



**Cooperation Centre for Scientific Research  
Relative to Tobacco**

## **CORESTA Guide N° 28**

**Technical Guide  
for Setting Method LOD and LOQ Values  
for the Determination of Metals in E-Liquid  
and E-Vapour Aerosol by ICP-MS**

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**E-Vapour Sub-Group**



## CORESTA TECHNICAL GUIDE N° 28

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Technical Guide for Setting Method LOD and LOQ Values for the Determination of Metals in E-Liquid and E-Vapour Aerosol by ICP-MS

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# 1. INTRODUCTION

## 1.1 Background

This Technical Guide provides a list of considerations for setting method Limit of Detection (LOD) and Limit of Quantification (LOQ) values when determining select metals in e-liquid and e-vapour aerosol by Inductively Coupled Plasma Mass Spectrometry (ICP-MS).

## 1.2 Purpose

This Guide details an approach for the determination of Limit of Detection (LOD) and Limit of Quantification (LOQ) values for trace elements in e-liquids and e-vapour aerosol using ICP-MS.

# 2. TERMS & DEFINITIONS

**Signal-to-Noise Ratio (S/N):** The ratio of analyte signal to that of the noise.

**Method Blank:** A sample free matrix that is prepared exactly as samples. The purpose of the Method Blank is to characterize contamination originating from reagents and the sample preparation process.

**Instrument Limit of Detection (LOD):** The lowest amount of an analyte which can be detected in a calibration standard. The LOD includes contamination arising from reagents, but not the sample preparation process.

**Method Limit of Detection (MLOD):** The lowest amount of analyte which can be detected in a sample prepared according to the analytical procedure. The MLOD includes contamination arising from reagents and the sample preparation process.

**Instrument Limit of Quantitation (LOQ):** The lowest amount of analyte which can be quantitatively determined with acceptable precision and accuracy in a calibration standard. The LOQ includes contamination arising from reagents, but not the sample preparation process.

**Method Limit of Quantitation (MLOQ):** The lowest amount of analyte, in a sample prepared according to the analytical procedure, which can be quantitatively determined with acceptable precision and accuracy. The MLOQ includes contamination arising from reagents and the sample preparation process.

**Noise:** The part of the data that contains extraneous information.

**Signal:** The part of the data that contains information about the chemical species of interest (i.e. analyte).

**Spiked Blank (or Fortification):** Sample to which all reagents and media are added in the same volumes or proportions as used in the sample preparation process, fortified known quantity of analyte.

# 3. TECHNICAL CONSIDERATIONS

The following list of technical considerations should be considered when developing and validating a method for the analysis of select metals in e-liquid and e-vapour aerosol by Inductively Coupled Plasma Mass Spectrometry (ICP-MS).

- Detection and quantitation limits must be based on sound scientific principles and the purpose of the resulting data.
- The definition of “quantitation” must account for both precision and accuracy.
- Detection limit procedures must take into account the variability and bias of unintentional sources of contamination.
- Specificity should be verified for all target analytes.
- Detection limit procedures must include procedures for ongoing demonstration of sensitivity and background contamination.
- Detection and quantitation levels must account for the effects of various matrices.
- If detection and quantitation limits is determined based on visual evaluation or based on signal to noise ratio, the presentation of the relevant chromatograms is considered acceptable for justification.

## 4. APPROACH

### 4.1 Detection Limit Approaches

Within the context of this technical guidance:

- Instrument LOD is used when no detectable metals are found within the method blanks.
- Method LOD is used when metals are detectable within the method blanks.

#### **Instrument LOD for metals that are not detected in all blanks.**

To determine the Instrument LOD for metals that are not detected in blank, use one or more of the following approaches:

1. The mean determined concentration plus three times the standard deviation of a set of method blanks (considered as conservative value).
2. The concentration value that corresponds to an instrument signal-to-noise ratio in the range of 3:1 to 2:1.
3. The concentration equivalent to three times the standard deviation of replicate instrumental measurements of spiked blanks.
4. The concentration equivalent to the Student’s t-statistic at a 99<sup>th</sup> percentile for sample size (n) minus 1 degrees of freedom, multiplied by the standard deviation ( $\sigma$ ) of replicate instrumental measurements of spiked blank values.
5. A specific calibration curve should be studied using samples containing an analyte in the range of detection limit. The residual standard deviation of a regression line or the standard deviation of y-intercepts of regression lines may be used as the standard deviation.
6. The region of the calibration where a significant change in sensitivity, i.e., a break in the slope of the calibration is found.
7. Visual evaluation of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be reliably detected.

### Method LOD for metals that are detected in blanks.

To determine the Method LOD for metals that are detected in blank, use one of the following approaches:

Note: A sufficient number of blank samples should be analyzed to assure a robust estimate of the method LOD. Method LOD should be determined periodically and when any change occurs in method, for example a change in filter lot number.

