Comparison of Quartz Filter Collection and Electrostatic Precipitation for Analysis of Trace Metals in ENDS Aerosol

2021_TSRC50_Jameson.pdf

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Introduction

The purpose of this study is to determine average method limit of detection (LOD) values for FDA HPHC list metals using the quartz filter (QF) collection method, compared to electrostatic precipitation (EP). Quartz filter collection is a common methodology for electronic nicotine delivery systems (ENDS) aerosol collection, and has been used routinely for analysis of metals in ENDS aerosol[1]. For metals analysis, QF are known to contain metals background, potentially increasing the method LOD, and background levels of metals can vary by QF lot, necessitating reassessment of background levels between lots. Electronic precipitation is an alternative methodology for aerosol collection which has been used for combustible cigarette aerosol collection[2] and was applied more recently to ENDS aerosol[3]. EP is not prone to high background levels of metals, and has a greater aerosol collection capacity than QF, allowing for increased method sensitivity by increasing collected aerosol mass when needed. High method sensitivity/low LOD is of particular importance for ENDS metals analysis, as ENDS aerosol generally has lower levels of metals than combustible cigarettes. For these reasons, EP is an attractive alternative to QF for analytical determination of metals in ENDS aerosol.

To compare these methodologies, a compilation of previously collected datasets using both QF and EP based methods was leveraged to calculate average method LODs using air blank measurements. Determination of method LOD is important for analytical measurements because it dictates the lowest concentration at which analyte present in the sample can be differentiated from the background. Method LOD is distinct from instrument LOD, the lowest concentration of analyte that can be detected by the instrument method used. Method LOD determination is of particular importance for QF collection-based trace metals analysis due to the potential for high metals background.
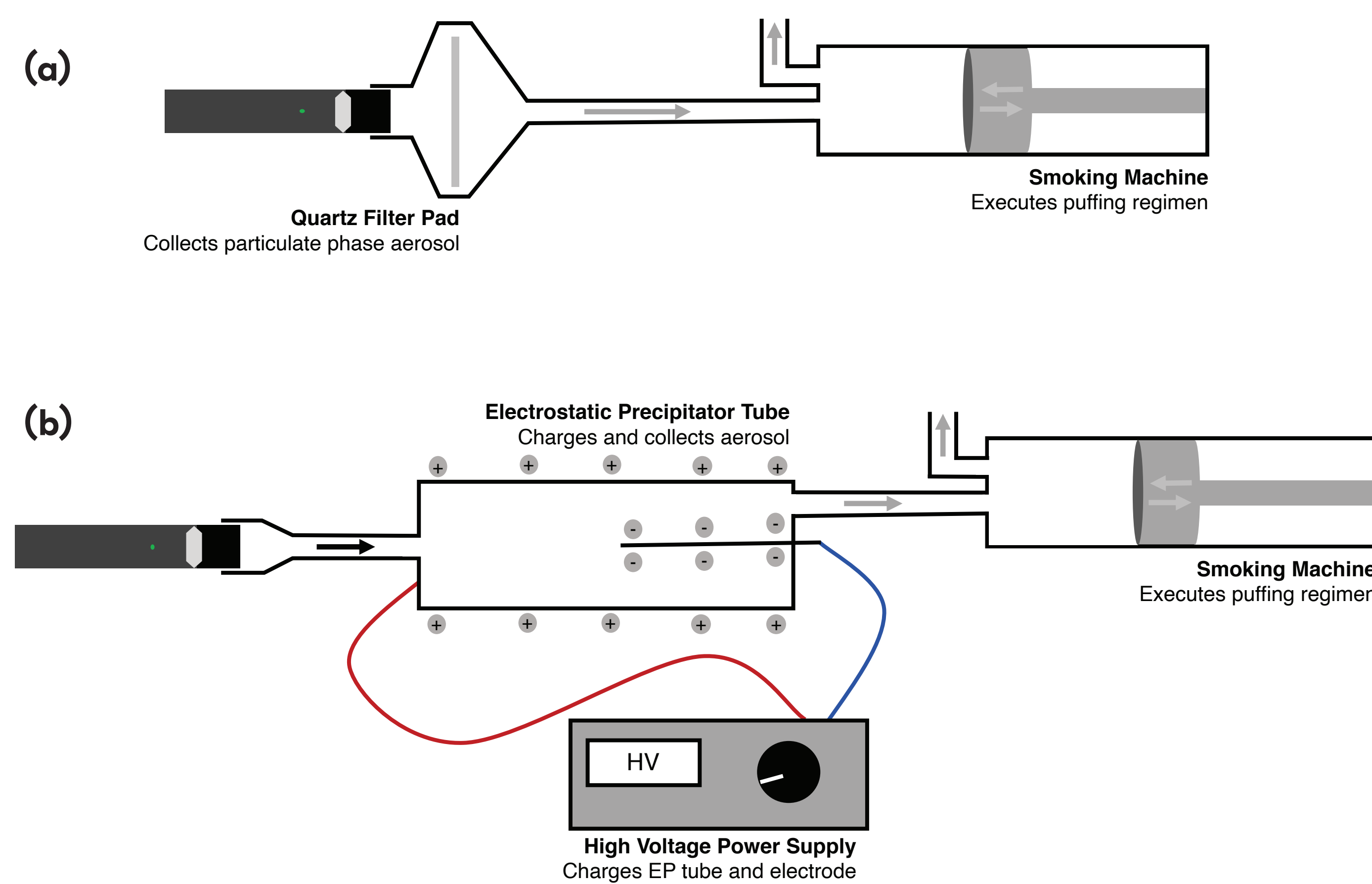

