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Analysis of Toxic Metals in Electronic Cigarette Aerosols Using a Novel Trap Design

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Abstract

Since 2006 the domestic popularity and sales of electronic cigarettes (i.e., electronic nicotine delivery systems or ENDS) have grown rapidly. Although the constituents of the aerosol produced by ENDS have been previously investigated, differences in puff regimens and aerosol trapping schema in published literature often complicate result comparisons and data interpretation. As the ENDS product designs continue to evolve, there is a critical need to develop and validate robust methodologies for laboratory testing, appropriate aerosol generation and trapping media required for accurate determinations of ENDS aerosol metals deliveries. A simple, high metals purity, fluoropolymer trap was developed and validated that meets standard machine puffing regimen (CORESTA Recommended Method 81) specifications and exhibits negligible acid extractable metal backgrounds. Using a standard machine puffing regimen in combination with a fluoropolymer condensation trap, aerosol was generated and collected from select ENDS devices for analysis of chromium, nickel, copper, zinc, cadmium, tin, and lead with triple quadrupole inductively coupled plasma mass spectrometry. Devices tested spanned a range of commercial products, including flavored variants of JUUL pods, refillable tank systems, rechargeable cartridges, and single-use ENDs devices. Results showed that for aerosols generated under a fixed puffing regimen (50 puffs/collection), metal concentrations ranged from below the detection limits (LOD) to 614 ng copper and 339 ng zinc per 10 puffs. Cadmium concentrations were below LOD for all devices tested. Device specific aerosol levels of Sn and Pb ranged from below LOD to low nanogram levels. Cr and Ni were transported in aerosols at levels equivalent to, or slightly higher than in mainstream cigarette smoke using a standard smoking regimen. The generally lower levels of specific metals, Cd and Pb, transmitted in ENDS aerosols compared to mainstream cigarette smoke reflect possible reduction of harm for smokers who substitute the use of ENDS as cessation devices in place of smoking cigarettes.

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Introduction

Electronic nicotine delivery systems (ENDS, electronic cigarettes) have become the most commonly used tobacco product among adolescents (1). Some evidence suggests that youth and young adults who begin using ENDS face increased odds of nicotine addiction and are more inclined to begin smoking traditional cigarettes compared with non-ENDS users (2, 3). The common perception that ENDS could aid in cigarette smoking cessation in adults is of great interest. However, current evidence suggests that increases in ENDS usage among adolescents and young adults may increase dual use of ENDS and cigarettes (1–6). Consequently, the public health community needs accurate and reliable analytical data to help support or invalidate conceptions that ENDS represent a less harmful alternative to traditional combustible products, such as cigarettes and little cigars (7).

The combustion temperature of cigarettes and little cigars reaches approximately 900°C during a puff (8, 9). Factors affecting toxic metal transfer from tobacco filler to mainstream smoke include tobacco mass, packing density, rod length, metal content in tobacco, volatility of the transported form of the metal relative to combustion temperature, filter length, ventilation, etc. (10–12). For ENDS devices, where combustion does not occur, the principal factors that may affect metals concentrations transported in aerosol are metal concentrations in the heated ENDS liquids. The heating elements in ENDS used to vaporize nicotine, glycerol and/or propylene glycol typically reach temperatures less than 300°C (13). These temperatures are sufficient to cause limited thermal decomposition of the solvent and other components of the liquid (14). Consequently, the transport mechanism from liquid to aerosol for toxic metals is unlike traditional, combustible cigarettes or cigar type products (8, 9). The temperatures to which ENDS liquids are heated are insufficient to support combustion or vaporization for most metals or metal compounds, thus toxic metal transport in ENDS aerosol likely are independent of metal volatility. Limited entrainment of metal particles, metal compounds, or dissolved metal compounds in aerosol droplets formed by passage of air over the liquid surface is a possible metal transport mechanism. Another possible metal transport mechanism could involve aerosolization within liquid droplets sputtered from the heating element as the liquid boils and vaporizes. Only the more volatile forms of some metals would vaporize at the relatively low ENDS heating element temperatures.

