2019 ANNUAL SUMMARY REPORT

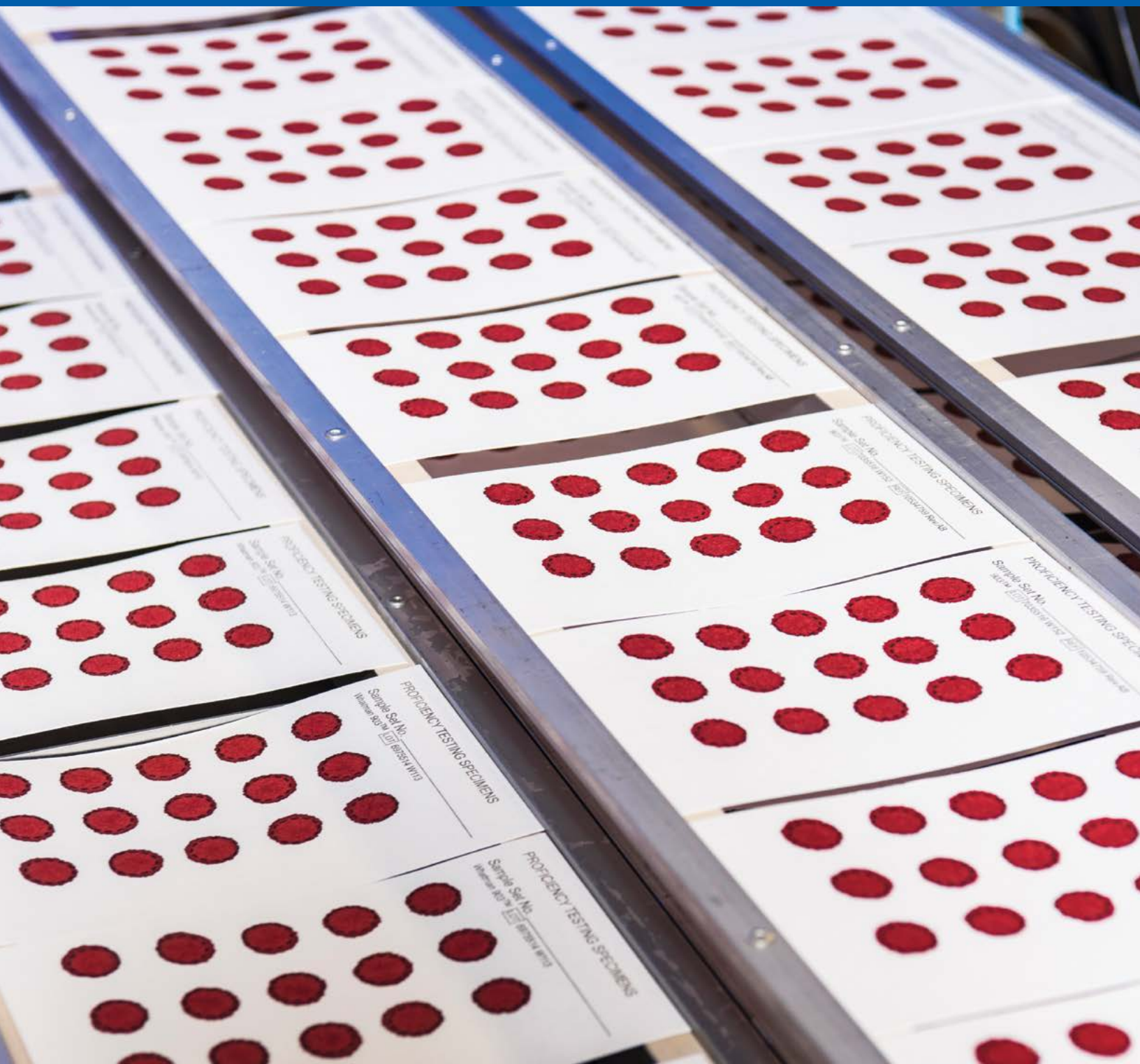
Newborn Screening Quality Assurance Program

Centers for Disease Control and Prevention
National Center for Environmental Health

Newborn Screening Quality Assurance Program

2019 Annual Summary Report, Volume 37

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention
National Center for Environmental Health
Division of Laboratory Sciences



Note for accessibility: Explanations for Figure 2 and a general explanation for Figures 3–38 (bias plots) are located in Appendix for Accessibility Descriptions, page 43.

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Introduction

Newborn screening is one of the most successful preventative health programs in the United States. Healthcare professionals collect dried blood spot (DBS) specimens from more than 98% of all U.S. newborns shortly after birth. State and public health laboratories or associated laboratories screen these DBS specimens for certain genetic, metabolic, and endocrine disorders. The Centers for Disease Control and Prevention's (CDC) Newborn Screening Quality Assurance Program (NSQAP) helps newborn screening laboratories with these testing processes.

NSQAP produces certified DBS materials for proficiency testing (PT) and quality control (QC) analysis, works to improve the quality and scope of laboratory services, and provides consultation to laboratories. State-operated and private newborn screening laboratories process thousands of DBS specimens daily. NSQAP helps newborn screening laboratories ensure that testing accurately detects disorders, does not delay diagnoses, minimizes false-positive reports, and sustains high-quality performance.

CDC's Newborn Screening and Molecular Biology Branch (NSMBB) has been granted International Organization for Standardization (ISO)/International Electrotechnical Commission (IEC) 17043 accreditation by the American Association for Laboratory Accreditation (A2LA). Accreditation was achieved after a thorough review of NSMBB's quality management system and ability to develop and administer specific PT protocols. The branch's NSQAP web-based PT programs are included in the A2LA Scope of Accreditation.

The accreditation does not include testing for glucose-6-phosphate dehydrogenase (G6PD) and NSQAP non-web-based PT programs. Consult A2LA Certificate#4190.01 for a list of accredited NSMBB PT programs.

About NSQAP

For more than 40 years, NSQAP and its cosponsor, the Association of Public Health Laboratories, have researched the development of DBS quality assurance materials for newborn screening tests and have assisted laboratories with DBS-related testing issues. NSQAP primarily supports U.S. newborn screening laboratories; however, private and international laboratories can enroll in the program. Participation is voluntary. NSQAP provides quality assurance services for the core (primary) and secondary conditions listed in the U.S. Recommended Uniform Screening Panel (RUSP) [1].

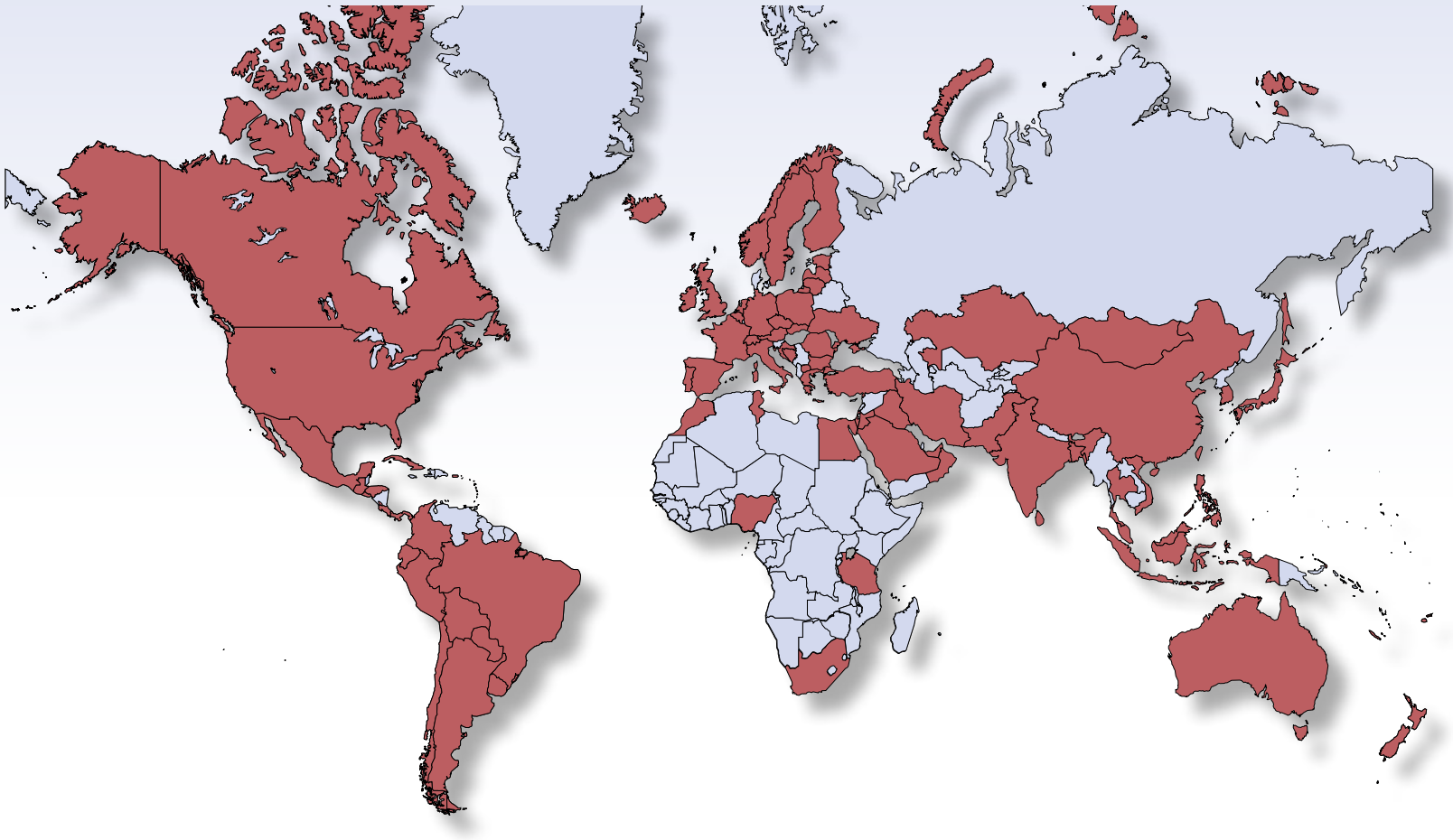
Over the years, NSQAP services and participation have grown substantially. In 2019, 648 newborn screening laboratories in 85 countries (at least one laboratory per country) participated in the program (Figure 1). Of these laboratories, 588 participated in PT (Table 1) and 522 in QC (Table 2). The program distributed DBS materials for 78 analytes to participating laboratories (Tables 1 and 2).

To offer more specialized services, NSQAP works with the Biochemical Mass Spectrometry Laboratory (BMSL) and the Molecular Quality Improvement Program (MQIP) in the NSMBB.

BMSL offers newborn screening tandem mass spectrometry (MS/MS) quality assurance, education, and research opportunities. It also oversees the amino acids, acylcarnitines, biotinidase, total galactose (TGal), galactose-1-phosphate uridyltransferase (GALT), G6PD, lysosomal storage disorders (LSD), and filter paper evaluation programs.

MQIP oversees the Cystic Fibrosis DNA (CFDNA) and T-cell receptor excision circle (TREC) PT programs and assists newborn screening laboratories with molecular testing. It also offers the Molecular Assessment Program (MAP), which conducts site visits at U.S. newborn screening laboratories that carry out molecular testing. These visits assess components of molecular testing and include program-tailored guidance for laboratory-specific needs and assistance in evaluating ongoing and future molecular testing procedures.

Figure 1. Eighty-five countries participated in the Newborn Screening Quality Assurance Program in 2019.



Argentina
Armenia
Australia
Austria
Bahrain
Belgium
Bolivia
Brazil
Bulgaria
Canada
Chile
China
Colombia
Costa Rica
Croatia
Cuba
Czech Republic
Denmark
Ecuador
Egypt
El Salvador
Estonia
Finland
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Malaysia
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Mexico
Mongolia
Morocco
Netherlands
New Zealand
Nigeria
Norway
Oman
Pakistan
Panama
Paraguay
Peru
Philippines
Poland
Portugal
Qatar
Romania
Saudi Arabia
Singapore
Slovak Republic
Slovenia
South Africa
South Korea
Spain
Sri Lanka
Sweden
Switzerland
Taiwan
Tanzania
Thailand
Tunisia
Turkey
Ukraine
United Arab Emirates
United Kingdom
United States
Uruguay
Vietnam

Table 1. Number of participants reporting proficiency testing analytes. (N = 588)

Note: A "2" after an analyte indicates 2nd tier

Analyte	Total PT Participation in 2019
17OHP	296
T4	91
TSH	367
TGal	193
BIOT	219
GALT	148
IRT	242
G6PD	112
CFDNA	66
HGB	77
Anti-HIV-1	23
TOXO	10
TREC	60
Arg	298
Cit	324
Leu	352
Met	337
Phe	446
SUAC	170
Tyr	349
Val	319
C0(L)	337
C2(L)	171
C3	340
C3DC	134
C3DC+C4OH	147
C4	317
C4OH	123
C5	348
C5:1	309
C5DC	333
C5OH	301
C6	322
C8	347
C10	334
C10:1	300
C10:2	219
C14	319
C14:1	328
C16	329
C16OH	326
C18	314
C18:1	303
C18OH	278
17OHP2	26
4AD2	26
CORT2	26
11D2	21
21D2	21
GALC	10
GAA	19
IDUA	19
24-LPC	15
26-LPC	20

Table 2. Number of participants reporting quality control analytes, 2019 (N = 522)

Note: A "2" after an analyte indicates 2nd tier

Analyte	Total QC participation in 2019
17OHP	278
T4	90
TSH	343
TGal	182
GALT	105
IRT	228
Ala	280
Arg	295
Cit	312
Gly	249
Leu	328
Met	320
Orn	258
Phe	380
SUAC	165
Tyr	323
Val	313
C0	314
C2	312
C3	313
C3DC	131
C3DC+C4OH	170
C4	311
C4OH	123
C5	320
C5:1	278
C5DC	302
C5OH	282
C6	314
C8	320
C10	320
C12	307
C14	312
C14:1	284
C16	313
C16OH	307
C18	310
C18OH	273
17OHP2	19
4AD2	18
CORT2	18
11D2	12
21D2	11
GALC	19
GAA	35
IDUA	33
GLA	31
ABG	29
ASM	15
20-LPC	26
22-LPC	28
24-LPC	39
26-LPC	42
GUAC	19
CRE2	15
ALE2	12
ILE2	12
LEU2	12
PHE2	14
TYR2	13
VAL2	13
MMA2	14
EMA2	7
MCA2	11
tHCY2	13
MA2	2

Filter Paper

NSQAP evaluates absorption characteristics of all filter paper lots approved by the Food and Drug Administration (FDA) as a newborn screening collection device [3]. Filter paper manufacturers must establish their own parallel evaluation. NSQAP's evaluations are an impartial and voluntary service offered as a function of our QC program; they do not constitute endorsement of any product.

The disk punched from a DBS specimen gives a volumetric measurement that requires a high degree of uniformity among and within production lots. NSQAP uses an isotopic method developed at CDC to evaluate and compare filter paper lots. It equates mean counts per minute of added radioisotope-labeled thyroxine (T4) contained within a 3.2-mm disk with the serum absorption volume of the disks made from blood with washed, intact red blood cells (RBCs). The latest version of Clinical Laboratory Standards Institute (CLSI) Standard NBS01-A6, Blood Collection on Filter Paper for Newborn Screening Programs, describes the method.

FDA-approved newborn screening filter paper manufacturers (GE Healthcare Biosciences Corporation and PerkinElmer Health Sciences) provide NSQAP with statistically valid sample sets of unprinted filter paper from each production lot. Tables 3 and 4 show serum absorption volumes from the 10 most recent lots of these two filter paper sources. The published standardized acceptable serum absorption volume per 3.2-mm disk (mean value and 95% confidence interval) is 1.44 ± 0.20 µL, using blood with washed intact RBCs [3]. The testing results in Tables 3 and 4 are informational only. Each mean value is within the acceptable range for the matrix used. All lots are homogenous (i.e., the measured within-spot, within-sheet, and among-sheets variances were within acceptable limits). CDC used 903™ filter paper lots W161, W171, and W181 to produce the QC and PT specimens distributed in 2019.

Table 3. PerkinElmer 226 specimen collection filter paper absorption characteristics by lot number—intact red cells

Filter Paper	Date of Evaluation	Serum Volume (µL) per 3.2 mm (1/8") Punch	Absorption Time (sec)	Spot Diameter (mm)
Lot No.	Month/Year	Average (StDev)	Average (StDev)	Average (StDev)
112911	June 2019	1.49 (0.16)	8.4 (1.1)	15.8 (0.7)
112147	Sept 2018	1.49 (0.11)	7.9 (0.9)	15.8 (0.6)
111064	July 2017	1.47 (0.20)	8.2 (1.0)	15.7 (0.5)
110092	July 2016	1.45 (0.09)	9.0 (1.2)	16.0 (0.7)
105617	May 2016	1.46 (0.08)	8.3 (1.8)	15.8 (0.5)
105616	Jan 2016	1.56 (0.11)	10.6 (2.0)	15.6 (0.5)
105178	Aug 2015	1.46 (0.09)	7.8 (1.1)	15.9 (0.6)
104568	March 2015	1.56 (0.10)	10.1 (2.1)	15.9 (0.7)
103649	March 2015	1.53 (0.10)	9.7 (3.1)	15.7 (0.7)
102928	Aug 2013	1.38 (0.09)	8.5 (0.9)	16.1 (0.5)

Table 4. 903™ specimen collection filter paper absorption characteristics by lot number—intact red cells

Filter Paper Lot No.	Date of Evaluation Month/Year	Serum Volume (µL) per 3.2 mm (1/8") Punch Average (StDev)	Absorption Time (sec) Average (StDev)	Spot Diameter (mm) Average (StDev)
W191	Oct 2019	1.43 (0.18)	12.2 (2.2)	16.0 (0.7)
W181	Sept 2018	1.42 (0.12)	16.1 (3.3)	16.2 (0.6)
W171	April 2017	1.39 (0.10)	19.7 (4.7)	16.0 (0.7)
W162	Jan 2017	1.43 (0.08)	12.9 (2.7)	16.0 (0.7)
W161	May 2016	1.41 (0.08)	14.8 (3.7)	16.2 (0.8)
W152	Aug 2015	1.37 (0.09)	15.8 (2.4)	16.2 (0.6)
W151	Aug 2015	1.39 (0.08)	15.2 (2.6)	16.2 (0.8)
W142	April 2015	1.46 (0.08)	11.0 (2.2)	16.0 (0.7)
W141	March 2014	1.53 (0.10)	13.8 (3.6)	15.9 (0.6)
W131	Aug 2013	1.40 (0.07)	10.4 (1.4)	16.1 (0.5)

Proficiency Testing

NSQAP distributes PT materials three times per year. PT panels consist of five blind-coded specimens. Specimen sets are packaged in a zip-closed, metalized plastic bag with desiccant. Instructions for analysis and reporting data are located online at https://www.cdc.gov/labstandards/nsqap_resources.html. These specimens provide an independent, external assessment of each laboratory's performance.

