We Can’t Wait on the FDA

Phillip S. Gardiner, Dr. P. H.
Policy and Regulatory Sciences Program Officer, Tobacco Related Disease Research Program (TRDRP) University of California Office of the President and Co-chair African American Tobacco Control Leadership Council (AATCLC)

2015 National Association Attorney’s General Summer Meeting
San Diego, California
June 17, 2015
The Fight To Regulate Menthol

Still A Burning Issue
• advance notice of proposed rulemaking (ANPRM) to obtain information related to the potential regulation of menthol in cigarettes. FDA is also making available its preliminary scientific evaluation of public health issues related to the use of menthol in cigarettes.
The exception of menthol from the flavor ban:
  – undermines the States’ attempts to curb youth smoking.
  – disproportionately endangers young people, women, African-Americans and other minorities, and people of lower socioeconomic status.
Chicago Moves Center Stage

• Call by Mayor Emmanuel to curb access and use of menthol and all flavored tobacco products (Summer and Fall, 2013)
  – Letter to FDA
  – Series of Town Hall Meetings
  – Aggressive Media Campaign
  – Coordination between national and local tobacco control activists
  – City Council Debate
Burned!
500 Foot Buffer Zone

- Passed December 2013; schools and childcare centers; flavored e-juices
  - Months to identify all menthol products
  - Notice to all affected Stores; ~12%
  - Launched November 2014
  - Tobacco Industry Sued November 2014
    - TRO thrown out of court; case still pending
No Menthol Sunday!

- May 31\textsuperscript{st} World No Tobacco Day; No Menthol Sunday
- 100's of Churches around the Country
  - From the pulpit
  - From the Pews
- Adopt Local Ordinances; continue pressure on the FDA
All Eyes on Baltimore!

- Councilwoman Helen Holton introduced on June 1, 2015 Legislation to erect a 500 foot buffer zone around Baltimore Public Schools that would prohibit the sale of menthol and other flavored tobacco products.
  - 12 Co-signing Councilwomen/men
  - Health Committee Hearings set for Fall 2015
  - Refining Legislation; Community Mobilization
Minnesota Funds Intervention to Curb the Use of Menthol

• $200,000 in fiscal year 2016 is for at least one grant
  – to implement strategies and interventions to reduce the disproportionately high usage of cigarettes by African-Americans, especially the use of menthol-flavored cigarettes
  – Health Commissioner Award
  – Buffer Zone Possibilities

(The Omnibus Health and Human Services Appropriations Bill)
Minneapolis or St. Paul Next?

• Series of Community Forums
• Flavors ban postponed
• Meetings with local elected officials
• Juneteenth no menthol celebration
• Fathers Day; no Menthol Sunday again
Canada Takes The Lead

- **Nova Scotia**: First jurisdiction in the world* to implement a ban on menthol cigarettes, May 31, 2015

- **Ontario**: Flavors ban including menthol will go into effect January 1, 2017

- **Alberta**: To ban menthol tobacco sales starting October 1, 2015

- **Quebec**: Flavors and menthol ban legislation introduced May 5, 2015
FDA/CTP

• ?
What’s The FDA Waiting On?

E-Cigarettes: Nicotine Addiction The Next Generation
E-Cigarettes

• **Nicotine Addiction: The Next Generation**
  – Aerosolizes Nicotine Laced Propylene Glycol, Glycerin, and Flavorings
  – Long Term Health Impact Unknown
  – Cessation Aid or Promoter of Nicotine Addiction and Continued Tobacco Use
  – Explosion in Popularity especially among youth; Emergence of a New Vaping Subculture
  – No National Regulations
E-Cigarettes: A Moving Target

• 400+ makes and models
  – Closed systems; cig-a-likes
  – Open systems; tanks
  – Hookah Pens, Vape Pens

• 7700+ Flavorings
  – Menthol
  – All Banned FDA flavors

• Tax the Liquid; the Nicotine; the Device
E-Cig Tank Systems; Mods
Youth Using E-Cigarettes More than Regular Cigarettes

- **8th Grade:** 9% e-cigarette; 4% regular cigarettes
- **10th Grade:** 16% e-cigarette; 7% regular cigarettes
- **12th-Grade:** 17% e-cigarette; 14% regular cigarettes  
  (MTF, 2014)
### tobacco industry Taking Over the E-Cigarette Industry

