Proposed Blood Lead Standards – Comments and Responses

Proposed Standards were made available to New York State permitted laboratories and laboratories in application for a permit on March 4th, 2020. The announcement was by e-mail to the facility and laboratory contact person's e-mail address and the Proposed Standards were posted to the CLEP website.

The comment period ended June 15th, 2020. Comments received from any regulated parties and responses are shown here.

Standards will be adopted July 13th, 2020, with an effective date of August 1st, 2020.

Blood Lead – Comprehensive Testing

Toxicology	
Blood Lead – Comprehensive Testing	
Proposed Standard	***Proposed Guidance***
Blood Lead Standard of Practice 1 (BL S1): Materials Contamination Control The laboratory must implement procedures to ensure that materials used for blood lead collection and processing are free from significant lead contamination.	Significant lead contamination refers to an amount of lead that would change the blood lead level by more than 0.2~~5~~ microgram**s**/dL. Blood collection tubes/containers should be either lot-tested, and certified by the testing laboratory as fit for purpose, or manufacturer-certified for blood lead use (or trace element testing) to ensure that they are free from significant lead contamination. Collection tubes/containers are suitable for use when the mean lead concentration or difference in blood lead is less than or equal to 0.2~~5~~ micrograms/dL. Collection materials such as alcohol swabs and blood tubes/containers must be fit for purpose. The laboratory must inform clients of proper collection techniques, especially the importance of thorough patient hand washing prior to collecting capillary specimens. Where appropriate, laboratory supplies (e.g., flasks,

Toxicology	
Blood Lead – Comprehensive Testing	
Proposed Standard	***Proposed Guidance***
	autosampler tubes, and pipet tips), used for blood lead testing must be pre-checked for contamination and/or acid-washed (e.g., with dilute nitric acid), and certified as fit for purpose. Disposable plastic ware can be verified as contamination-free by randomly checking materials by lot number.

Blood Lead Standard of Practice 1 (BL S1): Materials Contamination Control

COMMENT 1:

1) Significant lead contamination refers to an amount of lead that would change the blood lead level by more than 0.25 microgram/dL (CHANGED FROM 1ug/dL)
2) Collection tubes/containers are suitable for use when the mean lead concentration or difference in blood lead is less than 0.25 microgram/dL (CHANGED FROM 0.5ug/dL)

The changes are overly restrictive, not relevant to currently established clinical decision points, and not feasible
We are proposing that this change not be made.

RESPONSE: 1

The guidance provided reflects recommended laboratory practices. The original recommendation (0.5 µg/dL) was set almost 30 years when the CDC definition of a blood lead level (BLL) of concern was lowered from 25 µg/dL to 10 µg/dL. At that time, the level of background contamination deemed acceptable was set at 5% of the BLL of concern, i.e., 0.5 µg/dL. Today the definition of elevated BLL is 5 µg/dL in NYS and, according to the CDC, the current 97.5th percentile for BLL is 3.5 µg/dL, so revised guidance on acceptable background contamination is long overdue. Setting the minimum background contamination at 5% of the current NYS elevated BLL is 0.25 µg/dL. However, we recognize that some older laboratory methods for blood lead may not be capable of measuring BLLs to the second decimal place with confidence, so the proposed guidance on acceptable contamination has been modified to ≤0.2 µg/dL.

COMMENT 2:

The guidance for the proposed standard states that lead contamination concentrations greater than 0.25 micrograms/dL are significant. Laboratories' across the country have developed and validated the blood lead test to meet the guidance for the former standard that significant contamination is defined as lead concentrations greater than 1 microgram/dL; and certification as fit for purpose is defined as mean lead concentrations of less than or equal to 0.50 micrograms/dL. The former standard aligns with the CDC recommendations (https://www.cdc.gov/nceh/lead/publications/screening.htm appendix C.1, page 3). The guidance for the proposed standard would require laboratories to redevelop and revalidate the blood lead test to meet an analytical method sensitivity of 0.25 micrograms/dL. The level of effort to complete this would put an undue burden on the laboratories for an outcome which does not clinically impact the outcome of the testing.

RESPONSE 2:

The guidance provided reflects recommended laboratory practices. The original recommendation referenced in the comment (0.5 µg/dL) was set almost 30 years when the CDC definition of a blood lead level (BLL) of concern was lowered from 25 µg/dL to 10 µg/dL. At that time, the level of background contamination deemed acceptable was set at 5% of the BLL of concern, i.e., 0.5 µg/dL. Today the definition of an elevated BLL is ≥5 µg/dL in NYS and, according to the CDC, the current 97.5th percentile for BLL is 3.5 µg/dL, so revised guidance on acceptable background contamination is long overdue. Setting the minimum background contamination at 5% of the current NYS elevated BLL is 0.25 µg/dL. However, we recognize that some older laboratory methods for blood lead may not be capable of measuring BLLs to the second decimal place with confidence, so the proposed guidance on acceptable contamination has been modified to ≤0.2 µg/dL. Most comprehensive methods for blood lead should be able to achieve this level of precision without the need for re-validation.

