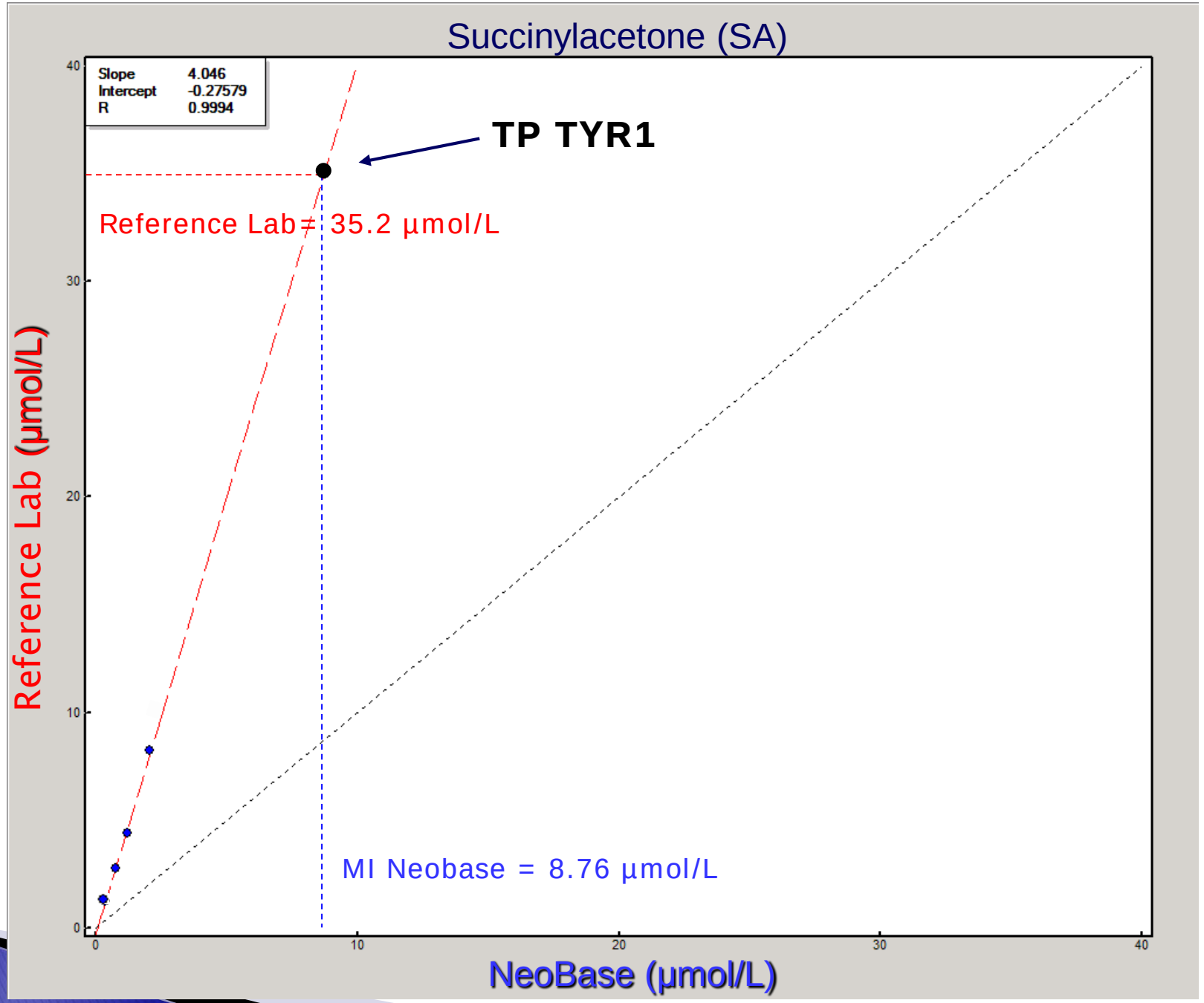
Normalization of Laboratory MS/MS Cutoffs using CDC NSQAP Quality Control Materials

Mary Seeterlin,[1] Victor De Jesus,[2]
Christopher Haynes,[2] Mark Morrissey,[3]
Adrienne Manning,[4] Konstantinos Petritis,[5]
Sonal Bhakta,[5] Patrice Held[6]

1. Michigan Department of Health & Human Services, Lansing, Michigan
2. US Centers for Disease Control and Prevention, Atlanta, Georgia
3. Wadsworth Center/New York State Department of Health, Albany, New York
4. Dr. Katherine A. Kelley State Public Health Laboratory, Connecticut Department of Public Health, Rocky Hill, Connecticut
5. Arizona Department of Health Services, Office of Newborn Screening, Phoenix, Arizona
6. Wisconsin State Laboratory of Hygiene, Madison, Wisconsin


Succinylacetone (SA)
Slope 4.046
Intercept -0.27579
R 0.9994
TP TYR1
Reference Lab = 35.2 µmol/L
MI Neobase = 8.76 µmol/L
Reference Lab (µmol/L)
NeoBase (µmol/L)
0
10
20
30
40

Goal:

- Accurately compare analyte cutoff values

Problem:

- Differences in testing methodologies
  - Derivatized vs. non-derivatized
  - Extraction techniques
  - Instrumentation
  - Internal Standards
  - Calibration Techniques
  - Standard Calibration Materials

Goal

- Accurately compare analyte cutoff values
- Accurately compare analyte concentrations for positive cases

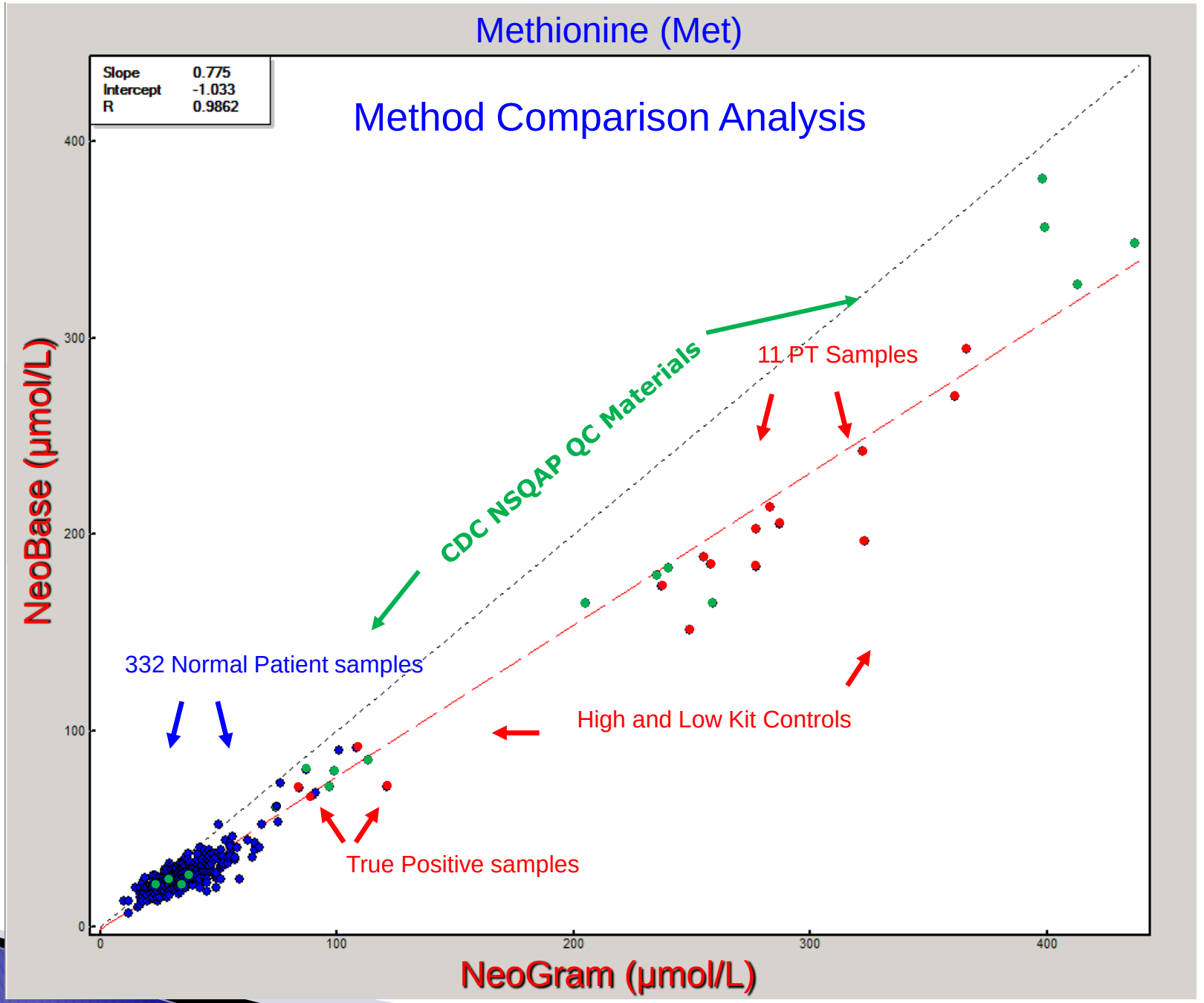
Problem

- Differences in testing methodologies
  - Derivatized vs. non-derivatized
  - Extraction technique
  - Instrumentation
  - Internal Standards
  - Calibration Techniques
  - Standard Calibration Materials

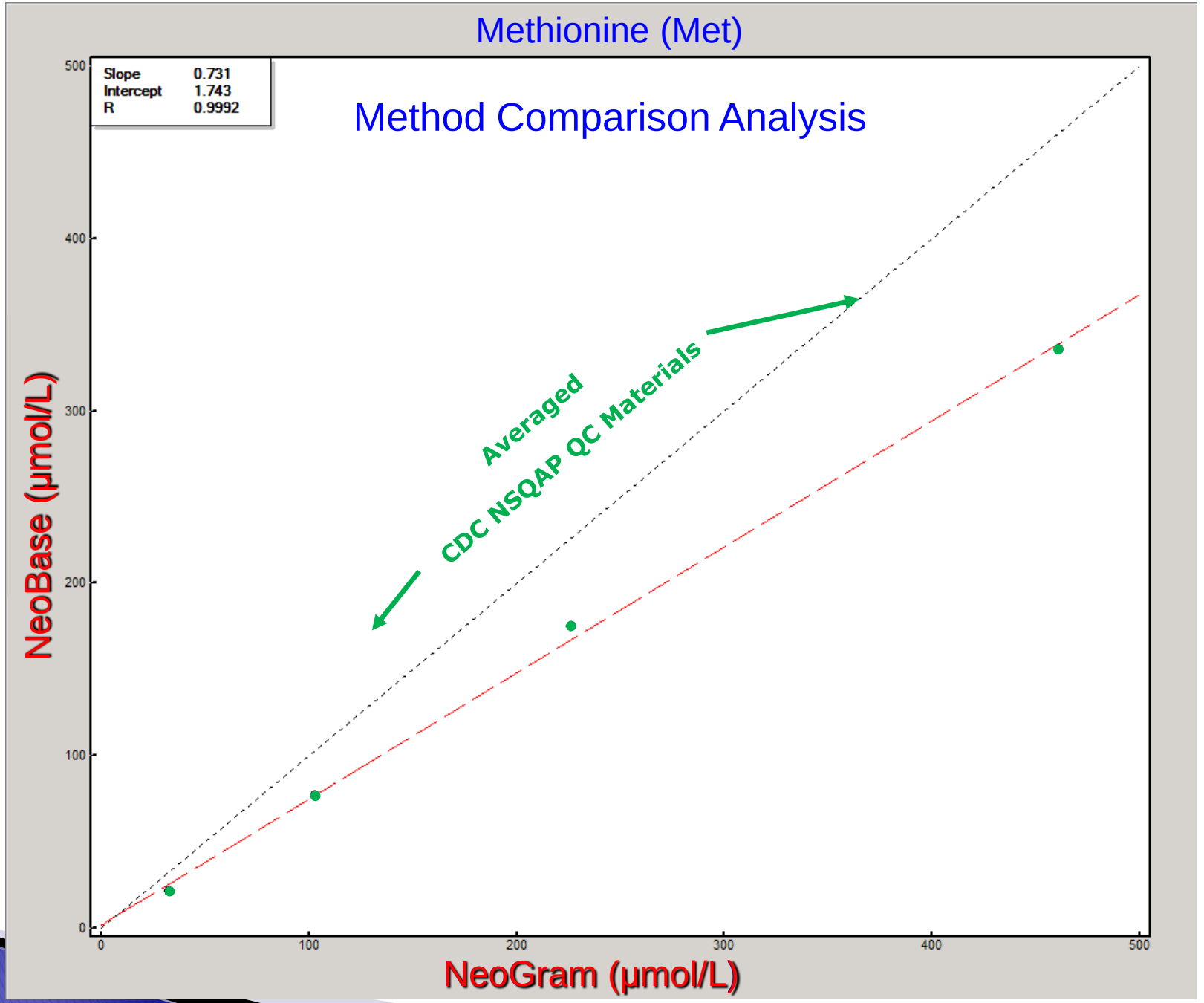
Solution

- Normalization using method comparison experiment
  - Laboratories test the NSQAP QC Materials
  - Linear regression equations generated
  - Normalized cutoffs calculated

