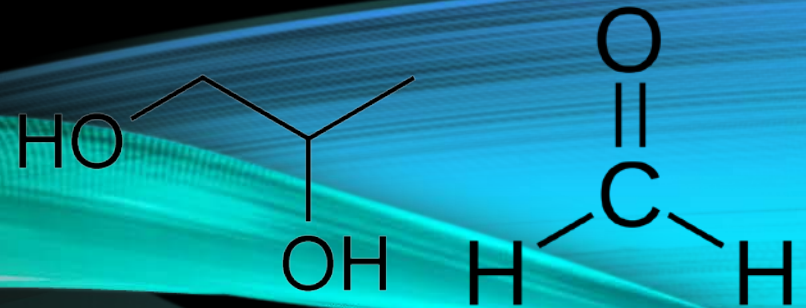


E-CIGARETTES TOXICITY THE RISK TO CHILDREN

Susan Smolinske, PharmD, DABAT, FAACT



DISCLOSURE

- This material was supported by the American College of Medical Toxicology (ACMT) and funded (in part) by the cooperative agreement FAIN: U61TS000238 from the Agency for Toxic Substances and Disease Registry(ATSDR).
- Acknowledgement: The U.S. Environmental Protection Agency (EPA) supports the PEHSU by providing partial funding to ATSDR under Inter-Agency Agreement number DW-75-92301301. Neither EPA nor ATSDR endorse the purchase of any commercial products or services mentioned in PEHSU publications

OBJECTIVES

- Evaluate the potential risk of exposure to vapor constituents on short and long term health of children who are exposed to electronic cigarettes
- Understand the risks of trauma or injury to children from accidental exposure to batteries or devices related to electronic cigarettes
- Discuss potential for child-resistant packaging to affect pediatric access to liquids

TYPES OF ELECTRONIC CIGARETTE DEVICES

- disposable/non-refillable e-cigarettes
- refillable e-cigarettes (tanks)
- refillable e-pens
- e-hookah pens (no nicotine)
- e-cigars

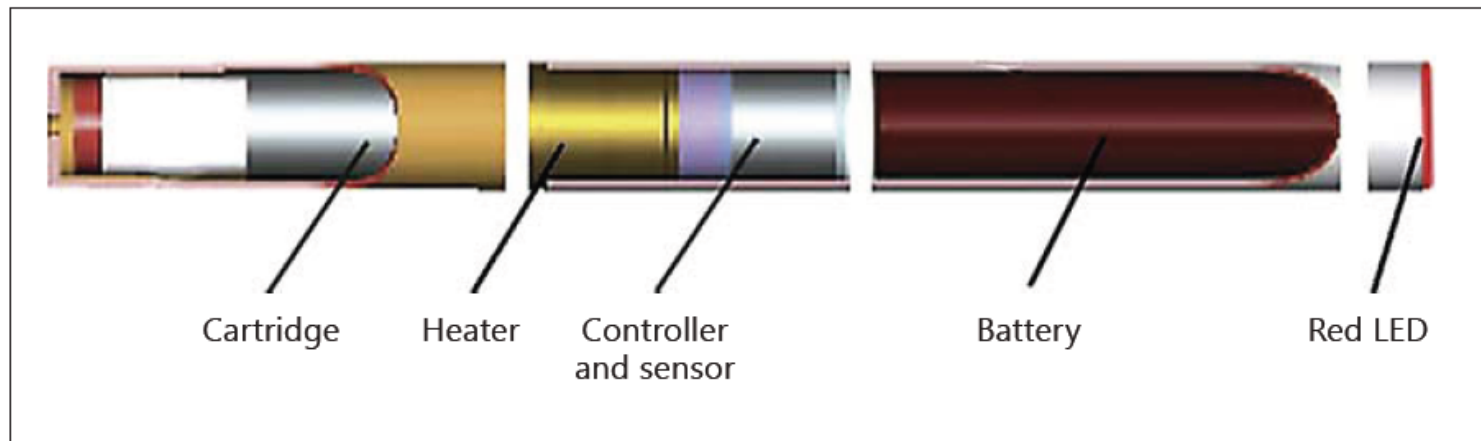


Electronic Cigarettes: A Short Review

J.F. Bertholon^{a, b, e} M.H. Becquemin^{a, c} I. Annesi-Maesano^{d, e} B. Dautzenberg^b

^aLaboratoire de Granulométrie et de Dépôt des Aérosols, Assistance Publique Hôpitaux de Paris,

^bUniversité Pierre et Marie Curie, Paris 6, ^cUniversité Denis Diderot et UPRES 2397, ^dInstitut National de la Santé et de la Recherche Médicale, Unité 707, and ^eDepartment of Epidemiology of Allergic and Respiratory Diseases,



Color version available online

CONSTITUENTS OF E-CIGARETTE LIQUIDS

- Nicotine
- Propylene glycol
- Ethylene glycol
- Diethylene glycol
- Polyethylene glycol
- Glycerin (prolongs duration of aerosol)
- Flavorings (thujone, vanillin, diacetyl)
- Carcinogens also found in tobacco (nitrosamines, PAH, formaldehyde)
- Adulterants (tadalafil, caffeine, vitamins)
- Metals (copper, cadmium, tin, silver, iron, silicate, aluminum)

PEDIATRIC CONCERNS

- Nicotine poisoning
- Propylene glycol inhalation (compare to theatrical smoke)
- Formaldehyde generation from propylene glycol
- Toxic constituents in tobacco-derived e-cigarette liquids
- Presence of known inhalation toxins from flavorings (diacetyl, acetylpropionyl)
- Use of the “dripping” technique
- Adulterants present in e-cigarette liquids
- Fire/explosion hazard from lithium batteries

NICOTINE POISONING DOSE-RESPONSE

- **Adult lethal dose 0.5-1g** (Mayer B. How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. Arch Toxicol. 2014 Jan;88(1):5-7.)
- **Pediatric lethal dose 6-13 mg/kg**
- **Significant toxicity 3 mg/kg**