Extreme care must go in to selecting appropriate laboratory glass and ceramic containers, and glass and quartz fiber filters, because many exhibit variable and high metal leaching, especially in the presence of acids required for extracting and maintaining metal solubility (15–21). In order to accurately determine the concentrations of metals transported in ENDS aerosol, sample collection materials must be acid resistant and contain low metal content to prevent metals leaching into acidic solvents. Thus, to maintain low metal background levels, trapping devices, sample containers, and drying surfaces should be free of glass and low purity quartz materials. Therefore, glass fiber filters are unsuitable for metals analysis because of high extractable metal concentrations.

A method is described for trapping toxic metals in ENDS aerosol using high purity fluoropolymer tubing with quantitative determination using triple quadrupole inductively coupled plasma mass spectrometry (QQQ-ICP-MS). This method was validated and applied

to a variety of ENDS aerosol samples. This new approach greatly reduces the potential for background interference and associated false positive detections.

Experimental

ENDS aerosol generation and sample preparation

Twelve different brands were tested in triplicate, consisting of four types: JUUL pods, refillable tank systems, rechargeable cartridges and single use ENDS devices. All products are trademarks of respective manufacturers and were obtained from vendors in the greater Atlanta, GA USA area or ordered online. ENDS aerosol was generated using a Cerulean (Richmond, VA, USA) CETI-8 e-cigarette aerosol machine. Condensed aerosol was collected from unused disposable products or from rechargeable or tank devices with freshly charged batteries for aerosol collection. Unused cartridges or pods were used for each replicate analytical run. Aerosol (50 puffs) was generated using CORESTA Method 81 parameters: 55 mL puff volume, 3 second puff duration, rectangular puff profile, flow path pressure drop ≤ 300 Pa, pressure drop ≤ 900 Pa with device in place, 30 second puff interval (22). Puff volume accuracies were verified daily using calibrated soap bubble meters. For the ENDS products with a manual heating button, the heating elements were activated at the beginning of the puff for aerosol generation. Since elevated pressure drops affect the puff profile shape and could delay activation of the heating elements, each tubing trap that was tested to assure that puff profiles met CORESTA Method 81 specifications to ensure consistency. The aerosols condensed inside ultrapure acid cleaned fluorinated ethylene propylene (FEP) tubing traps (Savillex, Eden Prairie, MN, USA) were removed from FEP traps by rinsing with 3 × 8 mL 1% v/v hydrochloric acid (Veritas double distilled, GFS, Columbus, OH, USA) + 2% v/v nitric acid (Environmental grade, GFS, further purified in a PFA sub-boiling still, CEM, Matthews, NC, USA). Samples were brought to 25 mL with the rinse solution in acid cleaned PMP class A volumetric flasks. Triplicate analyses were performed unless otherwise stated, and average values are reported.

Effect of tubing length on aerosol and metals recoveries

To optimize trap design and assess recoveries, aerosols from two different ENDS devices, a rechargeable cartridge system, 21st Century electronic cigarette and liquid cartridges (Beloit, WI, USA) and a refillable tank system, Vapin Plus 1100 electronic cigarette (Beloit, WI, USA) with Joyetech Full Flavor liquid (Tustin, CA, USA) were collected and analyzed. Traps were investigated with tubing lengths ranging from slightly greater than the CORESTA-specified puff volume to more than twice the specified puff volume: 518 cm, 3.97 mm i.d. (64 mL); 671 cm, 3.97 mm i.d. (83 mL); and 914 cm, 3.97 mm i.d. (113 mL). The percent aerosol mass recoveries were determined by dividing aerosol mass trapped in the tubing by the aerosol mass generated and delivered by the ENDS devices. Any aerosol mass that condensed on a post-tubing filter was subtracted from 100% recovery. Trapping efficiencies obtained using FEP tubing were compared with trapping efficiencies from experiments performed using commercially available, 44 mm glass fiber filters designed to trap mainstream cigarette smoke particulate (Borgwaldt, Richmond, VA, USA).