Methionine (Met)

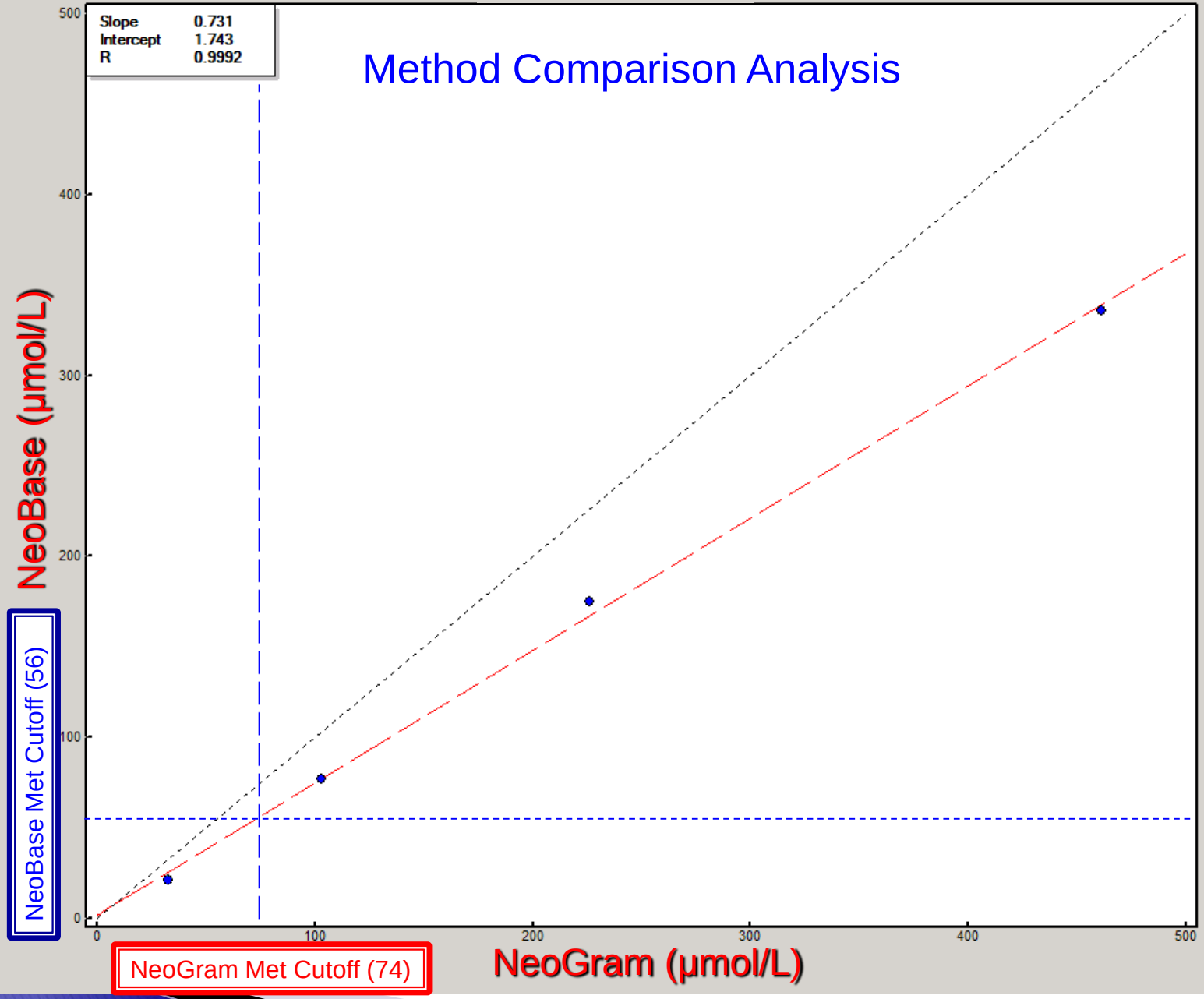


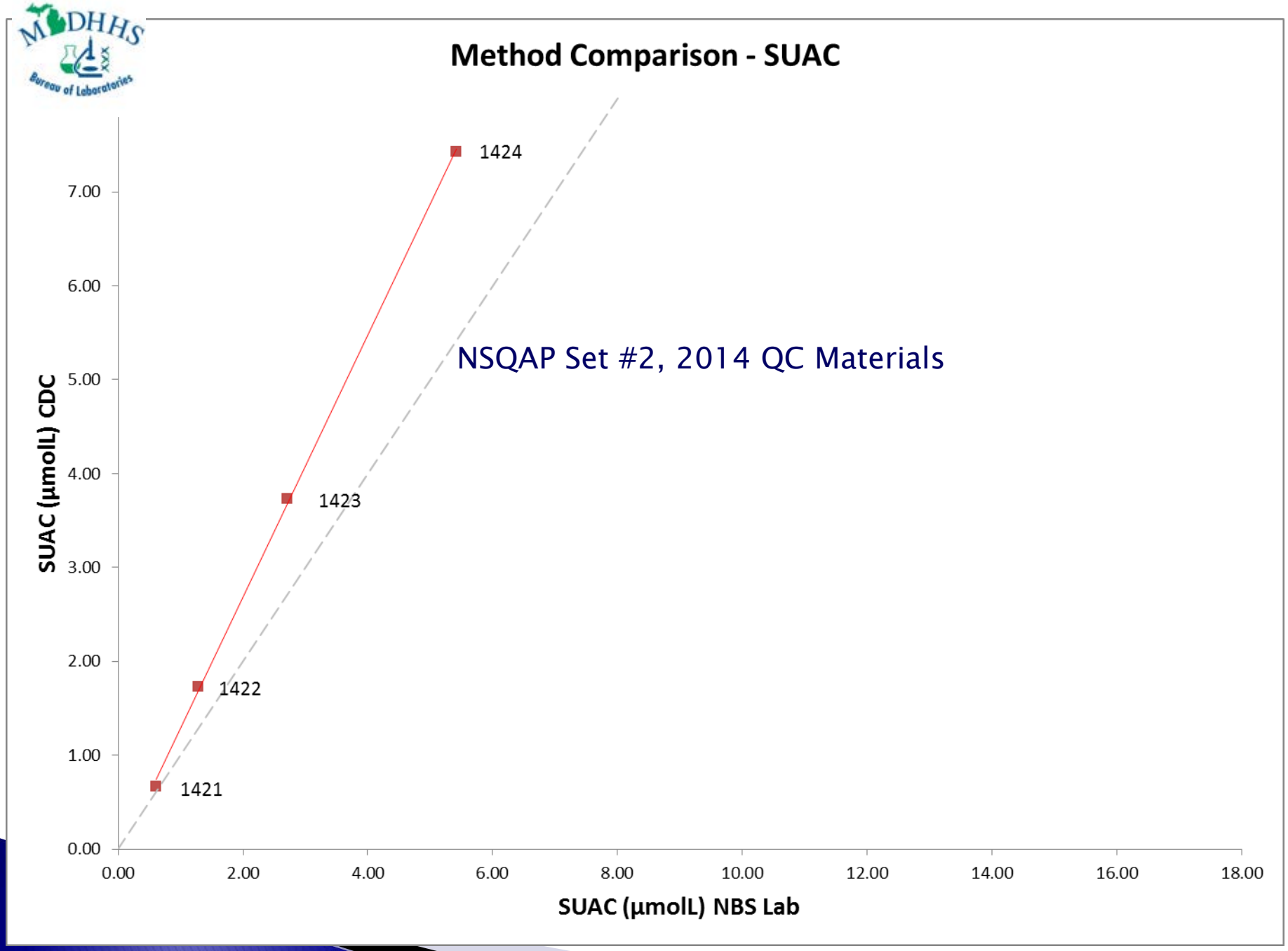
Methionine (Met)