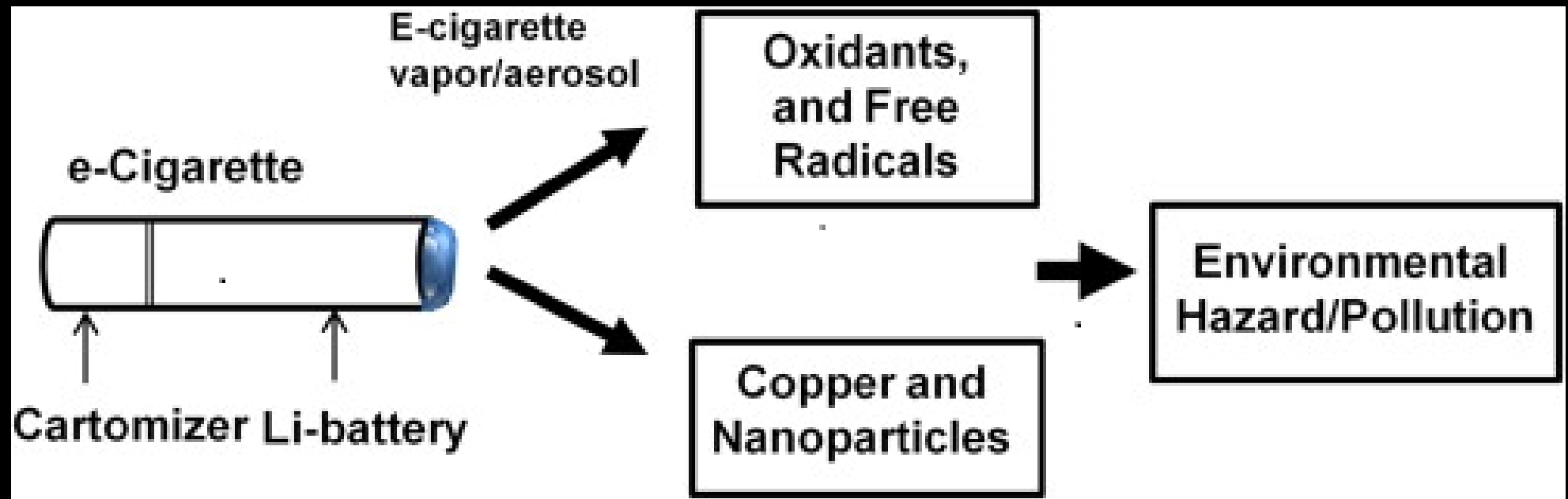
- **E-cig liquids contain 0, 3, 6, 12, 18, 24, 30, 48, 100 mg/mL**
 - In a 10 kg child 30 mg is the significantly toxic dose
 - This is equivalent to 10 mL of the lowest strength, 0.3 mL of the highest (6 drops)
- **There is one pediatric death reported (unk strength, unk amount)**

Aerosol particles
persist up to 4 hours

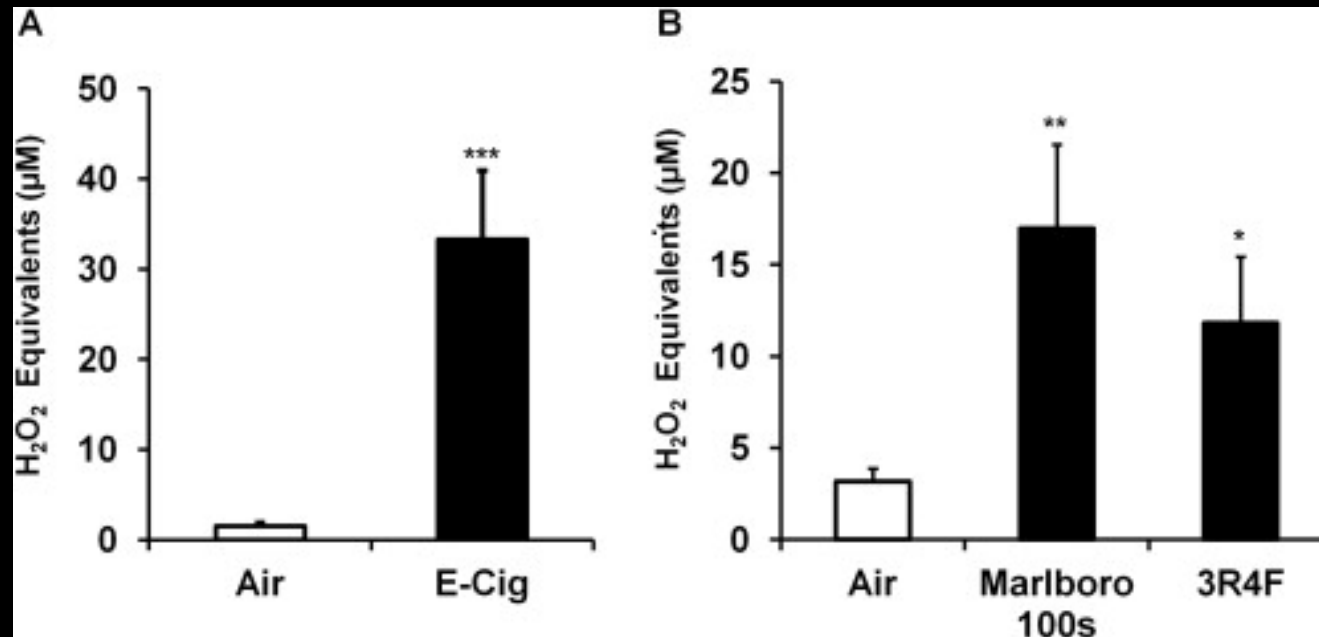
Deposition on
surfaces can cause
third-hand exposure



