E-cigarettes and Tobacco: What Do You Need to Know to Help Your Pharmacy Customers

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CPE Information and Disclosures

Jeannie Limpert and Tim Chen declare no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

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CPE Information

- Target Audience: Pharmacists & Technicians
- ACPE #: 0202-0000-15-201-LO4-P/T
- Activity Type: Knowledge-based

Pharmacist Learning Objectives

1. Identify the components of electronic cigarettes and how they work.
2. Explore concerns with product manufacturing, variability, and use.
3. Describe the federal government’s efforts to regulate and research electronic cigarettes.
4. Discuss both behavioral and intensive interventions.
5. State FDA-approved pharmacotherapy.
6. Describe the role of a pharmacist in tobacco cessation management.

Pharmacy Technician Learning Objectives

1. Identify the components of electronic cigarettes and how they work.
2. Explore concerns with product manufacturing, variability, and use.
3. Describe the federal government’s efforts to regulate and research electronic cigarettes.
4. State FDA-approved pharmacotherapy.
5. Describe the role of a technician in tobacco cessation management.

E-Cigarettes: A General Overview for Pharmacists and Technicians

Jeannie Limpert, MD
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FDA/CTP

Disclaimer: This information is not a formal dissemination of information by the FDA and does not represent the Agency’s position or policy.
OBJECTIVES

1. Identify the components of electronic cigarettes and how they work. (P/T)
2. Explore concerns with product manufacturing, variability, and use. (P/T)
3. Describe the federal government's efforts to regulate and research electronic cigarettes. (P/T)

GOAL

1. Identify the components of e-cigarettes and describe how they work
2. Discuss the potential health benefits and risks associated with e-cigarette use
3. Describe FDA's current regulatory authorities over e-cigarettes
4. Describe FDA/CTP's research initiatives

SELF ASSESSMENT QUESTION # 1

What are the three most basic components of an e-cigarette?

a. Battery, atomizer (heater), e-liquid
b. Battery, nicotine, propylene glycol
c. Atomizer (heater), nicotine, flavors
d. Battery, atomizer (heater), coils

SELF ASSESSMENT QUESTION # 2

Which of the following is true about e-liquids (choose all that apply)?

a. E-liquids usually contain nicotine, propylene glycol and/or glycerin, and flavorings.
b. Flavorants in e-liquids that are GRAS are safe for inhalation, and should not pose any toxicity risks.
c. E-liquids are available with a large range of nicotine concentrations and a large variety of flavorings.
d. The nicotine delivered to the users is not only impacted by the nicotine concentration in the e-liquid, but also by other factors such as the e-cigarette device and the way the e-cigarette is used.

SELF ASSESSMENT QUESTION # 3

A patient states that he heard that e-cigarettes are safer than combusted cigarettes and is interested in your opinion. Which of the following statements are true (choose all that apply)?

a. No tobacco product is safe, but some studies suggest that the chemical constituents in e-cigarette aerosols are less toxic than cigarette smoke.
b. E-cigarettes just produce water vapor.
c. Data on e-cigarettes is limited, but FDA CTP is funding research to learn more about the risks and benefits of e-cigarettes to inform future regulation.
d. Some e-cigarettes are approved by the FDA as being safe and effective as smoking cessation aids.

SELF ASSESSMENT QUESTION # 4

Possible means of reducing the risk of accidental poisoning from nicotine in young children may include:

a. Child-resistant e-liquid containers
b. Storage of e-liquids out of reach of children
c. Labeling warnings of toxicity risks on e-liquid bottles
d. All of the above
WHAT ARE E-CIGARETTES AND ELECTRONIC NICOTINE DELIVERY SYSTEMS?

ELECTRONIC NICOTINE DELIVERY SYSTEMS (ENDS)

- Generally: battery operated products designed to heat a liquid into aerosol that is inhaled by the user.
- The e-liquid contains humectants (propylene glycol and/or glycerin), flavorings, and usually nicotine.
- Diverse products

E-CIGARETTES

- Available in China ~2003
- Introduced into the US in ~2007
- Widely available for purchase in the US
  - internet, “vape shops,” retail stores
- US sales rapidly increasing

E-CIGARETTE PRODUCTS

- > 450 brands
- > 7500 unique flavors

TERMINOLOGY VARIED AND CONSTANTLY CHANGING

E-CIGARETTE ANATOMY BASICS

- Power source (battery)
- Heating element (atomizer)
- E-liquid

"Vape Pen"
"E-Hookah"
"Mod"
"Tank system"
"Personal Vaporizer"
**E-LIQUIDS**

Usually contain:
- Humectants: propylene glycol and/or glycerin
- Nicotine
- Flavorings

**MARKETING**

- No federal restrictions in the US for e-cigarettes that are marketed as tobacco products*
- TV, magazines, social media, sporting events
- Celebrity endorsement
- Coupons and samples

*If e-cigarettes make therapeutic claims (e.g., cessation claims), they are subject to marketing restrictions for drugs

**“JUST WATER VAPOR”**

**EVER E-CIGARETTE USE: US ADULTS**

![Graph showing the percentage of various groups over years](chart)

Source: King et al. Nicotine Tob Res; 2015.

