

**“Are E-Cigarettes a Bridge Product to Smoking  
or Abstinence? Or Neither?”**

**Warner Series Lecture  
September 16, 2009**

# Julia Cartwright

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- **Welcome to the Warner Series at the American Legacy Foundation®**
- ***Celebrating 10 Years of Building a World Where Young People Reject Tobacco and Anyone Can Quit***

# Julia Cartwright

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- Overview:
  - Speaker positions (10 minutes)
  - Moderator Q&A
  - Audience and Web Q&A
- EMAIL QUESTIONS: [press@americanlegacy.org](mailto:press@americanlegacy.org)
- Archive @ [www.americanlegacy.org](http://www.americanlegacy.org)

# Cheryl G. Heaton, DrPH

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**Moderator:**

President and CEO,  
American Legacy  
Foundation

# Nathan Cobb, M.D.

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Research Investigator,  
Steven A. Schroeder  
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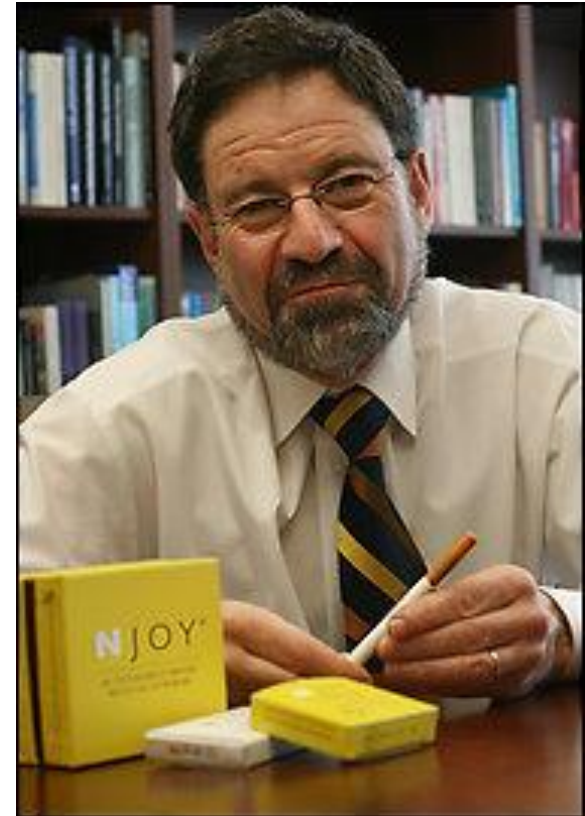
**Nathan Cobb, M.D.**

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**Electronic Nicotine Delivery Systems**

# Electronic Nicotine Delivery Systems

- Devices
  - Common characteristics
  - Vaporization process
- Use
- Refilling
  - Nicotine levels
  - Mechanism

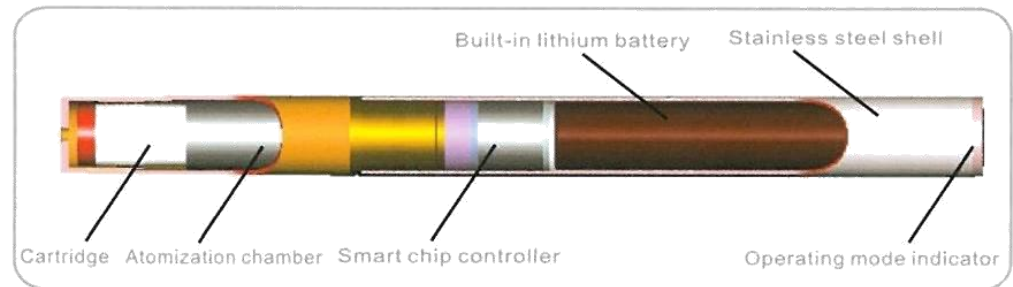
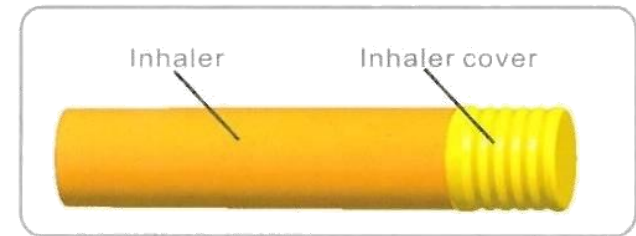