The Proficiency Testing Analytes

AMINO ACIDS

- arginine (Arg)
- citrulline (Cit)
- leucine (Leu)
- methionine (Met)
- phenylalanine (Phe)
- succinylacetone (SUAC)
- tyrosine (Tyr)
- valine (Val)

ACYLCARNITINES

- low free carnitine (C0)
- low acetylcarnitine (C2)
- propionylcarnitine (C3)
- malonylcarnitine (C3DC)
- butyrylcarnitine (C4)
- hydroxybutyrylcarnitine (C4OH)
- isovalerylcarnitine (C5)
- hydroxyisovalerylcarnitine (C5OH)
- hydroxyisovalerylcarnitine (C5OH)
- hexanoylcarnitine (C6)
- octanoylcarnitine (C8)
- decanoylcarnitine (C10)
- decenoylcarnitine (C10:1)
- decadienoylcarnitine (C10:2)
- dodecanoylcarnitine (C12)
- myristoylcarnitine (C14)
- tetradecenoylcarnitine (C14:1)
- palmitoylcarnitine (C16)
- hydroxypalmitoylcarnitine (C16OH)
- stearoylcarnitine (C18)
- oleoylcarnitine (C18:1)
- Hydroxystearoylcarnitine (C18OH)

OTHER ANALYTES

- 17 α-hydroxyprogesterone (17OHP)
- 20:0-lysophosphatidylcholine (C20-LPC)
- 22:0-lysophosphatidylcholine (C22-LPC)
- 24:0-lysophosphatidylcholine (C24-LPC)
- 26:0-lysophosphatidylcholine (C26-LPC)
- anti-HIV-1 Antibodies (HIV)
- α-L-iduronidase (IDUA)
- biotinidase (BIOT)
- cystic fibrosis DNA (CFDNA)
- Galactose-1-phosphate Uridyltransferase (GALT)
- galactocerebrosidase (GALC)
- glucose-6-phosphate dehydrogenase (G6PD)
- immunoreactive trypsinogen (IRT)
- Total Galactose (TGal)
- second-tier 17 α -hydroxyprogesterone (17OHP2)
- second-tier 4-androstenedione (4AD2)
- second-tier cortisol (CORT2)
- second-tier 11-deoxycortisol (11D2)
- second-tier 21-deoxycortisol (21D2)
- sickle cell and other hemoglobinopathies (Hb)
- T-cell receptor excision circle (TREC)
- Thyroid Stimulating Hormone (TSH)
- thyroxine (T4)
- anti-*Toxoplasma* Antibodies (TOXO)

Proficiency Testing Materials and Methods

NSQAP certifies PT specimens for homogeneity, accuracy, stability, and suitability for newborn screening assays. Most PT specimens are prepared from whole blood of 50% hematocrit. PT materials are produced from one of the following: unaltered donor blood, enriched single blood units, or pooled blood units.

Purified analytes are used for PT enrichments. Enrichments made with commercially available or custom-synthesized analytes are based on weight. Small variances in enrichments and recoveries might result from impurities in the purchased (synthesized) materials and endogenous analyte concentrations.

Congenital hypothyroid PT specimens are enriched with measured amounts of T4 and TSH after reconstituting washed RBCs with purchased T4-depleted charcoal-stripped serum.

IRT PT specimens are made from a washed, hematocrit-adjusted blood that is treated with a protease inhibitor then enriched with commercially purchased IRT.

TGal PT specimens are enriched with galactose and galactose-1-phosphate, allowing measurement of free galactose (galactose alone) and total galactose (free galactose plus galactose-1-phosphate).

BIOT PT specimens are made using heat-treated serum combined with compatible donor RBCs.

Deficient GALT PT specimens are made using a 50/50 saline/serum solution combined with compatible washed RBCs, and then heat-treating the pool.

C0(L) PT specimens are produced by washing fresh RBCs at least six times then combining with charcoal-stripped serum.

CFDNA PT specimens are prepared using blood from anonymous cystic fibrosis patients, carriers, or unaffected individuals without hematocrit adjustment.

Hb PT specimens are made from hematocrit-adjusted individual umbilical cord blood units.

HIV PT specimens are prepared by mixing purchased donor serum reactive for HIV-1 antibodies and washed RBCs to achieve the desired reactivity.

TREC receptor excision circle PT specimens are prepared from human blood, including cord blood from unaffected persons and modified adult blood depleted of mononuclear cells or leukocytes.

LSD PT specimens are prepared from human blood, including cord blood from unaffected persons and leukodepleted adult blood restored with lymphoblast cell lines derived from patients with LSD.

TOXO PT DBS specimens are prepared by combining human serum samples collected from patients exposed to Toxoplasma gondii with compatible washed RBCs.

Proficiency Testing Data Handling

Participants submit PT data and clinical assessments through the NSQAP data reporting website or by using an Excel form downloaded from the NSQAP section of the CDC website at https://www.cdc.gov/ labstandards/nsqap_resources.html. Laboratories that submitted results before the data reporting deadline receive an individual laboratory evaluation, and their data are included in the data summary report.

Proficiency Testing Errors

Screening programs are designed to minimize false-negative reports, but this precautionary approach could result in false-positive misclassifications. Laboratories should monitor false-positive misclassifications to keep them as low as possible.

Tables 5–8 show the PT errors reported in 2019 by domestic and international laboratories for qualitative assessments by disorder/analyte. Because of specific clinical assessment practices, presumptive clinical classifications (qualitative assessments) of some specimens might differ by participant. If participants provided their cutoff values, those values were applied in the final evaluation of the error judgment (Figure 2). The rates for false-negative misclassifications were based on the number of positive specimens tested; similarly, false-positive rates were based on the negative specimens tested.

The results of some PT specimens were near the decision level for clinical assessment. This rigorously tested the ability of laboratories to make the expected cutoff decision. Most specimens near the mean cutoff value are classified as not-evaluated specimens. As such, they were not included in the error calculations.

Table 5. Summary of non-MS/MS proficiency test errors by domestic laboratories

Analyte/ Disorders	Positive specimens assayed (N)	False negative errors (%)	Negative specimens assayed (N)	False positive errors (%)
Congenital Adrenal Hyperplasia	126	0%	504	0%
Biotinidase Deficiency	254	1%	381	4%
G6PD Deficiency	21	0%	24	0%
GALT Deficiency	214	0%	426	0%
Immunoreactive Trypsinogen	264	3%	396	1%
Congenital Hypothyroidism	94	0%	376	0%
Total Galactose	77	0%	308	0%

Table 6. Summary of non-MS/MS proficiency testing errors by international laboratories

Analyte/ Disorders	Positive specimens assayed (N)	False negative errors (%)	Negative specimens assayed (N)	False positive errors (%)
Congenital Adrenal Hyperplasia	655	2%	2620	1%
Biotinidase Deficiency	932	1%	1398	2%
G6PD Deficiency	642	4%	738	2%
GALT Deficiency	470	3%	940	0%
Immunoreactive Trypsinogen	1036	2%	1554	3%
Congenital Hypothyroidism	699	1%	2796	1%
Total Galactose	433	2%	1732	1%

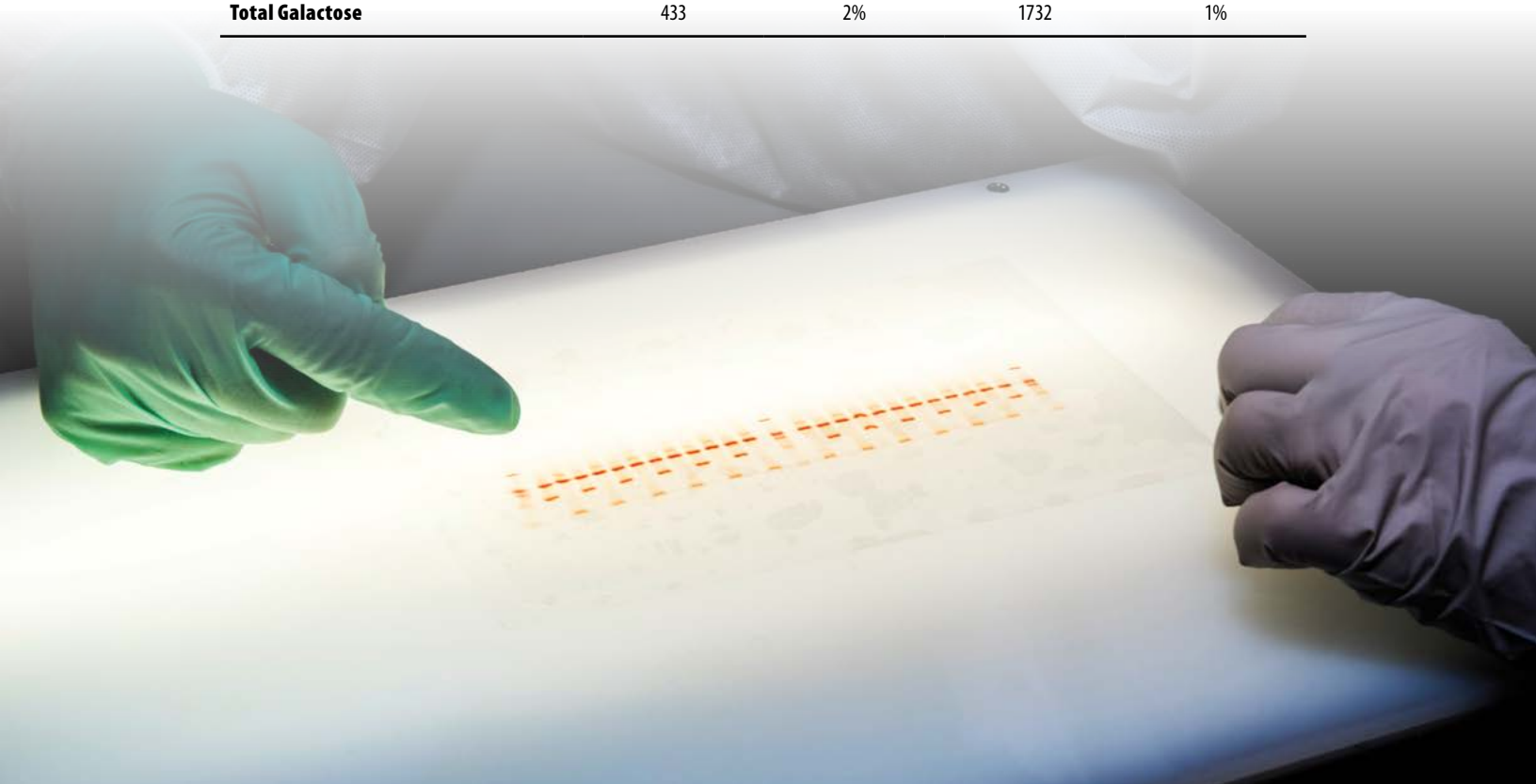


Table 7. Summary of amino acid and acylcarnitine proficiency test errors by domestic laboratories

Analyte	Positive specimens assayed (N)	False negative errors (%)	Negative specimens assayed (N)	False positive errors (%)
Arginine Screen	73	7%	477	0%
Citrulline Screen	133	1%	532	0%
Leucine Screen	92	0%	593	0%
Methionine Screen	134	1%	536	0%
Phenylalanine Screen	110	0%	720	1%
Succinylacetone Screen	110	0%	440	0%
Tyrosine Screen	50	0%	435	0%
Valine Screen	31	0%	279	0%
C0(L) Screen	188	7%	470	1%
C3 Screen	97	4%	628	0%
C3DC Screen	17	0%	238	0%
C3DC+C4OH Screen	48	0%	302	0%
C4 Screen	44	0%	606	0%
C4OH Screen	16	0%	229	0%
C5 Screen	48	0%	672	0%
C5:1 Screen	48	10%	662	0%
C5DC Screen	142	4%	520	0%
C5OH Screen	47	0%	663	0%
C6 Screen	46	0%	634	0%
C8 Screen	97	0%	628	0%
C10 Screen	45	0%	620	0%
C10:1 Screen	42	0%	578	0%
C10:2 Screen	29	0%	396	0%
C14 Screen	44	0%	621	0%
C14:1 Screen	96	0%	581	0%
C16 Screen	91	0%	589	0%
C16OH Screen	48	0%	629	0%
C18 Screen	85	6%	545	0%
C18:1 Screen	85	0%	550	0%
C18OH Screen	76	0%	499	0%

Table 8. Summary of amino acid and acylcarnitine proficiency testing errors by international laboratories

Analyte	Positive specimens assayed (N)	False negative errors (%)	Negative specimens assayed (N)	False positive errors (%)
Arginine Screen	453	4%	2977	1%
Citrulline Screen	737	1%	2948	1%
Leucine Screen	549	1%	3546	0%
Methionine Screen	779	3%	3116	1%
Phenylalanine Screen	708	2%	4542	2%
Succinylacetone Screen	330	3%	1320	2%
Tyrosine Screen	541	2%	3474	1%
Valine Screen	513	1%	3307	1%
C0(L) Screen	1044	0%	2590	7%
C3 Screen	521	1%	3369	1%
C3DC Screen	100	2%	1390	1%
C3DC+C4OH Screen	207	1%	1313	0%
C4 Screen	247	3%	3383	1%
C4OH Screen	88	2%	1287	0%
C5 Screen	266	2%	3759	1%
C5:1 Screen	240	3%	3295	1%
C5DC Screen	760	5%	2769	0%
C5OH Screen	222	2%	3158	3%
C6 Screen	252	2%	3443	0%
C8 Screen	544	2%	3506	0%
C10 Screen	264	2%	3636	1%
C10:1 Screen	238	3%	3257	1%
C10:2 Screen	171	3%	2359	1%
C14 Screen	245	7%	3470	1%
C14:1 Screen	506	3%	3055	1%
C16 Screen	513	4%	3297	1%
C16OH Screen	249	4%	3252	1%
C18 Screen	485	3%	3140	0%
C18:1 Screen	467	4%	3018	0%
C18OH Screen	421	7%	2754	1%

Non-Web Reported Analytes

Table 9 shows a summary of PT errors for programs not reported on the NSQAP database website. Those include the CFDNA, Hb, HIV, LSD, TREC, TOXO, XALD, and Second-tier CAH programs.

The CFDNA PT program provides evaluations based on allele identification and clinical assessment. Allele detection is dependent on the method used. Table 10 summarizes the CF variant challenges distributed in 2019.

Table 11 shows the challenges distributed in 2019 for sickle cell disease and other hemoglobinopathies. Participants are evaluated on hemoglobin phenotypes and ability to provide correct clinical assessments.

Table 9. Summary of non-Web based analyte proficiency test errors

Sickle Cell and Other Hemoglobinopathies

Proficiency Test	Domestic	International
Specimens assayed	664	485
Phenotype errors	0.2%	1.2%
Clinical assessment errors	0.3%	0.8%

Cystic Fibrosis DNA Variant

Proficiency Test	Domestic	International
Specimens assayed	504	532
Allele errors	0.2%	0.9%
Clinical assessment errors	0.2%	0.6%

Lysosomal Storage Disorders

Krabbe

Proficiency Test	Domestic	International
Specimens assayed	155	n/a
Clinical assessment errors	0.6%	n/a

Pompe

Proficiency Test	Domestic	International
Specimens Assayed	285	n/a
Clinical Assessment Errors	0.4%	n/a

Mucopolysaccharidosis Type I

Proficiency Test	Domestic	International
Specimens Assayed	280	n/a
Clinical Assessment Errors	0.7%	n/a

T-cell Receptor Excision Circle

Proficiency Test	Domestic	International
Total Specimens Assayed	598	230
Clinical Assessment Errors	0.7%	0.9%

Second-tier Congenital Adrenal Hyperplasia

Proficiency Test	Domestic	International
Specimens Assayed	85	260
Clinical Assessment Errors	4.7%	6.9%

X-linked Adrenoleukodystrophy

24:0 Lysophosphatidylcholine

Proficiency Test	Domestic	International
Specimens Assayed	85	49
Clinical Assessment Errors	0.0%	0.0%

26:0 Lysophosphatidylcholine

Proficiency Test	Domestic	International
Specimens Assayed	202	69
Clinical Assessment Errors	1.0%	0.0%

Table 10. Cystic Fibrosis DNA variant (CTFR gene) challenges distributed in 2019

Mutation (Legacy Name)	Mutation (HGVS Nomenclature)	Mutations Sent
F508del	(c.1521_1523delCTT)	7
S549N	(c.1646G>A)	1
711+1G>T	(c.579+1G>T)	1
P205S	(c.613C>T)	1
R1158X	(c.3472C>T)	1
A559T	(c.1675G>A)	1
W1282X	(c.3846G>A)	1
3905insT	(c.3773dupT)	1
A455E	(c.1364C>A)	1
F311del	(c.933_935delCTT)	1
Wild type	not applicable	14

Table 11. Hemoglobinopathies accepted presumptive phenotype distribution

Quarter	Specimen 1	Specimen 2	Specimen 3	Specimen 4	Specimen 5
Quarter 1	FS, FSU, UFS, FU	FAC	FA	FAS	FAS
Quarter 3	FAS	FS, FSU, UFS, FU	FAC	FA	FA
Quarter 4	FS, FSU	FAC	FAS	FA	α-Thalassemia carrier, normal

Proficiency Testing Cutoff Values

Participants report the decision level for sorting test results as presumptive positive (outside normal limits) from results reported as negative (within normal limits), based on their established cutoff value. Because CDC does not test newborns, establishing a population cutoff value is not possible. Therefore, CDC cutoff values are determined by using the mean of all domestic laboratory cutoff values. (Note: Each laboratory should establish its own cutoff values rather than using the CDC-reported cutoff values.)

For PT evaluations, the participating laboratory's reported cutoff value is applied to our grading algorithm. If no cutoff value is reported for a particular analytical result, the grading algorithm will default to the NSQAP-assigned cutoff value, which is based on the domestic mean cutoff value. (Figure 2)

Tables 12–15 summarize the reported cutoff values for domestic and international laboratories. The tables show summary statistics for each analyte. Tables 16–18 summarize domestic cutoff statistics by method.