Chromium, nickel, cadmium, tin, and lead (100 μL each, 1,000 μg/mL), and copper and zinc (100 μL each, 10,000 μg/mL (Inorganic Ventures, Christianburg, VA, USA)) were added to Joyetech (ShenZhen, China) Full Flavor Liquid (9.30 mL) to prepare an ENDS liquid fortified standard solution. These concentrations are in excess of concentration ranges observed in commercial samples and were used to estimate the transfer efficiency from ENDS liquid to aerosol and to evaluate the tubing length on aerosol metal recoveries (N=5). The fortified ENDS liquid density was 1.25 g/cm^3, just below the density of pure glycerol in the absence of solutes (1.26 g/cm^3). This resulted in a solution with 7% higher aqueous fraction than in the unfortified ENDS liquid. The concentration of analyte per gram liquid was determined using the density of the diluted solution. The 10.0 μg/mL and 100 μg/mL liquid concentrations were equivalent to 8.00 and 80.0 μg/g fortified liquid, respectively.

Metal recoveries obtained with varying lengths of 3.97 mm ID FEP tubing were compared to determine any significant statistical differences using ANOVA (SAS, Cary, NC, USA). If differences were significant among the three tubing lengths, individual paired comparisons were made for confirmation using the Tukey-Kramer test (SAS).

Analysis of samples

Calibration standards for analysis were prepared by dilution of NIST traceable single element standards obtained from High Purity Standards (Charleston, SC, USA) in 1% v/v hydrochloric acid + 2% v/v nitric acid + 0.25% v/v hydrofluoric acid. The calibration blank consisted of the acid solution used to prepare the standards. The calibration ranges for five standards were designed to bracket the majority of ENDS aerosol concentrations from just above LOD to elevated levels: 0.100 to 2.50 μg/L chromium, nickel, and lead; 0.200 to 5.00 μg/L copper; 2.00 to 50.0 μg/L zinc; and 0.0400 to 1.00 μg/L cadmium and tin. Calibration linearity was considered acceptable if $r \geq 0.999$ using standard linear regression. When any sample concentrations were determined to be greater than the calibration ranges, they were diluted to fall within the calibration range. Sample concentrations were multiplied by final analytical volume (0.0250 L) and by 1000 to convert μg to ng of metal transported. Sample results in ng obtained from 50 puffs were then divided by 5 to express concentrations in terms of ng per 10 puffs (Table 5), a puff number in the intermediate range among U.S. cigarettes smoked using WHO intense smoking regimen (10). The ENDS aerosol procedural blank results, not the calibration blank, in each analytical run were subtracted from sample concentrations.

Two second source QC samples were prepared by diluting single element standards (Inorganic Ventures, Christiansburg, VA, USA) in a 1:1 v/v propylene glycol (FCC grade, Sigma-Aldrich, St Louis, MO, USA) and glycerol (Bioultra, Sigma-Aldrich, St Louis, MO, USA) solution in 1% v/v hydrochloric acid + 2% v/v nitric acid + 0.25% v/v hydrofluoric acid (Veritas double distilled, GFS). Quality control was maintained using a modified Westgard plot (23) of the QC data using SAS software (Cary, NC, USA). Duplicate QCs were analyzed before and after samples during each analytical run. In the event that a QC failed, the run was repeated if sufficient ENDS liquid remained; the result was not reported if insufficient inventory remained.

Instrument parameters

Diluted ENDS aerosol samples were introduced into an Agilent (Tokyo, Japan) 8800 QQQ-ICP-MS with an Elemental Scientific (Omaha, NE, USA) SC2-DX FAST autosampler via 0.38 mm peristaltic pump tubing with pump speed of 0.40 rps. Samples were further diluted 1:1 by teeing in tubing of the same diameter with internal standard solution (1 μg/L rhodium, 1% v/v nitric acid, 1% v/v hydrofluoric acid, 2% v/v 2-propanol). Diluted samples were introduced into the plasma using an Elemental Scientific Apex desolvating introduction system and C400 concentric PFA nebulizer (Savillex, Minnetonka, MN, USA). Plasma was maintained at 1550 watts RF power, 15 L/min plasma gas, and 0.90 L/min auxiliary gas, optimized near 5.7 mm sampling position for low oxides. Since desolvation results in very low oxide formation, nebulizer gas was optimized for greatest signal stability and intensity. Lens parameters were optimized as needed with the exception of method and mode-specific parameters described in Table 1.