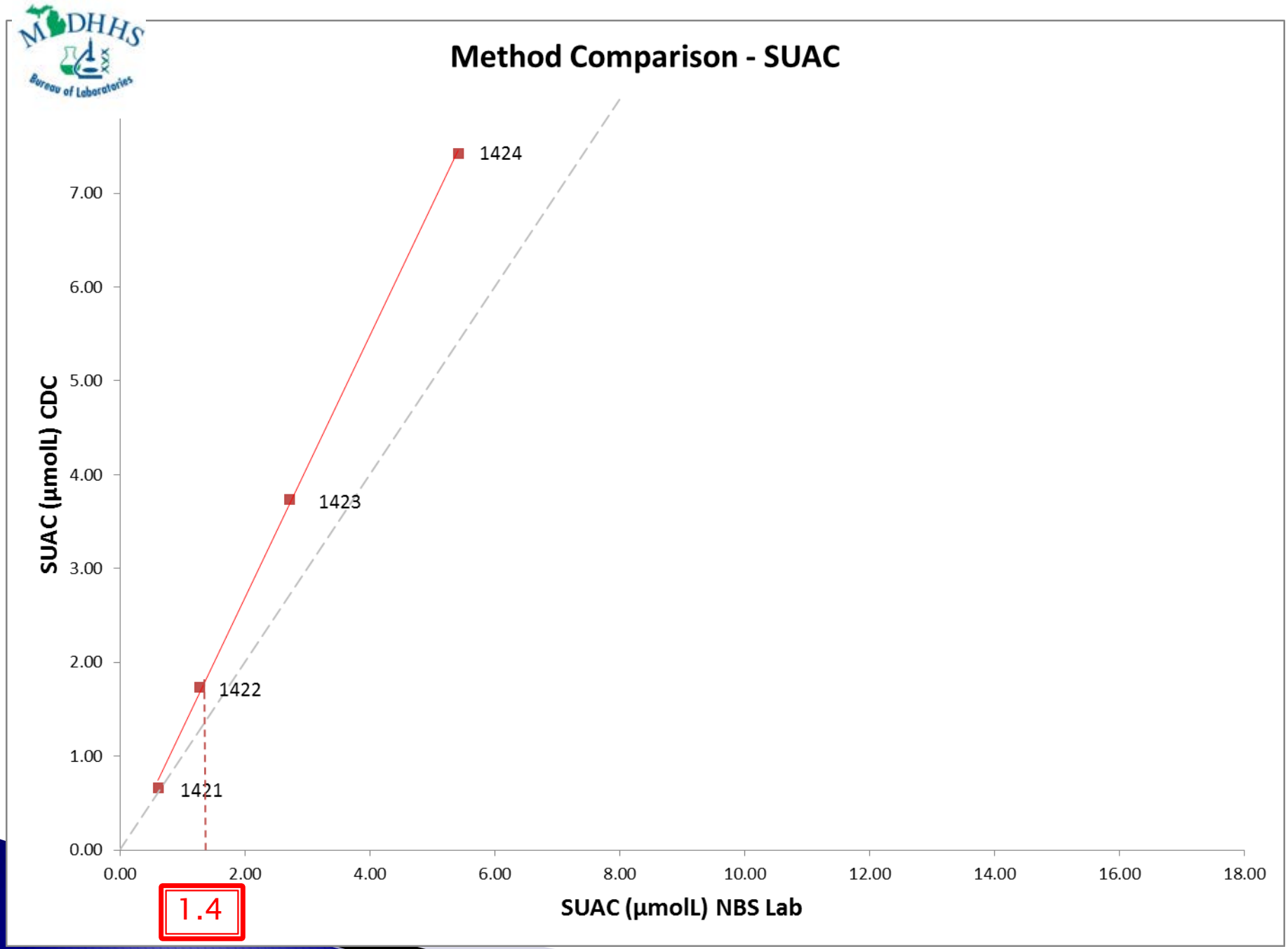


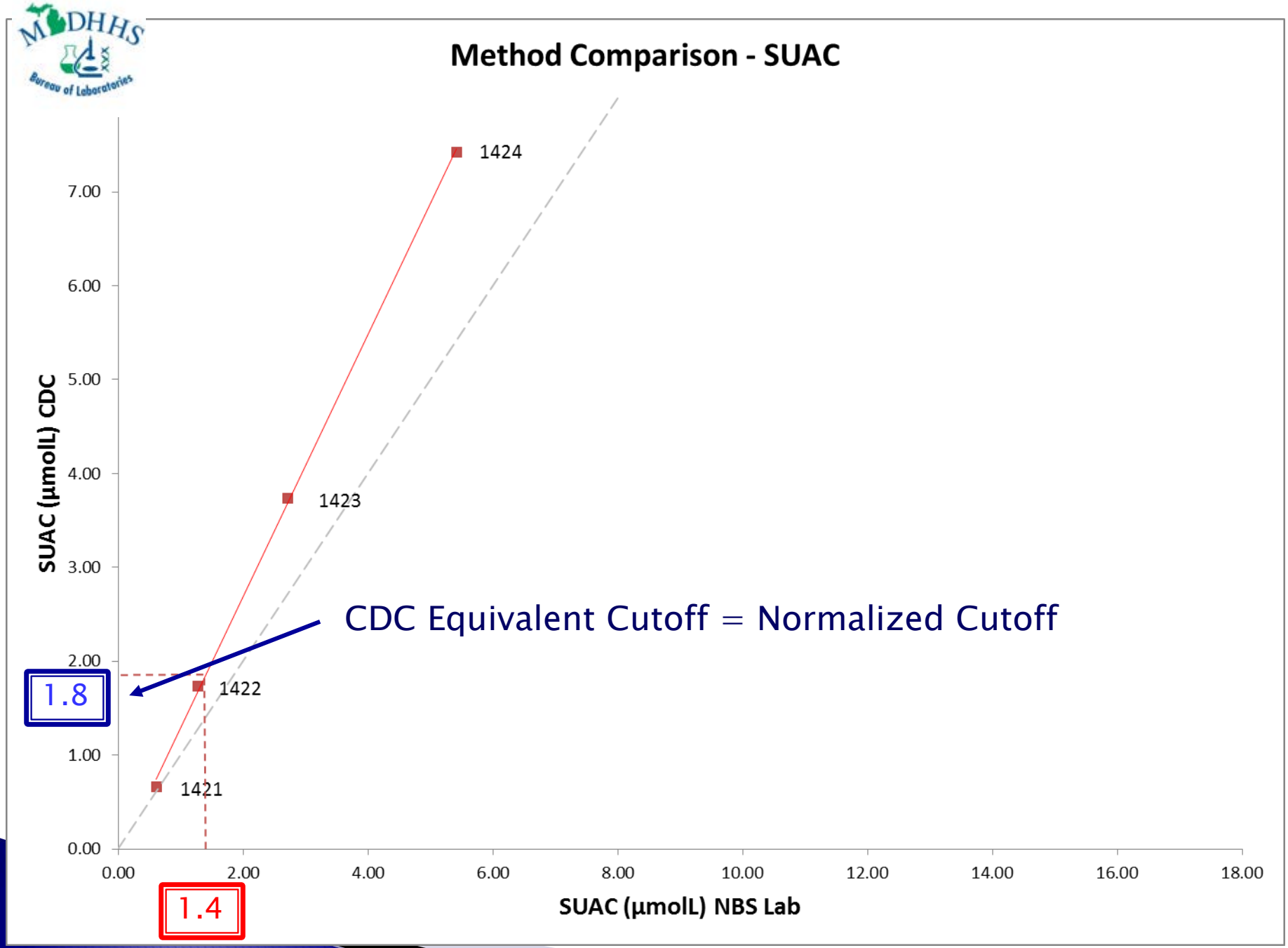
Methionine (Met)

