Potential Health Risks of Exposure to Toxic Metals in E-Cigarettes

Charlene Liu, Kristin Marano, Patrick Murphy, Courtney Culbert

RAI Services Company, Winston-Salem, NC

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Outline

- Introduction
- Problem Formulation
- Hazard Identification
- Toxicity Assessment
- Exposure Assessment
- Risk Characterization
- Conclusions

Electronic Cigarettes

The National Academies of Sciences, Engineering, and Medicine recently concluded that while e-cigarettes are not without health risks, they are likely to be far less harmful than conventional cigarettes

Metals in E-Cigarettes

- E-cigarettes generate an aerosol by heating an e-liquid with a metallic coil
- These products may present a potential for exposure to metals if transfer from the coil to the aerosol were to occur

Objective

To evaluate estimated potential health risks associated with exposure to metals in e-cigarette-generated aerosol in comparison to combustible cigarette mainstream smoke using quantitative risk assessment (QRA)

Hazard Identification

Metal Data

Journal of Analytical Toxicology 2014;38:204–211
doi:10.1093/jat/bku013 Advance Access publication February 16, 2014

Article

Toxic Metal Concentrations in Mainstream Smoke from Cigarettes Available in the USA

R. Steven Pappas[1]*, Mark R. Fresquez[2], Naudia Martone[1] and Clifford H. Watson[1]

[1]Division of Laboratory Sciences, Tobacco and Volatiles Branch, Centers for Disease Control and Prevention, National Center for Environmental Health, 4770 Buford Hwy NE Mail Stop F44, Atlanta, GA 30341-3717, USA, and [2]Battelle-Atlanta Analytical Services, Atlanta, GA, USA

*Author to whom correspondence should be addressed. Email: rpappas@cdc.gov

Public health officials and leaders of 168 nations have signaled their concern regarding the health and economic impacts of smoking by becoming signatory parties to the World Health Organization Framework Convention on Tobacco Control (FCTC). One of FCTC's purposes is to help achieve meaningful regulation for tobacco products in order to decrease the exposure to harmful and potentially harmful constituents (HPHCs) delivered to users and those who are exposed to secondhand smoke. Determining baseline delivery ranges for HPHCs in modern commercial tobacco products is crucial information regulators could use to make informed decisions. Establishing mainstream smoke delivery concentration ranges for toxic metals was conducted through analyses of total particulate matter (TPM) collected with smoking machines using standard smok

transported in smoke per cigarette. They further assessed the additive risk from the substances as classes of toxic chemicals. Among the substances which contributed to the cancer risk from inhaling tobacco smoke are the toxic metals arsenic, beryllium, cadmium, chromium (VI), nickel (International Agency for Research on Cancer (IARC) group 1 carcinogens) and lead (IARC group 2A carcinogen). Burns *et al.* also considered assessing health risk due to exposure to substances in smoke as a basis for product regulation, but they based their calculations on toxicant delivery per mg of nicotine in smoke instead of per cigarette (6). This provided justification and rationale for a regulation proposal by the WHO Study Group on Tobacco Product Regulation (TobReg) to lower toxicants in cigarette smoke. They also dis-

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Research

A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP2175.

Metal Concentrations in e-Cigarette Liquid and Aerosol Samples: The Contribution of Metallic Coils

Pablo Olmedo,[1,2,3] Walter Goessler,[4] Stefan Tanda,[4] Maria Grau-Perez,[1,2] Stephanie Jarmul,[1] Angela Aherrera,[1] Rui Chen,[1] Markus Hilpert,[2] Joanna E. Cohen,[5,6] Ana Navas-Acien,[1,2] and Ana M. Rule[1]

[1]Department of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
[2]Department of Environmental Health Sciences, Columbia University Mailman School of Public Health, New York, New York, USA
[3]Department of Legal Medicine and Toxicology, School of Medicine, University of Granada, Granada, Spain
[4]Institute of Chemistry, University of Graz, Graz, Austria
[5]Department of Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
[6]Institute of Global Tobacco Control, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

Background: Electronic cigarettes (e-cigarettes) generate an aerosol by heating a solution (e-liquid) with a metallic coil. Whether metals are transferred from the coil to the aerosol is unknown.