**CURRENT E-CIGARETTE USE: HIGH SCHOOL STUDENTS**

![Bar chart showing current e-cigarette use among high school students](chart)

Source: Arrazola et al. MMWR; 2015.

**HEALTH EFFECTS**


**ENDS HEALTH RISKS**

Health risks likely dependent on:
- Aerosol constituents
  - Device design
  - E-liquid constituents
  - Puff topography
- Sites of exposure/deposition/absorption
- Frequency and duration of use
- Individual health
  - Smoking status
  - Comorbid conditions
  - Pregnancy

**AEROSOL CONSTITUENTS**

Constituents identified, include:
- Carbonyl compounds
  - acetaldehyde, acrolein, formaldehyde, o-methylbenzaldehyde
- Fine and Ultrafine Particles
- Flavorings
- Metals
  - cadmium, lead, nickel
- Nicotine
- Polycyclic aromatic hydrocarbons
- Tobacco-specific nitrosamines
  - NNN, NNK
- Volatile organic compounds
  - p,m-xylene, toluene

**TOXICANTS: CONVENTIONAL CIGARETTE SMOKE VS. E-CIGARETTE AEROSOL**

Smoking machine data from 12 e-cigarettes

<table>
<thead>
<tr>
<th>Toxic compound</th>
<th>Conventional cigarette (μg in mainstream smoke)</th>
<th>Electronic cigarette (μg per 15 puffs)</th>
<th>Average ratio (conventional vs electronic cigarette)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formaldehyde</td>
<td>1.6-52</td>
<td>0.20-5.68</td>
<td>9</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>52-140</td>
<td>0.11-3.36</td>
<td>450</td>
</tr>
<tr>
<td>Acrolein</td>
<td>2.4-62</td>
<td>0.07-4.19</td>
<td>15</td>
</tr>
<tr>
<td>Toluene</td>
<td>8.3-70</td>
<td>0.02-0.63</td>
<td>120</td>
</tr>
<tr>
<td>NNK</td>
<td>0.005-0.19</td>
<td>0.00088-0.003043</td>
<td>380</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNK</td>
<td>0.002-0.11</td>
<td>0.00015-0.00283</td>
<td>40</td>
</tr>
</tbody>
</table>

NNK, N'-methyl-NNN, N'-methyl-NNK, NNN, N'-nitrosonornicotine.

- 9-450 fold reduction in some toxic compounds relative to conventional cigarettes

**NICOTINE DELIVERY**

Time course of plasma nicotine concentration as a function of electronic cigarette (ECD) nicotine concentration.

**SYSTEMATIC REVIEW ON HEALTH EFFECTS OF E-CIGARETTES**

- 76 studies included
  - Most common adverse events: light-headedness, throat irritation, dizziness, cough
  - Pulmonary and cardiovascular effects: variable
  - Authors’ conclusion:
    "Due to the many methodological problems, the relatively few and often small studies, the inconsistencies and contradictions in results and the lack of long-term follow-up, no firm conclusions can be drawn on the safety of ECs [e-cigarettes]."

USER EXPOSURE

<table>
<thead>
<tr>
<th>Toxicant of Interest</th>
<th>Urine E-Cigarette Users (n=28)</th>
<th>Urine Cigarette Smokers</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAH</td>
<td>1.58</td>
<td>0.97</td>
<td>0.0001</td>
</tr>
<tr>
<td>NNK</td>
<td>Total NNK</td>
<td>0.02</td>
<td>1.21</td>
</tr>
<tr>
<td>NNK</td>
<td>Total NNK</td>
<td>0.005</td>
<td>0.073</td>
</tr>
<tr>
<td>acrolein</td>
<td>1.36</td>
<td>4.30</td>
<td>0.00002</td>
</tr>
<tr>
<td>crotonaldehyde</td>
<td>0.05</td>
<td>0.005</td>
<td>0.001</td>
</tr>
<tr>
<td>propylene oxide</td>
<td>2.16</td>
<td>141</td>
<td>0.006</td>
</tr>
<tr>
<td>benzene</td>
<td>0.39</td>
<td>2.85</td>
<td>0.0001</td>
</tr>
<tr>
<td>nicotine</td>
<td>cotinine</td>
<td>1890</td>
<td>1930-2950</td>
</tr>
</tbody>
</table>

*Geometric means, g/ml urine

Source: adapted from Hecht et al. Nicotine & Tobacco Research, 2015.