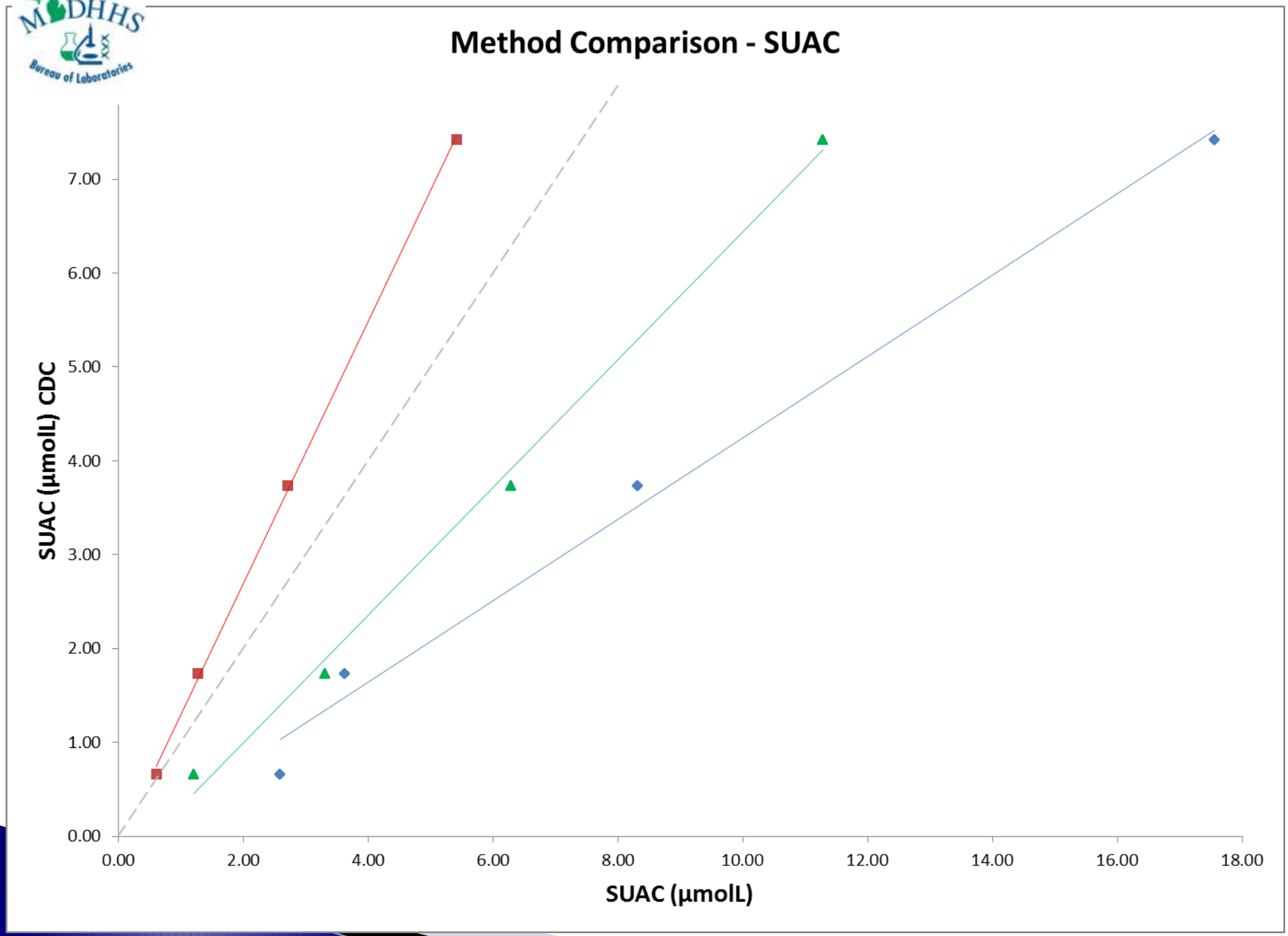
Method Comparison Analysis

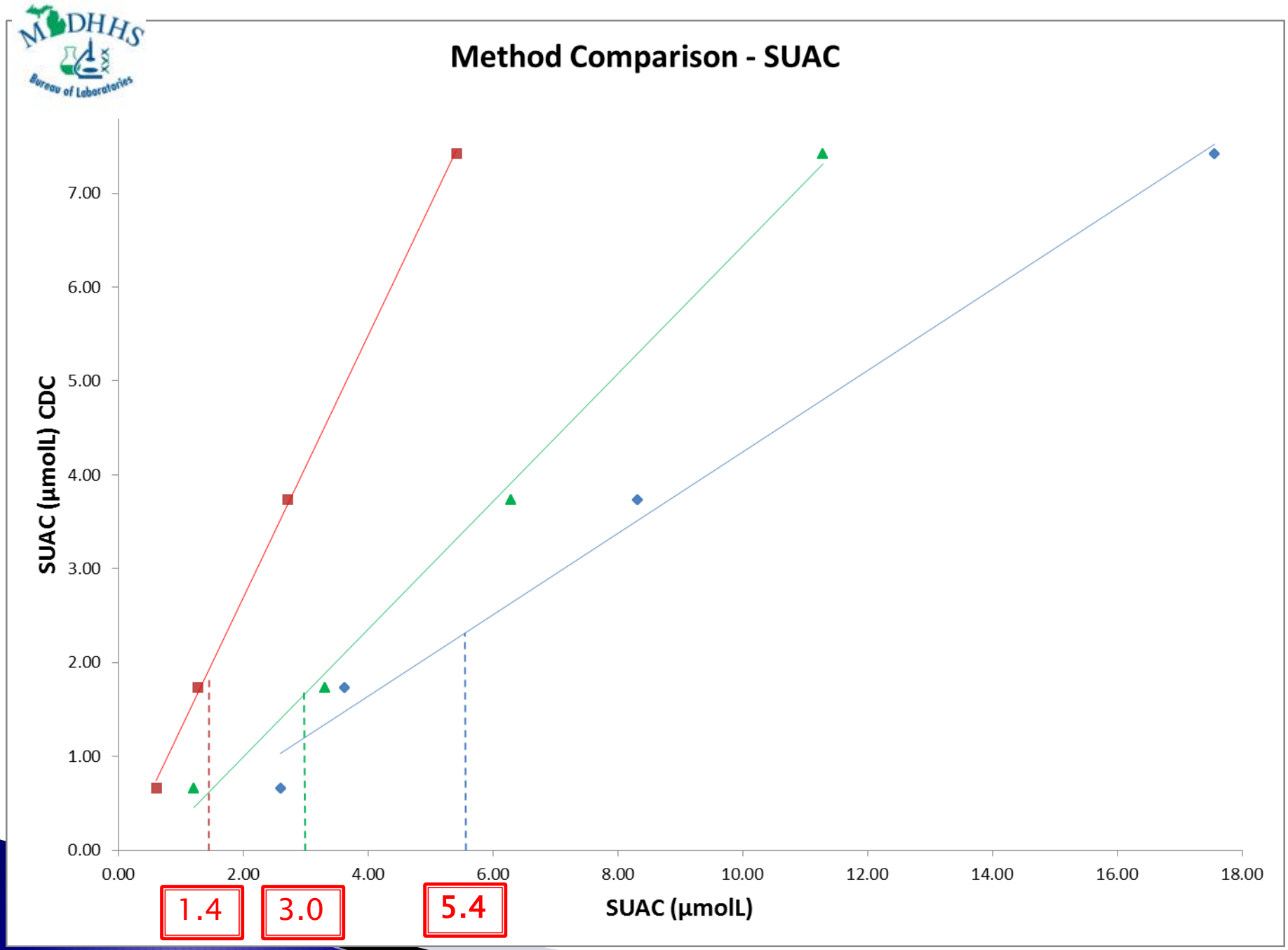


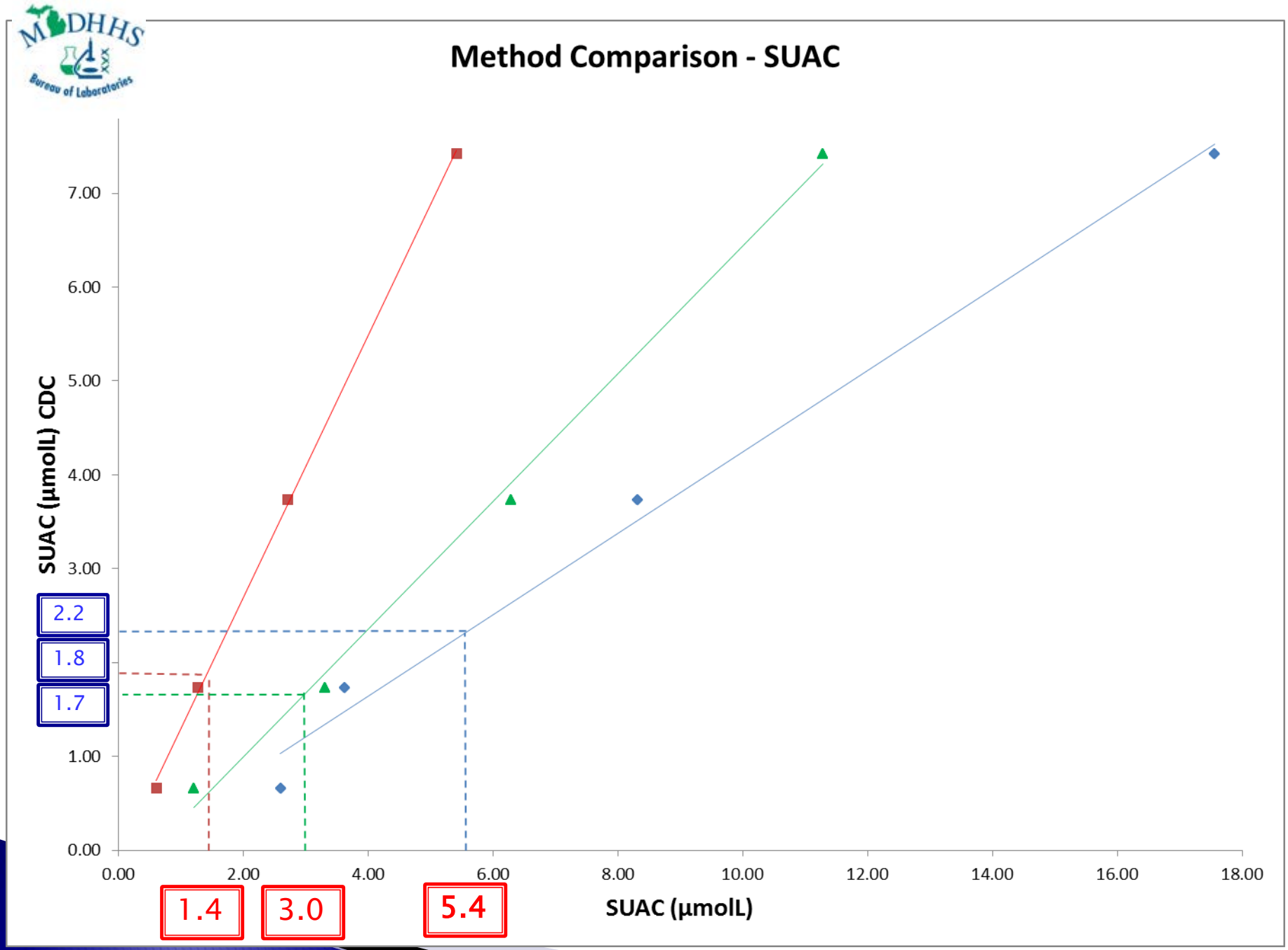

Method Comparison - SUAC
NSQAP Set #2, 2014 QC Materials
1424
1423
1422
1421
SUAC (µmolL) CDC
SUAC (µmolL) NBS Lab
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00


Method Comparison - SUAC
SUAC (µmolL) CDC
SUAC (µmolL) NBS Lab
1424
1423
1422
1421
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
1.4


Method Comparison - SUAC
1424
1423
1422
1421
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
SUAC (µmolL) CDC
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
SUAC (µmolL) NBS Lab
CDC Equivalent Cutoff = Normalized Cutoff
1.8
1.4


Method Comparison - SUAC
SUAC (µmolL) CDC
SUAC (µmolL)
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00


Method Comparison - SUAC
SUAC (µmolL) CDC
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
SUAC (µmolL)
1.4
3.0
5.4


Method Comparison - SUAC
SUAC (µmolL) CDC
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
2.2
1.8
1.7
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
1.4
3.0
5.4
SUAC (µmolL)

Collaborative

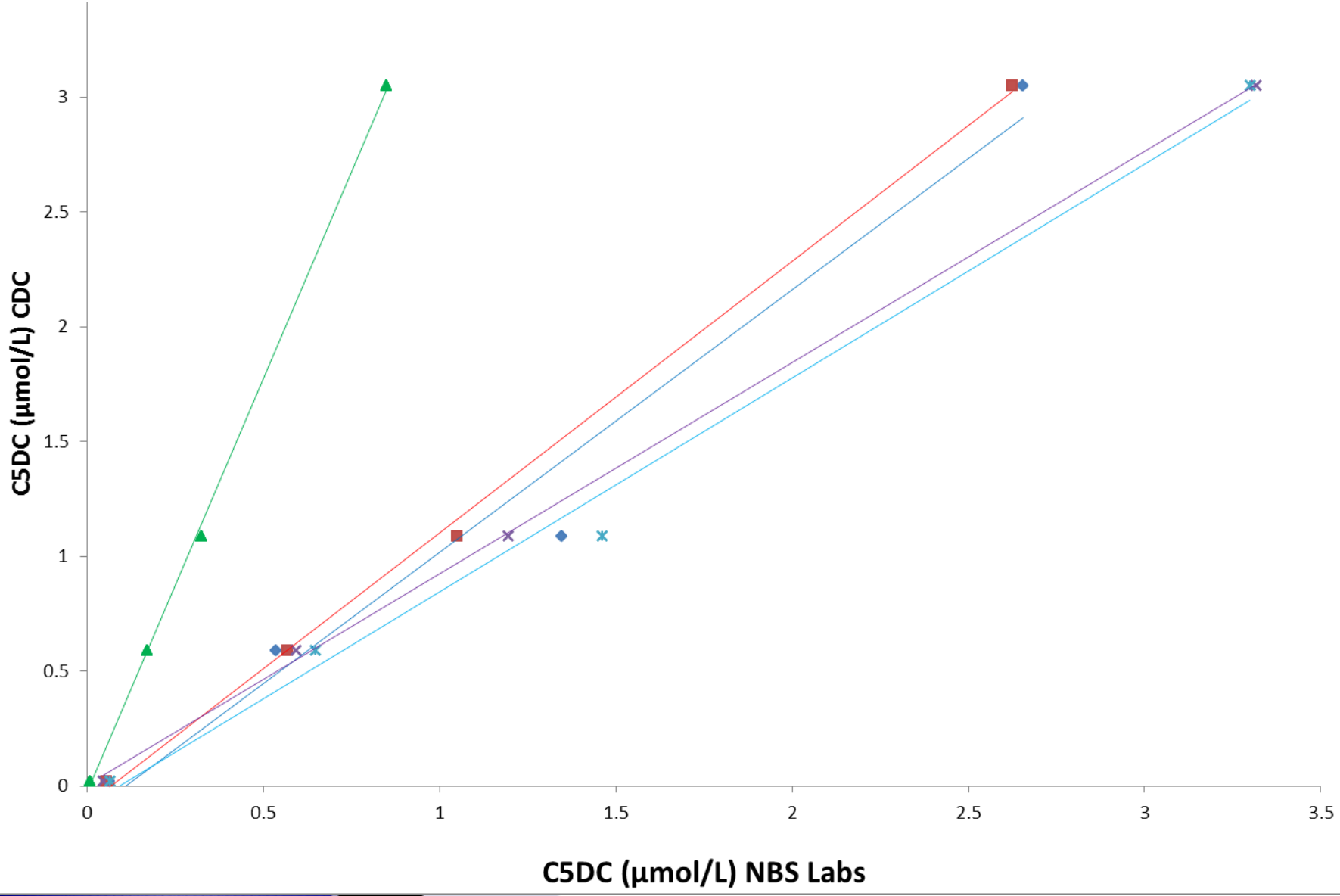
Methods:

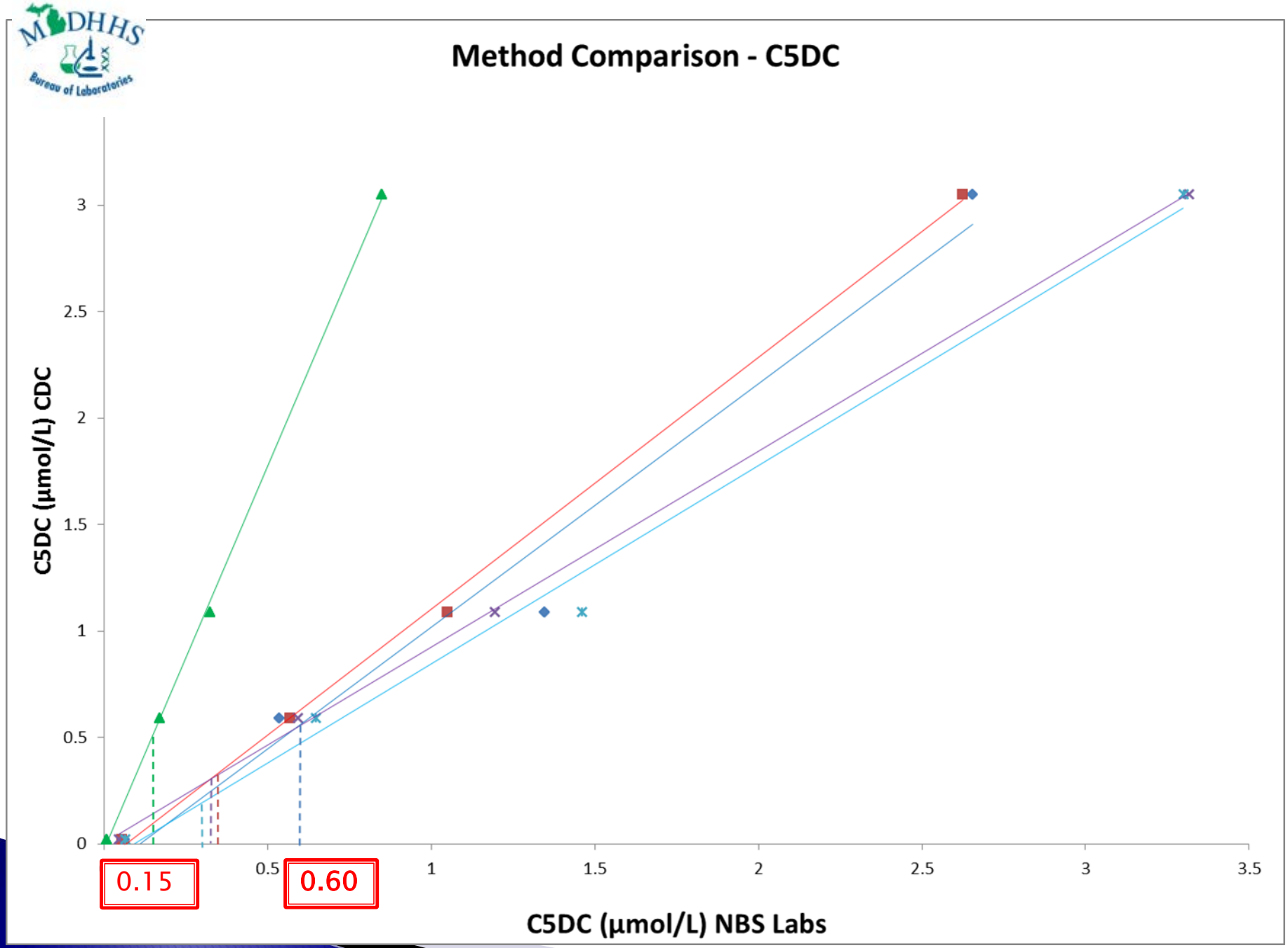
- Derivatized
- Non-Derivatized
- Laboratory Developed Test
- Kit Method