LERNER CA ET AL. ENVIRONMENTAL HEALTH HAZARDS OF E-CIGARETTES AND THEIR COMPONENTS: OXIDANTS AND COPPER IN E-CIGARETTE AEROSOLS. ENVIRONMENTAL POLLUTION 2015;198:100-7

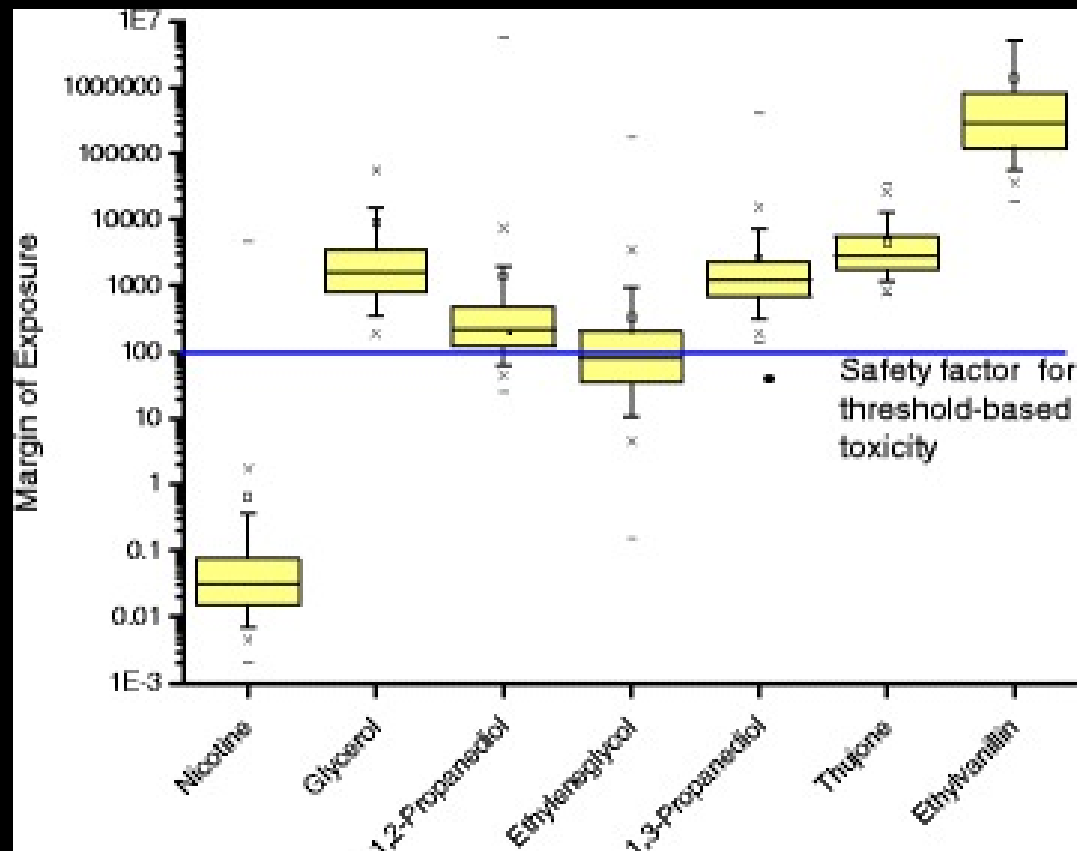


ROS DETECTED IN E-CIGARETTE AEROSOLS



COPPER LEVELS 6X THAT OF CONVENTIONAL CIGARETTE

MOST CONSTITUENTS ARE ABOVE SAFETY THRESHOLDS

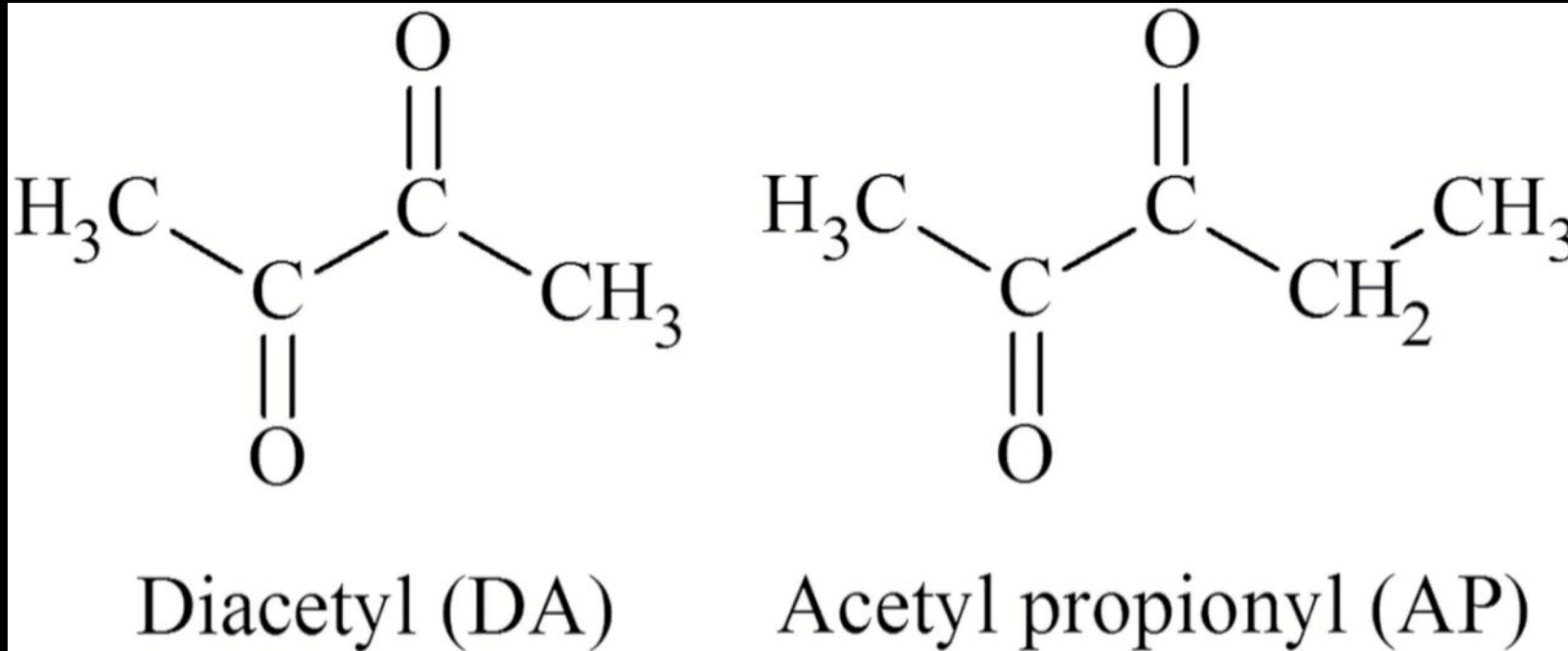


Hahn J et al. Electronic cigarettes: overview of chemical composition and exposure estimation. *Tob Induc Dis.* 2014 Dec 9;12(1):23.

TOXIC CONSTITUENTS IN TOBACCO-DERIVED E-CIGARETTE LIQUIDS

- Nitrates (100%)
 - Nitrosamines (lower 1-2 orders of magnitude compared to tobacco)
 - Nitrosamines can form from third-hand exposure on gas appliances
 - Phenols (catechol, cresol) (higher in TDE compared to other ecig)
-