Method limits of detection and quantitation

Method limits of detection (LODs) were determined according to Taylor's prescribed method (24), with standard deviations of the five calibration standards and the low and high QC readings after 20 analytical runs plotted against concentrations with regression lines extrapolated to S_0. S_0 was multiplied by 3 to determine the preliminary method LOD. For aerosol, method LODs were determined for 50 puffs. The final method LODs were statistically adjusted higher to avoid random overlaps between false positives, and false negatives (25). Lowest reportable level (LRL) was the respective lowest standard concentration for each analyte expressed in terms of ng aerosol (Table 2).

Results and Discussion

Electrostatic precipitation as a possible collection device

Commercial aerosol generation machines specifically designed for ENDS analysis are optimized for aerosol collection on glass fiber filters identical to those used to trap mainstream cigarette smoke particulate for organic smoke constituent analyses. One manufacturer offers an aerosol machine for electronic cigarettes that has an optional electrostatic precipitation trap for aerosol collection. While electrostatic precipitation in high purity, fused silica quartz tubes is a preferred aerosol trapping technique for mainstream cigarette and little cigar smoke particulate, ENDS aerosols are chemically and physically different from mainstream smoke produced by conventional combustible tobacco products. Typically, ENDS aerosol consists primarily of propylene glycol and/or glycerol vapor, which does not precipitate completely during transport through the electrostatic precipitation unit. Trapping efficiency with electrostatic precipitation can be variable depending on ENDS liquid composition. During preliminary method development for aerosol collection by electrostatic precipitation, we observed degradation of the quartz tube neoprene seals, causing them to disintegrate and eject neoprene particles into the collection tube, contaminating samples when propylene glycol containing aerosols passed through the tubes. Variable trapping efficiency and contamination problems were observed that rendered current electrostatic precipitation devices unsuitable for routine ENDS aerosol use.

ENDS aerosol recoveries with FEP condensation traps

Preliminary experiments using a 1524 cm × 2.16 mm i.d. FEP tube (56 mL internal volume) indicated resistance to air flow through the tube, which resulted in failure to achieve a rectangular puff profile specification. Additionally, the time required for the system to reach correct air flow specifications due to the restriction delayed heating element activation for some ENDS devices and led to lower aerosol mass than should have been generated under the specified puffing conditions (26). Therefore, no further work was performed using the 2.16 mm i.d. tubing. This finding highlights the importance of draw resistance and puff profile verification when assessing the reliability of published data obtained using laboratory devised aerosol trapping media.

Three 3.97 mm i.d. tubing lengths achieved a standard rectangular puff profile. Between 70 and 200 mg of aerosol was collected after 50 puffs from different ENDS devices. Table 3 shows the mass recoveries obtained from a tank system ENDS device using three different lengths of 3.97 mm i.d. FEP tubing as aerosol traps, along with the aerosol mass recovery obtained using a glass fiber filter as an aerosol trap. Unrecovered masses likely were from water (6% to 29% of ENDS liquids) (27, 28) or other volatile substances that did not condense during transport through the trap.

Aerosol mass recovery was slightly greater with 914 cm FEP tube length (Table 3). This likely resulted from increased internal surface area with the longer tubing, allowing condensation of water vapor or other volatile liquid constituents. ANOVA of aerosol metal recoveries in 3.97 mm i.d. FEP tubing showed no statistically significant differences for any of the metal concentrations in aerosol collected from the 518 cm, 671 cm, and 914 cm FEP tube lengths (Table 4). Therefore, the longest tubing length is advisable for more volatile substances, but is not essential to efficiently trap metals, as the metals are not in aerosol vapor phase.