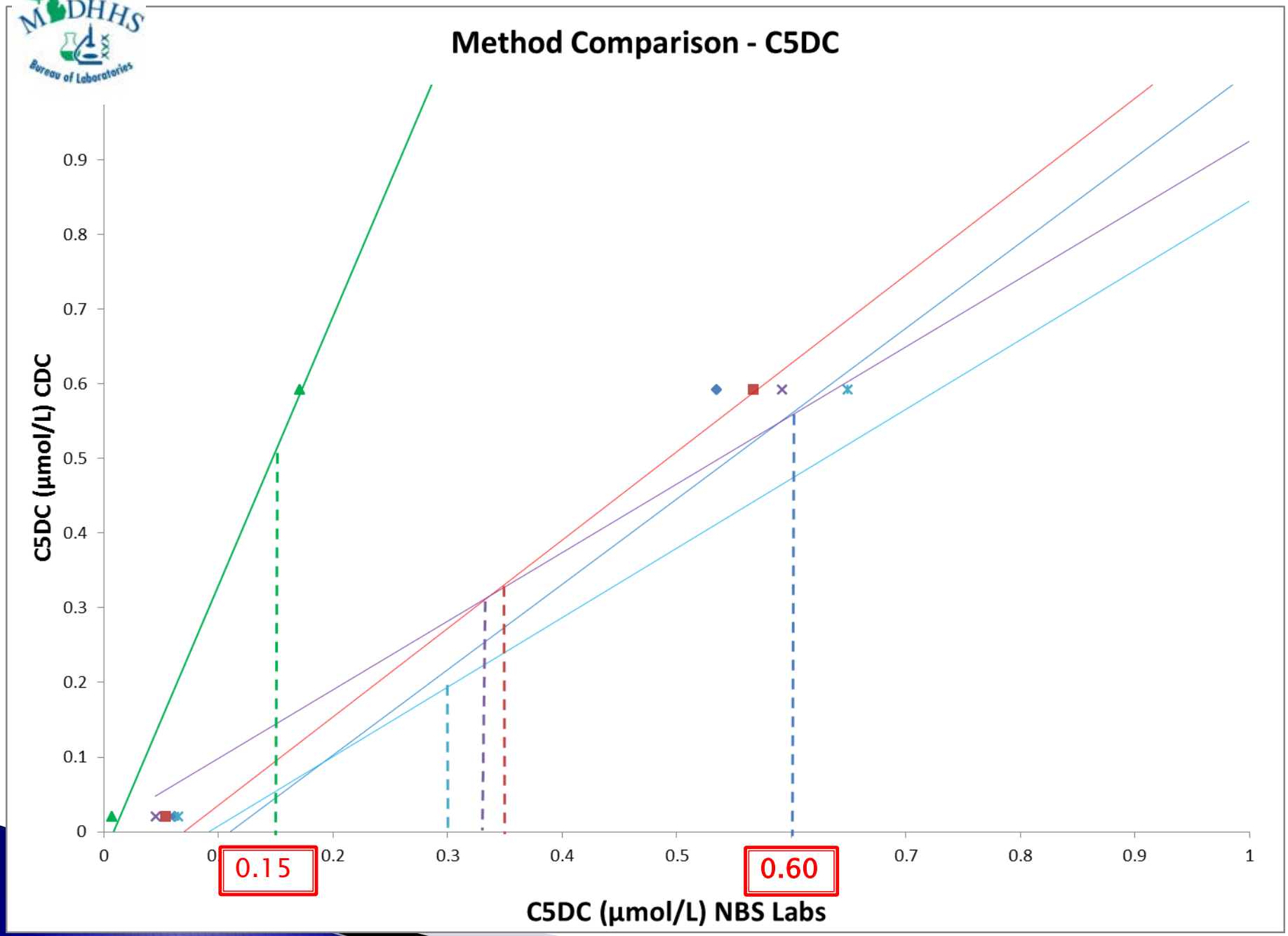
Analytes:

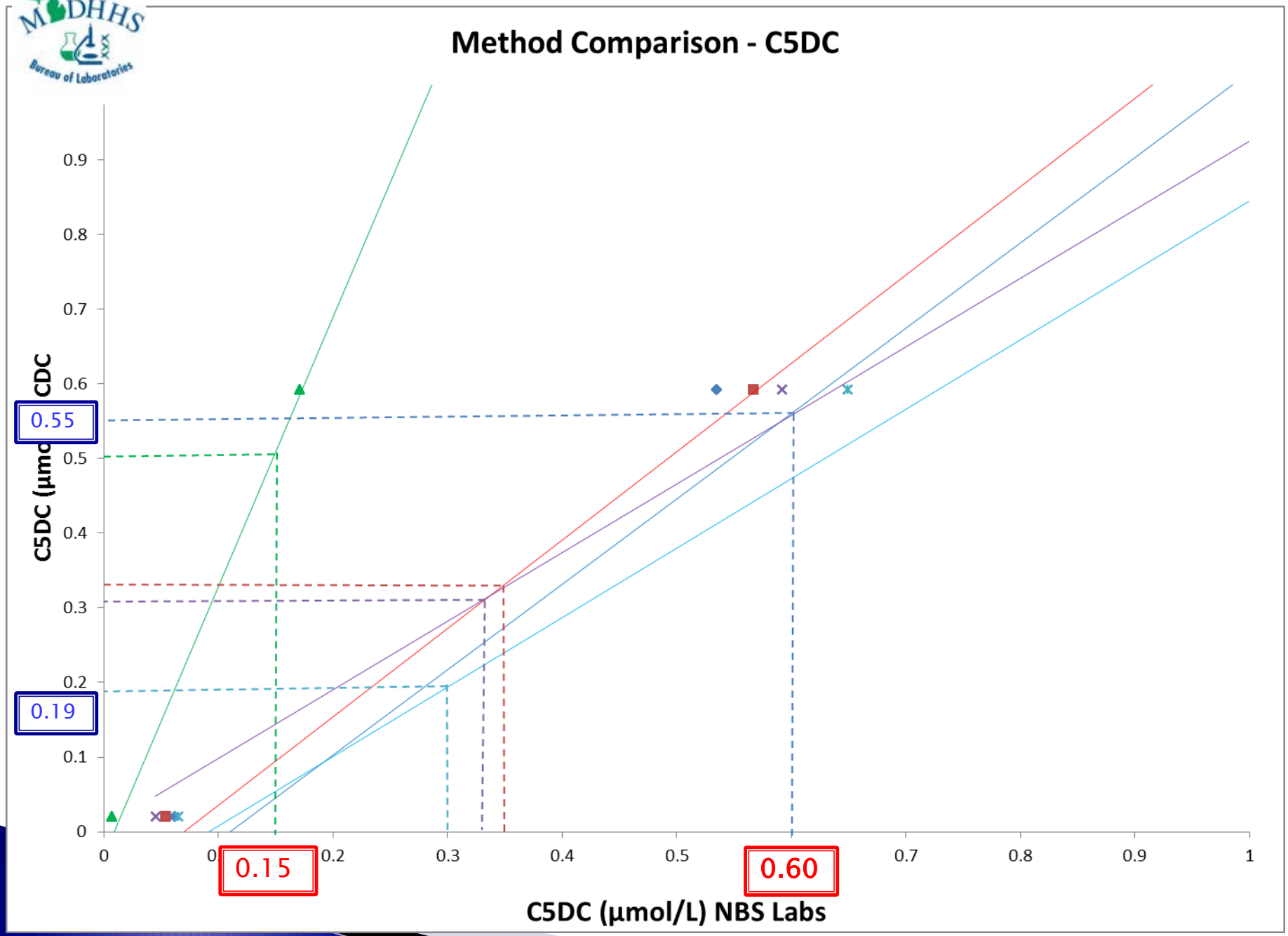
- Arginine (Arg)
- Citrulline (Cit)
- Phenylalanine (Phe)
- Succinylacetone (SUAC)
- Free carnitine (C0)
- Octanoylcarnitine (C8)
- Malonylcarnitine (C3DC)
- Glutarylcarnitine (C5DC)
- Myristoylcarnitine (C14)