Table 12. Summary of non-MS/MS cutoff values for domestic laboratories

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	42	35.1	33.0	25.0	17.8	65.0
IRT (ng/mL blood)	43	64.6	60.0	55.0	42.2	112.1
T4 (µg/dL serum)	21	6.4	6.1	5.0	5.0	8.0
TGal (mg/dL blood)	23	11.4	10.0	10.0	6.0	20.0
TSH (µIU/mL serum)	43	29.9	25.0	20.0	12.6	58.0
Phe (µmol/L blood)	3	148.7	137.0	N/A	121.2	188.0

Table 13. Summary of non-MS/MS cutoff values for international laboratories

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	216	24.1	20.0	35.0	5.2	103.5
IRT (ng/mL blood)	173	65.5	65.0	70.0	35.0	121.4
T4 (µg/dL serum)	42	8.3	6.0	6.0	3.0	60.0
TGal (mg/dL blood)	142	12.8	10.0	10.0	5.0	30.0
TSH (µIU/mL serum)	281	21.8	20.0	20.0	7.0	50.0
Phe (µmol/L blood)	64	155.6	150.0	120.0	96.9	303.0

Table 14. Summary of amino acid and acylcarnitine cutoff values for domestic laboratories (µmol/L blood)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine	37	74.2	70.0	50.0	27.0	120.0
Citrulline	46	57.9	55.0	60.0	30.0	200.0
Leucine	46	285.1	275.0	250.0	145.0	400.0
Methionine	45	73.6	75.0	100.0	44.0	100.0
Phenylalanine	53	140.4	150.0	150.0	74.0	182.0
Succinylacetone	37	2.5	2.0	4.5	0.8	5.4
Tyrosine	50	390.3	350.0	300.0	19.0	850.0
Valine	31	293.3	300.0	300.0	180.0	530.0
C0(L)	47	8.15	7.50	6.00	5.00	24.00
C2(L)	18	6.73	7.00	9.00	2.00	9.50
C3	49	5.75	6.00	6.30	2.82	9.69
C3DC	17	0.21	0.20	0.20	0.10	0.45
C3DC+ C4OH	24	0.51	0.40	0.38	0.25	3.03
C4	44	1.31	1.30	1.70	0.49	3.24
C4OH	16	0.61	0.65	0.65	0.30	0.80
C5	48	0.73	0.70	0.60	0.39	1.20
C5:1	48	0.20	0.15	0.10	0.03	0.50
C5DC	48	0.37	0.40	0.50	0.05	0.80
C5OH	48	0.84	0.80	0.80	0.25	1.50
C6	46	0.38	0.30	0.20	0.14	0.95
C8	49	0.45	0.43	0.60	0.20	0.73
C10	45	0.44	0.40	0.40	0.22	0.70
C10:1	42	0.28	0.25	0.25	0.13	0.45
C10:2	29	0.15	0.12	0.10	0.04	0.39
C14	45	0.74	0.70	0.70	0.26	1.20
C14:1	49	0.61	0.65	0.60	0.17	0.80
C16	46	7.61	7.60	10.00	2.14	10.36
C16OH	49	0.13	0.10	0.10	0.06	0.25
C18	42	2.32	2.25	3.50	0.70	3.50
C18:1	43	3.50	3.00	2.50	2.00	7.00
C18OH	39	0.09	0.10	0.10	0.03	0.16

Table 15. Summary of amino acid and acylcarnitine cutoff values for international laboratories (µmol/L blood)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine	227	58.5	55.9	70.0	10.0	150.0
Citrulline	246	52.1	47.5	55.0	20.0	200.0
Leucine	275	305.7	295.0	300.0	142.0	686.7
Methionine	261	55.1	50.0	75.0	10.0	140.0
Phenylalanine	286	135.9	125.0	150.0	48.0	300.0
Succinylacetone	111	2.0	1.5	1.5	0.3	8.0
Tyrosine	268	301.4	287.3	350.0	79.9	600.0
Valine	257	265.7	265.0	300.0	136.0	470.0
C0(L)	254	11.82	8.20	10.00	2.00	100.00
C2(L)	143	21.63	8.98	7.00	0.00	85.00
C3	254	5.21	5.12	5.65	0.81	11.00
C3DC	96	0.33	0.25	0.25	0.07	4.50
C3DC+ C4OH	102	0.49	0.44	0.45	0.10	3.14
C4	240	0.97	0.92	1.30	0.16	3.80
C4OH	89	0.59	0.60	0.65	0.05	1.40
C5	265	0.68	0.60	0.70	0.13	2.00
C5:1	236	0.15	0.12	0.25	0.01	1.20
C5DC	251	0.33	0.30	0.35	0.08	0.90
C5OH	224	0.72	0.77	0.80	0.21	2.50
C6	244	0.29	0.24	0.40	0.04	3.32
C8	271	0.42	0.31	0.45	0.05	21.38
C10	254	0.37	0.38	0.45	0.07	1.10
C10:1	231	0.25	0.25	0.30	0.05	1.00
C10:2	166	0.15	0.12	0.15	0.01	2.00
C14	243	0.61	0.56	0.75	0.08	1.30
C14:1	253	0.46	0.42	0.60	0.10	2.50
C16	249	6.78	7.00	7.50	0.70	14.00
C16OH	246	0.31	0.10	0.10	0.02	48.00
C18	238	2.12	2.02	2.30	0.17	6.32
C18:1	233	3.04	3.00	3.50	0.03	5.80
C18OH	208	0.10	0.08	0.10	0.01	2.00

Table 16. Summary of cutoff values by analyte and method for domestic laboratories—hormones, galactose, and immunoreactive trypsinogen, (methods N<3 not shown)

17 α-Hydroxyprogesterone ng/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**35.1**	**33.0**	**25.0**	**17.8**	**65.0**
AutoDelfia	19	35.6	33.0	33.0	17.8	60.0
PerkinElmer GSP Neonatal	23	34.6	32.0	25.0	25.0	65.0

Immunoreactive Trypsinogen ng/mL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**64.6**	**60.0**	**55.0**	**42.2**	**112.1**
AutoDelfia	21	72.6	68.0	68.0	52.0	112.1
PerkinElmer GSP Neonatal	22	57.1	55.0	55.0	42.2	100.0

Thyroxine µg/dL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**21**	**6.4**	**6.1**	**5.0**	**5.0**	**8.0**
AutoDelfia	6	7.1	7.0	n/a	6.0	8.0
PerkinElmer GSP Neonatal	14	6.2	6.0	5.0	5.0	8.0

Thyroid-Stimulating Hormone µIU/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**29.9**	**25.0**	**20.0**	**12.6**	**58.0**
AutoDelfia	17	36.1	28.5	58.0	12.6	58.0
PerkinElmer GSP Neonatal	25	26.0	25.0	20.0	19.0	37.0

Total Galactose mg/dL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**23**	**11.4**	**10.0**	**10.0**	**6.0**	**20.0**
Astoria-Pacific 50 Hour Reagent Kit	4	11.5	10.5	10.0	10.0	15.0
Fluorometric manual (e.g. Hill or Misuma)	3	14.7	14.0	n/a	10.0	20.0
PerkinElmer GSP Neonatal	11	11.1	10.0	10.0	7.3	14.0

Table 17. Domestic cutoff summary by analyte and method—amino acids (µmol/L blood), (methods N < 3 not shown)

Arginine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**37**	**74.2**	**70.0**	**50.0**	**27.0**	**120.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	76.7	70.0	n/a	60.0	100.0
Derivatized - MS/MS non-kit	10	64.7	63.0	n/a	27.0	115.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	21	80.6	90.0	50.0	48.0	120.0

Continued

Citrulline

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**46**	**57.9**	**55.0**	**60.0**	**30.0**	**200.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	51.7	50.0	n/a	40.0	65.0
Derivatized - MS/MS non-kit	12	53.1	52.5	40.0	36.0	75.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	3	46.7	45.0	45.0	45.0	50.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	57.9	60.0	60.0	40.0	75.0

Leucine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**46**	**285.1**	**275.0**	**250.0**	**145.0**	**400.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	291.7	275.0	275.0	275.0	325.0
Derivatized - MS/MS non-kit	12	279.8	294.5	300.0	222.0	350.0
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	180.0	145.0	145.0	145.0	250.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	301.4	288.0	250.0	225.0	400.0
Non-derivatized - MS/MS non-kit	3	270.0	255.0	n/a	250.0	305.0

Methionine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**45**	**73.6**	**75.0**	**100.0**	**44.0**	**100.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	76.7	75.0	75.0	75.0	80.0
Derivatized - MS/MS non-kit	12	66.3	66.0	50.0	44.0	100.0
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	55.0	45.0	45.0	45.0	75.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	80.1	80.0	100.0	54.5	100.0

Phenylalanine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**53**	**140.4**	**150.0**	**150.0**	**74.0**	**182.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	138.3	135.0	n/a	130.0	150.0
Derivatized - MS/MS non-kit	15	135.3	139.0	n/a	86.0	182.0
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	125.7	125.0	n/a	100.0	152.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	149.0	152.0	165.0	120.0	180.0
Non-derivatized - MS/MS non-kit	6	124.2	125.5	150.0	74.0	150.0

Succinylacetone

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**37**	**2.5**	**2.0**	**4.5**	**0.8**	**5.4**
Derivatized - MS/MS non-kit	9	2.9	2.5	2.0	1.6	5.0
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	1.5	1.0	1.0	1.0	2.4
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	2.4	2.0	4.5	0.8	4.5

Tyrosine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**50**	**390.3**	**350.0**	**300.0**	**19.0**	**850.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	293.3	300.0	300.0	280.0	300.0
Derivatized - MS/MS non-kit	14	292.9	300.0	300.0	99.0	500.0
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	358.3	350.0	350.0	350.0	375.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	511.5	450.0	850.0	300.0	850.0
Non-derivatized - MS/MS non-kit	6	224.4	270.0	n/a	19.0	400.0

Valine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**31**	**293.3**	**300.0**	**300.0**	**180.0**	**530.0**
Derivatized - MS/MS non-kit	9	276.1	280.0	200.0	200.0	420.0
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	220.0	180.0	180.0	180.0	300.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	14	317.6	300.0	300.0	250.0	530.0
Non-derivatized - MS/MS non-kit	3	266.7	250.0	250.0	250.0	300.0

Table 18. Domestic cutoff summary by analyte and method—acylcarnitines (µmol/L blood), (methods N < 3 not shown)

C0(L)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**8.15**	**7.50**	**6.00**	**5.00**	**24.00**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	11.15	10.46	n/a	9.00	14.00
Derivatized - MS/MS non-kit	15	10.31	10.00	10.00	5.00	24.00
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	6.60	6.00	6.00	5.00	10.00

C2(L)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**18**	**6.73**	**7.00**	**9.00**	**2.00**	9.50
Derivatized - MS/MS non-kit	6	5.67	5.50	n/a	2.00	9.50
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	6	6.87	7.00	7.00	4.00	9.00

C3

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**49**	**5.75**	**6.00**	**6.30**	**2.82**	**9.69**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	5.38	5.20	n/a	5.00	5.94
Derivatized - MS/MS non-kit	16	5.20	5.63	6.00	2.82	7.30
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	6.16	4.80	n/a	4.00	9.69
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	5.99	6.25	6.30	4.80	7.50
Non-derivatized - MS/MS non-kit	3	6.81	6.92	n/a	6.50	7.00

C3DC

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**17**	**0.21**	**0.20**	**0.20**	**0.10**	**0.45**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.24	0.22	n/a	0.19	0.30
Derivatized - MS/MS non-kit	14	0.20	0.20	0.20	0.10	0.45

C3DC + C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**24**	**0.51**	**0.40**	**0.38**	**0.25**	**3.03**
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	20	0.40	0.39	0.38	0.25	0.60

Continued

C4

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**1.31**	**1.30**	**1.70**	**0.49**	**3.24**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.90	0.90	n/a	0.81	1.00
Derivatized - MS/MS non-kit	14	1.34	1.35	1.40	0.49	3.24
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	1.24	1.33	n/a	1.00	1.40
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	1.37	1.30	1.70	1.00	1.70

C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**16**	**0.61**	**0.65**	**0.65**	**0.30**	**0.80**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.63	0.65	n/a	0.55	0.70
Derivatized - MS/MS non-kit	13	0.60	0.65	0.40	0.30	0.80

C5

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**0.73**	**0.70**	**0.60**	**0.39**	**1.20**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.65	0.70	0.70	0.54	0.70
Derivatized - MS/MS non-kit	15	0.75	0.70	0.50	0.39	1.20
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.65	0.60	0.60	0.60	0.75
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.74	0.70	1.00	0.45	1.00

C5:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**0.20**	**0.15**	**0.10**	**0.03**	**0.50**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.18	0.15	0.15	0.15	0.25
Derivatized - MS/MS non-kit	16	0.20	0.15	0.07	0.05	0.50
Non-derivatized - MS/MS NeoBase™2	3	0.11	0.10	0.10	0.10	0.14
PerkinElmer	3	0.11	0.10	0.10	0.10	0.14
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	0.23	0.19	0.10	0.03	0.50

C5DC

Method	N	Mean	Median	Mode	Min	Max
All Methods	**48**	**0.37**	**0.40**	**0.50**	**0.05**	**0.80**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.26	0.25	n/a	0.24	0.30
Derivatized - MS/MS non-kit	16	0.18	0.18	0.15	0.05	0.30
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.33	0.24	0.24	0.24	0.51
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	0.50	0.50	0.50	0.30	0.80

C5OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**0.84**	**0.80**	**0.80**	**0.25**	**1.50**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.70	0.67	n/a	0.60	0.83
Derivatized - MS/MS non-kit	16	0.82	0.80	0.80	0.25	1.36
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	1.34	1.50	1.50	1.03	1.50
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	0.80	0.80	0.85	0.60	1.05

Continued

C6

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**46**	**0.38**	**0.30**	**0.20**	**0.14**	**0.95**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.27	0.25	0.25	0.25	0.30
Derivatized - MS/MS non-kit	15	0.33	0.31	0.24	0.14	0.63
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.25	0.24	0.24	0.24	0.26
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	0.46	0.29	0.95	0.17	0.95

C8

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**49**	**0.45**	**0.43**	**0.60**	**0.20**	**0.73**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.36	0.35	0.35	0.35	0.38
Derivatized - MS/MS non-kit	16	0.43	0.40	0.50	0.20	0.73
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.57	0.60	0.60	0.50	0.60
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.48	0.45	0.60	0.32	0.70

C10

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.44**	**0.40**	**0.40**	**0.22**	**0.70**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.31	0.30	n/a	0.27	0.35
Derivatized - MS/MS non-kit	14	0.39	0.40	0.40	0.22	0.55
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.50	0.55	0.55	0.39	0.55
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	0.48	0.45	0.65	0.22	0.70

C10:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**0.28**	**0.25**	**0.25**	**0.13**	**0.45**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.28	0.30	0.30	0.25	0.30
Derivatized - MS/MS non-kit	13	0.27	0.25	0.17	0.17	0.42
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.16	0.13	0.13	0.13	0.22
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	21	0.30	0.30	0.45	0.15	0.45

C10:2

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**29**	**0.15**	**0.12**	**0.10**	**0.04**	**0.39**
Derivatized - MS/MS non-kit	12	0.18	0.16	0.10	0.06	0.39
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	12	0.13	0.10	0.10	0.04	0.30

C14

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.74**	**0.70**	**0.70**	**0.26**	**1.20**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.61	0.60	n/a	0.52	0.70
Derivatized - MS/MS non-kit	15	0.66	0.70	0.80	0.26	0.96
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.65	0.60	0.60	0.60	0.76
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	0.82	0.70	0.70	0.58	1.20

Continued

C14:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**49**	**0.61**	**0.65**	**0.60**	**0.17**	**0.80**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.52	0.45	n/a	0.40	0.70
Derivatized - MS/MS non-kit	16	0.54	0.63	0.60	0.17	0.77
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.61	0.60	0.60	0.60	0.64
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.68	0.68	0.80	0.50	0.80

C16

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**46**	**7.61**	**7.60**	**10.00**	**2.14**	**10.36**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	6.78	6.65	n/a	6.50	7.20
Derivatized - MS/MS non-kit	15	6.69	7.00	7.00	2.14	9.00
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	7.45	6.00	6.00	6.00	10.36
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	8.33	8.00	10.00	6.00	10.00

C16OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**49**	**0.13**	**0.10**	**0.10**	**0.06**	**0.25**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.15	0.14	n/a	0.12	0.18
Derivatized - MS/MS non-kit	16	0.14	0.15	0.10	0.06	0.25
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.12	0.10	0.10	0.10	0.16
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.11	0.10	0.10	0.07	0.20

C18

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**2.32**	**2.25**	**3.50**	**0.70**	**3.50**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	2.06	2.00	n/a	1.89	2.29
Derivatized - MS/MS non-kit	12	1.88	1.88	n/a	0.70	2.80
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	2.56	2.30	2.30	2.30	3.09
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	2.57	2.38	3.50	1.55	3.50

C18:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**3.50**	**3.00**	**2.50**	**2.00**	**7.00**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	2.79	2.50	n/a	2.43	3.43
Derivatized - MS/MS non-kit	13	2.71	2.70	3.00	2.00	3.50
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	2.69	2.70	2.70	2.67	2.70
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	4.22	3.46	7.00	2.27	7.00

C18OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**39**	**0.09**	**0.10**	**0.10**	**0.03**	**0.16**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.13	0.12	n/a	0.10	0.16
Derivatized - MS/MS non-kit	11	0.10	0.10	0.10	0.03	0.16
Non-derivatized - MS/MS NeoBase2 PerkinElmer	3	0.06	0.04	0.04	0.04	0.10
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	20	0.09	0.10	0.10	0.03	0.16

Explanation of the NSQAP's Grading Algorithm

NSQAP provides PT evaluations based on qualitative clinical assessments. The algorithm for determining PT errors (Figure 4) is as follows:

Part 1: The **NSQAP expected clinical assessment** for PT specimens is determined by comparing the **NSQAP expected value** to the **NSQAP cutoff value**.