- Farsalinos KE et al. Nicotine levels and presence of selected tobacco-derived toxins in tobacco flavoured electronic cigarette refill liquids. *Int J Environ Res Public Health*. 2015 Mar 24;12(4):3439-52

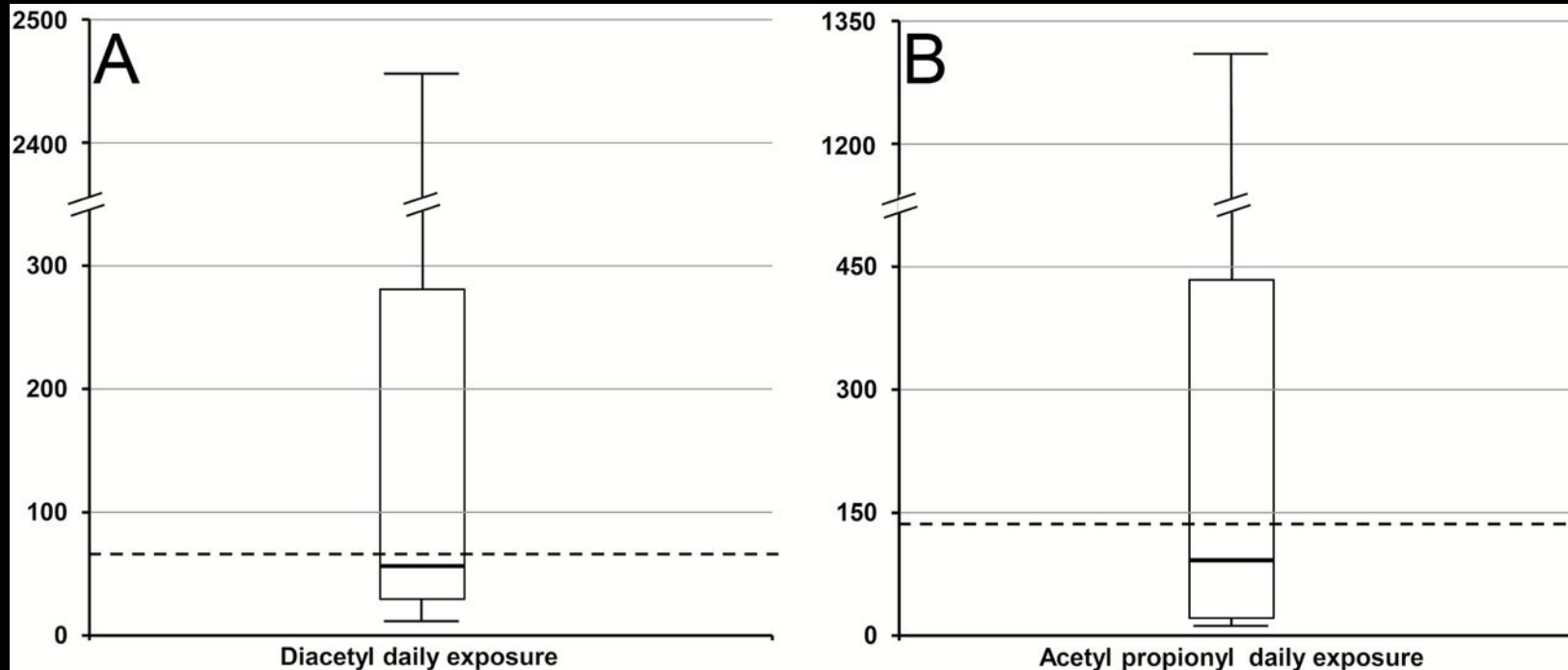
Chemical structures of diacetyl (DA) and acetyl propionyl (AP)



RISKS OF EXPOSURES TO DIACETYL AND ACETYL PROPIONYL

- Found in heated microwave popcorn
- Inhalation results in decline in FEV₁
- bronchiolitis obliterans (rare)
- Workers had 2.6 times the expected rate of respiratory symptoms(chronic cough, shortness of breath and 3.3 times the expected rate of airway obstruction
- This is an avoidable risk for e-cigarettes

Analysis of liquid e-cigarette sweet flavored products



Median levels were slightly lower than NIOSH safety levels. A substantial proportion of the positive samples would expose consumers to levels higher than the NIOSH limits.