#### Convenience Store Sales Volume

<table>
<thead>
<tr>
<th>Brand</th>
<th>E-Cigarette Brand</th>
<th>Sales Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds</td>
<td>Vuse</td>
<td>30.1%</td>
</tr>
<tr>
<td>Imperial</td>
<td>blu</td>
<td>21.6%</td>
</tr>
<tr>
<td>JTI</td>
<td>Logic</td>
<td>14.5%</td>
</tr>
<tr>
<td>Altria</td>
<td>Mark Ten</td>
<td>10.9%</td>
</tr>
<tr>
<td>NJOY*</td>
<td>NJOY</td>
<td>4.4%</td>
</tr>
</tbody>
</table>

* (Herzog, March, 2015) * Privately held
Vape Shops on the Rise

• The "Starbucks of e-vapor"
  – It is estimated that there are somewhere between 5,000-10,000 vape shops in the U.S.
  – Tank systems; Refills; Mix-your-Own
  – Vapers can hang out, work, socialize and vape
  – Purchase products; sample new ones
  – Eating and Drinking
    – (Herzog, 2014)
E-Cigarette Liquid: The “Juice”
E-Cigarette Liquid: The “Juice”

• E-Cigarette Liquid contains:
  – **Nicotine**, extracted from tobacco leaves
    • Large variation in content between and within brands
      (Cheah et al 2012; Trtchounian et al 2011; Goniewicz et al 2013)
    • Lethal if ingested; 60 mg Adult; 6 mg Children
    • Detrimental to fetuses (Martz, 2009)
    • Tobacco specific nitrosamines (TSNAs) (Laugesen, 2008; Westenberger, 2009; Goniewicz et al 2013)
    • 1.2mg of nicotine in each cigarette, or 24mg of nicotine per pack (1.2mg x 20 cigarettes) = ~ 1 e-cigarette
Nicotine Is Not Benign

• Nicotine can be acutely toxic; Poisonous and addictive

• Nicotine activates multiple biological pathways through which smoking and aerosolizing increases risk for disease.

• Nicotine exposure during fetal development has a lasting adverse consequences on brain development and contributes to multiple problematic birth outcomes including low birth weight and still birth.

  – RSG, 2014
E-Cigarette Liquid: The “Juice”

• E-Cigarette Liquid contains:
  – **Propylene Glycol** - the vapor; the fog
    • FDA approved food additive (humectant, solvent for colors and flavors), cosmetics, and medicines.
    • Short term exposure causes eye, throat, and airway irritation (Wieslander et al 2001; Vardavas et al 2012,)
    • Long term exposure can result in children developing asthma. (Choi et al 2010)
    • Chemical composition changes when heated (Henderson et al, 1981)
E-Cigarette Liquid: The “Juice”

- E-Cigarette Liquid contains:
  - **Glycerin**: A humectant used instead of or in combination with propylene glycol in EC fluids for aerosol production.
  - FDA Approved for ingestion.
  - Slightly hazardous in case of skin and eye contact, ingestion, and inhalation; prolonged exposure may cause organ damage.
- **Metals**
  - Tin particles found in E-liquid (Williams et al., 2013)
E-Cigarette Liquid: The “Juice”

- E-Cigarette Liquid contains:
  - **Flavorants. Key one Menthol; Candy flavoring**
    - Anesthetic effects, promotes deeper inhalation, greater cell permeability
    - Allows the poison to go down easier!
  - Not GRAS! Ingestion vs. Inhalation
  - 7000+ flavors; appeals to kids (bubblegum, strawberry, gummy bears, etc.)
  - Exotic for adults (Sex on the Beach, Aces and 8’s)

- Mix your Own (ala roll your own)
The Aerosol: It’s Not Just Water Vapor

- E-Cigarette Aerosol Contains:
  - Propylene glycol, glycerol, flavorings, and nicotine, which are found in the e-liquid, are also found in the e-vapor
  - Propylene oxide
  - Volatile Organic Compounds: Benzene and Toluene
The Aerosol: It's Not Just Water Vapor

- **E-Cigarette Aerosol Contains:**
  - **Carbonyl Compounds:** Formaldehyde, acetaldehyde, and acrolein
  - **Metals:** tin, silver, iron, nickel, aluminum, sodium, chromium, copper, magnesium, manganese, lead, potassium and silicate nanoparticles
  - **Tobacco specific nitrosamines (TSNAs)**: carcinogenic compounds found in tobacco and tobacco smoke.