ENDS aerosol metal recoveries using FEP condensation traps

Experiments comparing ENDS aerosol metal ion recoveries from the FEP traps showed 3 × 8 mL rinses were sufficient to assure complete recovery from the condensation tube. Table 4 shows blank rinses and aerosol recoveries from both Joyetech liquid aerosolized with a Vapin 1100 Plus and from the same liquid fortified with 10 mg/L chromium, nickel, cadmium, tin and lead, and 100 mg/L copper and zinc.

Statistical analysis (ANOVA) of metal concentrations in rinses from the tubing showed no significant differences for metals from the three 3.97 mm i.d. tube lengths with the exception of the fortified liquid aerosol nickel results. These results were reevaluated with the Tukey-Kramer test (analysis of results of individually paired tube lengths) and showed significantly higher average nickel from the 671 cm tube than from either the 518 cm tube ($p = 0.036$) or the 914 cm tube ($p = 0.019$), but no significant difference between the 518 cm and 914 cm tubes ($p = 0.929$).

High run-to-run and device-to-device variability in aerosol metals concentrations is indicated by standard deviations in excess of 50% of the means in several cases (Table 4). The variability is likely due to differences in the metal concentrations entrained in aerosol

according to the transport mechanisms discussed below, and to variable efficiency of aerosolization, even among the same brands of devices (27). Assuming the aerosol concentration of chromium in unfortified ENDS liquid were negligible, then spiking the liquid to 8.00 μg/g should provide 1,600 ng chromium in 0.2 g aerosol if the chromium were completely aerosolized. However, spiking the liquid only increased the mean aerosol chromium concentration to 3.7 ng/50 puffs for a transfer efficiency of 0.23%. The mean nickel recovery represented a transfer efficiency of 1.73%. The mean recoveries of copper, zinc, tin, and lead represented transfer efficiencies of 0.86%, 0.63%, 1.15% and 1.16%, respectively. These metals and their compounds are not generally volatile. Thus, even when fortified to very high concentrations, these metal ions were not efficiently transported in aerosol. Cadmium exhibited a slightly greater transfer efficiency, an average of 4.7% of the fortified amount transferred from the ENDS liquid into the aerosol. This data supports earlier statements suggesting that non-volatile metal forms would have to be transported in aerosol droplets, since heating element temperatures are insufficient to vaporize them.

Metal concentrations in aerosol from ENDS products

All devices were analyzed in 2018, and the dates obtained are shown in Table 5. Within each of the four device types, with the exception of the refillable tank systems, multiple brands or flavors were analyzed. The mean and standard deviations are presented in Table 5. The ENDS aerosol metal concentrations were generally low, with the exceptions of copper and zinc from some devices. Aerosol metals concentrations measured from all JUUL devices were below LOD or LRL, including copper and zinc concentrations. The devices with highest aerosol copper and zinc concentrations were single-use products and one cartridge device, suggesting the internal metal content in contact with the ENDS liquid, the corrosive nature of the liquid in a given device, and device age could be important factors influencing aerosol concentrations.

Most chromium concentrations were below LOD or LRL. For a few devices with quantifiable aerosol levels, chromium masses transported in 10 aerosol puffs were of similar magnitude to those from mainstream cigarette smoke using WHO intense regimen (10, 29). Nickel was transported at quantifiable levels in aerosol from most single-use and cartridge devices. For these products, the aerosol nickel mass in ten puffs was higher than that in the mainstream smoke from one cigarette (10). This finding demonstrates the possible effect of internal device corrosion over time, although freshly manufactured devices are not likely to have high levels of corrosion. Nickel was not quantifiable in aerosol from one Markten cartridge, two NJOY single-use devices, one Fin cartridge device, or JUUL products. Tin and lead were transported in the aerosols at generally low levels; several less than LOD or LRLs. The highest lead aerosol concentration was from the tank device examined. The highest ENDS lead mass transported in ten puffs was lower than that in mainstream smoke obtained from one cigarette using the WHO intense regimen, and was similar to conventional cigarette deliveries using the ISO 3308 regimen (10). For most ENDS products, however, aerosol lead concentrations were low relative to cigarette smoke.