Objective: Our goal was to investigate the transfer of metals from the heating coil to the e-liquid in the e-cigarette tank and the generated aerosol.

Methods: We sampled 56 e-cigarette devices from daily e-cigarette users and obtained samples from the refilling dispenser, aerosol, and remaining e-liquid in the tank. Aerosol liquid was collected via deposition of aerosol droplets in a series of conical pipette tips. Metals were reported as mass fractions (μg/kg) in liquids and converted to mass concentrations (mg/m^3) for aerosols.

Results: Median metal concentrations (μg/kg) were higher in samples from the aerosol and tank vs. the dispenser (all $p < 0.001$): 16.3 and 31.2 vs. 10.9 for Al; 8.38 and 55.4 vs. <0.5 for Cr; 68.4 and 233 vs. 2.03 for Ni; 14.8 and 40.2 vs. 0.476 for Pb; and 515 and 426 vs. 13.1 for Zn. Mn, Fe, Cu, Sb, and Sn were detectable in most samples. Cd was detected in 0.0, 30.4, and 55.1% of the dispenser, aerosol, and tank samples respectively. Arsenic was detected in 10.7% of dispenser samples (median 26.7 μg/kg) and these concentrations were similar in aerosol and tank samples. Aerosol mass concentrations (mg/m^3) for the detected metals spanned several orders of magnitude and exceeded current health-based limits in close to 50% or more of the samples for Cr, Mn, Ni, and Pb.

Conclusions: Our findings indicate that e-cigarettes are a potential source of exposure to toxic metals (Cr, Ni, and Pb), and to metals that are toxic when inhaled (Mn and Zn). Markedly higher concentrations in the aerosol and tank samples versus the dispenser demonstrate that coil contact induced e-liquid contamination. https://doi.org/10.1289/EHP2175

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Metal Data

Product Type	Puff Regime*	# Products	% Products with Metals > Limit of Quantitation					
			As	Cd	Cr	Mn	Ni	Pb
Combustible[1]	35/60/2	53	96%	98%	0%	98%	13%	96%
Combustible[1]	55/30/2	53	100%	100%	0%	100%	70%	100%
Open ENDS[2]	67/30/4	56	18%	30%	64%	64%	86%	95%
Closed ENDS[3]	55/30/3	37	NA	0%	0%	NA	0%	0%
Closed ENDS[3]	80/15/5**	37	NA	0%	0%	NA	0%	0%

Product Type	Puff Regime*	Puffs per Collection	Metals in Smoke/Aerosol (ng/puff)					
			As	Cd	Cr	Mn	Ni	Pb
Combustible[1]	35/60/2	~8.5	0.37	4.4	< 0.1	0.15	0.046	1.6
Combustible[1]	55/30/2	~11	0.85	11	< 0.1	0.32	0.07	3.8
Open ENDS[2]	67/30/4	30-50	NQ	NQ	0.0056	0.0013	0.03	0.0071
Closed ENDS[3]	55/30/3	100-200	NA	< 0.01	< 0.06	NA	< 1.5	< 0.7
Closed ENDS[3]	80/15/5**	30-135	NA	< 0.03	< 0.12	NA	< 3	< 1.4

ENDS = Electronic nicotine delivery system
NA = Not analyzed in this study
NQ = Not quantifiable

*Puff Regime represents puff volume (mL) / puff interval (sec) / puff duration (sec)
**14 products automatically cut off after 4 seconds and were tested at 80/15/4

[1]Pappas et al., 2014, Toxic Metals Concentrations in Mainstream Smoke from Cigarettes Available in the USA. Journal of Analytical Toxicology, 38, 204-211.
[2]Olmedo et al., 2018. Metal Concentrations in E-Cigarette Liquid and Aerosol Samples: the Contribution of Metal Coils. Environmental Health Perspectives, February 21, 126(2).
[3]R.J. Reynolds vapor products (28) and market products (9) analyzed by Eurofins Lancaster Laboratories, Professional Scientific Services, Winston-Salem.