Flavorings GRAS? Not For Inhalation

• GRAS certification by the Flavor Extracts Manufacturers Association (FEMA) pertains only to ingestion, not inhalation.
  – “E-cigarette manufacturers should not represent or suggest that the flavor ingredients used in their products are safe because they have FEMA GRAS™ status for use in food because such statements are false and misleading.”
Flavorings GRAS? Not For Inhalation

- Aldehydes toxicologically are primary irritants of the mucosa of the respiratory tract

- The lungs have a different spectrum of toxicity than the intestinal tract, substances known to be safe when swallowed can still be dangerous when inhaled

  – (Williams, James and Robert, 2015)
“Popcorn lung" comes from inhaling diacetyl, a chemical widely used in the flavor industry to simulate dairy (e.g. butter, cheese, yogurt), fruit flavors (e.g. strawberry, bananas), and so-called brown flavors (e.g. coffee, butterscotch)

In flavoring-induced lung disease, the tiny bronchial passages located near the air exchanging alveoli become gradually scarred shut. One can become progressively shorter of breath due to poor oxygen absorption

Diacetyl has been found in many e-cigarette vapors, especially sweet flavors.

(Tierney et al., 2015; Farsalinos, 2014)
**E-Cigarette Emit Metals used in Their Manufacturing**

- Zinc and Nickel concentrations were found to be higher in e-cigarette emissions compared to conventional Cigarette emissions, originating from the cartridges holding the e-liquids.

- “Considering the potential adverse health effects associated with the inhalation of these metals (particularly Ni and Zn, and the emission observed both in our analysis as well as the study by Williams et al. 13), attention should be directed toward eliminating the use of these metals in the cartridges during the manufacturing process of e-cigarettes.”
  
  – (Saffari et al., 2014)
E-Cigarettes: The Second Generation

• **1st Generation:**
  – Cig-a-likes; Most Toxins Emitted in the Aerosol Lower than Regular Cigarettes (Goniewicz et al., 2013)
  – Aerosolizing Temperature 40 – 65c

• **2nd Generation**
  – Tank Systems; refillables
  – Some Toxins Emitted Approaching Levels found in Regular Cigarettes
  – Aerosolizing Temperatures >65c
As Battery Voltage Increase, Toxins Increase

- On Average, Toxins were 13 – 807 Fold Lower than Tobacco Cigarettes
- **However, when voltage was increased from 3.2 to 4.8V:**
  - 4 to over 200 times increase in formaldehyde, acetaldehyde, and acetone levels
  - The levels of formaldehyde were in the range of levels reported in tobacco smoke

(Kosmider et al., 2014)
# E-Cig Aerosol Composition

- Propylene glycol
- Glycerin
- Flavorings (many)
- Nicotine
- NNN
- NNK
- NAB
- NAT
- Ethylbenzene
- Benzene
- P,m,xylene
- Toluene
- Acetaldehyde
- Formaldehyde
- Naphthalene
- Styrene
- Benzo(b)fluoranthene

- Chlorobenzene
- Crotonaldehyde
- Propionaldehyde
- Benzaldehyde
- Valeric acid
- Hexanal
- Fluorine
- Anthracene
- Pyrene
- Acenaphthylene
- Acenaphthene
- Fluoranthene
- Benz(a)anthracene
- Chrysene
- Retene
- Benzo(a)pyrene
- Indeno(1,2,3-cd)pyrene

- Benzo(ghi)perylene
- Acetone
- Acrolein
- Silver
- Nickel
- Tin
- Sodium
- Strontium
- Barium
- Aluminum
- Chromium
- Boron
- Copper
- Selenium
- Arsenic

- Cadmium
- Silicon
- Lithium
- Lead
- Magnesium
- Manganese
- Potassium
- Titanium
- Zinc
- Zirconium
- Calcium
- Iron
- Sulfur
- Vanadium
- Cobalt
- Rhubidium

Compounds in **yellow** are from FDA 2012, Harmful and Potentially Harmful Substances – Established List
Secondhand Vaping and Nicotine

• The levels of airborne nicotine and cotinine concentrations in the homes with e-cigarette users were significantly higher than control homes. “Our results show that non-smokers passively exposed to e-cigarettes absorb nicotine.”  
  – (Fernandez et al., 2014)
E-Cigarettes Source of Thirdhand Smoke Exposure

• Conclusions: This study indicates that there is a risk of thirdhand exposure to nicotine from e-cigarettes. Thirdhand exposure levels differ depending on the surface and e-cigarette brand.