Figure 1: Experimental setups for (a) QF and (b) EP aerosol collection

Methods

For QF collections, pads were positioned just in front of the JUUL device mouthpiece (**Figure 1a**). After puffing, QF was removed from the pad holder using non-metallic tweezers and extracted/digested with a nitric acid solution. The sample solution was analyzed by Inductively Coupled Plasma Mass Spectrometry (ICP-MS).

Methods (cont.)

For EP collections, the JUUL device was puffed directly into an EP tube (**Figure 1b**). The EP setup consisted of a high voltage power supply, creating a high voltage between a glass tube (positively charged), and an inert electrode (negatively charged) suspended within the tube. When aerosol particles enter the tube, they acquire negative charge by interaction with the electrode, and the charged vapor particles then deposit on the positively charged tube walls. The the glass tube was removed and extracted with methanol, then the sample solution was digested with nitric acid before analysis by ICP-MS.

Blank measurements were made by collecting room air alongside ENDS aerosol collections for both QF and EP collection methods and analyzing identically to aerosol samples. Blanks were compiled across eight separate trace metals analysis studies. The dataset included 372 individual blank measurements for QF and 41+ blank measurements for EP.

Method LOD values were computed for each analyte and collection methodology using CORESTA guide no. 28.

Blank Results

Using QF collection, a large proportion of blank measurements for chromium, lead, and nickel were above the instrument LOD. By contrast, EP collection yielded blank measurements below LOD in the majority of cases (**Table 1**).

	Quartz Filter			Electrostatic Precipitation		
Analyte	Blanks Examined	Blanks >LOD	Percent >LOD	Blanks Examined	Blanks >LOD	Percent >LOD
Cadmium	372	16	4.3%	41	0	0%
Chromium	372	372	100%	41	1	2.4%
Lead	372	195	52%	41	2	4.8%
Nickel	372	130	35%	42	1	2.4%

Table 1: Comparison of the proportion of >LOD blank measurements via QF and EP collections

The observed background levels of chromium, lead, and nickel found for QF in this study were also highly variable within the study results. Relative standard deviations of chromium, lead and nickel in QF blanks were 100%, 116%, and 67%, respectively. Mean and standard deviation for QF and EP blanks are shown in **Figure 2**.
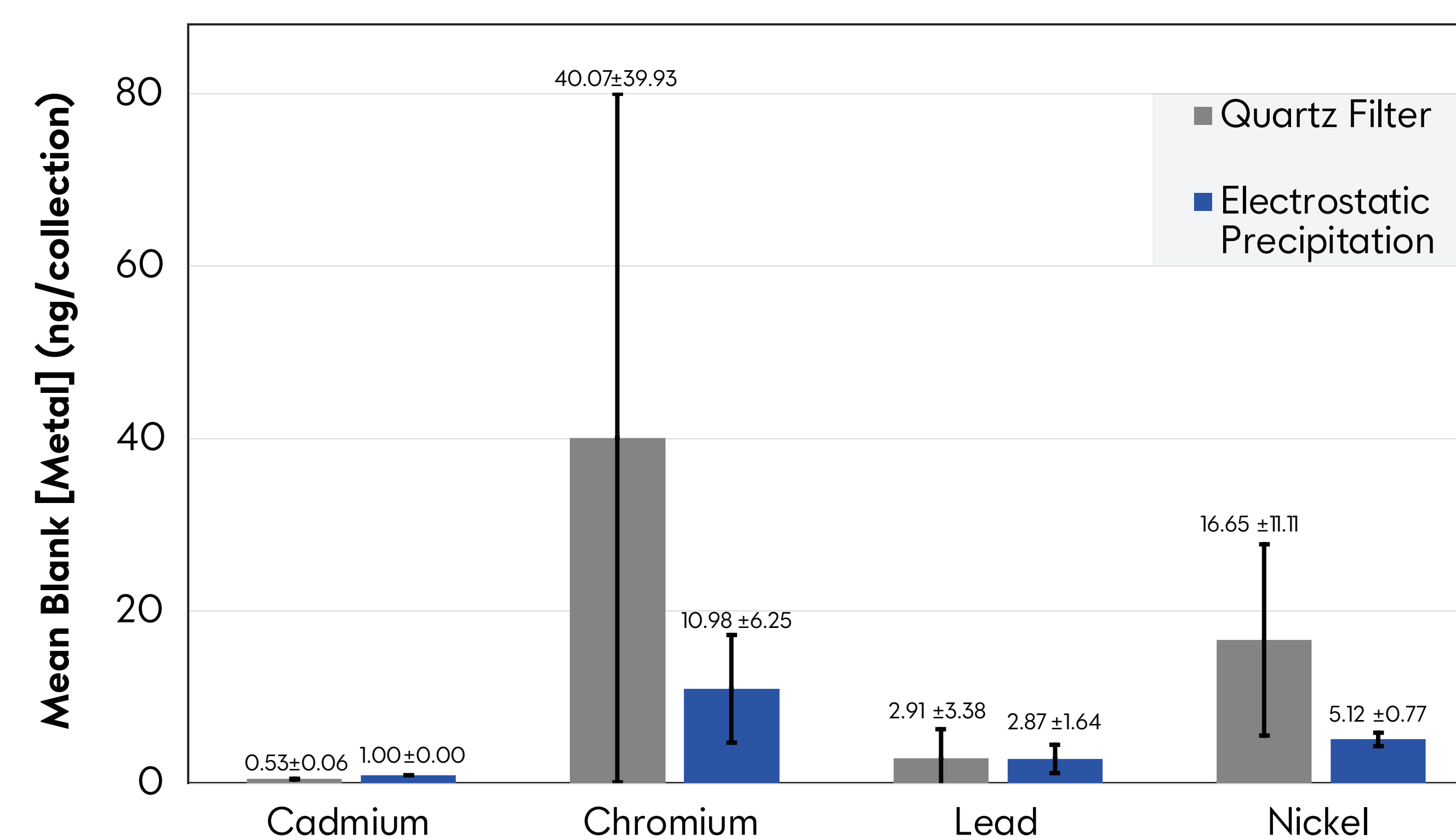