Toxicity Assessment

Toxicity Factors Sources

- USEPA's Integrated Risk Information System (IRIS) and National Ambient Air Quality Standard (NAAQS)
- Agency for Toxic Substances and Disease Registry (ATSDR)

Toxicity Factors

Constituent	Reference Concentration (mg/m^3)	Source	Inhalation Unit Risk $(\mu g/m^3)^{-1}$	Source
Arsenic	1.5E-05	IRIS	4.3E-03	IRIS
Cadmium	1.0E-05	ATSDR	1.8E-03	IRIS
Chromium[a]	1.0E-04	IRIS	8.4E-02	IRIS
Manganese	5.0E-05	IRIS	NA	-
Nickel	1.4E-05	IRIS	2.4E-04	IRIS
Lead[b]	1.5E-04	NAAQS	NA	-

[a] Toxicity factors for chromium are based on the most toxic form: hexavalent chromium (Cr[VI]). Per USEPA Regional Screening Levels, the Cr(VI) specific inhalation unit risk value (assuming 100% Cr(VI)) is derived by multiplying the IRIS Cr(VI) value by 7. This is considered to be a health-protective assumption.
[b] Lead is considered a carcinogen and a noncancer toxicant by USFDA; however, toxicity values are not available. RfC is based on USEPA National Ambient Air Quality Standard (NAAQS).
IRIS – USEPA Integrated Risk Information System
ATSDR – Agency for Toxic Substances and Disease Registry

Exposure Assessment

Assumptions: Combustible Cigarettes

- Initiation: 12.5 years of age[1]
- Consumption Rate: 1 pack per day[2]
- Exposure Frequency: 365 days per year
- Exposure Duration: 57.5 years assuming a 70-year lifespan[1,2,3]

[1]SAMHSA. 2015. Behavioral Health Trends in the United States: Results for the 2014 National Survey on Drug Use and Health.
[2]CDC. 2018. Current Cigarette Smoking among Adults – United States, 2016. Morbidity and Mortality Weekly Report, 67(2).
[3]EPA. 2011. Exposure Factors Handbook: 2011 Edition.

Assumptions: E-Cigarettes

- Initiation: 12.5 years of age[1]
- Consumption Rate:
  - 50[2] and 150[3] puffs per day
- Exposure Frequency: 365 days per year
- Exposure Duration: 57.5 years assuming a 70-year lifespan[1,4,5]

[1]SAMHSA. 2015. Behavioral Health Trends in the United States: Results for the 2014 National Survey on Drug Use and Health.
[2]Olmedo et al., 2018. Metal Concentrations in E-Cigarette Liquid and Aerosol Samples: the Contribution of Metal Coils. Environmental Health Perspectives, February 21, 126(2).
[3]Weighted mean value from 10 studies
[4]CDC. 2018. Current Cigarette Smoking among Adults – United States, 2016. Morbidity and Mortality Weekly Report, 67(2).
[5]EPA. 2011. Exposure Factors Handbook: 2011 Edition.

Exposure Concentration (EC)

- *Combustible Cigarettes:*

$$EC = \frac{HPHC\ yield \times CpD \times EF \times ED}{Inhalation\ Rate \times AT} = \frac{\mu g}{m^3}$$

- E-Cigarettes:
  - $EC = \frac{Metal\ Daily\ Mass \times EF \times ED}{Inhalation\ Rate \times AT} = \frac{\mu g}{m^3}$

CpD = cigarettes per day
EF = exposure frequency
ED = exposure duration
Inhalation Rate = 20 m^3/day[1]
AT = averaging time
[1]EPA. 2011. Exposure Factors Handbook: 2011 Edition