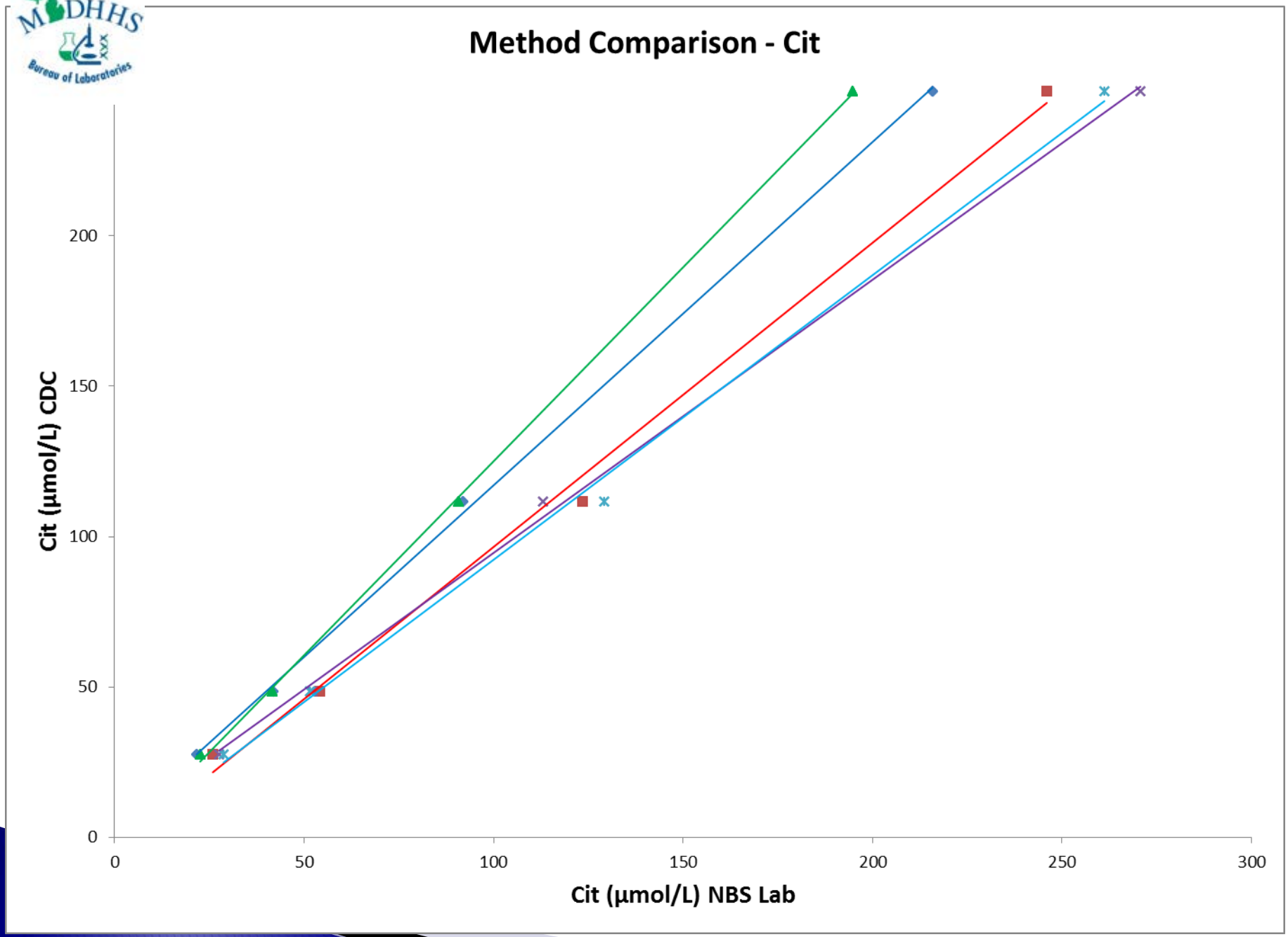
Method Comparison - C5DC

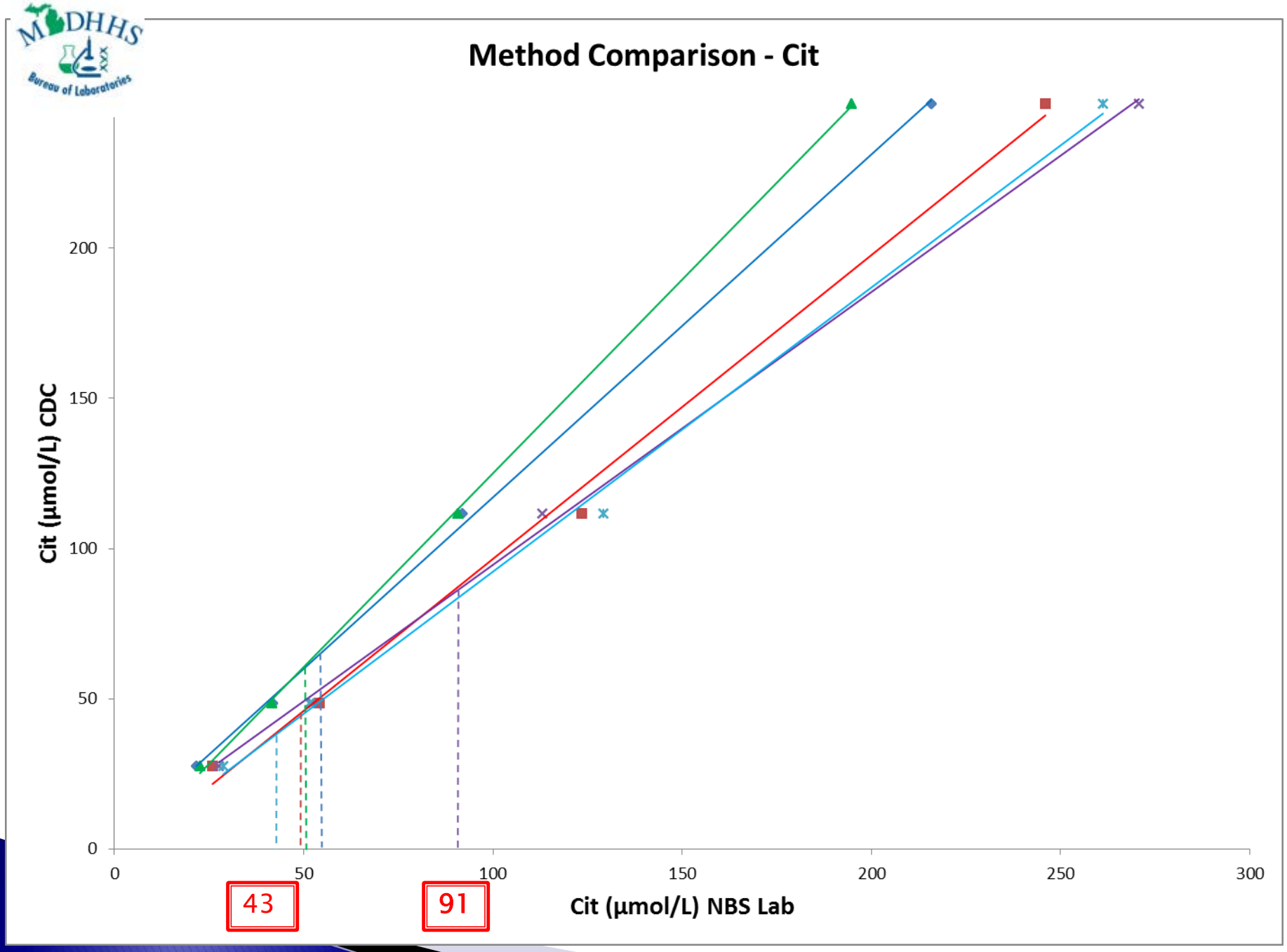


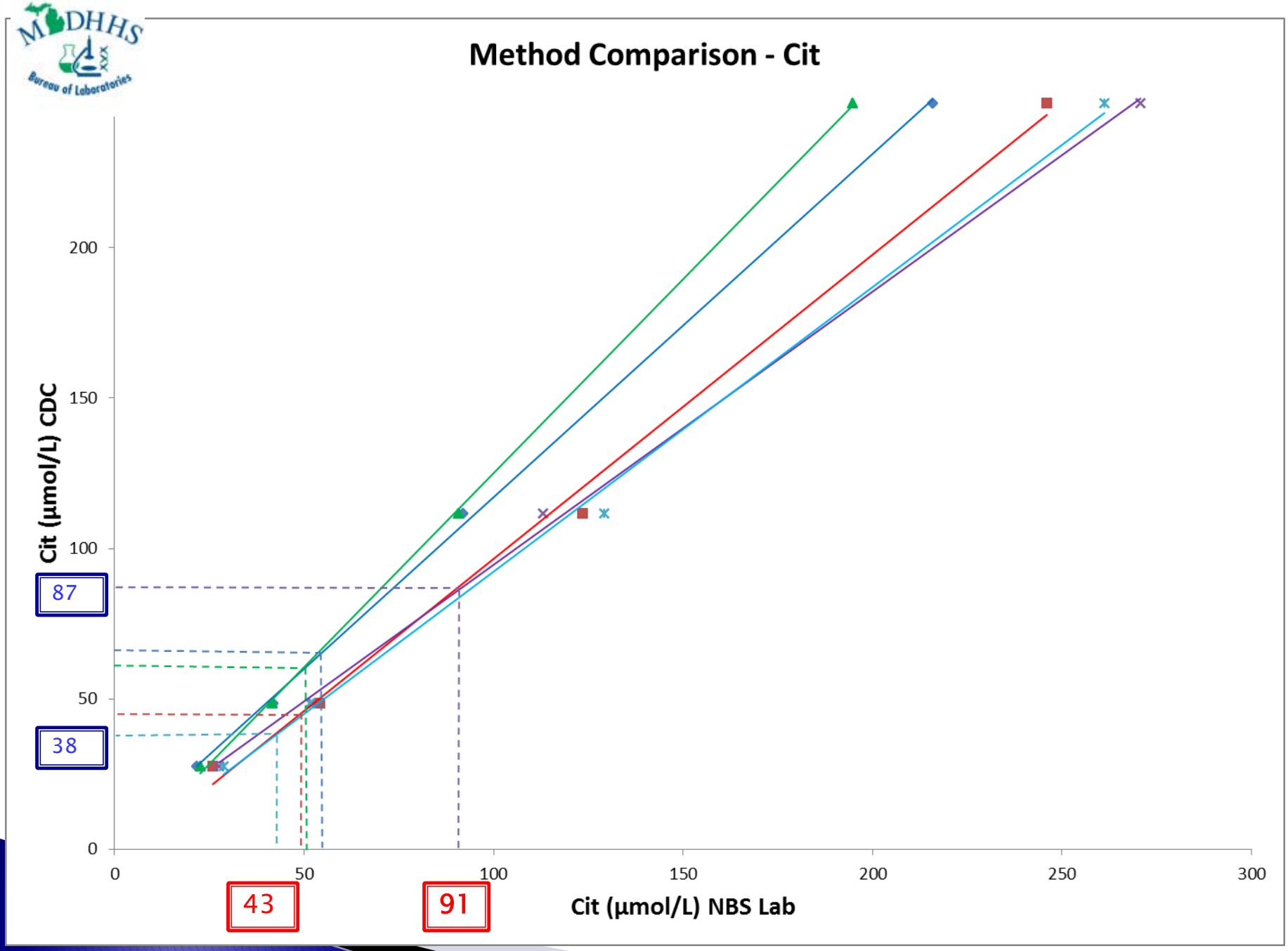

Method Comparison - C5DC
C5DC (µmol/L) CDC
C5DC (µmol/L) NBS Labs
0
0.5
1
1.5
2
2.5
3
3.5
0.15
0.60

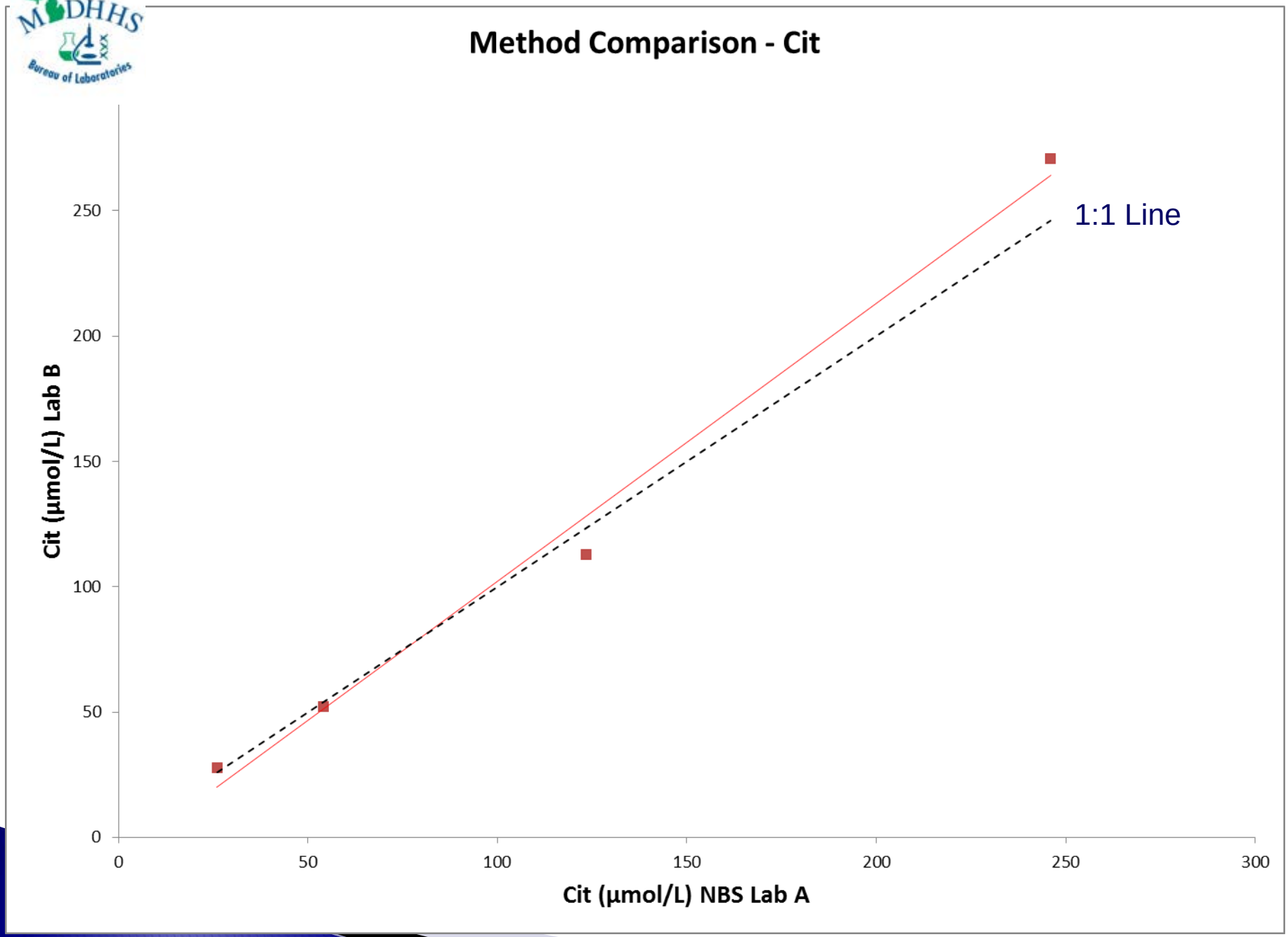

Method Comparison - C5DC
C5DC (µmol/L) CDC
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.15
0.2
0.3
0.4
0.5
0.60
0.7
0.8
0.9
1
C5DC (µmol/L) NBS Labs

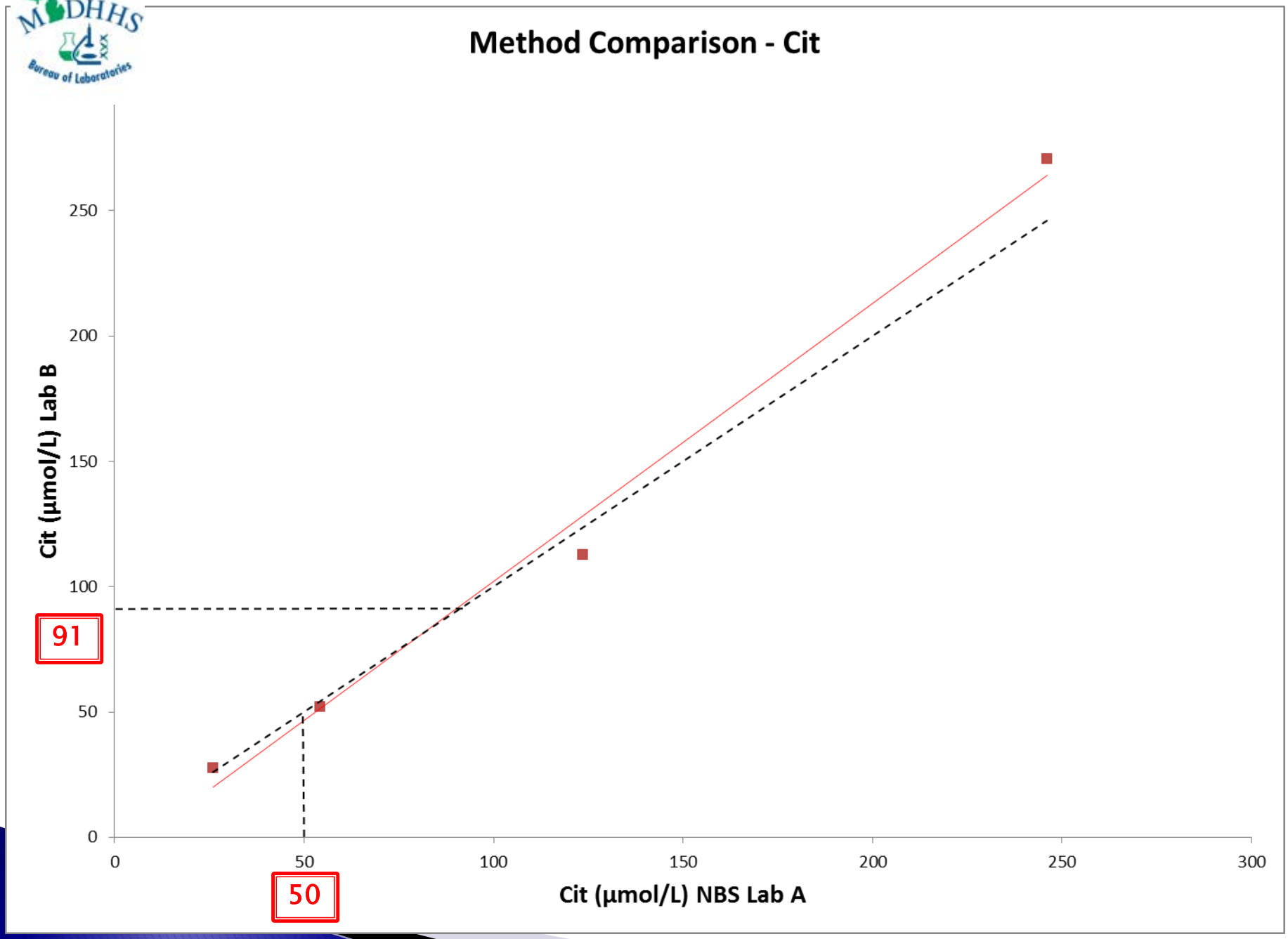

Method Comparison - C5DC
C5DC (µmol/L) NBS Labs
0.55
0.19
0.15
0.60
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