• Future research should explore the potential risks of thirdhand exposure to carcinogens formed from nicotine released from e-cigarettes (Goniewicz and Lee, 2014)
Health Effects of E-Cigarettes

• Long Term Health Effects are unknown

• Short-term Health Effects include:
  – Decreased Fractional exhaled Nitric Oxide (FeNO) [a measure of lung function retardation]
  – Increased respiratory resistance; constricts peripheral airways
  – Decreases in the eye’s tear film stability
  – Acute nicotine poisoning
    – (Vardavas, 2012; Norback and Lindfren, 2001)
Health Effects of E-Cigarette

• Adversely effects epithelial functions of young people.
• Even nicotine-free e-liquid promotes pro-inflammatory response and HRV infection.
• Both e-liquid without nicotine and with nicotine inhibits lung innate immunity (e.g., SPLUNC1) that is involved in lung defense against HRV infection.
• “These findings strongly suggest the deleterious health effects of e-cigarettes in the airways of young people.” (Wu, et al., 2014)
Poison center calls involving e-cigarettes

215 Calls per Month

1 Call per Month

September 2010 to February 2014
European Union E-Cigarettes Regulation

Starting in 2016

• Advertising Banned
• Graphic Health Warning Labels
• Child-Proof
• Nicotine Limited to 20mgs
• Outlawing Menthol Cigarettes (4-year delay)
• Indoor and Outdoor use NOT Regulated
The Road to FDA Regulation (or lack thereof)

- No FDA Regulation
  - Blocked imports in 2008
  - Launch toxicological studies 2009
  - Seized NJOY/Sottera shipments 2009
  - Sottera sued the FDA, claiming the e-cigarettes should be regulated like cigarettes, not a medicine
  - 2010, both the lower and appelate court agreed with Sottera
  - 2014, FDA posted limited deeming regulations
NAAG Letter to FDA, September 2013

• Immediate regulatory oversight of e-cigarettes
• Immediate bio-chemical effects on the brain and body at any dosage, and is toxic in high doses.
• The Tobacco Control Act imposed restrictions on advertising and marketing to youth. These restrictions should be applied to e-cigarettes
• Register with FDA and report product and ingredient listings
• Only market new tobacco products after FDA review
• Only make claims of reduced risk if FDA confirms that scientific evidence supports the claim and that marketing the product will benefit public health as a whole
• Not distribute free samples
FDA Deeming Regulations

- Minimum age and identification restrictions to prevent sales to underage youth
- Requirements to include health warnings
- Prohibition of vending machine sales, unless in a facility that never admits youth
FDA Deeming Regulations: A Cautionary Tale

• TV, Radio and Social Media Advertising Remain
• 7000 + Candy Flavorings, including Menthol Remain
• Internet and Mail Order Sales Continue with No Age Restrictions
• WSJ, Wells Fargo, the tobacco industry and E-Cigarette Manufacturers Like the Regulations (or lack thereof)
FDA Deeming Regulations: A Cautionary Tale

- No Child-Proofing Requirements
- No Warning Labels
- A Minimum of 2 years to Enact, by then the E-Cigarette horse will be even further out of the Barn, Down the Road and Coming to a Clinic, Office and or Home Near You.
California Laws on E-Cig Laws

• 60 California Cities Regulate E-cigarettes

• UC Prohibits the use of E-Cigarettes

• California State HEALTH AND SAFETY CODE
  SECTION 119405 Prohibits the Sale to Minors
  http://www.leginfo.ca.gov/cgi-bin/displaycode?section=hsc&group=119001-120000&file=119405
The Aerosol This Time? Precaution Advised

• E-Cigarette Vapor
  – Concentrations of pollutants and carcinogens less than in cigarettes; still many toxic substances
  – Great variation within and between products; no product standards
  – Renormalization; youth uptake on the rise
  – Intermediate and long term health effects unknown
  – *Maybe* safer, but this doesn’t mean safe
Thank You!

TRDRP
Research for a Healthier California

www.trdrp.org
phillip.gardiner@ucop.edu

AATCLC
Saving Black Lives