Risk Characterization

Risk Characterization

- Noncancer Health Hazard

$$Hazard\ Quotient = \frac{EC}{RfC}$$

$$Hazard\ Index = \sum Hazard\ Quotient$$

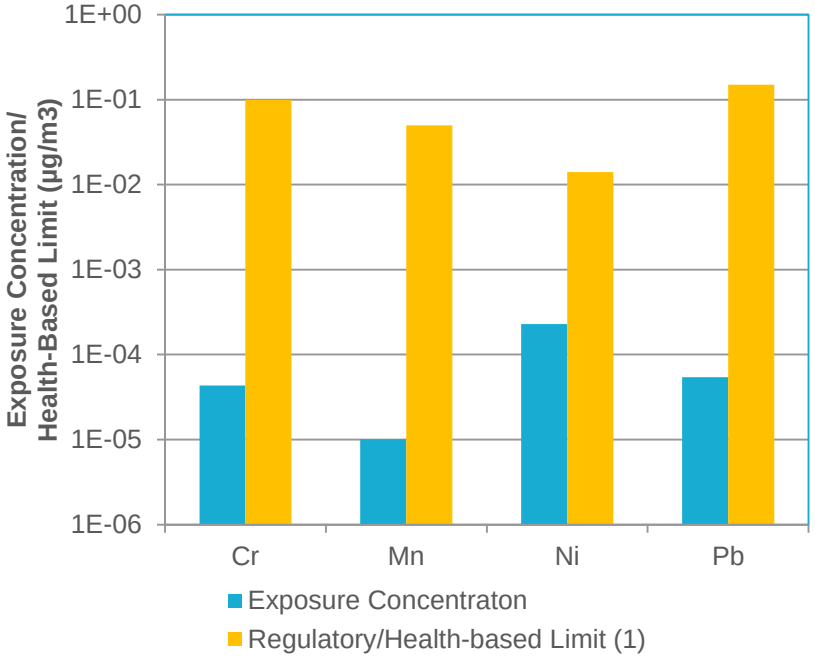
- Excess lifetime cancer risk

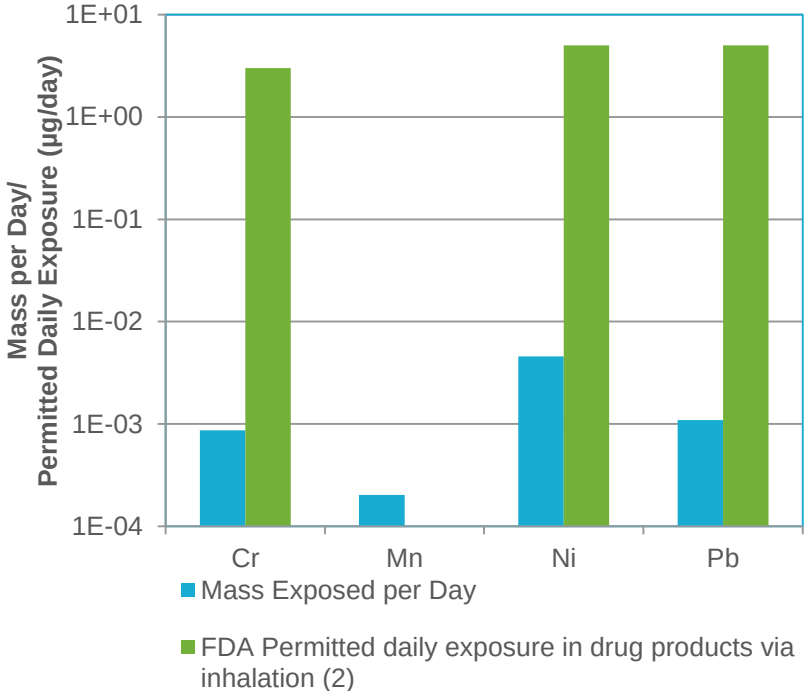
$$ELCR = EC \times IUR$$

$$Total\ ELCR = \sum ELCR$$

EC = exposure concentration
RfC = reference concentration
IUR = inhalation unit risk