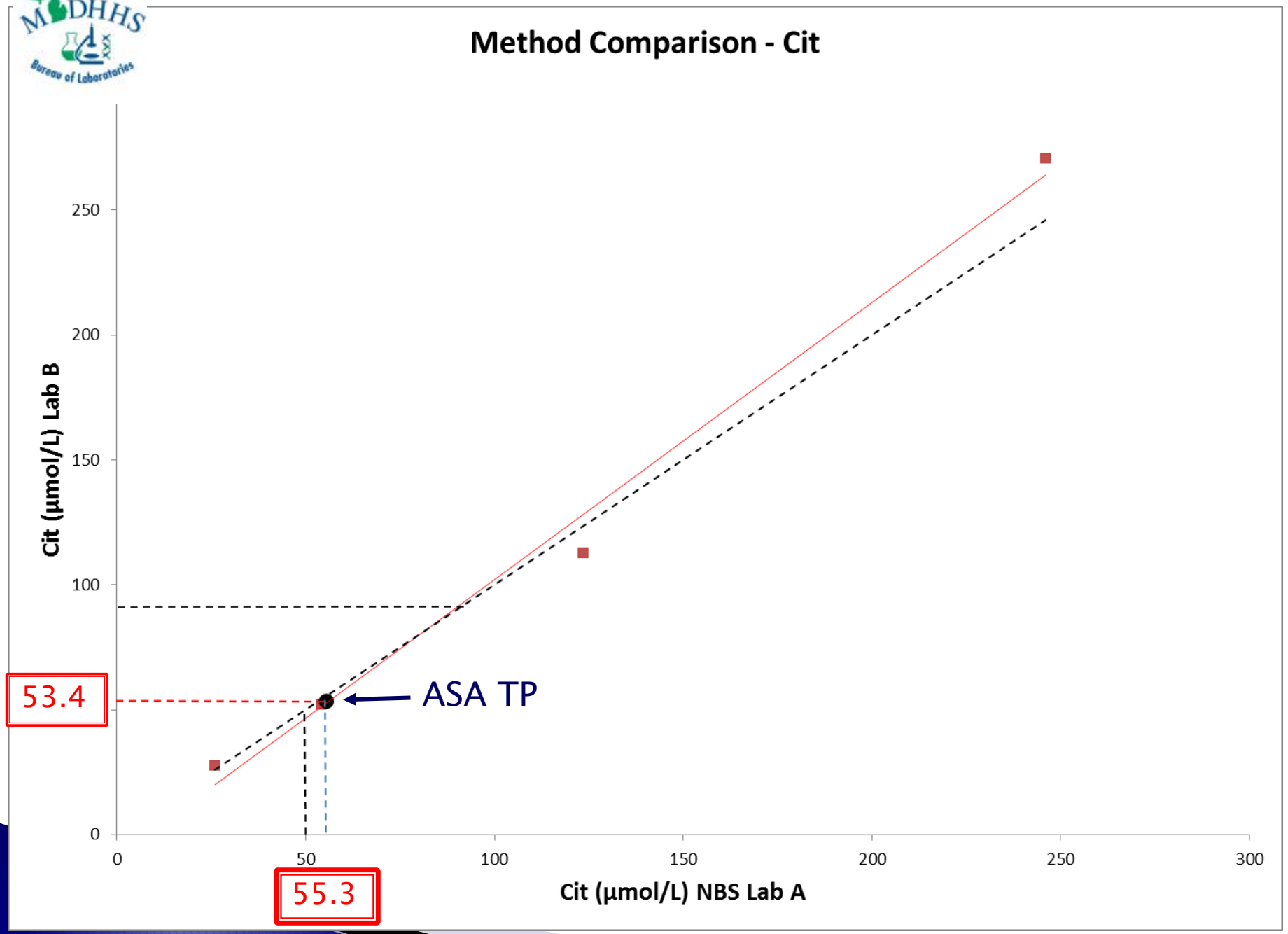

Method Comparison - Cit
Cit (µmol/L) CDC
Cit (µmol/L) NBS Lab
0
50
100
150
200
250
300


Method Comparison - Cit
Cit (µmol/L) CDC
0
50
100
150
200
0
50
100
150
200
250
300
Cit (µmol/L) NBS Lab
43
91

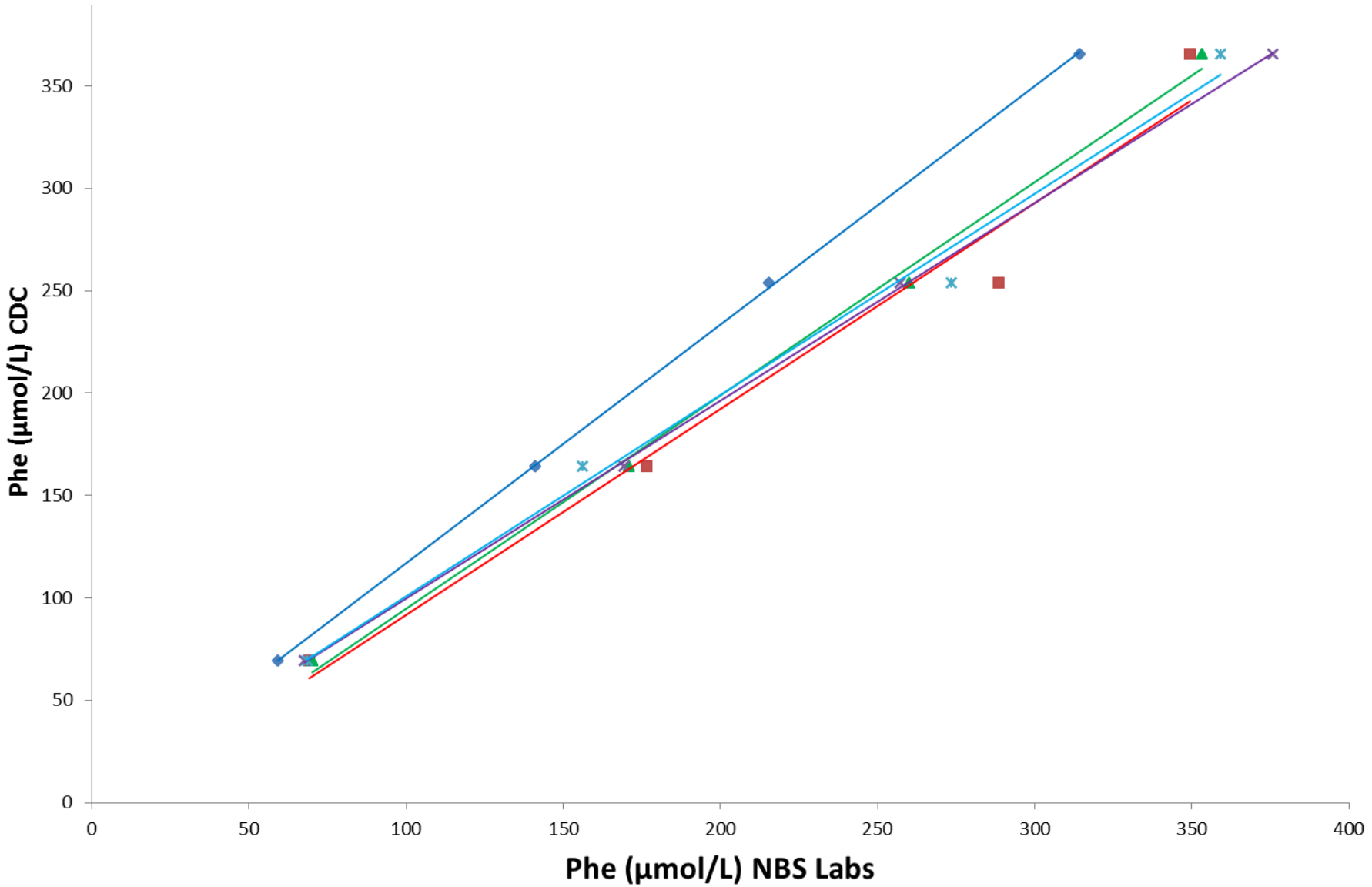

Method Comparison - Cit
Cit (µmol/L) CDC
Cit (µmol/L) NBS Lab
0
50
100
150
200
250
300
87
38
43
91


Method Comparison - Cit
1:1 Line
Cit (µmol/L) Lab B
Cit (µmol/L) NBS Lab A
0
50
100
150
200
250
300

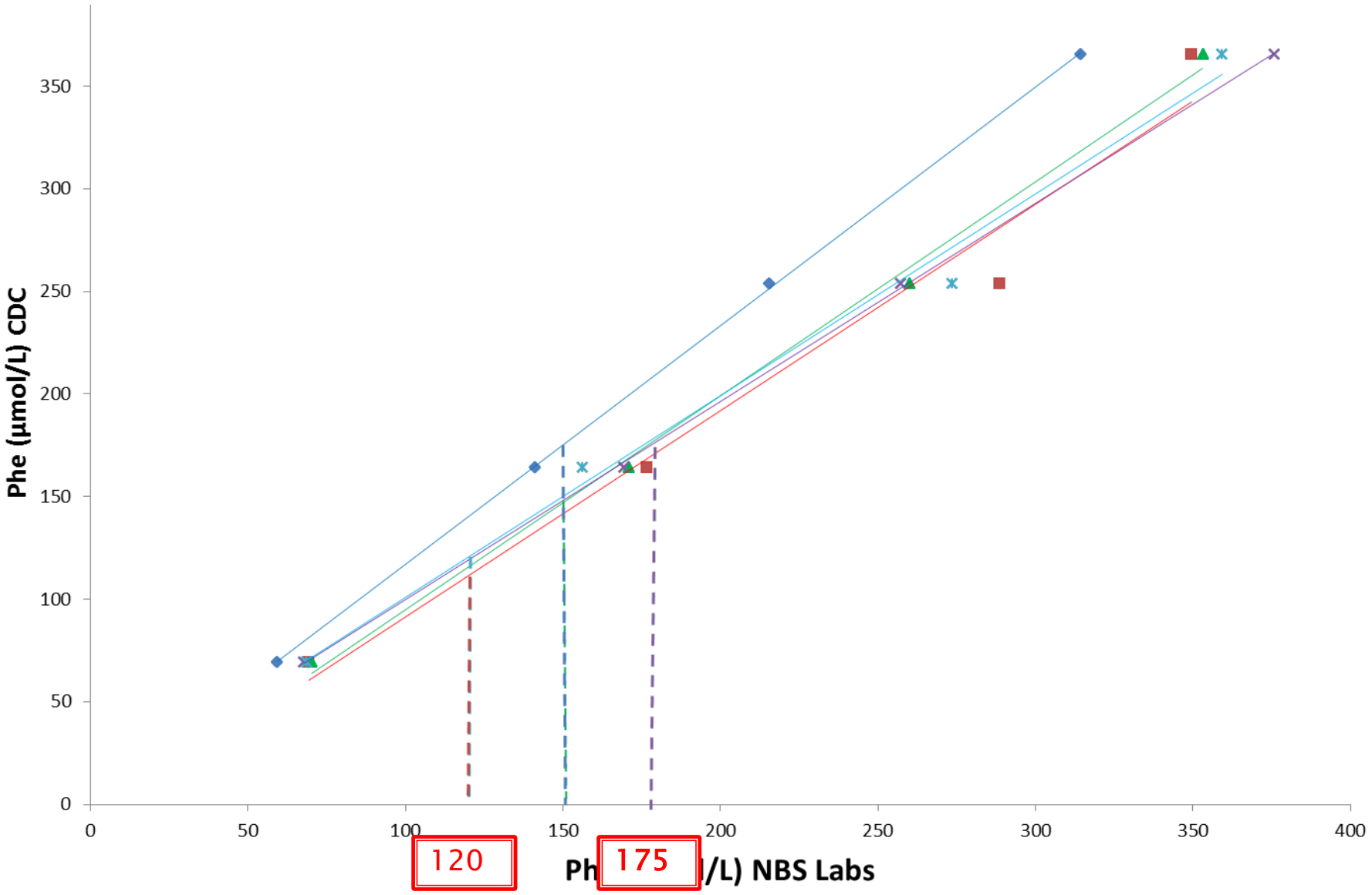

Method Comparison - Cit
Cit (µmol/L) Lab B
Cit (µmol/L) NBS Lab A
0
50
100
150
200
250
300
91
50