One would expect very low cadmium contributions from internal leaching or corrosion, since the components used do not contain significant cadmium impurities. This expectation

was confirmed by determining that cadmium concentrations were below method LODs for all ENDS aerosols.

These results suggest that, for the products examined, metal concentrations in liquids from which the aerosols were generated would be important, especially if their concentrations correlate with the device's composition materials. This is an important topic that will be addressed in a subsequent study. From the results reported here, it is apparent that nickel, an IARC group 1 carcinogen, and lead, an IARC group 2 carcinogen, may be important ENDS device regulatory targets. Arsenic and cadmium, which are important for regulatory consideration with regard to cigarette emissions, are not components of commercial ENDS devices and unlikely to be important regulatory targets for ENDS products. Since the metals in aerosol were generally derived from ENDS device components with which the liquids were in contact, it may be possible to decrease the rates of metal corrosion within device components and pods by increasing the pH. Increasing the pH, however, would have other consequences. Some liquids are formulated with lower pH to slow pulmonary absorption of nicotine and provide a longer duration of satisfaction, whereas higher pH that would slow the rates of metal corrosion would cause nicotine to be more quickly absorbed in the free base form.

Conclusions

A reliable method for the collection and quantitative analysis of seven toxic metals in ENDS aerosol was developed and validated using the standard CORESTA Method 81 puff regimen. The use of this standard regimen was important given the level of ENDS industry regulation in Europe (30). The acid resistant, high purity fluoropolymer tube used to trap ENDS aerosol provides good aerosol mass recovery and negligible background levels of acid leachable metal, while meeting standardized puff profile specifications. To minimize false positive detection, when measuring metals in ENDS aerosols, the trap configuration and subsequent sample preparation steps must take into account possible sources of leachable metals background in the materials used. In this method, the absence of leachable metals permitted determination of LODs for quantitative metal analyses in aerosol from several ENDS devices using QQQ-ICP-MS. Experimental results showed that even when ENDS liquid was fortified to high metal concentrations, metals in the aerosol have low transport efficiencies, as would be expected for substances such as metals and metal compounds that are not volatile at temperatures attained by ENDS devices.

The metal transport efficiencies from ENDS liquid to aerosol were, in general, quite low, averaging less than 1% to 4.7%. However, in several devices with masses of chromium and nickel transported in ten CORESTA puffs from older devices were comparable to or slightly higher than their levels in mainstream cigarette smoke using WHO intense regimen (10, 29). For the products examined, lead aerosol deliveries were generally lower than in mainstream cigarette smoke on a per cigarette basis using WHO intense regimen (10). Unlike cigarettes, from which cadmium is transported at concentrations higher than many other metals in mainstream cigarette smoke using WHO intense regimen (10), cadmium concentrations were below reportable levels in ENDS aerosol for the tested products. As ENDS devices

continue to evolve in design and construction, it is prudent to monitor aerosol metals deliveries to evaluate any potential harmful exposures that could occur.

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Table I.

ENDS Aerosol Instrument modes and Internal Standard Assignments

Element, isotope	Instrument Mode	Cell gas	Quantitated ion	Quantitated mass	Internal Standard
^{52}Cr	MS-MS	NH_3	$^{52}Cr(NH_3)_2^+$	86	$^{103}Rh(NH_3)_4^+$
^{60}Ni	MS-MS	O_2	$^{60}NiO^+$	76	$^{103}RhO^+$
^{63}Cu	MS-MS	NH_3	$^{63}Cu(NH_3)_2^+$	97	$^{103}Rh(NH_3)_4^+$
^{66}Zn	MS-MS	NH_3	$^{66}Zn(NH_3)_3^+$	117	$^{103}Rh(NH_3)_4^+$
^{111}Cd	MS-MS	O_2	$^{111}Cd^+$	111	$^{103}RhO^+$
^{118}Sn	SQ	No Gas	$^{118}Sn^+$	118	$^{103}Rh^+$
$^{206+207+208}Pb$	SQ	No Gas	$^{206,207,208}Pb^+$	206+207+208	$^{103}Rh^+$

Cell parameters: No cell gas with −8 V octopole bias, 5 V energy discrimination; 0.45 mL/min O_2 cell gas with −20 V octopole bias, −8 V energy discrimination; 3.5 mL/min 10% NH_3, 90% He cell gas with −18 V octopole bias, −8 V energy discrimination

Table II.