FLAVORANTS AND ADDITIVES

- Toxicity of flavorings and additives of concern
  - “GRAS” Generally Recognized as Safe = ingestion e-inhalation
  - E-liquid cytotoxicity correlated with the number and concentration of chemicals used to flavor e-liquids
- Specific Flavorants
  - Cinnamon:
    - Two cinnamon flavorants in e-liquids: highly cytotoxic
  - Butter:
    - Diacetyl (DA; 2,3-butanedione) & Acetyl Propionyl (AP; 2,3-pentanedione)
    - GRAS but known adverse respiratory effects: bronchiolitis obliterans, decreased respiratory function

HEALTH EFFECTS OF NICOTINE

- Cardiovascular effects (increased HR and BP)
- Alters thrombosis risk
- Adverse pregnancy outcomes
- Adverse impact on developing brain

ADVERSE EXPERIENCES IN NONUSERS

Nonuser exposures:
- Secondary exposures to aerosols may have adverse health effects
- Tertiary exposures may also be of concern

ENDS users
ENDS nonusers

ACCIDENTAL EXPOSURES: ACUTE NICOTINE TOXICITY

- Accidental exposure through ingestion and dermal absorption can lead to toxicity
- Concern about accidental exposures and poisonings, especially in young children
  - Marked increase in calls to US poison centers
  - Two accidental deaths in toddlers related to e-liquid ingestion
- Potential strategies to prevent poisonings include:
  - Child-resistant e-liquid containers
  - Storage of e-liquids out of the reach of children
  - Clear labeling
  - Safe handling of e-liquid

FDA/CTP SAFETY REPORTING PORTAL

www.safetyreporting.hhs.gov
FDA REGULATORY AUTHORITY

THE FAMILY SMOKING PREVENTION AND TOBACCO CONTROL ACT

- Gives FDA authority to regulate the manufacture, distribution, and marketing of tobacco products to promote and protect public health
- Immediate jurisdiction over cigarettes, cigarette tobacco, roll-your-own, and smokeless
- The ability to assert jurisdiction over other tobacco products (including e-cigarettes)

Signed June 22, 2009

ENDS LARGELY UNREGULATED

State and Locality Regulations Include:
- Prohibition of sales to minors
- Prohibition of use in some public places
- Child resistant packaging for e-liquids

PROPOSED RULE: DEEMING

In April 2014 FDA proposed a new rule that would extend CTP's authority to cover additional tobacco products, including:
- e-cigarettes
- cigars
- pipe tobacco
- nicotine gels
- waterpipe
- tobacco dissolvables not already under the FDA's authority

PROVISIONS IN PROPOSED DEEMING RULE

Requirements for:
- ingredient listing
- product listing
- reporting of harmful and potentially harmful constituents (HPHCs)
Prohibition of:
- misleading descriptors and unproven modified risk claims
- adulteration and misbranding
- free samples
- sale to individuals under the age of 18 years
The Tobacco Control Act gives the FDA authority and resources to conduct research to inform regulation.

Tobacco Regulatory Science Program (TRSP):
- Interagency partnership with NIH
- Coordinates CTP research funding across NIH

E-cigarette Regulatory Science Program (ERSP):
- Interagency partnership with NIH
- Coordinates CTP research funding across NIH

E-CIGARETTE RESEARCH PROJECTS
- CTP is currently funding >70 projects related to e-cigarettes, including:
  - PATH Study
    - Longitudinal study of 46,000 adults and youth
  - Tobacco Centers for Regulatory Science (TCORS)
    - 11/14 centers identified e-cigarettes as a project of interest
  - Partnerships with CDC and NIH to expand existing surveys to track e-cigarette issues
  - Funding Opportunity Announcements
  - Supplements to existing grants or cooperative agreements

CONCLUSIONS
- E-cigarettes are a diverse group of products
- Health effects data are limited
  - E-cigarettes may be a less harmful source of nicotine
  - Short and long-term benefits and risks for users and nonusers not fully characterized
  - Public health impact unknown
- FDA/CTP currently does not regulate e-cigarettes
  - In April 2014, FDA/CTP issued a proposed rule to assert jurisdiction over these products but it is not yet finalized
- CTP is actively engaged in research to gather science to inform future regulatory actions related to these products

ANSWER TO SELF ASSESSMENT QUESTION # 1
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**ACKNOWLEDGEMENTS**

- Beth Durmowicz, MD

**THANK YOU**