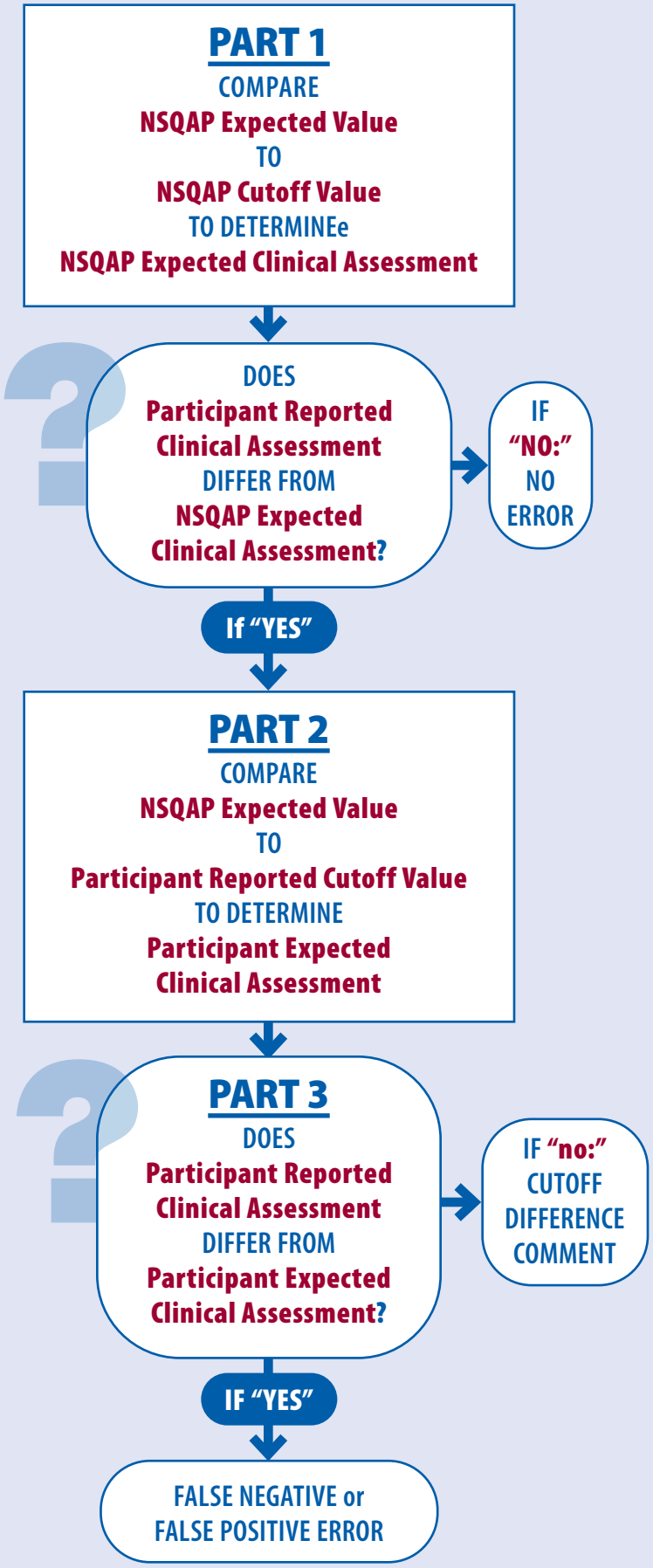
Clinical assessments are reported as "within normal limits" or "outside normal limits." The NSQAP expected value is the sum of the endogenous value plus the enrichment value for an individual analyte. The NSQAP cutoff value is determined annually using the mean of all domestic laboratories' reported cutoff values as a guideline.

Part 2: The **participant reported clinical assessment** is then compared with the **NSQAP expected clinical** assessment. If these assessments agree, the algorithm stops and no error is reported. If these assessments do not agree, the grading algorithm is continued.

Part 3: If the algorithm was not completed in part 2, the **participant expected clinical assessment** is determined by comparing the **NSQAP expected value** to the participant's reported cutoff value. If the **participant reported clinical assessment** differs from the **participant expected clinical assessment** a false positive or false negative error will be noted. If the **participant reported clinical assessment** agrees with the **participant expected clinical assessment** a cutoff difference comment will be noted.

Determination of a final evaluation for a specimen is based on Clinical Laboratory Improvement Amendments (CLIA) regulations. These require the PT provider to compare the laboratory's response for each analyte with the response that reflects agreement of 80% or more of all laboratories. (CLIA Regulations, 2004). An NSQAP gradable specimen must have 80% or more agreement among domestic laboratories. For analytes with less than 10 domestic participants, the specimen will be evaluated unless the sample is deemed ungradable by the review committee.

Figure 2. NSQAP's Grading Algorithm Flow chart



2019 Bias Plots

Proficiency Testing Bias Plots

Figures 3–38 are illustrated for PT analytes reported using the NSQAP data reporting website. A wide range of quantitatively measured PT challenges was selected for the bias plots. Comparisons of results by different methods are illustrated with the participants' reported PT data for one selected challenge for each analyte. The expected value of each specimen equals the sum of the enriched value and the endogenous (non-enriched) value. IRT standard cannot be fully recovered by any IRT analytical method; therefore, IRT PT uses CDC-assayed values.

Non-derivatized MS/MS methods for amino acids and acylcarnitine analysis cannot distinguish between analytes C3DC and C4OH (i.e., they are isobaric). Laboratories using a non-derivatized MS/MS method report C3DC+C4OH, while derivatized MS/MS method users report those analytes separately. These bias plots show the difference of the reported value (positive or negative) by laboratory and method subtracted from the expected or assayed value. To illustrate method-related differences in analyte recoveries, the PT quantitative results are grouped by kit or method.

For each plot, note the scale-changes of the y-axis. A reported value matching the expected value (endogenous value plus enriched value) falls on the plot's "0" line. For each figure, a summary of the specimen data for the selected PT challenge is tabulated in the left margin. Ideally, a reasonable bias is less than 20% of the expected value.

The bias plots illustrate the 95% confidence interval for the participant mean. A tight scatter within this interval indicates good performance for a method or a group of methods. In general, the quantitative comparisons for PT challenges are reasonable within a method but vary among methods. Because some of the pools in a routine PT survey represent a unique donor specimen, differences in endogenous materials in the donor specimens might influence method-related differences

Note for accessibility:
For Figures 3–38, the bias plot's explanation follows each figure title.

Figure 3. Reproducibility of Results: Bias Plot of 17 α-Hydroxyprogesterone (17OHP) Values by Method Quarter 1, Specimen 11913 Expected Value (EV) = 86.1 ng/mL serum

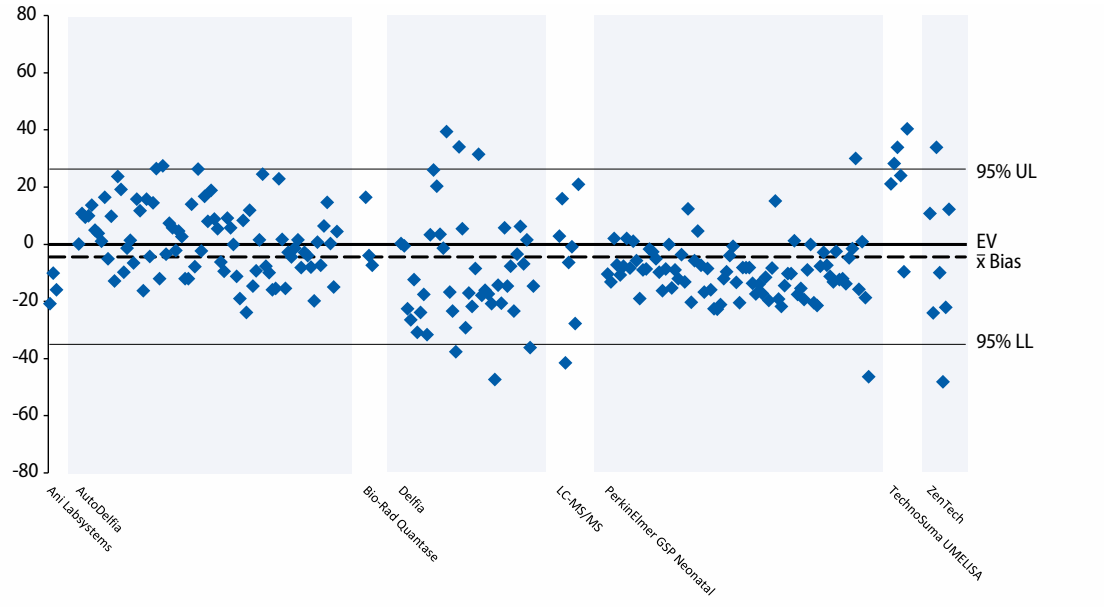
17OHP ng/mL serum

Enriched: 85.0

CDC Assayed: 85.5

Participant Mean: 81.7

Participant Bias: -4.4



The 17OHP bias plot shows units of measure on the y-axis ranging from 80 ng/mL serum to -80 ng/mL serum. The bias for this plot is -4.4 ng/mL serum. The data on this plot shows a tight scatter among all participants.

T4

Figure 4. Reproducibility of Results: Bias Plot of Thyroxine (T4) Values by Method Quarter 1, Specimen 11913 Expected Value (EV) = 14.5 µg/dL serum

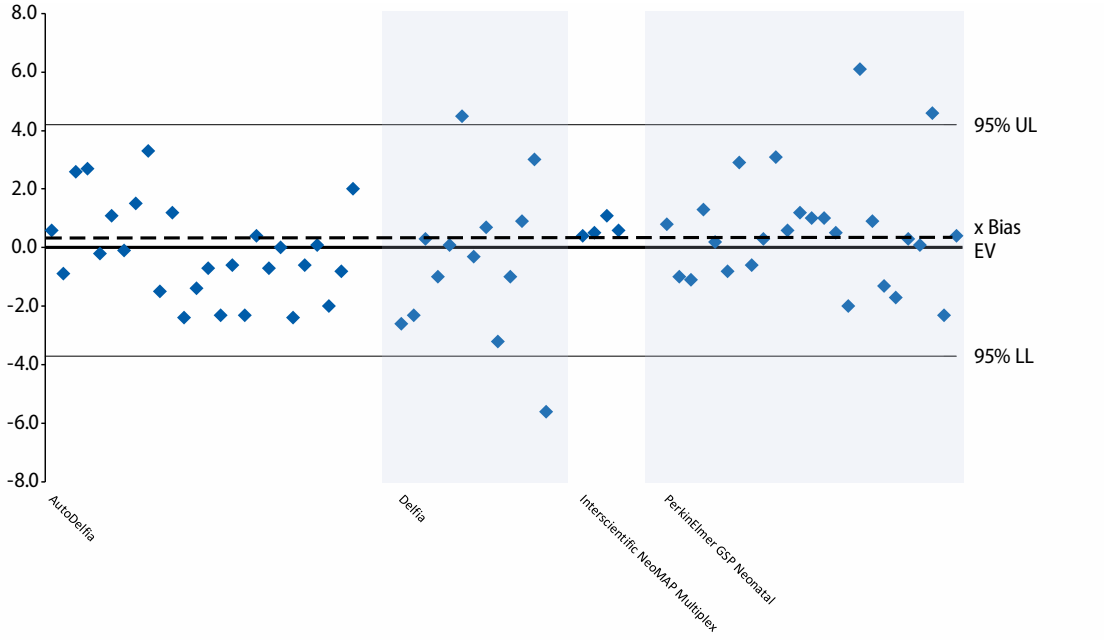
T4 µg/dL serum

Enriched: 10.0

CDC Assayed: 14.0

Participant Mean: 14.7

Participant Bias: 0.2



The T4 bias plot shows units of measure on the y-axis ranging from 8 µg/dL serum to -8 µg/dL serum. The bias for this plot is 0.2. The data on this plot shows a good agreement among participants.

Figure 5. Reproducibility of Results: Bias Plot of Thyroid-Stimulating Hormone (TSH) Values by Method Quarter 4, Specimen 41911 Expected Value (EV) = 85.4 µIU/mL serum

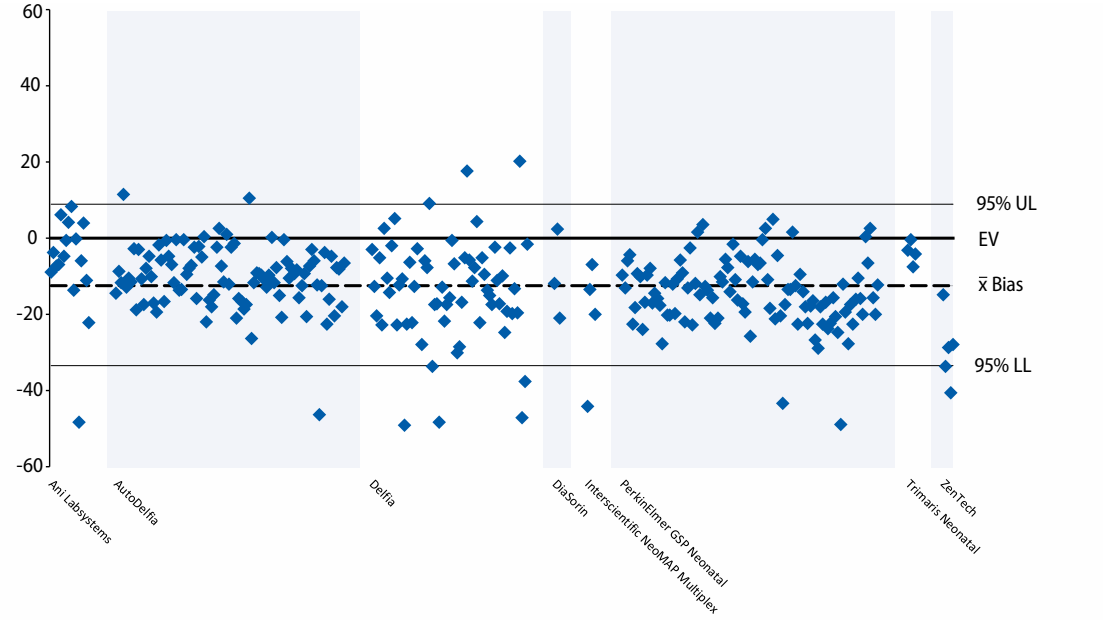
TSH µIU/mL serum

Enriched: 85.0

CDC Assayed: 79.4

Participant Mean: 67.0

Participant Bias: -18.4



The TSH bias plot shows units of measure on the y-axis ranging from 100 µIU/mL serum to -100 µIU/mL serum. The bias for this plot is -18.2. The data on this plot shows a negative bias across all methods

Figure 6. Reproducibility of Results: Bias Plot of Total Galactose (TGal) Values by Method Quarter 3, Specimen 31911 Expected Value (EV) = 25.0 mg/dL blood

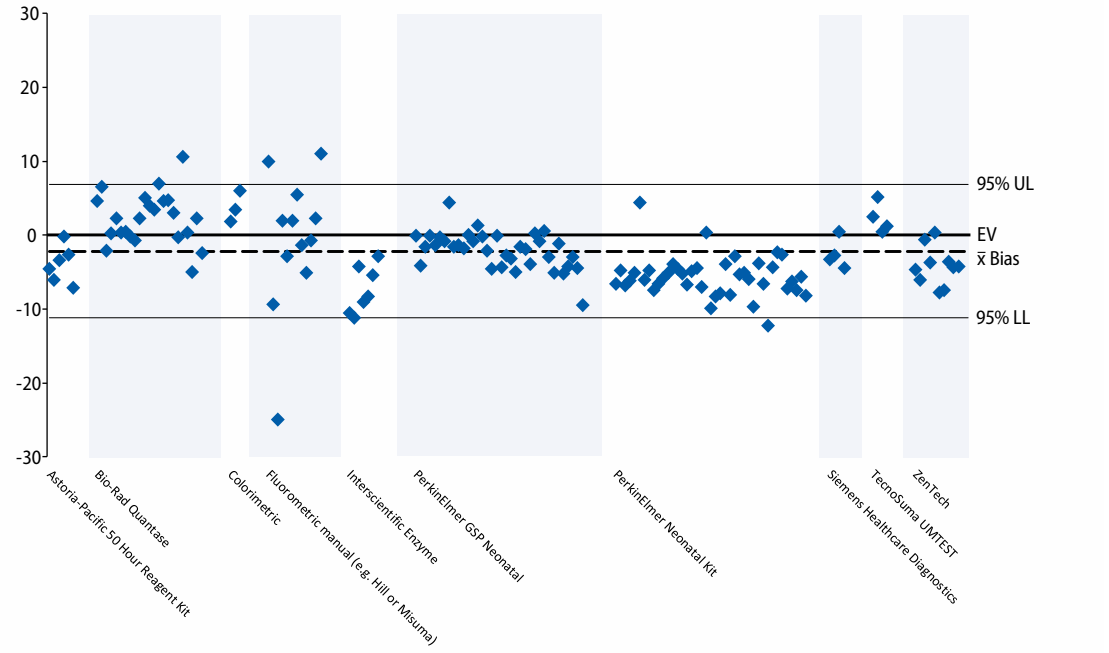
TGal mg/dL blood

Enriched: 25.0

CDC Assayed: 19.6

Participant Mean: 22.8

Participant Bias: -2.2



The TGal bias plot shows units of measure on the y-axis ranging from 30 mg/dL blood to -30 mg/dL blood. The bias for this plot is -2.2. The data on this plot shows good agreement among participants, however some methods show a positive bias while other methods show a negative bias.

Figure 7. Reproducibility of Results: Bias Plot of Immunoreactive Trypsinogen (IRT) Values by Method Quarter 1, Specimen 11981 Assayed Value (AV) = 143.5 ng/mL blood

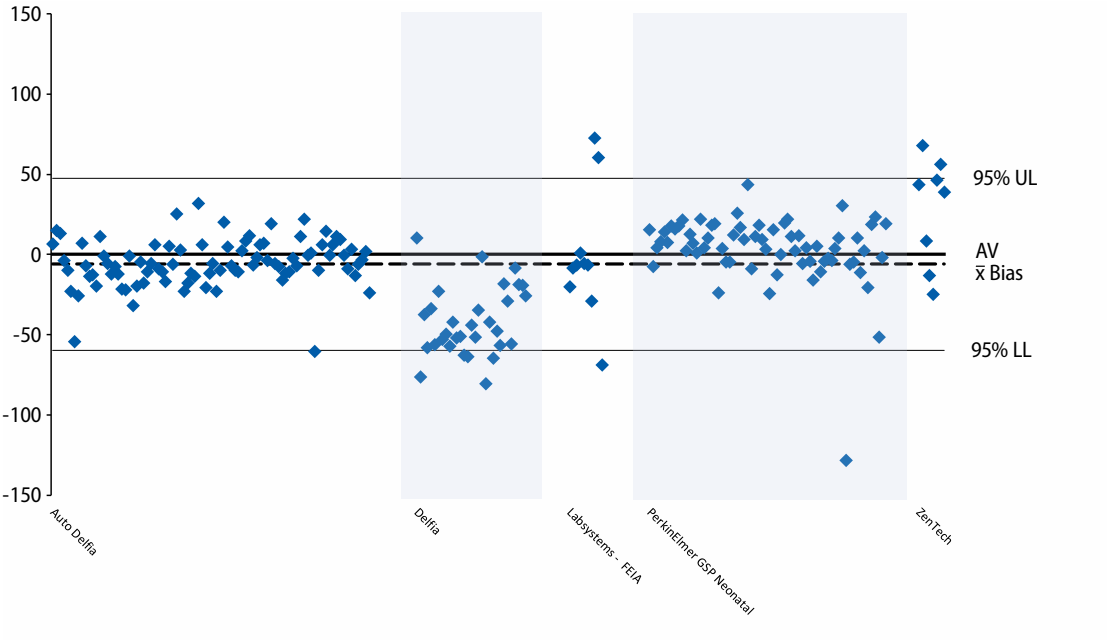
IRT ng/mL blood

Enriched: 250.0

CDC Assayed: 143.5

Participant Mean: 137.4

Participant Bias: -6.1



The IRT bias plot shows units of measure on the y-axis ranging from 150 ng/mL blood to -150 ng/mL blood. The bias for this plot is -6.1. Data on this bias plot shows one method having a more negative bias than the other two methods.