# Sample Devices



# Common Components

- Battery
- Heating element
- Absorbent with solution
  - Nicotine
  - Propylene glycol
  - Flavorings



# Vaporization

- As propylene glycol (or other alcohol) is heated to 40-65C and forcibly drawn through the device, it vaporizes.
  - Theoretically, nicotine is carried along in this process.
- FDA found ~6 mg of nicotine in tested cartridges
  - Estimated 0.027 to 0.045 milligrams per puff



# Use

- *“Electronic cigarette uses advanced microelectronic technology and supercritical physical atomization technology to atomize the high-purity and exciting nicotine dilution extracted from tobacco into smoke for smoker’s sucking and accordingly meet the needs of those smokers.”*

- Smoking Anywhere Manual

to theatrical fog.

# Refilling

- Multiple suppliers of “juice” independent of device manufacturers
- Marketed for 1-1.3ml refill per cartridge
  - Current high is 36mg/refill
  - Single bottle may contains as much as 1 gram of nicotine in the volume of a shot glass.



# Refill Process



# Peter Shields, M.D.

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Deputy Director,  
Lombardi Comprehensive  
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# Scientific Evaluation of ENDS Products and Health Claims

- ENDS manufacturer's making health claims
  - Liken themselves to cigarettes and so no regulation as NRT is needed
  - Cliché: Less ought to be better
- No comprehensive framework exists for evaluating tobacco products and health claims
- These products are nicotine-delivery devices and so a safety and efficacy assessment is needed
  - Is it really an alternative to smoking? Safer?
  - No unintended consequences? Quality control?
- There is no single ENDS product, and so each unique design needs to be tested

# Scientific Evaluation of ENDS and Associated Health Claims

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- Safety Assessment
  - Chemical and toxicological studies of filler and aerosol
    - Human use conditions (limited human testing)
    - Comparator is other nicotine delivery devices
- Health claims assessment
  - Randomized switching studies and cross-sectional studies, accounting for compensation
  - Consumer use, perception and abuse liability measures
  - Biomarkers and Topography
  - Adverse Events
- Surveillance – use, impact on smoking, and health effects

# FDA Testing Of ENDS - Methods



- Small pilot study
- Compared “Njoy” and Smoking “Everywhere” to Nicotrol Inhaler
- Analyzed cartridge content and the vapor specifically for nicotine, tobacco smoke alkaloids, TSNAs, and DEG
- 100 cc puffs every 60s

# FDA Testing Of ENDS - Findings

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- Lower nicotine content and delivery than claimed, although FDA concluded that “high” yields exceeded Nicotrol levels
  - QC issues and the 0 nicotine cartridges still had some nicotine
- TSNAs found at trace levels
- Diethylene glycol found in one cartridge
  - DEG is not in cigarettes
- Anabasine detected in some cartridges

# FDA Nicotine Testing

Product	Nicotine/Cartridge (mg)		Nicotine/puff (ug)		
	Manufacturer Claim	FDA Report	Manufacturer claim	FDA per 100ml puff	Apples to Apples
Smoking Everywhere – High	16 (20 cigs)	5.98	NA	31.5	<ul style="list-style-type: none"> <li>• 1 cartridge = 20 cigarettes</li> <li>• See note*</li> </ul>
Njoy - Menthol High	18 (20 cigs)	6.76	NA	26.8-43.2	1 cartridge = 20 cigarettes
Nicotrol Inhaler	10 (1 cig)	Not tested	50**	15.2	80 puffs over 20min = 1 cigarette

\*“Security system which stops automatically if too many inhalations occur within a short time space ...”