Figure 2: Mean and standard deviation for all QF and EP blank measurements

CORESTA Guide No. 28

CORESTA Guide No. 28 provides a list of considerations for setting method LOD and Limit of Quantification values when determining select metals in e-liquid and aerosol by ICP-MS. Equation 1 (Eq. 1) from Guide No. 28 was selected to be used for the determination of method LODs in this study.

$$L_D = (T_{0.99} \times \sigma_{Blanks}) + x \quad \text{(Eq. 1)}$$

Where:

L_D = Method LOD

$T_{0.99}$ = Student's t-value appropriate for the single-tailed 99th percentile t statistic and a standard deviation estimate with sample size (n) minus 1 degrees of freedom.

σ = Standard deviation of blank values

x = Average blank value (use zero if the mean is negative)

LOD Results

Equation 1 was used to calculate the method LODs for Chromium, Nickel, Cadmium, and Lead by QF collection and by EP collection. **Table 2** compares instrument LOD to method LOD for both collection methods. Instrument LOD values are similar for both methods because ICP-MS is used for analyte quantitation, independent of collection method. Because method LOD accounts for analyte background levels, the high metals background in QF results in higher method LODs.

	Quartz Filter		Electrostatic Precipitation		
Analyte	Instrument LOD (ng/collection)	Method LOD (ng/collection)	Instrument LOD (ng/collection)	Method LOD (ng/collection)	Method LOD Percent Diff
Cadmium	0.53	0.68	1.00	1.00	48%
Chromium	5.25	133.36	10.00	26.11	-80%
Lead	1.05	10.81	2.50	6.83	-37%
Nickel	10.50	42.60	5.00	6.99	-84%

Table 2: Reported instrument LOD and calculated method LOD for trace metals analysis

Conclusions

Method LOD dictates the lowest concentration at which analyte present in the sample can be differentiated from the background. Significant reductions in method LOD for analysis of trace metals from the FDA ENDS PMTA HPHC guidance were achieved by switching from QF to EP collection. The computed method LODs for QF and EP collection, respectively, were 0.68 ng and 1.00 ng for cadmium (48% increased, due to instrument LOD), 133.36 ng and 26.11 ng for chromium (80% reduced), 10.81 ng and 6.83 ng for lead (37% reduced), and 42.60 ng and 6.99 ng for nickel (84% reduced). Notably, due to the high variability in QF metals background, there were five instances with chromium, one instance with lead, and three instances with nickel where blank measurements from this dataset exceeded the method LODs calculated here. These instances suggest that false positive metals reporting is still expected in large sample sets using QF collection, even after proper LOD calculation. Due to lower method LODs and greater method reliability, EP collection is superior to QF collection for ENDS trace metals analysis.

1. Long, G. A., 2014. Comparison of select analytes in exhaled aerosol from e-cigarettes with exhaled smoke from a conventional cigarette and exhaled breaths. Int J Environ Res Public Health. 11, 11177-91.
2. Determination of Toxic Trace Metals (Ni, Pb, Cd, Cr, As, Se) in Mainstream Tobacco Smoke. Health Canada. T- 109, Second Edition. November 1, 2017.
3. Ohashi, S., 2018. Development and Validation of an ICP-MS Method for Simultaneous Determination of Selected Metals in Electronic Cigarette Aerosol. Beiträge zur Tabakforschung International. 28, 2-13.