Figure 8. Reproducibility of Results: Bias Plot of Arginine (Arg) Values by Method Quarter 1, Specimen 11954 Expected Value (EV) = 130.2 µmol/L blood

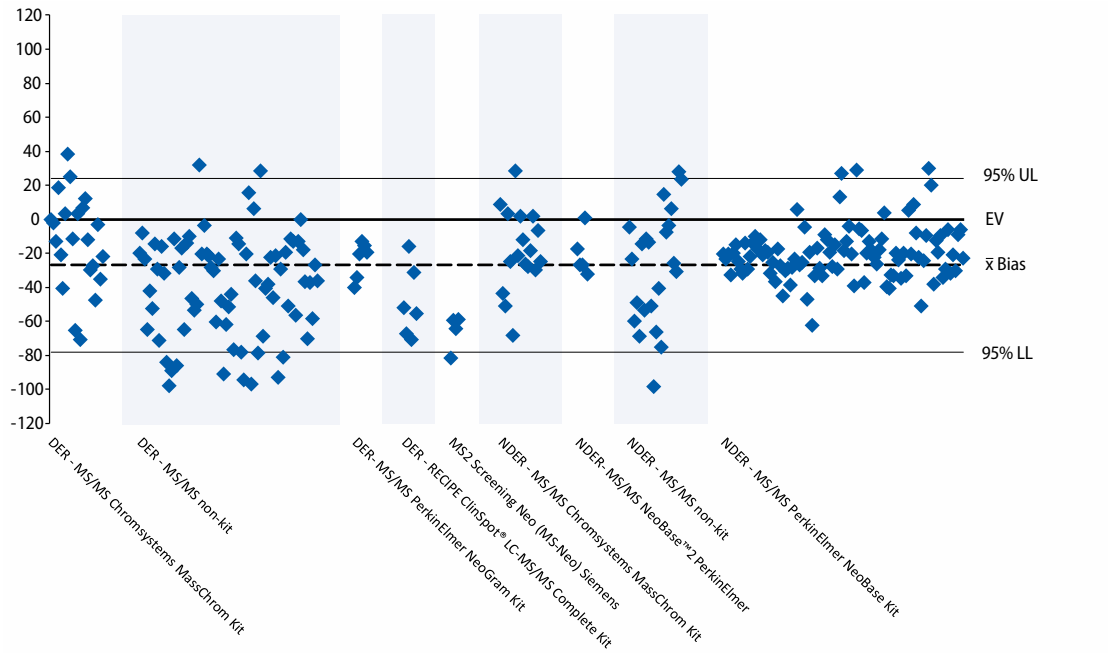
Arg µmol/L blood

Enriched: 123.9

CDC Assayed: 99.5

Participant Mean: 103.2

Participant Bias: -27.0



The Arg bias plot shows units of measure on the y-axis ranging from 120 µmol/L blood to -120 µmol/L blood. The mean bias for this plot is -27.0 µmol/L blood . All methods show a significantly negative bias.

Figure 9. Reproducibility of Results: Bias Plot of Citrulline (Cit) Values by Method Quarter 1 , Specimen 11951 Expected Value (EV) = 181.3 µmol/L blood

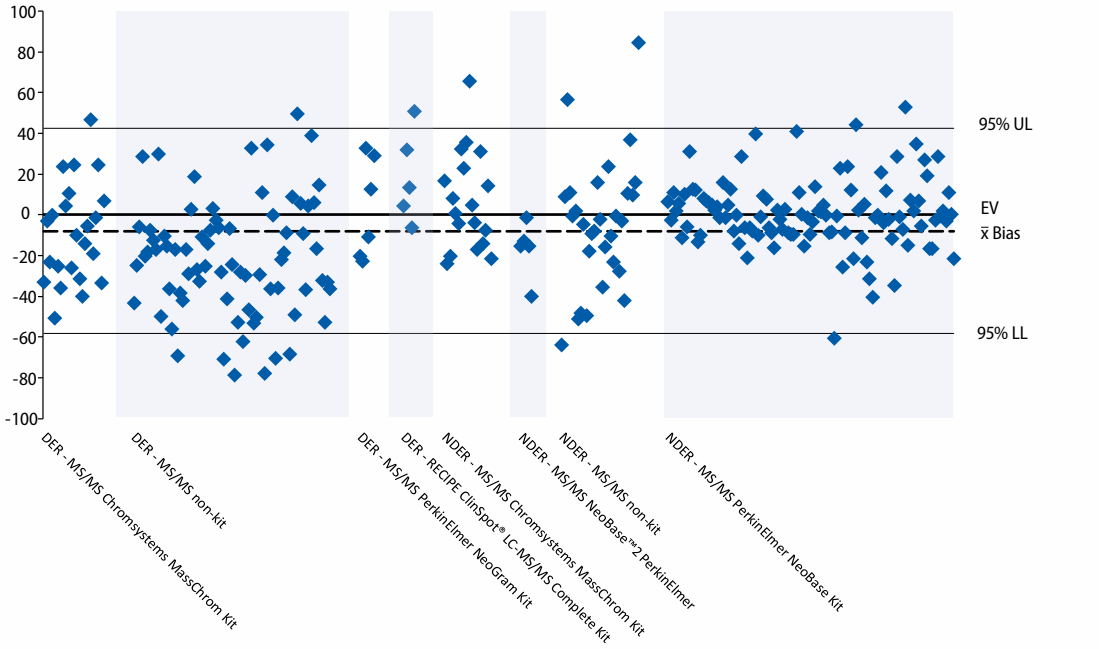
Cit µmol/L blood

Enriched: 168.0

CDC Assayed: 167.6

Participant Mean: 173.4

Participant Bias: -7.9



The Cit bias plot shows units of measure on the y-axis ranging from 100 µmol/L blood to -100 µmol/L blood. The mean bias for this plot is -7.9 µmol/L blood . Most methods show a evenly scattered bias.

Figure 10. Reproducibility of Results: Bias Plot of Leucine (Leu) Values by Method Quarter 4, Specimen 41951 Expected Value (EV) = 573.3 µmol/L blood

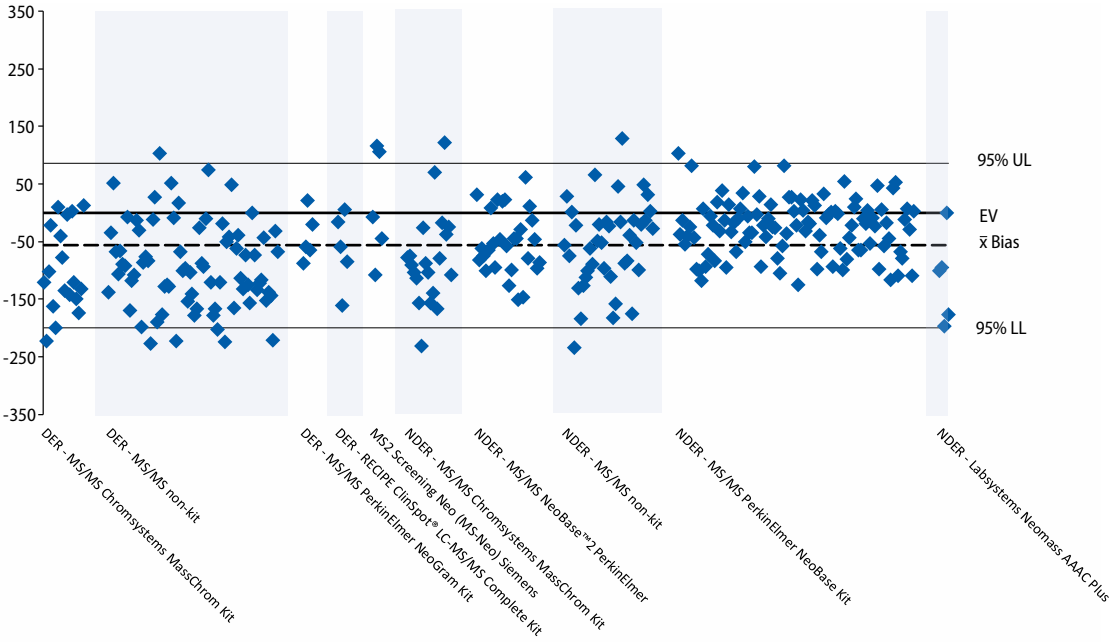
Leu µmol/L blood

Enriched: 450.0

CDC Assayed: 599.4

Participant Mean: 516.6

Participant Bias: -56.7



The Leu bias plot shows units of measure on the y-axis ranging from 350 µmol/L blood to -350 µmol/L blood. The mean bias for this plot is -56.7 µmol/L blood. There is good scatter around a negative bias

Figure 11. Reproducibility of Results: Bias Plot of Methionine (Met) Values by Method Quarter 3, Specimen 31952 Expected Value (EV) = 169.6 µmol/L blood

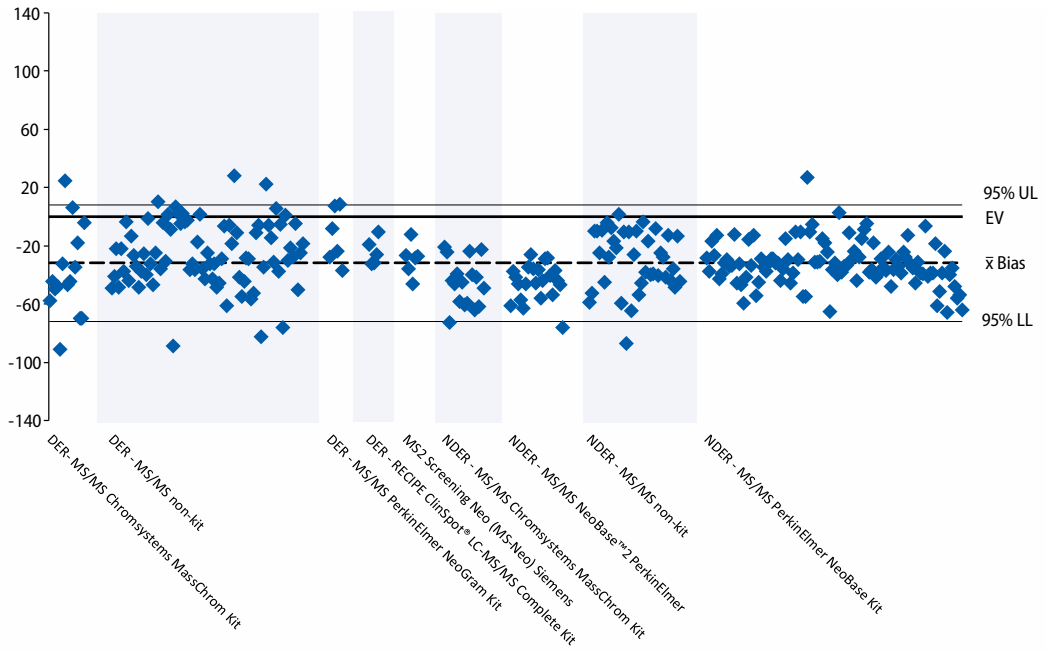
Met µmol/L blood

Enriched: 155.6

CDC Assayed: 130.6

Participant Mean: 137.6

Participant Bias: - 32.0



The Met bias plot shows units of measure on the y-axis ranging from 140 µmol/L blood to -140 µmol/L blood. The mean bias for this plot is -32.0 µmol/L blood . All methods show a significantly negative bias

Figure 12. Reproducibility of Results: Bias Plot of Phenylalanine (Phe) Values by Method Quarter 1, Specimen 11952 Expected Value (EV) = 311.4 µmol/L blood

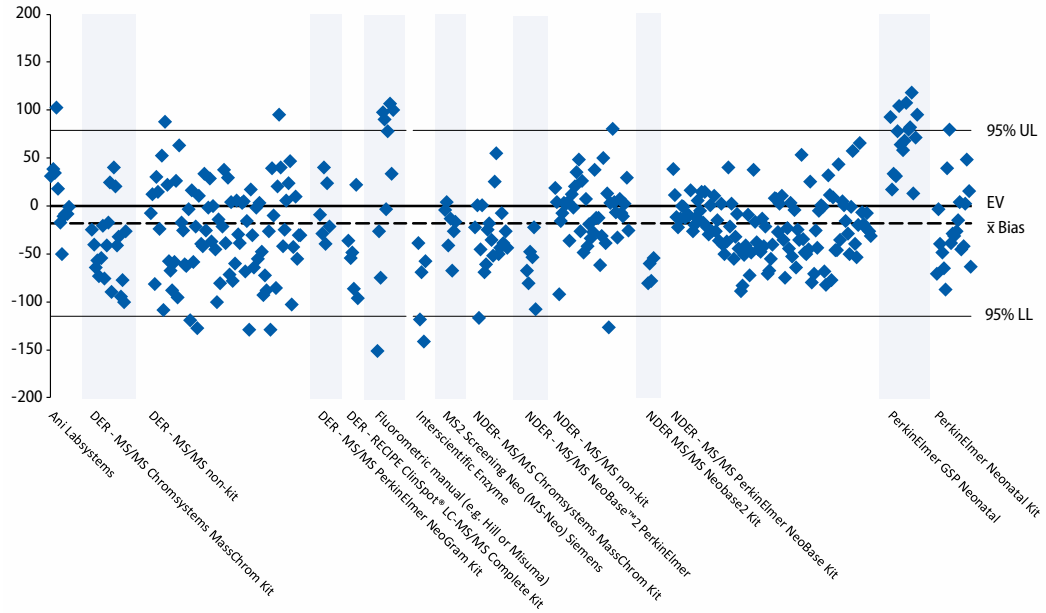
Phe µmol/L blood

Enriched: 296.0

CDC Assayed: 298.1

Participant Mean: 293.2

Participant Bias: - 18.2



The Phe bias plot shows units of measure on the y-axis ranging from 200 µmol/L blood to -200 µmol/L blood. The mean bias for this plot is -18.2 µmol/L blood. One method shows a positive bias while others show a slight negative bias.

Figure 13. Reproducibility of Results: Bias Plot of Succinylacetone (SUAC) Values by Method Quarter 3, Specimen 31955 Expected Value (EV) = 49.3 µmol/L blood

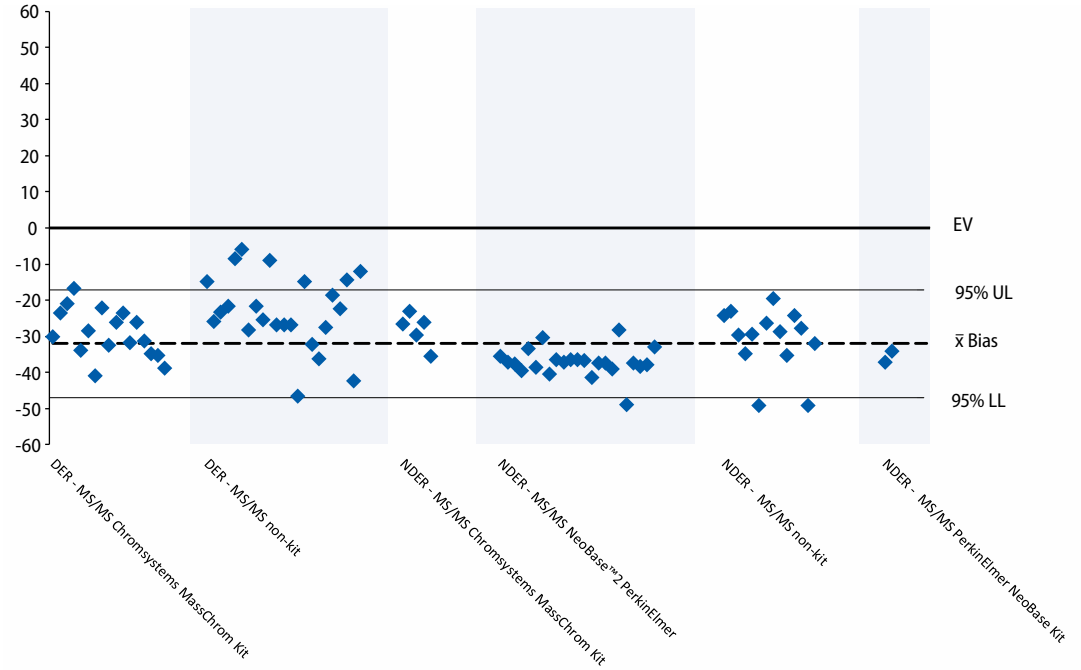
SUAC µmol/L blood

Enriched: 49.2

CDC Assayed: 15.5

Participant Mean: 17.3

Participant Bias:-32.0



The SUAC bias plot shows units of measure on the y-axis ranging from 60 µmol/L blood to -60 µmol/L blood. The mean bias for this plot is -32.0 µmol/L blood . All methods show a strongly negative bias, which is historically consistent for this analyte.