\*\*Nicotrol inhaler puff yield calculated by prescribing info claim of 4 mg yield based on 80 deep inhalations over 20 minutes (50% absorption follows, mostly through buccal mucosa)

# FDA Testing Limitations

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- Pilot study with sound methodology
- Unknown optimal puffing profile
  - Initial use and compensatory use for smokers, former smokers and initiators
  - Puff volume, duration, frequency and number of puffs
- Unknown changes in vapor with later puffs or battery charge
- Limited chemical assessment
- Not a market survey
- Not a human study with biomarkers

# Laugesen Report - 2008

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- Ruyan e-cigarette
- Private company – Health New Zealand
  - Activities funded by Runyon Ltd
  - Assays done by commercial laboratories
- Methods
  - Variety of methods to detect multiple chemical constituents
  - Puffing methods poorly described

# Laugesen Report - 2008

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- Also found trace levels of TSNAs in the cartridge
- Other compounds detected
  - Acetaldehyde
  - Acetone
  - Formaldehyde
  - PAHs
- Lower levels than cigarettes, but higher than FDA-approved NRT
- Limitations of FDA testing apply here

# Laugesen Report - 2008

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- “Propylene glycol is virtually non-toxic”
  - Effects of electronic heating not tested on long term toxicity including cancer for humans or animals
    - “Fog machine analogy” and cosmetics does not apply
  - Metabolism is different for persons with kidney and liver disease, some racial groups
  - Higher levels than in tobacco

# Unintended Consequences of ENDS – What needs to be studied?

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- Exposure to harmful chemicals leading to health effects such as lung and other cancers through laboratory and human studies
- Nicotine toxicity
- Delaying or subverting smoking cessation
- Enticing former smokers to resume smoking
- Serving as a gateway for new smokers

# Conclusions

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- The study of ENDS is doable and can be done within a reasonable time period for many endpoints
- Following a safety assessment, even if ENDS were considered safer than cigarettes, smokers may need to be informed that they are still at risk of some adverse health outcomes, if that is the case
  - This can only be determined through adequate studies

# David Abrams, Ph.D.

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Executive Director,  
Steven A. Schroeder  
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# Jack Henningfield, Ph.D.

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Vice President, Research and  
Health Policy, Pinney &  
Associates

Department of Psychiatry and  
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Johns Hopkins University  
School of Medicine

Tobacco Regulation Study  
Group, the World Health  
Organization



# World Health Organization Tobacco Regulation Study Group (TobReg)

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- The study group was formed by the WHO to provide scientific guidance on tobacco issues addressed by the Framework Convention on Tobacco Control (WHO FCTC), aka, the “Tobacco Treaty”.
- TobReg’s focus is on issues related to Treaty Articles, 9, 10, and 11, which address tobacco product contents, disclosures and packaging and labelling. And, with respect to ENDS, Article 8, which requires protection from exposure to tobacco smoke.

## WHO TobReg (cont.)

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- TobReg convened in November, 2008, in part to address issue posed by ENDS. A draft abbreviated advisory was released early in 2009. The Final Advisory from that meeting is forthcoming.

# ENDS: WHO TobReg Scientific Advisory and Recommendation

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- This recommendation was developed within the context of the WHO Framework Convention on Tobacco Control ("FCTC") but is similarly relevant to the United States.
- The recommendation was developed because ENDS pose significant public health issues and raise questions for tobacco control policy and regulation. ENDS do not meet definitions of conventional tobacco products but most claim lung delivery of nicotine and other substances.