PROPYLENE GLYCOL

- Metabolized to pyruvic and **lactic acid**, acetic acid and propionic aldehyde
- Oxidation at high temps can do the same
- Can cause intoxication (1/3 potent as ethanol)
- One of the constituents involved in theatre mist toxicity

THEATRE MIST COMPARISON

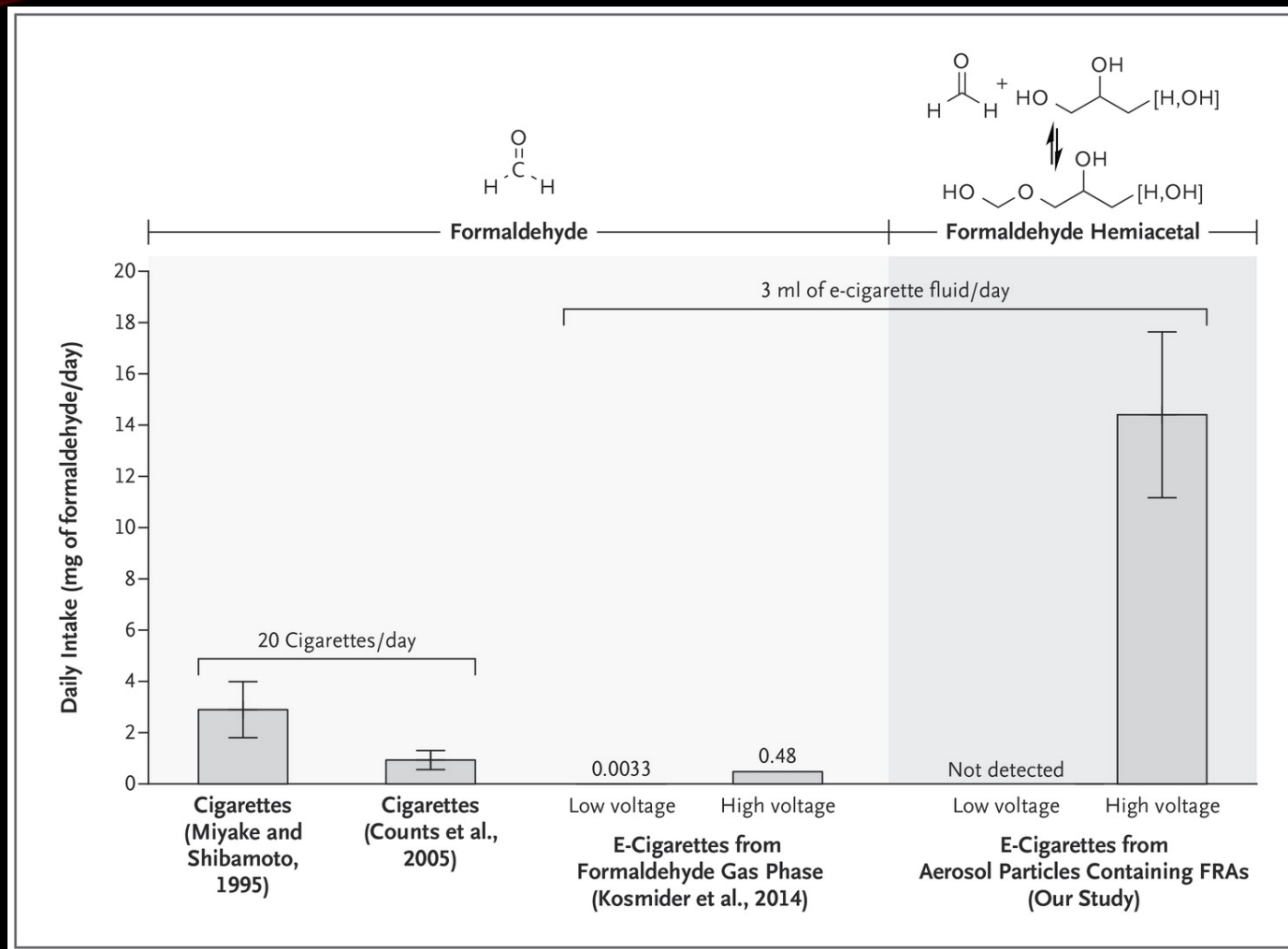
- Aerosol persists 3-4 hours
- Mild respiratory irritation
 - Cough
 - Throat irritation
- Risk for asthmatics unclear
- 3-4 X risk for respiratory, eye, skin
- Those within 10 ft of fog had 5% less FEV1 and FVC than those further away
- Glycol smoke associated with systemic effects
 - Headache
 - Dizziness
 - drowsiness



- Rossol. Occup Med 2001;16:595
- Teschke. Am J Indust Med 2005;47:411

Daily Exposures to Formaldehyde Associated with Cigarettes and E-Cigarettes.

formaldehyde-releasing agents may deposit more efficiently in the respiratory tract than gaseous formaldehyde



Tank system

FACTORS DETERMINING POWER/HEAT OF VAPED AEROSOL

- Voltage
- Coil resistance
- Device geometry
- Liquid flow in wick
- Catalytic actions
- airflow



Identification of amino-tadalafil and rimonabant in electronic cigarette products using high pressure liquid chromatography with diode array and tandem mass spectrometric detection[☆]

Michael E. Hadwiger*, Michael L. Trehy, Wei Ye, Terry Moore, James Allgire, Benjamin Westenberger

Food and Drug Administration, Division of Pharmaceutical Analysis, 1114 Market St., Saint Louis, MO 63101, USA

ARTICLE INFO

Article history:

Received 18 May 2010

Received in revised form 27 August 2010

Accepted 4 October 2010

Available online 11 October 2010

Keywords:

E-cigarettes

Electronic cigarettes

HPLC

Mass spectrometry


Multi-mode ionization

ABSTRACT

A high-pressure liquid chromatography-diode array detection and multi-mode ionization tandem mass spectrometry (HPLC-DAD-MMI-MS/MS) method was used to identify amino-tadalafil and rimonabant in electronic cigarette (e-cigarette) cartridges. Amino-tadalafil is a drug analogue of the commercially approved Cialis[™] (i.e. tadalafil). Rimonabant is a drug that was, at one time, approved for weight loss in Europe (although approval has been retracted), but not in the United States. In addition, poor quality control over the e-cigarette products analyzed here is shown by the presence of nicotine in products labeled as containing no nicotine or by the presence of significant amounts of rimonabant oxidative degradant in e-cigarette products containing rimonabant. Identification was accomplished by comparing the retention time of relevant peaks in the sample with those of standard compounds, in addition to comparison of the UV spectra, mass spectra and/or product ion mass spectra.


