cigars and Weak Warning Labels for Cigars Do Not  
Protect the Public Health

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In its proposed deeming rule, FDA proposes to exempt a subset of cigars from FDA regulation, and proposed warning labels for cigars that are not based on scientific evidence. These proposals are not appropriate for the protection of the public health, and would result in negative public health consequences.

The FDA should not exempt "premium" cigars from regulation (i.e., reject "Option 2") and should include the fifth FTC warning (Tobacco Use Increases the Risk of Infertility, Stillbirth and Low Birth Weight) on the packaging of all cigars.

Although large, expensive cigars may be used differently by different sectors of society, there are still plenty of people in the U.S. who can afford to smoke them regularly. Premium cigar smokers should neither be excluded from the education that health warnings provide, nor spared the emotional distress the warnings may provoke. All tobacco and nicotine deliver products need to be labeled clearly and consistently. Failure to do so creates the false impression that products without health warnings are less risky to use than labeled products. In the case of premium cigars, this is certainly not true.

It is particularly important to include the warning about reproductive risk on all cigars. Cigars are a combustible tobacco product and while epidemiological studies have not yet proven that cigar smoking causes reproductive harm, the preponderance of the evidence suggests that it does. In 2001 the Federal Trade Commission mandated that cigar packaging and advertisements must display the Surgeon General's Warnings, including the reproductive warning (U.S. Federal Trade Commission 2001). As the FDA recognizes in the draft rule, a large cigar can contain as much nicotine as a pack of cigarettes (National Cancer Institute 1998) and also emits massive amounts of carbon monoxide, respirable particles, carcinogens and other oxidant chemicals (National Cancer Institute 1998, Klepeis, Ott et al. 1999). Although the proportional uptake of the total nicotine from cigars is lower than that from cigarettes, even exposure to secondhand cigarette smoke causes reproductive harm (U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention et al. 2006).

It is vitally important to include reproductive health warnings on all cigars because of the intersection of cigar use and reproductive risk. Conception is a focal event that can be disrupted by a single toxic assault. **Smoking a large, expensive, celebratory cigar presents a significant risk to conception and to the health of an unborn child.**

Smoking by men reduces the number of term pregnancies among couples conceiving by in-vitro fertilization (Fuentes, Munoz et al. 2010). Exposure to secondhand cigarette smoke in women is associated with the recovery of fewer oocytes during assisted reproductive procedures. According to the 2014 Surgeon General's report:

Basic characteristics of embryologic and fetal development include cell growth, differentiation, interaction, and migration. Teratogenic factors can disturb one or more of these processes, resulting in abnormalities in fetal structure or function, including growth retardation, malformations due to abnormal growth or morphogenesis, and altered CNS performance (Hacker, Gambone et al. 2010). In addition, there is a growing appreciation that teratogenic substances can have effects throughout the duration of pregnancy, and that those effects can be more subtle than gross anatomic anomalies (Yaffe and Aranda 2010). Thus, for women of reproductive age, a comprehensive exploration of the known and potential harms of the range of available tobacco products, all of which contain nicotine, is needed. (U.S. Department of Health and Human Services, Centers for Disease Control and Prevention et al. 2014)

Here is an overview of the reproductive health effects of cigar use as they relate to health effects caused by the use of tobacco products during pregnancy.

- a) According to the 2014 Surgeon General's report, "Tobacco use during and after pregnancy remains a major cause of reduced fertility as well as maternal, fetal, and infant morbidity and mortality" (U.S. Department of Health and Human Services, Centers for Disease Control and Prevention et al. 2014).
- b) It is critical that women of reproductive age be warned of health risks associated with use of tobacco products during pregnancy. Adverse reproductive health effects include (but are not limited to): increased risk of sudden infant death syndrome (SIDS) (U.S. Department of Health and Human Services 2004), orofacial clefts (Jia, Shi et al. 2011, Mirilas, Mentessidou et al. 2011, Zandi and Heidari 2011, Zhang, Jiao et al. 2011), anorectal atresia (Miller, Manning et al. 2009, Hackshaw, Rodeck et al. 2011), and ectopic pregnancy (Bouyer, Coste et al. 2003, Karaer, Avsar et al. 2006, Roelands, Jamison et al. 2009).