Figure 14. Reproducibility of Results: Bias Plot of Tyrosine (Tyr) Values by Method Quarter 3, Specimen 31955 Expected Value (EV) = 786.6 µmol/L blood

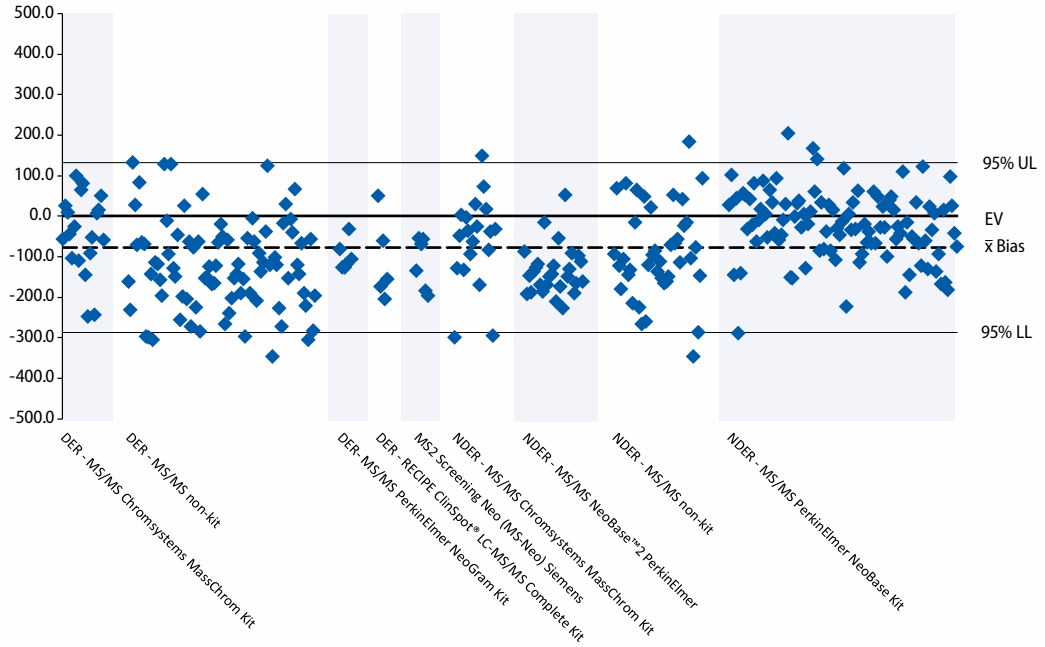
Tyr µmol/L blood

Enriched: 741.4

CDC Assayed: 689.9

Participant Mean: 709.3

Participant Bias: -77.3



The Tyr bias plot shows units of measure on the y-axis ranging from 500 µmol/L blood to -500 µmol/L blood. The mean bias for this plot is -77.3 µmol/L blood . All methods show a good scatter around the bias.

Figure 15. Reproducibility of Results: Bias Plot of Valine (Val) Values by Method Quarter 3, Specimen 31954 Expected Value (EV) = 628.4 µmol/L blood

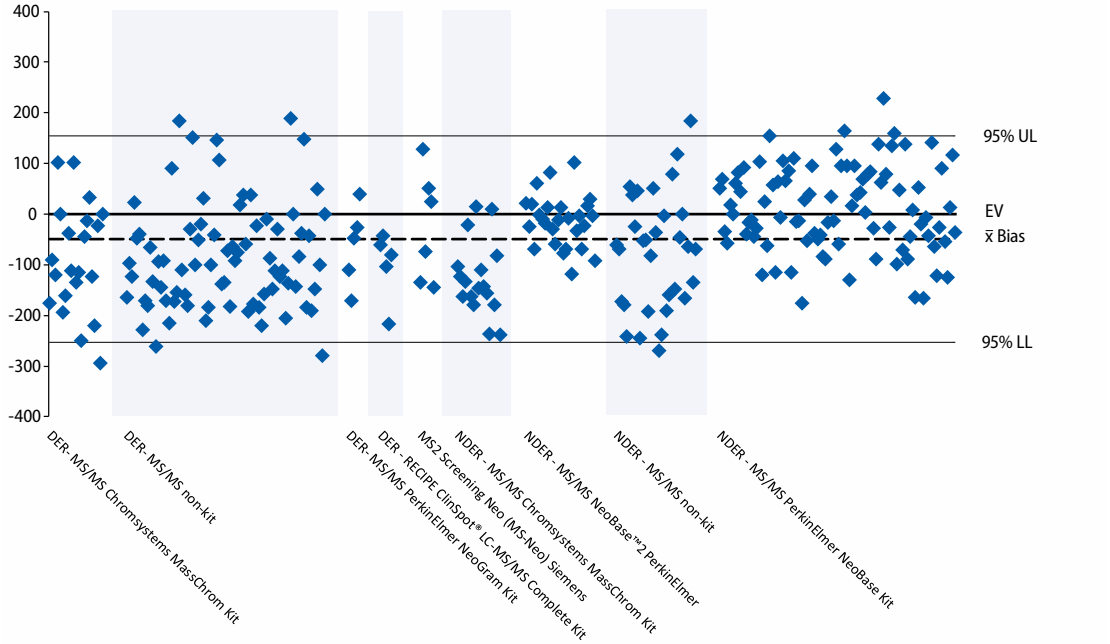
Val µmol/L blood

Enriched: 544.6

CDC Assayed: 590.6

Participant Mean: 579.6

Participant Bias: -48.8



The Val bias plot shows units of measure on the y-axis ranging from 400 µmol/L blood to -400 µmol/L blood. The mean bias for this plot is -48.8 µmol/L blood . Most methods show a slightly negative bias while one is evenly scattered.

Figure 16. Reproducibility of Results: Bias Plot of Low Free Carnitine (C0(L)) Values by Method Quarter 4, Specimen 41964 Expected Value (EV) = 32.52 µmol/L blood

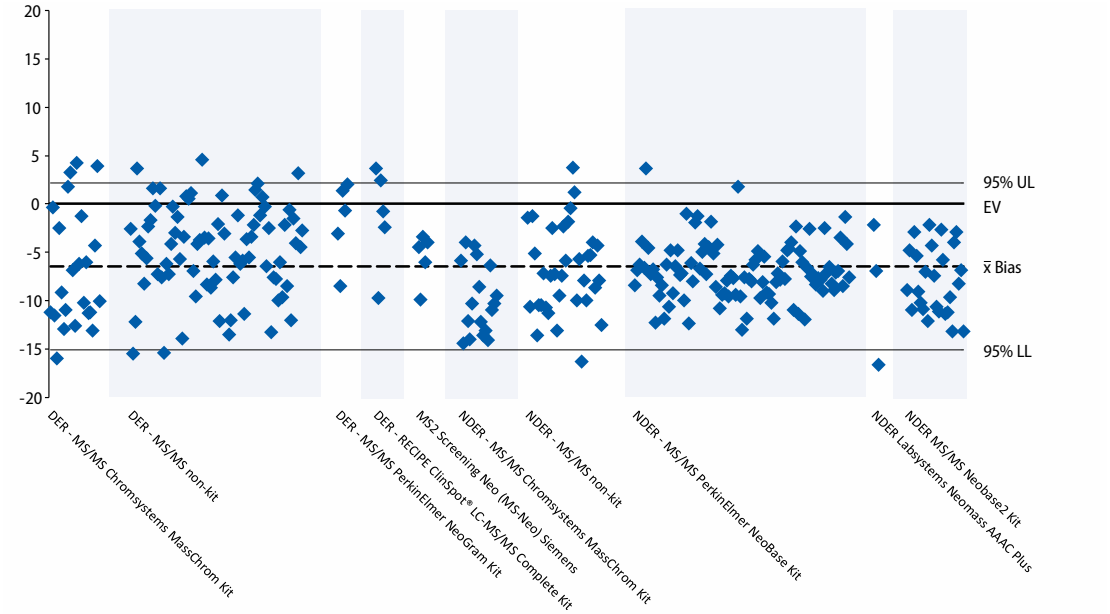
C0(L) µmol/L blood

Enriched: 0.00

CDC Assayed: 31.82

Participant Mean: 26.06

Participant Bias: -6.46



The C0(L) bias plot shows units of measure on the y-axis ranging from 20 µmol/L blood to -20 µmol/L blood. The mean bias for this plot is -6.46 µmol/L blood . All methods show a significantly negative bias.

Figure 17. Reproducibility of Results: Bias Plot of Low Acetylcarnitine(C2(L)) Values by Method Quarter 4 , Specimen 41965 Expected Value (EV) = 17.22 µmol/L blood

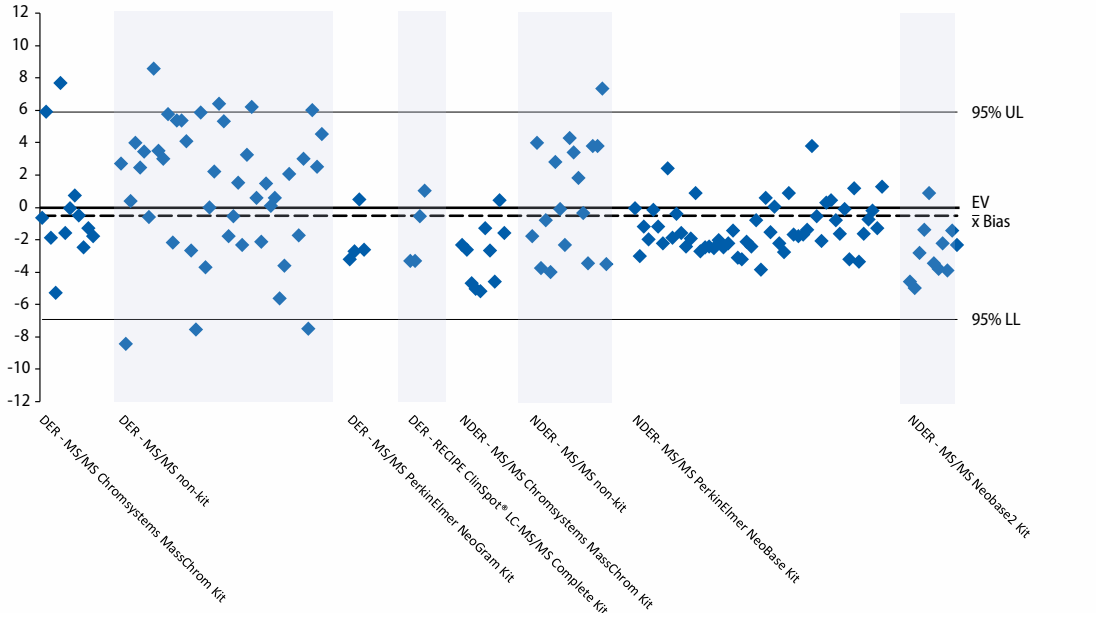
C2(L) µmol/L blood

Enriched: 0.00

CDC Assayed: 17.52

Participant Mean:16.72

Participant Bias: -0.50



The C2(L) bias plot shows units of measure on the y-axis ranging from 12 µmol/L blood to -12µmol/L blood. The mean bias for this plot is -0.50 µmol/L blood . Each method shows tight scatter among its participants.

Figure 18. Reproducibility of Results: Bias Plot of Propionylcarnitine (C3) Values by Method Quarter 3, Specimen 31964 Expected Value (EV) = 11.04 µmol/L blood

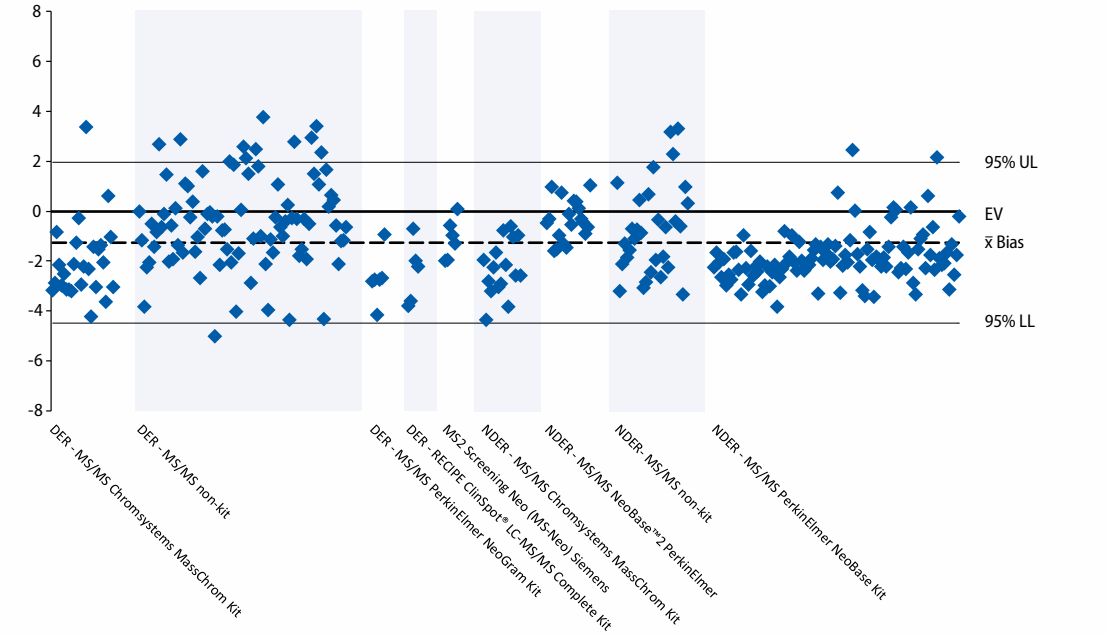
C3 µmol/L blood

Enriched: 10.75

CDC Assayed: 11.64

Participant Mean: 9.79

Participant Bias: -1.25



The C3 bias plot shows units of measure on the y-axis ranging from 8 µmol/L blood to -8 µmol/L blood. The mean bias for this plot is -1.25 µmol/L blood . One method is clustered below the bias while other methods show good scatter.

Figure 19. Reproducibility of Results: Bias Plot of Malonylcarnitine (C3DC) Values by Method Quarter 3, Specimen 31965 Expected Value (EV) = 25.03 µmol/L blood

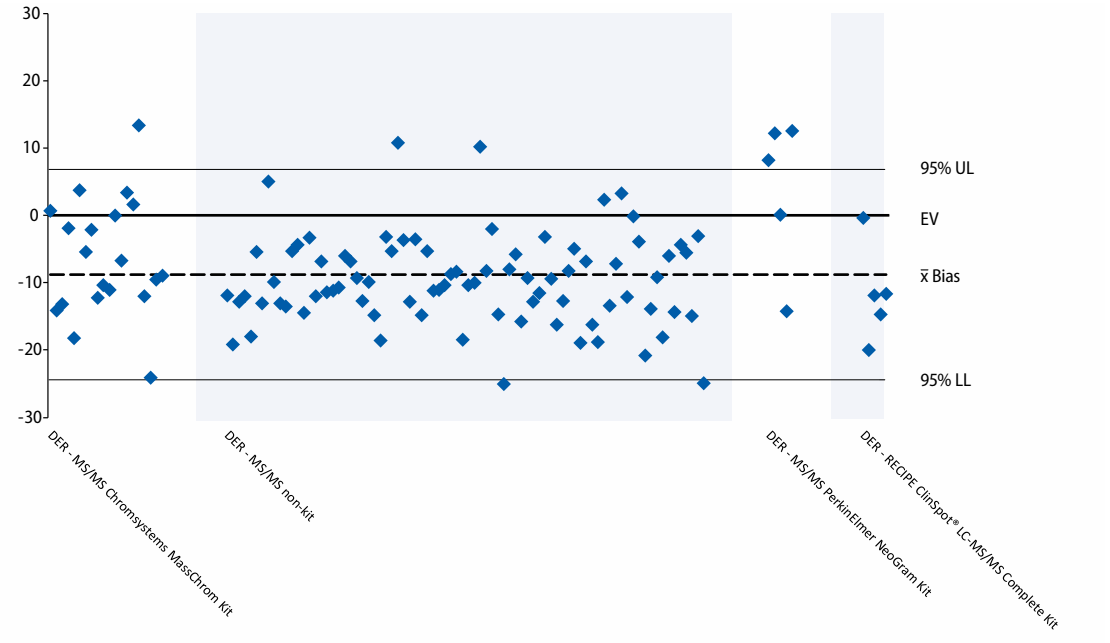
C3DC µmol/L blood

Enriched: 25.00

CDC Assayed: 25.03

Participant Mean: 16.25

Participant Bias: -8.78



The C3DC bias plot shows units of measure on the y-axis ranging from 30 µmol/L blood to -30 µmol/L blood. The mean bias for this plot is -8.78 µmol/L blood. Most methods show a slightly negative bias while one is slightly positive.

Figure 20. Reproducibility of Results: Bias Plot of C3DC+C4OH Non-derivatized Values by Method Quarter 3, Specimen 31965 Expected Value (EV) = 25.03 µmol/L blood

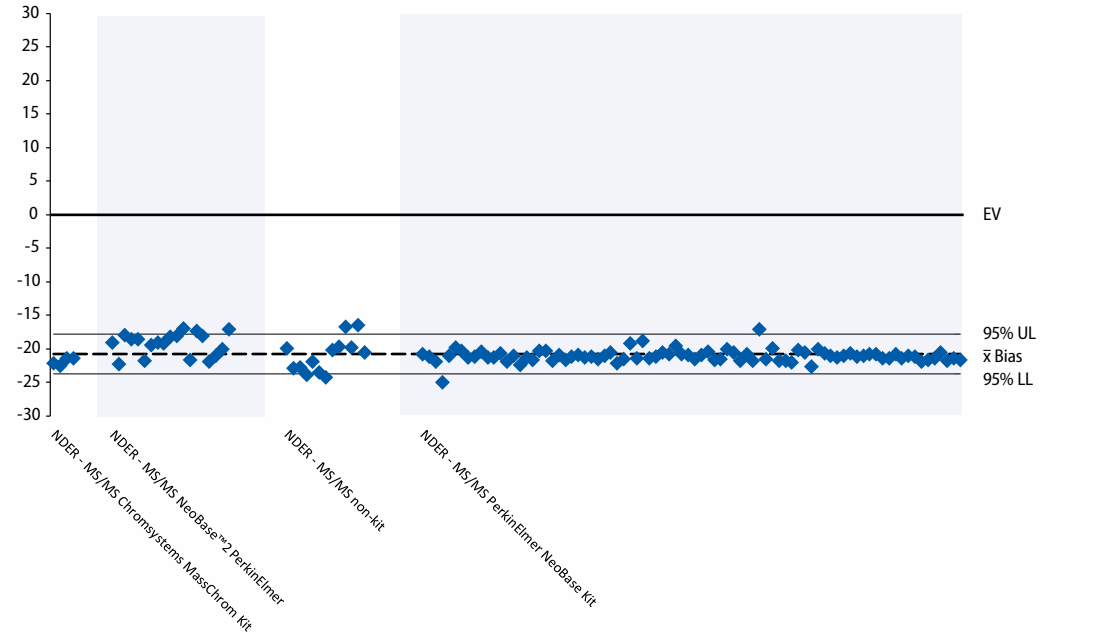
C3DC+C4OH
µmol/L blood

Enriched: 25.00

CDC Assayed: 2.62

Participant Mean: 4.26

Participant Bias: -20.77



The C3DC+C4OH bias plot shows units of measure on the y-axis ranging from 30 µmol/L blood to -30 µmol/L blood. The mean bias for this plot is -20.77 µmol/L blood .

All methods show a strongly negative bias, which is historically consistent for this analyte.