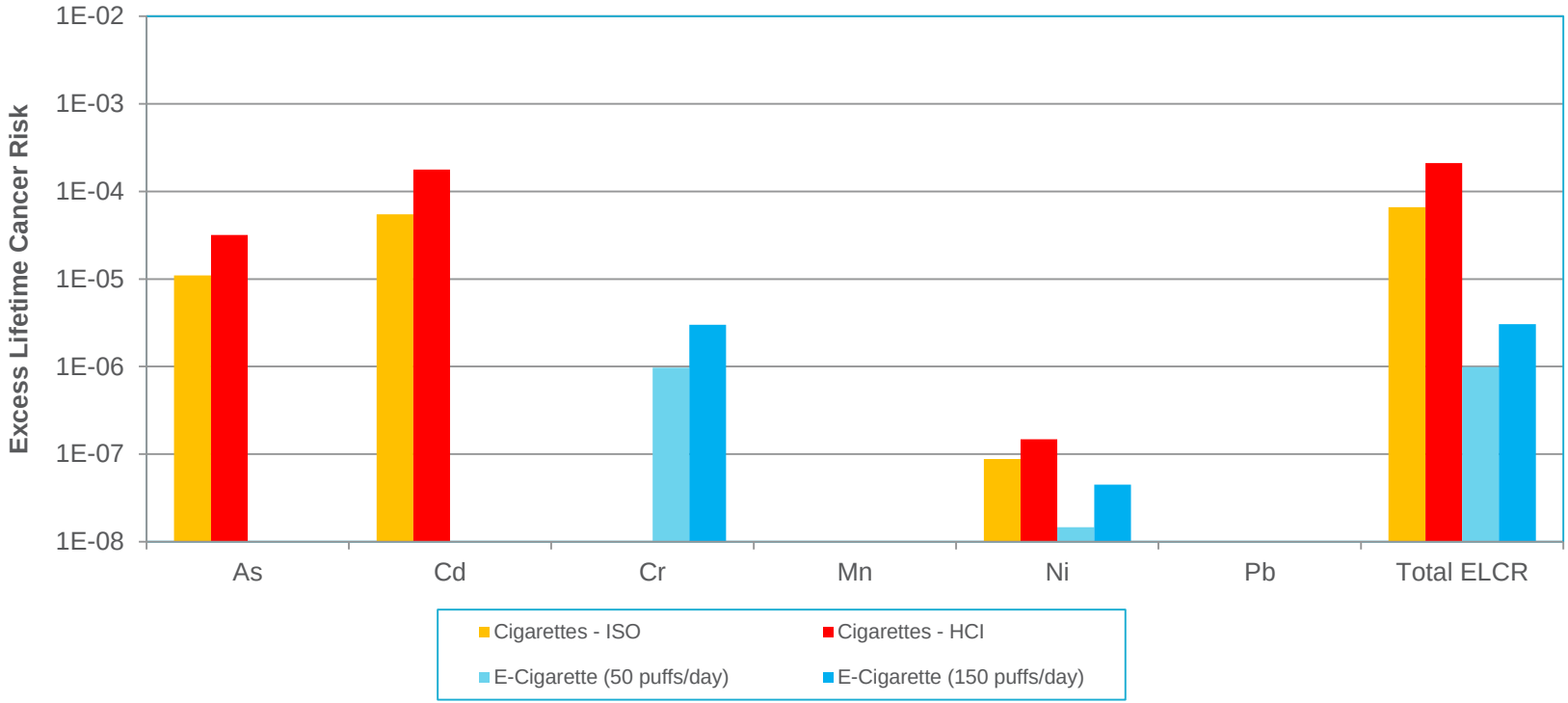
Estimated Exposure vs. Regulatory and Health-based Limits