## **Infertility**

- a) There is sufficient evidence to infer a causal relationship between smoking and erectile dysfunction in men (U.S. Department of Health and Human Services, Centers for Disease Control and Prevention et al. 2014)
- b) Tobacco smoke has been shown to adversely affect sexual health and erectile function (Bornman and du Plessis 1986, Juenemann, Lue et al. 1987, Mannino, Klevens et al. 1994, Polsky, Aronson et al. 2005, Shiri, Hakkinen et al. 2006).
- c) Several lines of evidence support a causal relationship between smoking and erectile dysfunction (ED):
  - o Nicotine pharmacologically induces vasospasm of the penile arteries, thus altering the dynamics of the local blood flow required for erection (Adaikan

and Ratnam 1988, Harte and Meston 2008. Nicotine also has adverse effects on the physiology of arousal in women {Harte, 2008 #33}. Studies in animals point to damaging effects of smoking on tissue-dependent erection regulatory factors (Xie, Garban et al. 1997).

- d) A review of the literature provides mounting evidence that smoking constitutes a risk factor for erectile dysfunction, including:
- Case studies (Wabrek et al. 1983; Condra et al. 1986; Tengs and Osgood 2001)
  - Cross-sectional studies (Moreira et al. 2006; Lam et al. 2006b; He et al. 2007)
  - Prospective population-based studies (Kleinman et al. 2000; Bacon et al. 2003; Kupelian et al. 2010)

### **Stillbirth and perinatal mortality**

Studies support a role for nicotine in the effects of smoking on stillbirth and perinatal mortality. Animal models show that nicotine in the fetus causes cell damage, reduces cell number, and impairs synaptic activity (Slotkin, Orband-Miller et al. 1987, Slotkin 1998, Dwyer, Broide et al. 2008). Nicotinic acetylcholine receptors (nAChRs) are receptors that are ordinarily activated by endogenous acetylcholine, but that can also be stimulated by nicotine, resulting in disruption of normal cholinergic signaling (Albuquerque, Pereira et al. 2009).

- a) In the 2001 Surgeon General's report, it was noted that cigarette smoking was consistently associated with stillbirth (U.S. Department of Health and Human Services, Public Health Service et al. 2001), with an increased risk of 40% (Cnattingius, Haglund et al. 1988) to 60% (Raymond, Cnattingius et al. 1994).
- b) Nicotine exposure in animal models has also been shown to interfere with the fetus's critical protective response to hypoxia, which would lead to an increased risk of infant mortality (Slotkin 1998).

### **Low birth weight**

- a) Tobacco use during pregnancy leads to reduced birth weight (U.S. Department of Health and Human Services, Centers for Disease Control and Prevention et al. 2014). The 2004 Surgeon General's report found the evidence sufficient to infer causal relationships between smoking and fetal growth restriction and between smoking and decreased gestation/increased preterm delivery. Likewise, the 2006 Report on the Health Consequences of Involuntary Exposure to Tobacco Smoke found that secondhand smoke exposure causes sudden infant death syndrome and low birth weight (U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention et al. 2006).
- b) Maternal smoking is associated with a 27% increase in the risk of preterm delivery compared with nonsmokers (Shah and Bracken 2000). Similarly, Baba et al. 2012 found an increased risk of preterm birth associated with smoking during pregnancy (Baba, Noda et al. 2011).

- c) Studies of gene-environment interactions have shown that genes that encode enzymes associated with the metabolism of compounds found in tobacco smoke, including polycyclic hydrocarbons (PAHs) and nitrosamines, have been associated with restricted fetal growth in smokers (Wang, Zuckerman et al. 2002, Nukui, Day et al. 2004, Grazuleviciene, Danileviciute et al. 2009, Aagaard-Tillery, Spong et al. 2010).

### **Concluding remarks**

Despite the numerous health risks described above, over 400,000 live-born infants in the United States are exposed in utero to tobacco from maternal smoking annually (Hamilton, Martin et al. 2013, Tong, Dietz et al. 2013). We should not remove the fifth FTC warning from premium cigars, or exclude premium cigars from the FDA regulation (i.e., reject "Option 2) and risk increasing this number.

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