Toxicology	
Blood Lead – Comprehensive Testing	
Proposed Standard	***Proposed Guidance***
Blood Lead Standard of Practice 4 (BL S4): Calibration Protocols On each day of testing, the laboratory must run a calibration curve that: a) includes a blank and at least three (3) calibration standards; b) is matrix matched to the specimens being tested, unless validation studies indicate the absence of matrix effects; and c) is run at least every eight (8) hours of testing, unless longer instrument stability is validated, but no longer than twenty-four (24) hours.	Information on Departmental approval of laboratory developed tests (LDTs) is available at: https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval. a) For laboratory developed tests (LDTs), this type of calibration is considered robust. b) Typically, graphite furnace AAS can be calibrated with aqueous lead standards, plus modifier; however, ICP-MS is more sensitive to matrix effects and must be matrix-matched, i.e., base blood is added to calibration standards for simple dilution methods, unless validation studies indicate the absence of matrix effects.

Blood Lead Standard of Practice 4 (BL S4): Calibration Protocols

COMMENT 1:

Reword to state in Guidance section b)Typically, graphite furnace AAS can be calibrated with aqueous lead standards, plus modifier; ICP-MS is more sensitive to matrix effects and must be matrix-matched, i.e., base blood is added to calibration standards for simple dilution methods, unless validation studies indicate the absence of matrix effects.
The current way that it is worded seems to contradict the standard that the guidance is referring to where it allows for validation work to show that matrix effects are not significant. Phrase the guidance standard similarly to the Trace Elements Standard of Practice 5 (TE S5) for Calibration for consistency.

RESPONSE 1:

We agree with the proposed revision and have modified the guidance as suggested.

COMMENT 2:

Section (b) of the proposed standard requires that calibration curves be matrixed matched, unless validation studies indicate the absence of matrix effects. However, the guidance for this standard appears to require a matrix matched calibration curve even if the laboratory has validated the absence of matrix effects for the blood lead test by ICP-MS. If validation studies indicate the absence of matrix effects for blood lead by ICP-MS, then aqueous lead standards should be acceptable for calibration. Aqueous lead standards are acceptable for calibration if the laboratory has validated the absence of matrix effects.

RESPONSE 2:

We have modified the guidance as suggested.

Toxicology	
Blood Lead – Comprehensive Testing	
Proposed Standard	***Proposed Guidance***
Blood Lead Standard of Practice 5 (BL S5): Quality Control Three (3) levels of quality control (QC) must be included with each test run to include a low, intermediate and elevated concentration.	The controls should include a low (approximately three (3) to five (5) micrograms/dL), an intermediate (ten (10) to fifteen (15) micrograms/dL), and an elevated level (greater than twenty (20) micrograms/dL) level material. The Department anticipates that these suggested ranges will be modified as control materials from commercial vendors that are in compliance with CDC recommendations become available. Laboratories using furnace AAS methods with an upper calibration point of thirty (30) micrograms /dL must also run an elevated control (greater than or equal to thirty (30) micrograms /dL) when diluting samples greater than or equal to thirty (30) micrograms /dL.

Toxicology	
Blood Lead – Comprehensive Testing	
Proposed Standard	***Proposed Guidance***
	Laboratories using ICP-MS methods for blood lead ~~**cannot**~~ may be unable to simply dilute specimens exceeding the upper calibration standard because of matrix effects. Alternative protocols ~~must~~ may need to be used to handle such samples and must be validated as appropriate.

Blood Lead Standard of Practice 5 (BL S5): Quality Control

COMMENT 1:
Would documented dilution protocol validation and satisfactory recovery address the concern regarding matrix factor?

RESPONSE 1:
Yes. The guidance has been modified to state that alternative protocols may need to be used to handle such samples and must be validated as appropriate.

COMMENT 2:
The guidance for this standard states that laboratories cannot dilute specimens exceeding the upper calibration standard due to matrix effects. Laboratories that have validated the absence of matrix effects for the blood lead test by ICP-MS at the high end of the calibration curve should be permitted to dilute samples greater than or equal to the upper calibration standard, provided they also run an elevated control. Recommend updating the standard to define that laboratories may dilute if they have validated the absence of matrix effects.

RESPONSE 2:
The guidance has been modified to state that alternative protocols may need to be used to handle such samples and must be validated as appropriate.