Published by Elsevier B.V.

E-RECTILE DYSFUNCTION PRODUCT?!



Cialis flavor E-liquid
E-liq
Cialis flavor E-liquid
Category : Root > E-liquids
From 11,20 €
Condition : New
Rating(s) and review(s) :
Cialis flavor E-liquid
★★★★☆
Average: 4 / 5
Based on 6 rating(s) and 5 user review(s).

Notice

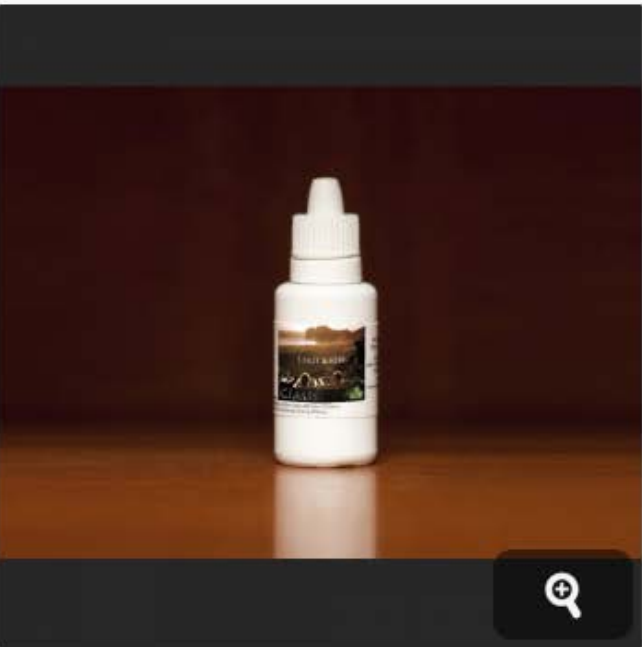
Save vaping!
Support
European Free Vaping
Initiative 

Categories

E-liquids

Home > E-liquids > Cialis flavor E-liquid

CIALIS FLAVOR E-LIQUID



Price Lowered

By Vaping, Improve Your Sexual Capacity !

Milliliters : 10 ML

Nicotine : 0 mg (no ni)

Base type : Ice blade (F)

Reference: E-liq

Quantity: 1

Availability: In stock

11,20 €
~~16,00 €~~ -30%

Int. J. Environ. Res. Public Health **2015**, *12*, 4796–4815; doi:10.3390/ijerph120504796

OPEN ACCESS

International Journal of
**Environmental Research and
Public Health**

ISSN 1660-4601

www.mdpi.com/journal/ijerph

Article

Toxicity Assessment of Refill Liquids for Electronic Cigarettes

Vincent Varlet¹, **Konstantinos Farsalinos**^{2,3}, **Marc Augsburger**¹, **Aurélien Thomas**^{1,4}
and **Jean-François Etter**^{5,*}

METHODS

- Convenience sample of 42 models from 14 brands of e-liquid refills (USA, UK, France, Switzerland)
- Tested for microbes, diethylene glycol, ethylene glycol, hydrocarbons, ethanol, aldehydes, solvents.
- Toxicity assessment:
 - Acute oral ingestion of 10 grams of e-liquid
 - Chronic consumption of 3 grams/day of e-liquid

RESULTS

- EG/diethylene glycol: No liquids above FDA/USP limits
- ETOH: maximum concentration 0.4%
- Limonene most common hydrocarbon
- Formaldehyde detected in all samples (thermal decomposition of PG)
- Risk of acute toxicity (aside from nicotine): "not significant"





LIMITATIONS


- Not all brands included
- Only one batch per product (inter-batch variability)
- Rapidly changing marketplace
- No comment on propylene glycol
- Difference between oral vs. inhalational toxicity


DIRECT DRIPPING


A HIGH-TEMPERATURE, HIGH-FORMALDEHYDE EMISSION ELECTRONIC CIGARETTE USE METHOD


 **How to use your 306 atomizer and drip tip**


- 

1 The 306 atomizer ships with a black cover piece attached.
- 

2 Screw the 306 on to any 510 threaded device such as an eGo battery.
- 

3 Then remove the cover piece by pulling it off.
- 

4 What you now have is an exposed 306 atomizer.
- 

5 Attach any compatible 306 drip tip of choice.
- 

6 Add a few drops of your favorite e-liquid, vape and repeat!

WHY DRIP?

- Better control of rate of liquid delivery to the heater coil
- Greater vapor yield
- Greater throat "hit"
- More consistent flavor
- Way to test new flavors without wasting liquid