Limits of Detection

ng/50 puffs	Cr	Ni	Cu	Zn	Cd	Sn	Pb
LOD	0.625	1.25	1.00	25.0	0.250	0.500	0.250
LRL	2.50	2.50	5.00	50.0	1.00	1.00	2.50

Lowest Reportable Level (LRL) is the concentration of the lowest standard expressed in ng/50 puffs.

Table III.

Percent aerosol mass recovery using high purity FEP tubes of different lengths versus standard glass fiber filters

Aerosol Collection Media	Aerosol Mass Recovered*	%Mass Recovery
Glass Fiber Filter	0.178 ± 0.007	98.0 ± 8.8 %
518 cm FEP Tube	0.157 ± 0.052	84.8 ± 4.2 %
671 cm FEP Tube	0.146 ± 0.026	89.2 ± 1.9 %
914 cm FEP Tube	0.148 ± 0.026	95.3 ± 2.0 %

* Devices can yield aerosol masses that vary from session to session

Table IV.

Anayses of tube blank rinses, Vapin 100 Aerosol metals recoveries, and the spiked aerosol recoveries (mean and standard deviation, ng obtained in 50 puffs)

	Cr	Ni	Cu	Zn	Cd	Sn	Pb
Method LOD (ng/50 puffs)	0.625	1.25	1.00	25.0	0.250	0.500	0.250
Lowest Reportable Limit (ng/50 puffs)	2.50	2.50	5.00	50.0	1.00	1.00	2.50
Blank Tube Rinse ng/50 puffs							
518 cm FEP Tube	<LRL	<LRL	6.27 ± 3.00	<LRL	<LRL	<LRL	<LRL
671 cm FEP Tube	<LRL	<LRL	14.4 ± 7.9	<LRL	<LRL	<LRL	<LRL
914 cm FEP Tube	<LRL	<LRL	5.98 ± 4.41	<LRL	<LRL	<LRL	<LRL
ANOVA p value	**N/A**	**N/A**	**0.0549**	**N/A**	**N/A**	**N/A**	**N/A**
ENDS Device: Vapin Plus - Joyetech E-liquid ng/50 puffs							
518 cm FEP Tube	<LRL	10.4 ±7.5	34.4 ± 32.9	91.2 ± 68.6	<LRL	5.01 ± 6.77	13.1 ± 8.6
671 cm FEP Tube	<LRL	10.2 ± 2.7	16.9 ± 5.0	107 ± 74	<LRL	2.22 ± 1.07	16.1 ± 11.4
914 cm FEP Tube	<LRL	10.8 ± 9.9	18.8 ± 8.3	86.5 ± 97.5	<LRL	1.37 ± 0.81	8.11 ± 6.22
ANOVA p value	**N/A**	**0.993**	**0.341**	**0.917**	**N/A**	**0.352**	**0.392**
ENDS Device: Vapin Plus - spiked Joyetech E-liquid ng/50 puffs							
518 cm FEP Tube	3.27 ± 1.48	19.6 ± 14.0	71.9 ± 48.1	178 ± 107	76.9 ± 92.6	21.6 ± 15.5	30.6 ± 33.6
671 cm FEP Tube	5.67 ± 3.10	83.1 ± 58.7	361 ± 397	265 ± 123	42.9 ± 33.4	19.5 ± 11.7	26.2 ± 13.2
914 cm FEP Tube	2.17 ± 1.25	11.5 ± 8.9	50.6 ± 30.8	146 ± 60	107 ± 89	22.7 ± 8.6	36.1 ± 23.5
ANOVA p value	**0.06**	**0.014**[§]	**0.101**	**0.194**	**0.445**	**0.918**	**0.821**

[§]Reevaluated with the Tukey Kramer test.