#### Equation 1.

$$L_D = (T_{0.99} \times \sigma_{Blanks}) + x$$

Where:

$L_D$  = Method Limit of Detection

$T_{0.99}$  = 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.

$\sigma$  = Standard deviation of Blank Values

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

or

#### Equation 2.

$$L_D = \frac{3.3 \sigma}{S}$$

Where:

$L_D$  = Method Limit of Detection

$\sigma$  = Standard Deviation of Blank Values

S = Slope of the Calibration Curve

## 4.2 Quantitation Limit Approaches

Within the context of this technical guidance:

- Instrument LOQ is used when no detectable metals are found within the method blanks.
- Method LOQ is used when metals are detectable within the method blanks.

### Instrument LOQ for metals that are not detected in method blanks.

When metals are not detected in method blanks, estimate the LOQ using one or more of the following:

1. The concentration value that corresponds to an instrument signal-to-noise ratio in the range of 10.
2. The concentration equivalent to 10 times the standard deviation of replicate instrumental measurements of spiked blanks. Spike blanks should be prepared near the expected instrument LOQ.

3. A specific calibration curve should be studied using samples, containing an analyte in the range of quantitation limit. The residual standard deviation of a regression line or the standard deviation of y-intercepts of regression lines may be used as the standard deviation.
4. The lowest concentration value that meets the method requirements for accuracy and precision.
5. The lowest point of the calibration range if the lowest point meets the method requirements for accuracy and precision.
6. Visual evaluation of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be reliably quantified in blanks.

### **Method LOQ for metals that are detected in blanks.**

Once the lowest spike blank sample that meets the method requirements for accuracy and precision, calculate the LOQ as follows:

#### **Equation 3.**

$$L_Q = L_D + R$$

Where:

$L_Q$  = Method Limit of Quantification

$L_D$  = Method Limit of Detection

$R$  = Validated Lowest Spike Recovery

or

#### **Equation 4.**

$$L_Q = \frac{10 \sigma}{S}$$

Where:

$L_Q$  = Method Limit of Quantification

$\sigma$  = Standard Deviation of Blank Values

$S$  = Slope of the Calibration Curve

Note: Any outlier detection in the data set should follow accepted statistical methods.

## **4.3 Examples**

### **Example of metals that are detected in blanks**

Aerosol method LODs/LOQs are established based on manufactured filter pad and/or reagent lots. The following examples exhibit how equations can be used to calculate method LODs and LOQs.

**Example 1.** How Method LOD is determined, for element values above the instrument LOQ:

$$L_D = (T_{0.99} \times \sigma_{Blanks}) + x$$

Where:

n = 25 Blanks tested for Chromium

$T_{0.99} = 2.492$

$\sigma = 0.2186$  ng/mL

$x = 1.75169$  ng/mL

$L_D = 2.30$  ng/mL

**Example 2.** How Method LOQ is determined, for element values above the instrument LOQ (continued):

$$L_Q = L_D + R$$

Where:

$L_D = 2.30$  ng/mL

R = 2.0 ng/mL (minimum value with +/- 20 % accuracy)

$L_Q = 4.30$  ng/mL

**Example 3.** How Method LOD is determined, for element values below the validated instrument LOD collected during the aerosol blank run:

**Equation 5.**

$$L_D = I_D$$

Where:

$x = < 0.5$  ng/mL

$I_D = 0.5$  ng/mL (Validated Instrument Method of Detection)

$L_D = 0.5$  ng/mL

**Example 4.** How Method LOQs are determined for element values below the validated instrument LOD collected during the aerosol blank run (continued):

$$L_Q = L_D + R$$

Where:

$L_D = 0.5$  ng/mL

R = 1.0 ng/mL

$L_Q = 1.5$  ng/mL

**Example 5.** How Method LOD is determined, for element values above the instrument LOQ:

$$L_D = \frac{3.3 \sigma}{S}$$

Where:

n = 25 Blanks tested for Chromium  
x = 1.75169 ng/mL  
 $\sigma$  = 0.2186 ng/mL  
S = 0.30  
L<sub>D</sub> = 2.41 ng/mL

**Example 6.** How Method LOQs is determined by for element values above the validated instrument LOD collected during the aerosol blank run (continued):

$$L_Q = \frac{10 \sigma}{S}$$

Where:

n = 25 Blanks tested for Chromium  
x = 1.75169 ng/mL  
 $\sigma$  = 0.2186 ng/mL  
S = 0.30  
L<sub>Q</sub> = 7.29 ng/mL

## 5. SUMMARY

The principal goal of this technical guide is to address potential approaches to setting method LOD and LOQ values when determining select metals within e-liquid and e-vapour aerosol samples.

## 6. REFERENCES

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