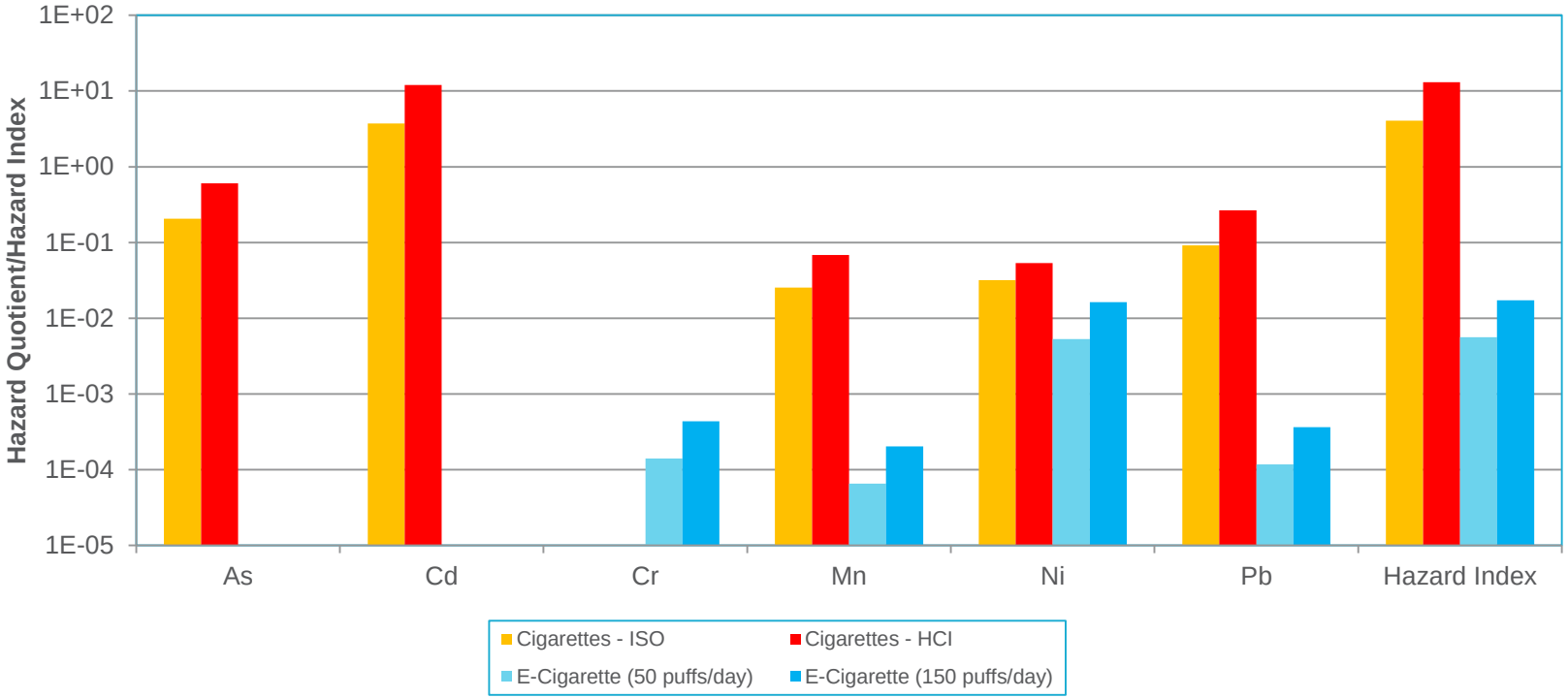


(1) Based on chronic Reference Concentration or National Ambient Air Quality Standard
(2) FDA. 2015. Q3D Elemental Impurity Guidance for Industry. Center for Drug Evaluation and Research.

Estimated Cancer Risk



Estimated Noncancer Hazard



Results

- Estimated exposure to metals in e-cigarette aerosol were 60 to 5,000 times below regulatory and health-based limits.
- Estimated Health Risk:
  - Cancer risk: 10^{-6} range, within USEPA acceptable levels
  - Noncancer Hazard: 60 to 5,000 times lower than USEPA acceptable level
- Compared to combustible cigarettes:
  - > 95% reduction in cancer risk
  - > 99% reduction in noncancer hazard

Conclusions

- Risk estimates for metals in e-cigarette aerosols represent greater than 95% reduction compared with combustible cigarette smoke
- Potential health risks from exposure to metals from e-cigarettes are orders of magnitude below estimated risk from combustible cigarettes