Figure 21. Reproducibility of Results: Bias Plot of Butyrylcarnitine (C4) Values by Method Quarter 3, Specimen 31965 Expected Value (EV) = 3.04 µmol/L blood

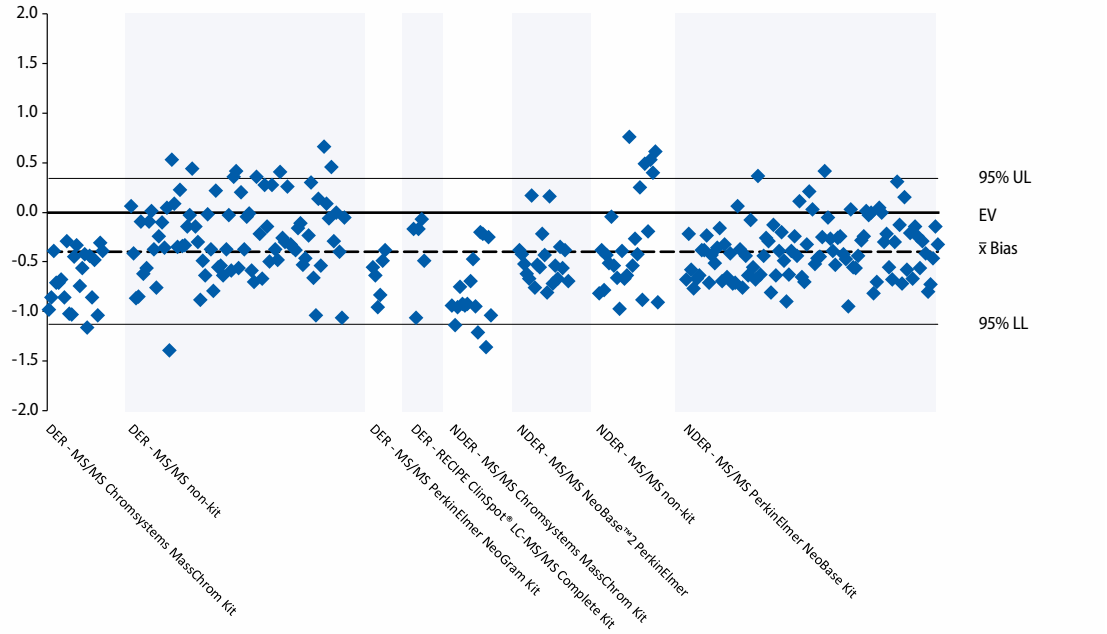
C4 µmol/L blood

Enriched: 3.00

CDC Assayed: 2.83

Participant Mean: 2.64

Participant Bias: -0.40



The C4 bias plot shows units of measure on the y-axis ranging from 2 µmol/L blood to -2 µmol/L blood. The mean bias for this plot is -0.40 µmol/L blood . All methods show a good scatter around a moderately negative bias.

Figure 22. Reproducibility of Results: Bias Plot of Hydroxybutyrylcarnitine (C4OH) Values by Method Quarter 4, Specimen 41961 Expected Value (EV) = 3.04 µmol/L blood

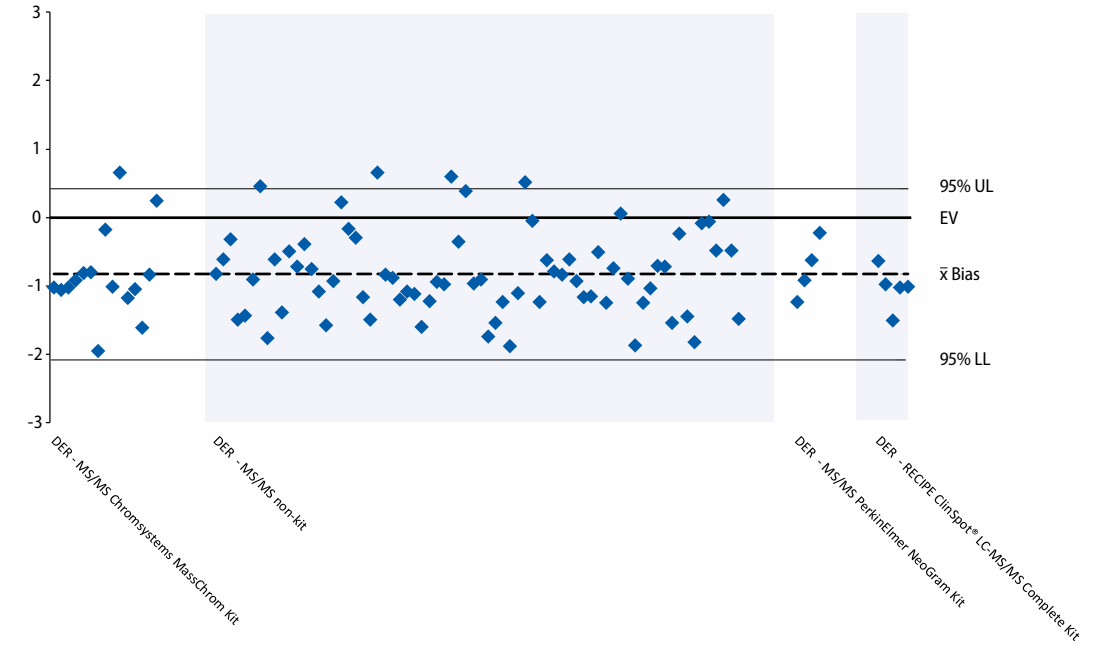
C4OH µmol/L blood

Enriched: 3.00

CDC Assayed: 2.62

Participant Mean: 2.21

Participant Bias: -0.83



The C4OH bias plot shows units of measure on the y-axis ranging from 3 µmol/L blood to -3 µmol/L blood. The mean bias for this plot is -0.83 µmol/L blood . All methods show a significantly negative bias.

Figure 23. Reproducibility of Results: Bias Plot of Isovalerylcarnitine (C5) Values by Method Quarter 4, Specimen 41965 Expected Value (EV) = 1.55 µmol/L blood

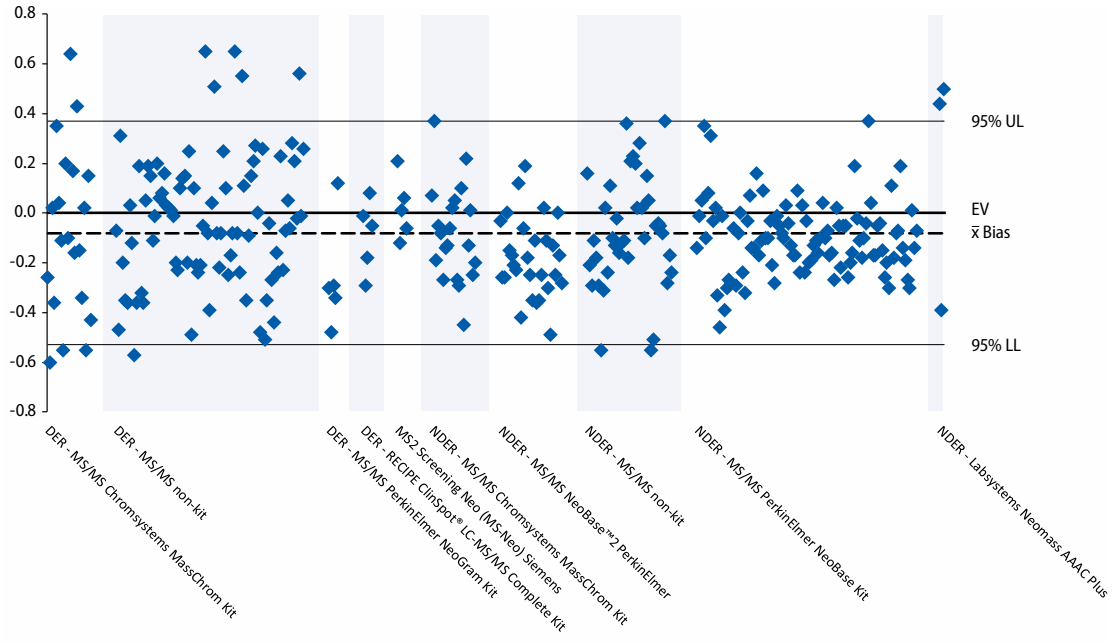
C5 µmol/L blood

Enriched: 1.50

CDC Assayed: 1.61

Participant Mean: 1.47

Participant Bias: -0.08



The C5 bias plot shows units of measure on the y-axis ranging from 0.8 µmol/L blood to -0.8 µmol/L blood. The mean bias for this plot is -0.08 µmol/L blood . All methods show a slightly negative bias.

Figure 24. Reproducibility of Results: Bias Plot of Tiglylcarnitine (C5:1) Values by Method Quarter 3, Specimen 31965 Expected Value (EV) = 0.76 µmol/L blood

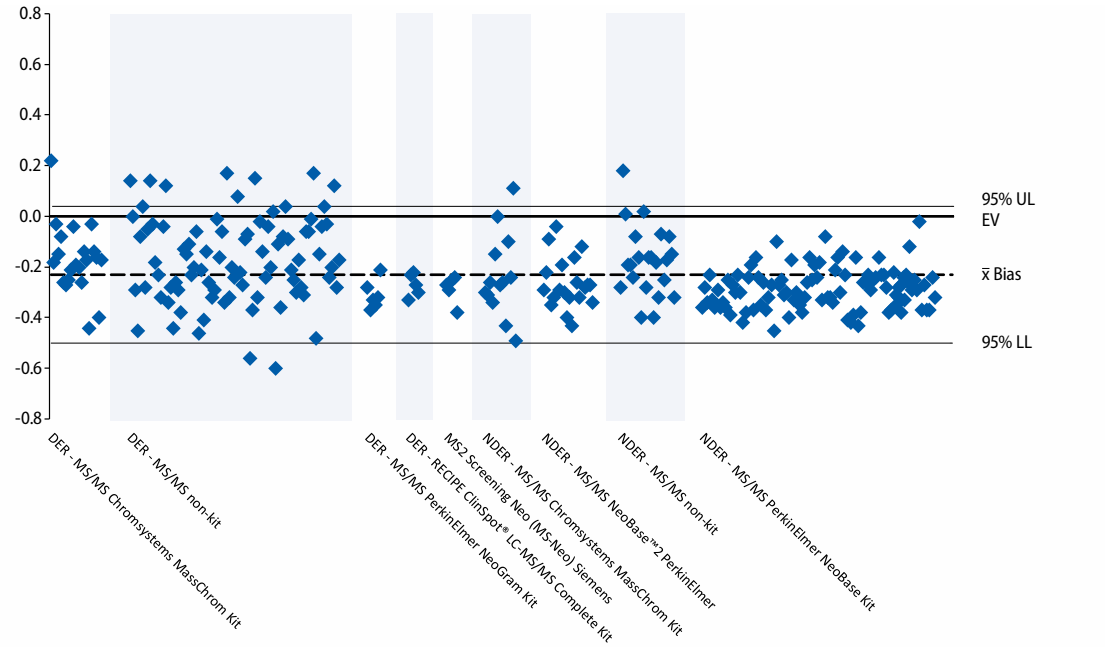
C5:1 µmol/L blood

Enriched: 0.75

CDC Assayed: 0.66

Participant Mean: 0.53

Participant Bias: -0.23



The C5:1 bias plot shows units of measure on the y-axis ranging from 0.8 µmol/L blood to -0.8 µmol/L blood. The mean bias for this plot is -0.23 µmol/L blood . All methods show a significantly negative bias.

Figure 25. Reproducibility of Results: Bias Plot of Glutarylcarnitine (C5DC) Values by Method Quarter 3, Specimen 31962 Expected Value (EV) = 1.82 µmol/L blood

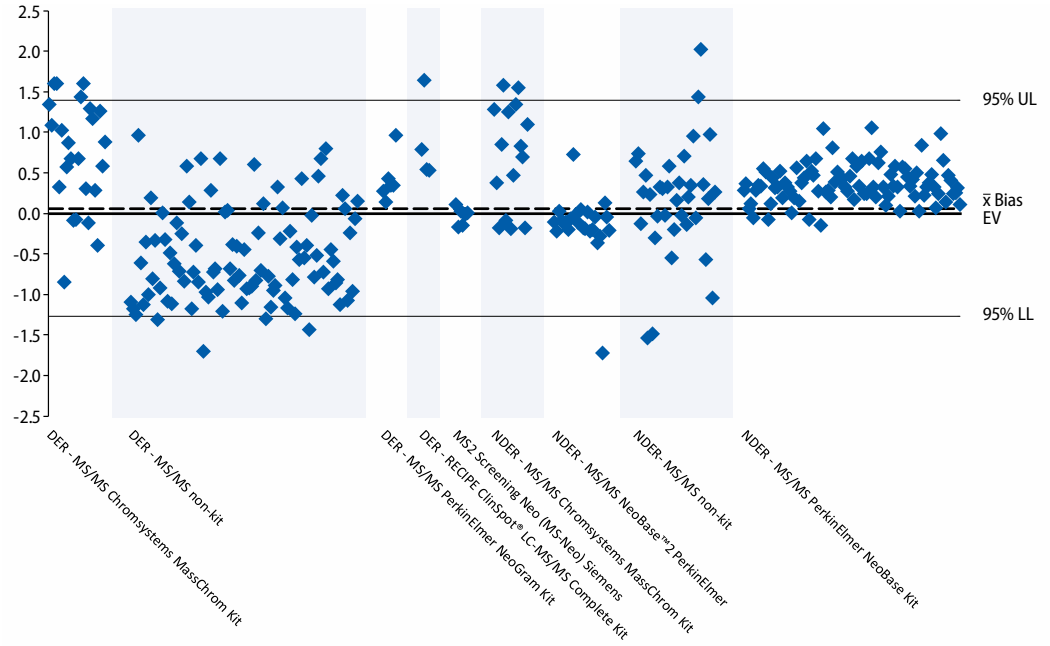
C5DC µmol/L blood

Enriched: 1.80

CDC Assayed: 2.17

Participant Mean: 1.88

Participant Bias: 0.06



The C5DC bias plot shows units of measure on the y-axis ranging from 2.5 µmol/L blood to -2.5 µmol/L blood. The mean bias for this plot is 0.06 µmol/L blood . Two methods show a significantly negative bias, while others show a positive bias.

Figure 26. Reproducibility of Results: Bias Plot of Hydroxyisovalerylcarnitine (C5OH) Values by Method Quarter 4, Specimen 41964 Expected Value (EV) = 1.91 µmol/L blood

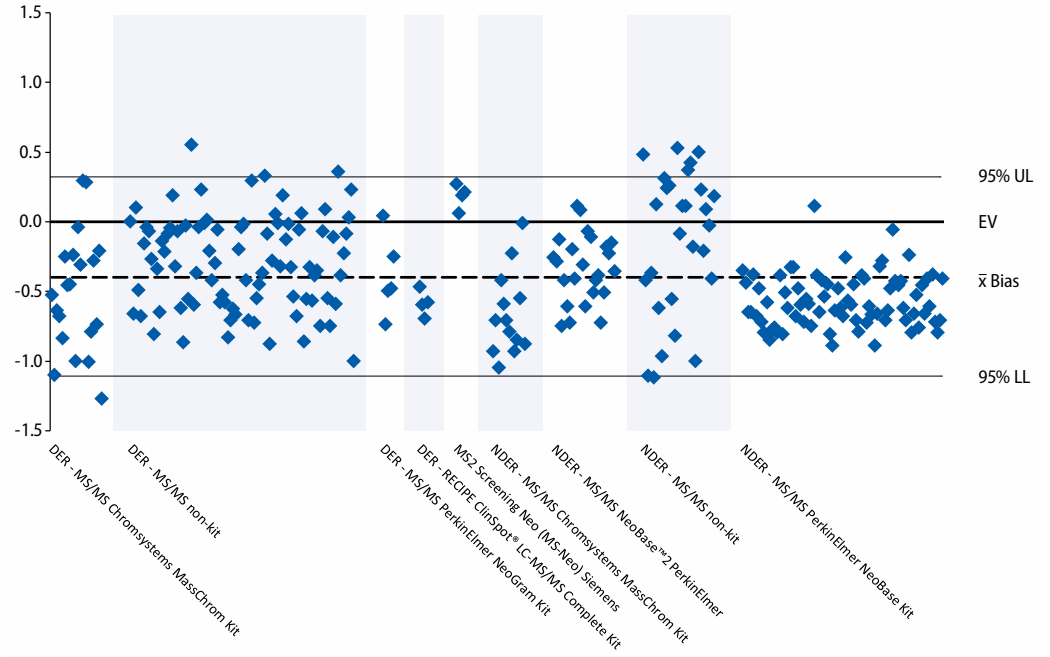
C5OH µmol/L blood

Enriched: 0.80

CDC Assayed: 1.84

Participant Mean: 1.51

Participant Bias: -0.40



The C5OH bias plot shows units of measure on the y-axis ranging from 1.5 µmol/L blood to -1.5 µmol/L blood. The mean bias for this plot is -0.40 µmol/L blood . All methods show a significantly negative bias.

Figure 27. Reproducibility of Results: Bias Plot of Hexanoylcarnitine (C6) Values by Method Quarter 3, Specimen 31963 Expected Value (EV) = 2.71 µmol/L blood

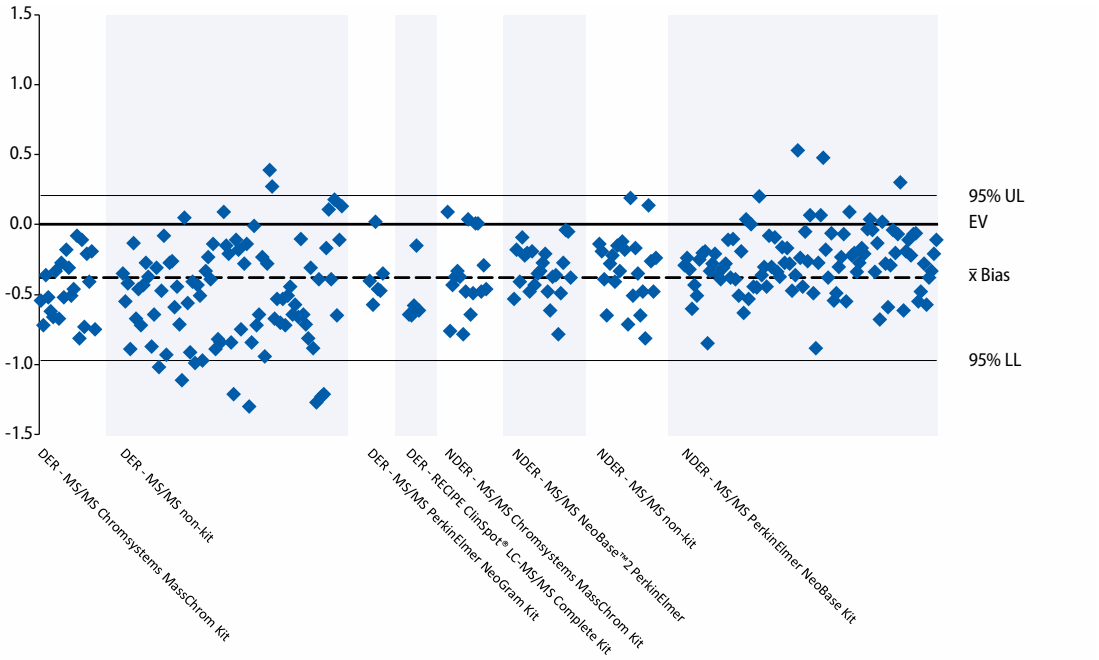
C6 µmol/L blood

Enriched: 2.70

CDC Assayed: 2.35

Participant Mean: 2.33

Participant Bias: -0.38



The C6 bias plot shows units of measure on the y-axis ranging from 1.5 µmol/L blood to -1.5 µmol/L blood. The mean bias for this plot is -0.38 µmol/L blood . All methods show a significantly negative bias.