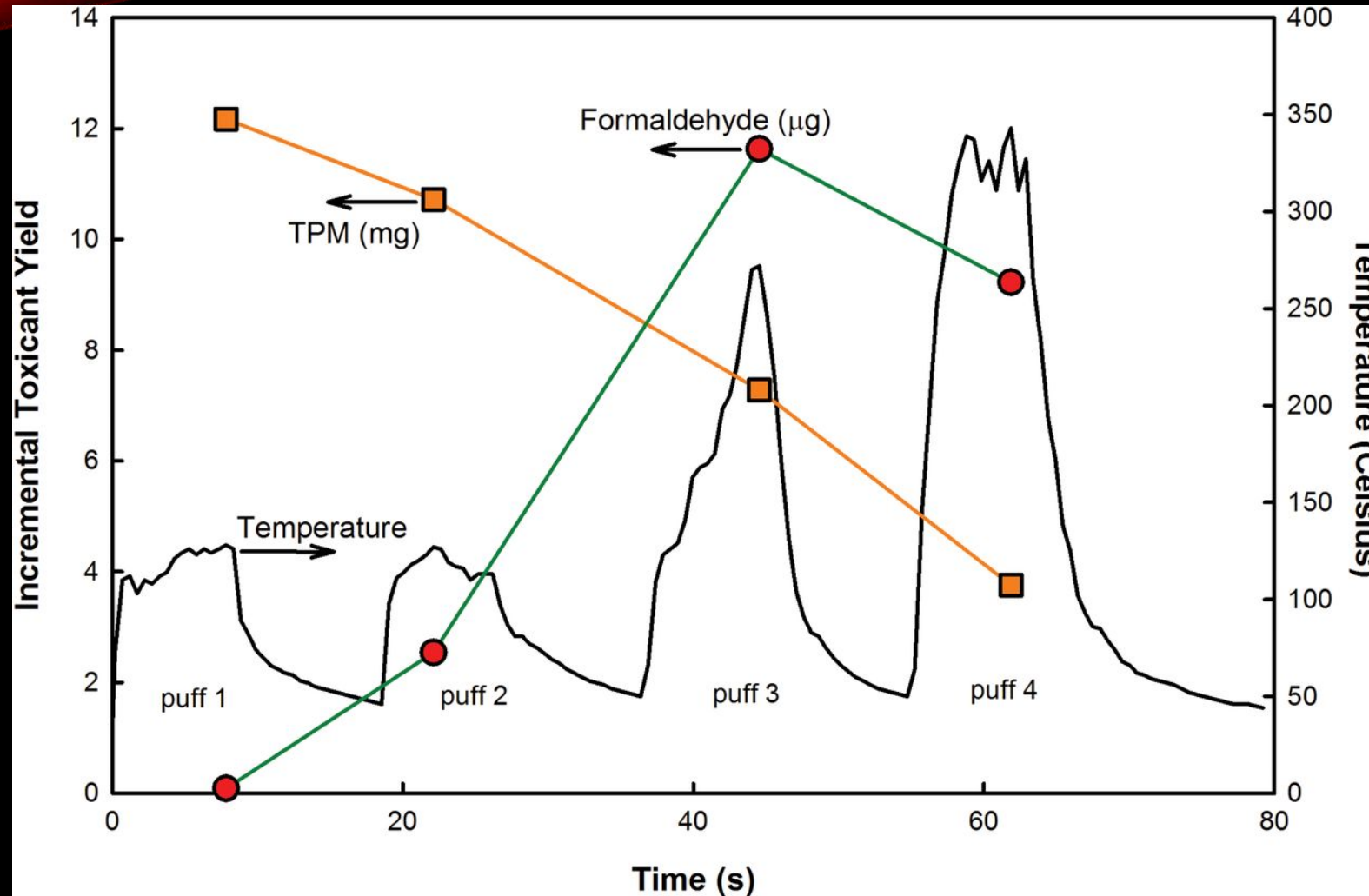
HOW DO YOU DO IT?

- Most common method:
- Inhale a few puffs until taste is “burning”; “dry puff”
- Add drops and resume puffing
- Inter-drip average 3-6 puffs

SO WHAT'S THE PROBLEM?

- Higher temperatures generated as liquid evaporates between drips
- Higher aldehyde formation
- Temperature increases with each puff
- 10-20 puffs = fomaldehyde of 1 or more cigarettes

Typical maximum heater coil temperature vs. time for four consecutive puffs (8 seconds puff duration, 19.1mL/s puff velocity).



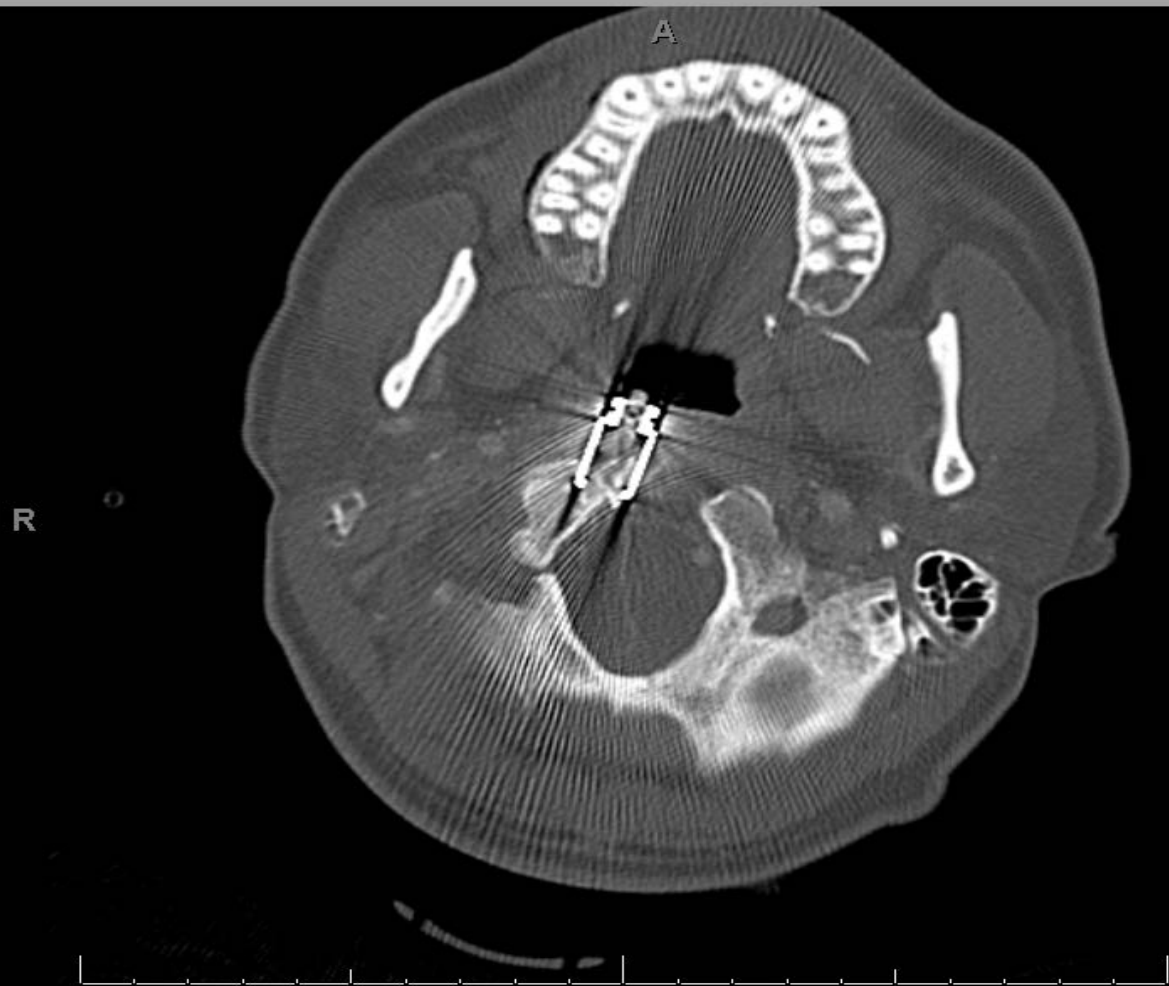
SOHA TALIH ET AL. NICOTINE TOB RES 2015;NTR.NTV080