Method Comparison - Cit
Cit (µmol/L) Lab B
Cit (µmol/L) NBS Lab A
0
50
100
150
200
250
300
53.4
55.3
ASA TP

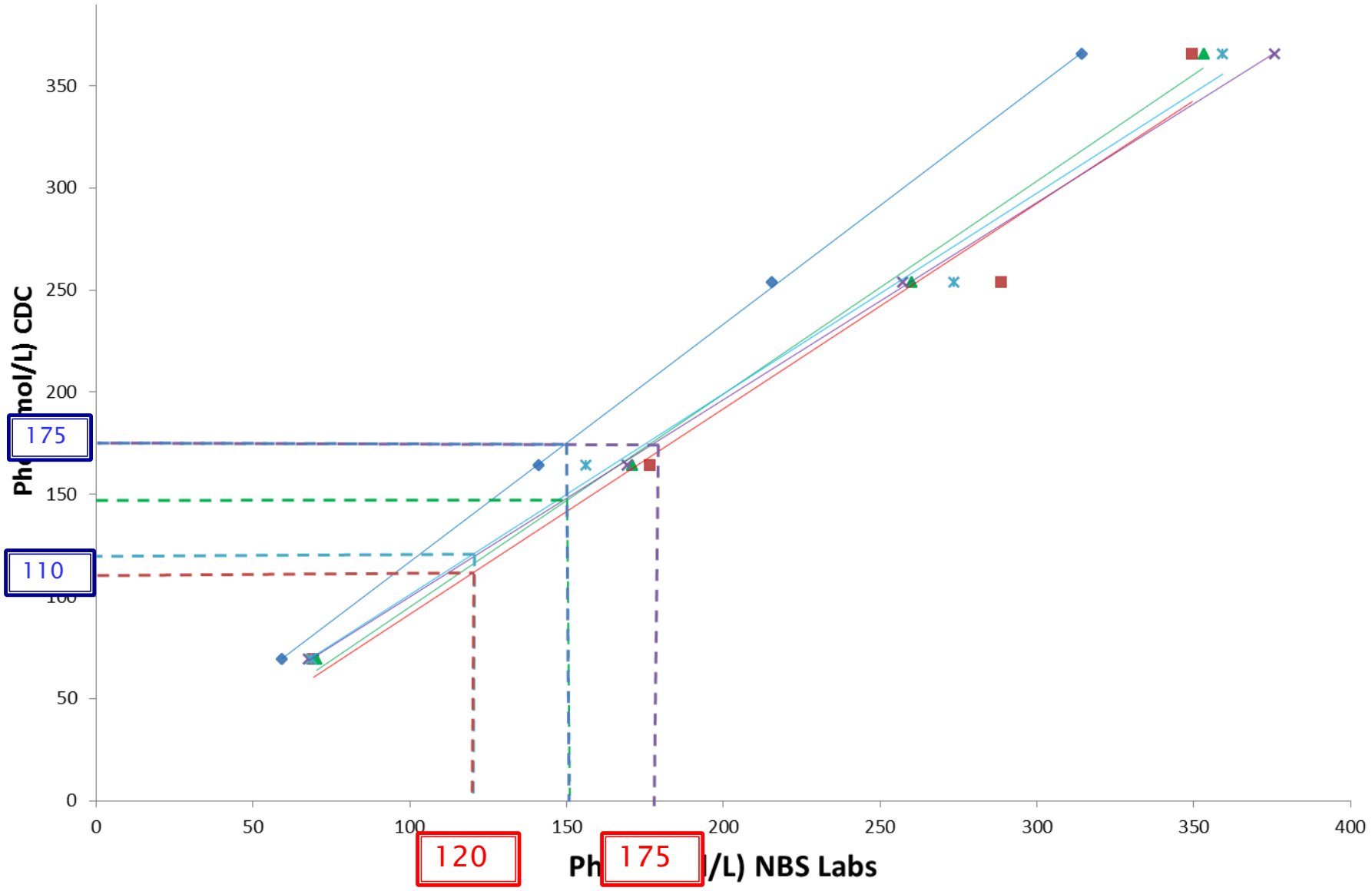
Method Comparison - Phe



Method Comparison - Phe



Method Comparison - Phe

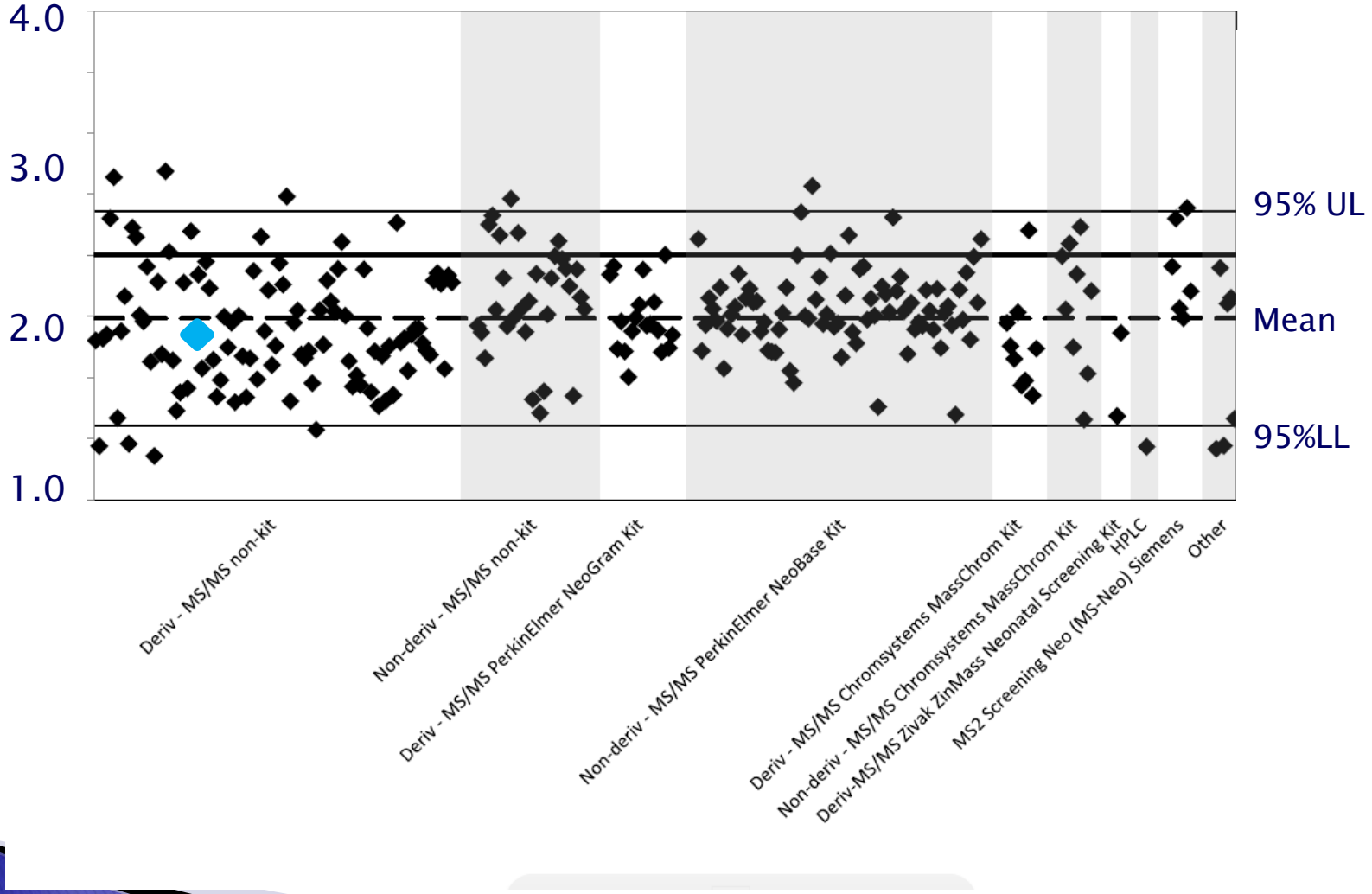


Conclusions:

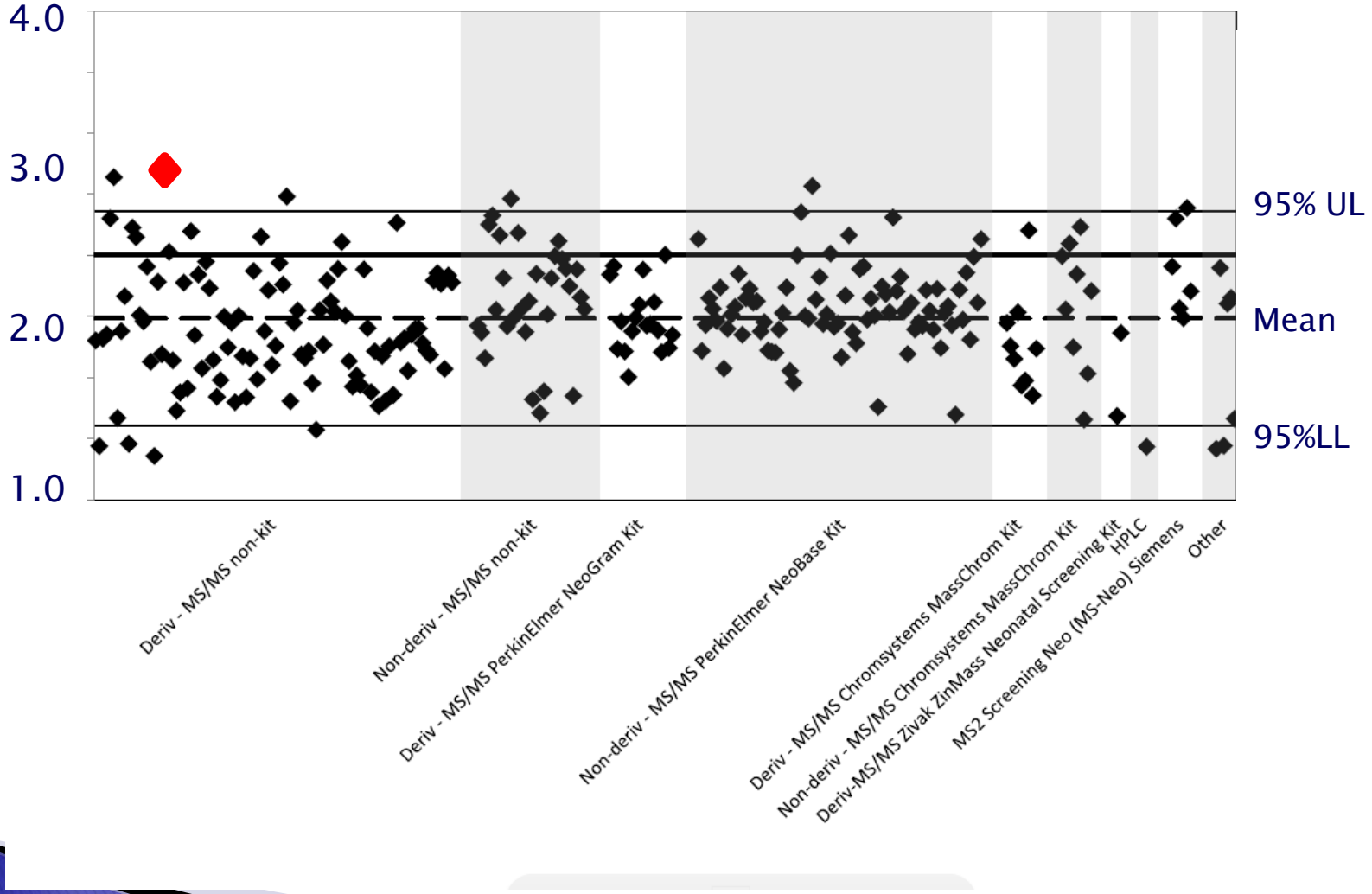
Normalization Technique Using CDC NSQAP QC Materials + Method Comparison

- Provides normalized cutoff values
- Allows accurate comparison of cutoffs regardless of testing methodology.
- Provides a foundation for comparison and discussion.

Hypothetical Normalized Succinylacetone (SUAC) Cutoffs by Method



Hypothetical Normalized Succinylacetone (SUAC) Cutoffs by Method



Acknowledgements:

Victor De Jesus – CDC NSQAP

Christopher Haynes – CDC NSQAP

Mark Morrissey – New York

Adrienne Manning – Connecticut

Konstantinos Petritis – Arizona

Sonal Bhakta – Arizona

Patrice Held – Wisconsin

MI NBS Team – Eleanor Stanley