Table V.

Metal concentrations in ENDS aerosols with respect to device type (JUUL, single-use, cartridge, tank refill) and year obtained (mean and standard deviation, ng obtained in 10 puffs)

	Cr	Ni	Cu	Zn	Cd	Sn	Pb
LOD (ng/10 puffs)	0.125	0.250	0.200	5.00	0.050	0.100	0.050
LRL (ng/10 puffs)	0.500	0.500	1.00	10.0	0.200	0.200	0.500
Refillable Tank system; obtained in 2016							
Joyetech™ eGo tank system with My Vapor Store Gold Premium 24mg Nicotine	<LOD *	4.95 ± 1.93	7.47 ± 6.69	33.4 *	<LOD *	0.40 ± 0.15	11.4 ± 4.1
JUUL® pods; obtained in 2018							
Cool Mint, Mango & Virginia Tobacco	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Crème Brulee & Fruit Medley	<LOD	<LOD	<LRL	<LRL	<LOD	<LOD	<LOD
Cartridges; obtained in 2017							
Fin® Bold 2.4% Nicotine	<LOD	0.459 ≠	6.43 ± 5.60	<LRL	<LOD	<LOD	0.228 ≠
Mistic® Traditional 1.8% Nicotine	1.14 ± 0.62	4.97 ± 3.01	488 *	265 ± 111	<LOD	1.16 ± 0.78	3.28 ± 2.56
Vuse Menthol	1.12 ± 0.22	4.63 ± 2.00	<LRL	<LRL	<LOD	<LOD	<LOD
Vuse Original	0.293 ≠	1.89 ± 0.55	1.28 ± 0.88	<LRL	<LOD	<LOD	<LOD
Cartridges; obtained in 2016							
Krave Menthol 1.8% Nicotine	<LOD	1.73 ± 0.90	5.36 ± 2.72	<LOD	<LOD	0.639 ± 0.346	0.163 ≠
Krave Classic Tobacco 1.8% Nicotine	0.243 ≠	4.01 ± 2.14	87.1 *	40.1 ± 15.3	<LOD	1.71 ± 0.51	2.45 ± 0.60
Markten® 2.5% Nicotine	<LOD	0.472 ≠	97.2 ± 15.5	103 ± 21	<LOD	<LOD	<LOD
21st Century® Regular 2.0% Nicotine	1.85 ± 1.11	8.75 ± 5.32	6.75 ± 2.21	<LOD *	<LOD	0.507 ± 0.349	0.128 ≠
21st Century® Regular Zero Nicotine	0.622 ± 0.305	9.63 ± 0.81	8.95 ± 4.72	27.9 ± 29.4	<LOD	0.603 ± 0.755	1.46 ± 1.94
single use; obtained in 2016							
Flavor Vapes® Blueberry 18 mg nicotine	0.231 ≠	1.67 ± 1.93	614 ± 64	339 ± 90	<LOD	1.44 ± 1.66	<LOD
single use; obtained in 2017							
blu™ Classic Tobacco	0.373 ≠	1.14 ± 0.25	49.5 *	60.4 ± 52.5	<LOD	<LOD	<LOD
Logic Power 2.4% nicotine	0.789 ± 0.422	2.28 ± 0.96	360 ± 186	175 ± 101	<LOD	0.341 ± 0.067	1.06 ± 0.33
NJOY® Bold	<LOD	<LOD	2.53 ± 3.62	<LOD	<LOD	0.453 ± 0.402	<LOD
NJOY® Menthol	<LOD	0.507 ± 0.015	<LRL	<LOD	<LOD	0.961 ± 0.500	<LOD

* Due to insufficient inventory, only two replicates are reported.

≠ Value between the LOD and LRL.