chemical	2 puff IDI	3 puff IDI	4 puff IDI	cigarette	Cartridge ecig	Tank ecig a = 2X volts B = 1X volt
formaldehyde	19.7	71.3	88.1	21.5	0.025–0.77	NR
acetaldehyde	269	822	1172	540	0.11–1.36	0.17–4.23 ^a
acetone	28.3	103	196	214	NR	0.34–7.59 ^a
acrolein	BDL	1.97	1.75	49	0.07–4.19	NR
propionaldehyde	51.6	185	314	42.6	NR	ND ^b
butyraldehyde	0.61	2.9	6.3	26.7	NR	NR
valeraldehyde	29.1	83.9	92.5	NR	NR	BQL ^b
Total aldehydes	398	1272	1872	NR	NR	NR

CASE REPORT NMPDIC

- 27-year-old male presented to the Emergency Department after attempting to use an e-cigarette that subsequently exploded while in his mouth, lodging the mouth piece in the posterior soft palate.
- Patient drove himself to healthcare facility, presenting with pain, noted edema, pain while swallowing, and tachycardia.
- Physical examination revealed upper lip edema with apparent linear burn and chipped upper teeth. The visible wound was black, described as "charred-like" skin.
- Imaging revealed a a metallic-appearing foreign body lodged between the atlanto-occipital junction, without clear evidence of violating the spinal canal. Radiology findings reveal small fractures involving C1 and C2. Fracture fragments are displaced posteriorly but not as far as the spinal cord, or in close proximity to the vertebral artery.
- Removal of foreign body was successfully completed through ENT transoral approach. Patient was seen at an orthopedic clinic 9 days post-removal. Imaging revealed no appreciable fractures or subluxations, and was clear to return to work with "as needed" use of a C-spine collar.

7/12/2015 11:22:09



U.S. FIRE ADMINISTRATION ELECTRONIC CIGARETTE FIRES AND EXPLOSIONS OCTOBER 2014

- Twenty-five separate incidents of explosion and fire involving an e-cigarette were reported in the US media between 2009 and August 2014
- Two injuries were serious burns
- 80% occurred while battery was charging
- Shape and construction of e-cigarettes can make them more likely than other products with lithium-ion batteries to behave like “flaming rockets” when a battery fails
- No regulation, code or law applies to the safety of the electronics or batteries in e-cigarettes. No UL testing is required. Not in CPSC regulations.

CHILD BURNED IN PROVO UT

An electronic cigarette, which was being charged via her car's cigarette lighter, exploded. A hot piece of metal flew from the e-cigarette into the back of the car, landing in her child's car seat, which caught fire.

The child sustained 1st and 2nd degree burns on elbow, lower back, and buttocks



CHILD-RESISTANT PACKAGING IN NEW MEXICO

- Challenges
 - Duplicate bills; one on sales to minors, one on packaging
 - Definition of "child-resistant"
 - CPSC experiments are not going to happen
 - CPSP definition is vague
 - CPSP does not regulate e-cig packaging hence we need state laws
 - Had to exclude cartridges because they are "contained"
 - NM law does not allow referral to federal regulations
 - Liquid tank refills come with two dropper bottles
 - One is empty with smaller tube
 - One is full
 - Child-resistant packaging could not be mandated on the empty container
 - Who enforces this?

CHILD-RESISTANT PACKAGING IN NEW MEXICO PROVISIONS

HB 213 mandates child-resistant packaging on any product containing nicotine liquid

- "The attorney general may institute a civil action in district court for a violation of the provisions of this section or to prevent a violation of the provisions of this section. Relief may include a permanent or temporary injunction, a restraining order or any other appropriate order, including a civil penalty not to exceed one thousand dollars (\$1,000) for each violation."

CHILD-RESISTANT DEFINITION IN NEW MEXICO HB 213

- "a package or container that is designed or constructed to be significantly difficult for children under five years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and not difficult for normal adults to use properly, but does not mean a package or container that all such children cannot open or obtain a toxic or harmful amount within a reasonable time."

CONCLUSIONS

- More research needed to assess risk of second and third hand exposure to excipients in e-cigarettes
- Dripping delivery methods should be discouraged
- Use only the charging device provided by the product
- Wipe surfaces of gas appliances frequently
- Avoid use in presence of children
- Encourage adoption of child-resistant packaging for tank refills
- Cartridge types are safer around small children
 - Risk is very high of accidental ingestion for tank types