# ENDS: WHO TobReg Scientific Advisory and Recommendation

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- ENDS have the potential to undermine public smoking bans and undermine prevention and cessation by serving as attractive nicotine/tobacco starter products and by their claims as safe alternatives to tobacco products.
- There are at least 24 licensed companies and many more brands and model names, their marketing websites make diverse claims concerning their contents, sensory properties, and uses which include cigarette substitution, smoking cessation, craving and for use where smoking is not permitted.

# ENDS: WHO TobReg Conclusions

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- ENDS products deliver nicotine, a addictive chemical, via the respiratory system with the purpose of facilitating and perpetuating nicotine addiction.
- The safety and extent of nicotine uptake from using ENDS products have not been established. Although ENDS may cause and sustain addiction, evidence on the potential for addiction and the frequency with which addiction occurs does not currently exist.

# ENDS: WHO TobReg Conclusions

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- Manufacturers have marketed ENDS as smoking cessation aids and these products have the potential to be effective in this use; however, scientific evidence sufficient to establish cessation efficacy and safety of use is not yet available.
- There are safety concerns that nicotine delivery to the lung may result in stronger toxicological, physiological and addictive effects. Scientific studies must address these concerns.

# ENDS: WHO TobReg Conclusions

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- Lung delivery of medications, independent of the effects of nicotine, is of global importance and must be addressed with scientific studies.

# ENDS: WHO TobReg Policy Recommendations #1

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- (1)ENDS products should be regulated as combination drug/medical devices and not as tobacco products. Notwithstanding the various marketing strategies, ENDS facilitate and perpetuate nicotine addiction.

# ENDS: WHO TobReg Policy Recommendations #1

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- (2)Regulators should weigh the incremental benefits of ENDS as smoking cessation aids over current NRT products against the risk of the products' appeal to non-smokers, that is, the risk of non-smokers being drawn into nicotine addiction.

# ENDS: WHO TobReg Policy Recommendations #1

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- (3) If ENDS products are regulated under tobacco control laws, then the manufacture, sale or importation of these products should be subject to regulation of contents and labelling (Articles 9-11), prohibitions against public use that might expose others to emissions (Article 8), and restrictions on advertising, promotion and sponsorship that appeal to adolescents (Article 13). Nations may consider granting exemption and concurrent jurisdiction with drug regulatory authorities only if ENDS products are proven safe and effective as smoking cessation aids.

# ENDS: WHO TobReg

## Policy Recommendations #2

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- (4) Manufacturers and retailers must provide evidence defining the appropriate uses, exposures and safety of ENDS and regulatory authorities should confirm the accuracy of this evidence prior to approval for sale and marketing.

# ENDS: WHO TobReg

## Policy Recommendations #2

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- (5) Claims implying health benefits or reduced harm relative to cigarettes should be prohibited unless the safety of these devices, when used as intended, are scientifically proven to the satisfaction of regulatory authorities.
- (6) Claims that ENDS assist smoking cessation should be prohibited unless the efficacy of these devices, when used as intended, are scientifically proven to the satisfaction of regulatory authorities.

# ENDS: WHO TobReg Research Recommendations

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- (1) Research is needed on the delivery and absorption of nicotine through ENDS use, both acutely and chronically, in order for regulators to establish the dosage and formulation for regulatory approval.
- (2) Research is needed on the behavioural and physiological consequences of using ENDS.

# ENDS: WHO TobReg Research Recommendations

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- (3) The dependence potential (also known as “abuse liability”) relative to cigarettes and NRTs needs to be studied.
- (4) Short and long-term effects of human exposure to determine potential harm needs to be monitored.

# ENDS: WHO TobReg Research Recommendations

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- (5) Post-marketing studies need to be conducted to determine patterns of use, such as dual use, monitor adverse effects, and the individual and population effects on initiation and cessation.

# Cheryl G. Heaton, DrPH

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## Moderator Questions

Web: [press@americanlegacy.org](mailto:press@americanlegacy.org)

# Cheryl G. Heaton, DrPH

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## Audience Questions

# Julia Cartwright

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**THANK YOU FOR COMING!**

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