Figure 28. Reproducibility of Results: Bias Plot of Octanoylcarnitine (C8) Values by Method Quarter 3, Specimen 31963 Expected Value (EV) = 24.42 µmol/L blood

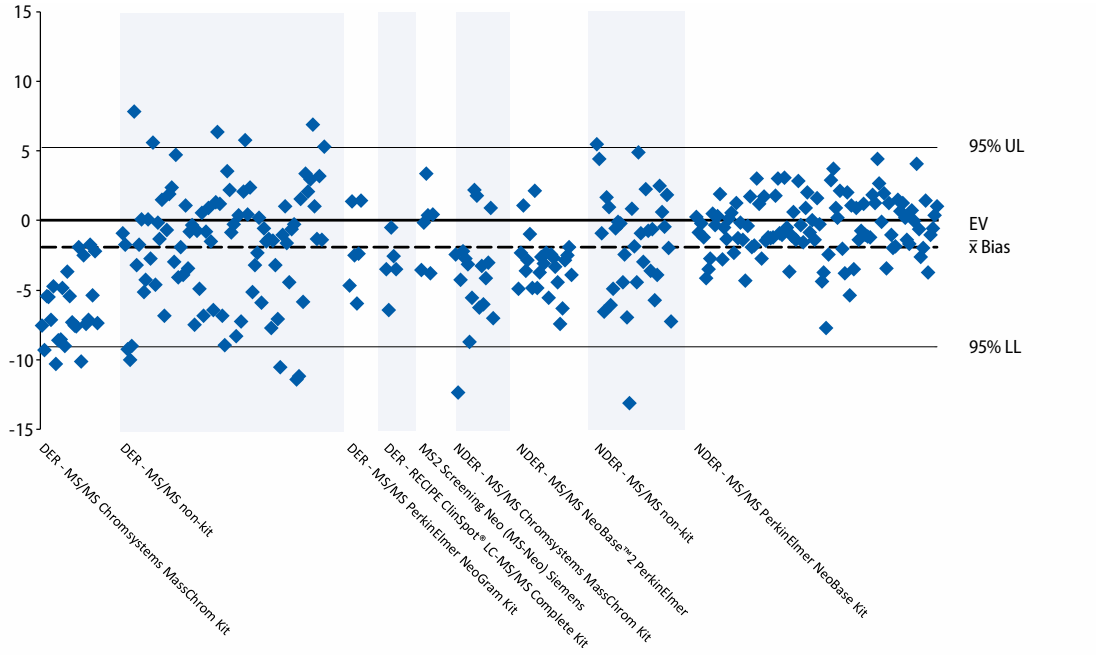
C8 µmol/L blood

Enriched: 24.41

CDC Assayed: 24.08

Participant Mean: 22.51

Participant Bias: -1.91



The C8 bias plot shows units of measure on the y-axis ranging from 15 µmol/L blood to -15 µmol/L blood. The mean bias for this plot is -1.91 µmol/L blood . All methods show a slightly negative bias.

Figure 29. Reproducibility of Results: Bias Plot of Decanoylcarnitine (C10) Values by Method Quarter 3, Specimen 31963 Expected Value (EV) = 1.95 µmol/L blood

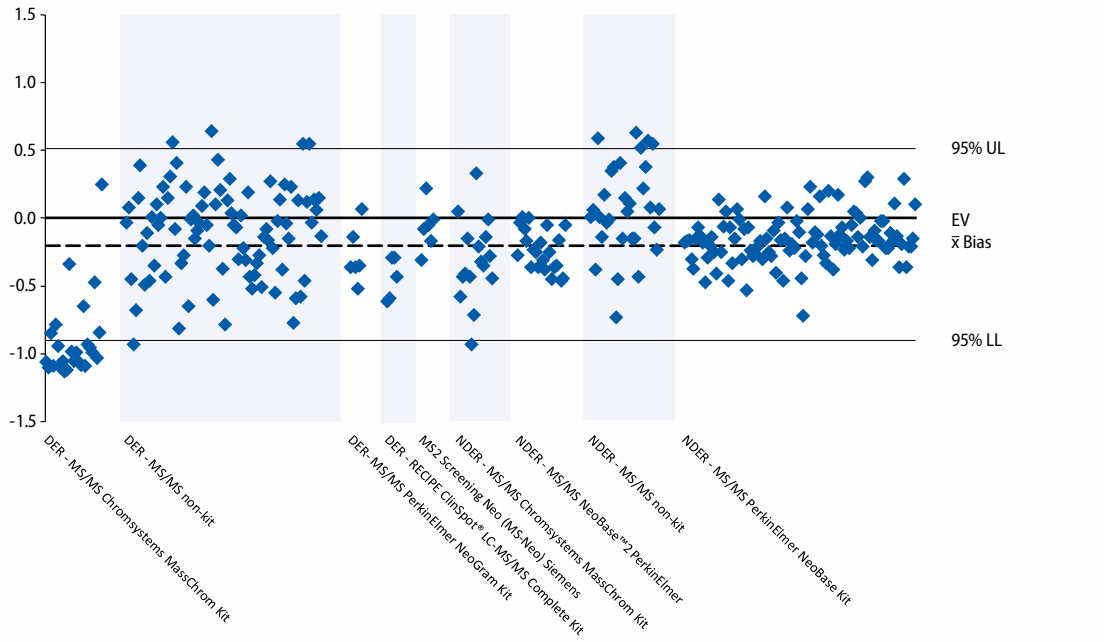
C10 µmol/L blood

Enriched: 1.94

CDC Assayed: 1.90

Participant Mean: 1.75

Participant Bias: -0.20



The C10 bias plot shows units of measure on the y-axis ranging from 1.5 µmol/L blood to -1.5 µmol/L blood. The mean bias for this plot is -0.20 µmol/L blood . Most methods show a negative bias, while two show an even scatter across the EV.

Figure 30. Reproducibility of Results: Bias Plot of Decenoylcarnitine (C10:1) Values by Method Quarter 3, Specimen 31963 Expected Value (EV) = 1.65 µmol/L blood

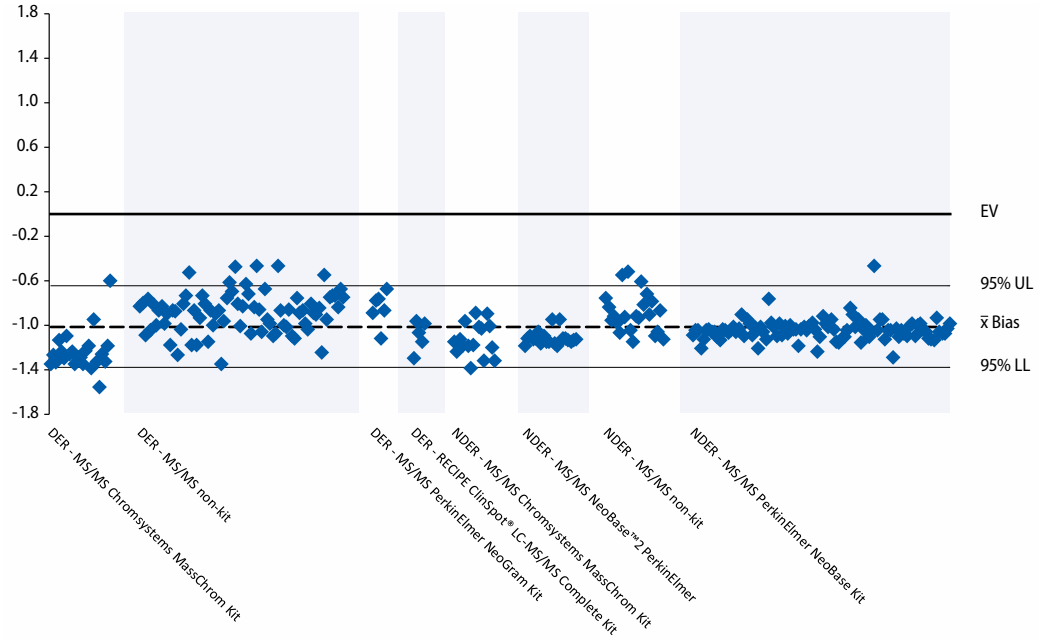
C10:1 µmol/L blood

Enriched: 0.82

CDC Assayed: 0.78

Participant Mean: 0.63

Participant Bias: -1.02



The C10:1 bias plot shows units of measure on the y-axis ranging from 1 µmol/L blood to -1 µmol/L blood. The bias for this plot is -0.03 µmol/L blood. On the C10:1 bias plot, there is good agreement within methods but some methods show a positive bias and others show a negative bias.

Figure 31. Reproducibility of Results: Bias Plot of Decadienoylcarnitine (C10:2) Values by Method Quarter 3, Specimen 31965 Expected Value (EV) = 1.00 µmol/L blood

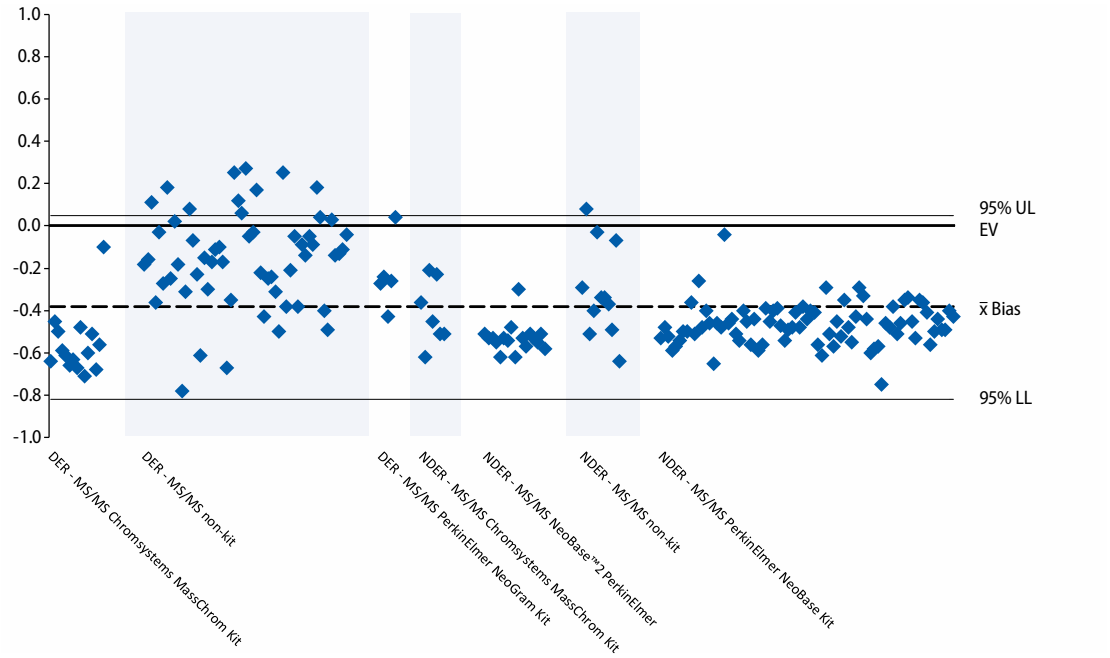
C10:2 µmol/L blood

Enriched: 1.00

CDC Assayed: 0.92

Participant Mean: 0.62

Participant Bias: -0.38



The C10:2 bias plot shows units of measure on the y-axis ranging from 1 µmol/L blood to -1 µmol/L blood. The mean bias for this plot is -0.38 µmol/L blood . All methods show a negative bias.

Figure 32. Reproducibility of Results: Bias Plot of Myristoylcarnitine (C14) Values by Method Quarter 4, Specimen 41962 Expected Value (EV) = 1.59 µmol/L blood

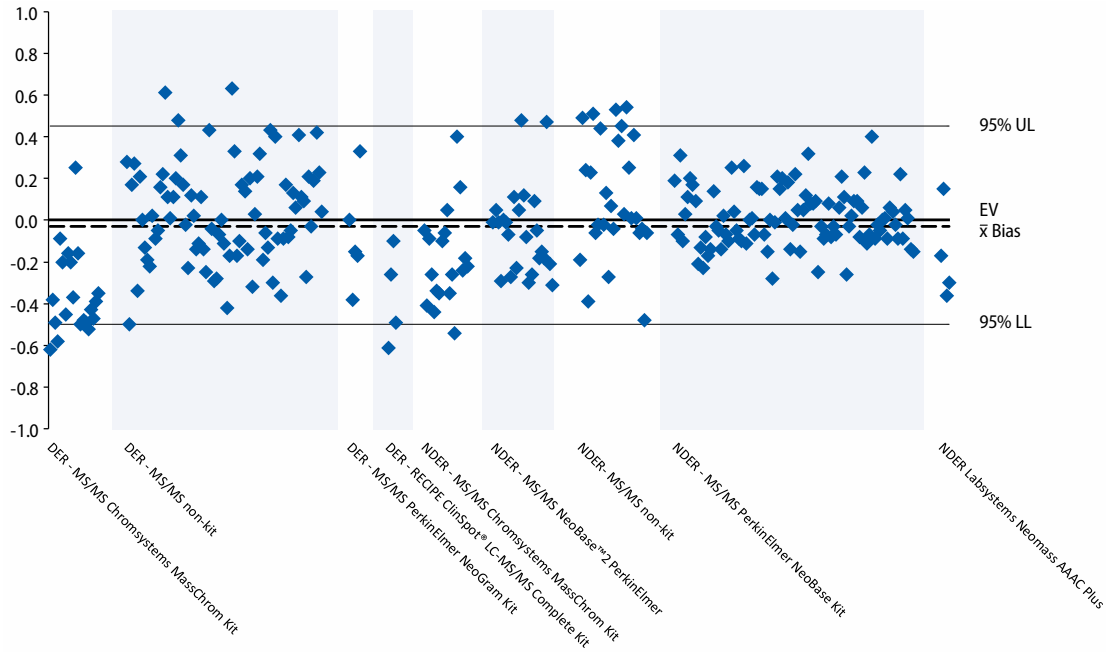
C14 µmol/L blood

Enriched: 1.50

CDC Assayed: 1.64

Participant Mean: 1.56

Participant Bias: -0.03



The C14 bias plot shows units of measure on the y-axis ranging from 1 µmol/L blood to -1 µmol/L blood. The mean bias for this plot is -0.03 µmol/L blood . Most methods show an even scatter across the EV.

Figure 33. Reproducibility of Results: Bias Plot of Tetradecenoylcarnitine (C14:1) Values by Method Quarter 4, Specimen 41962 Expected Value (EV) = 1.75 µmol/L blood

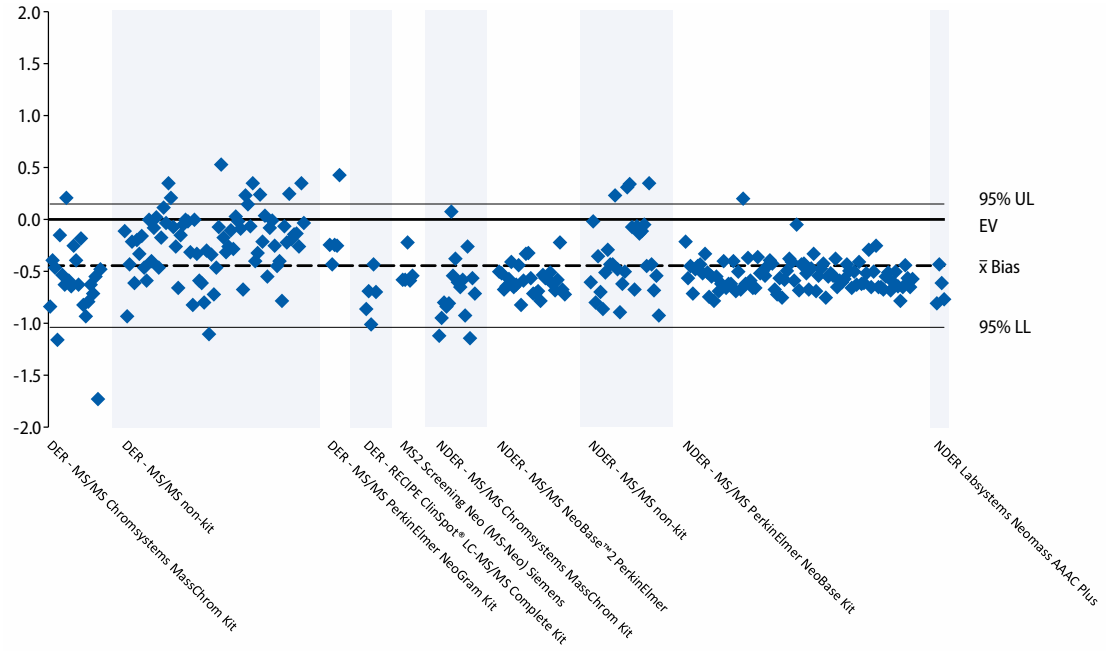
C14:1 µmol/L blood

Enriched: 1.70

CDC Assayed: 1.48

Participant Mean: 1.30

Participant Bias: -0.45



The C14:1 bias plot shows units of measure on the y-axis ranging from 2 µmol/L blood to -2 µmol/L blood. The mean bias for this plot is -0.45 µmol/L blood . All methods show a significantly negative bias.

Figure 34. Reproducibility of Results: Bias Plot of Palmitoylcarnitine (C16) Values by Method Quarter 1, Specimen 11965 Expected Value (EV) = 12.82 µmol/L blood

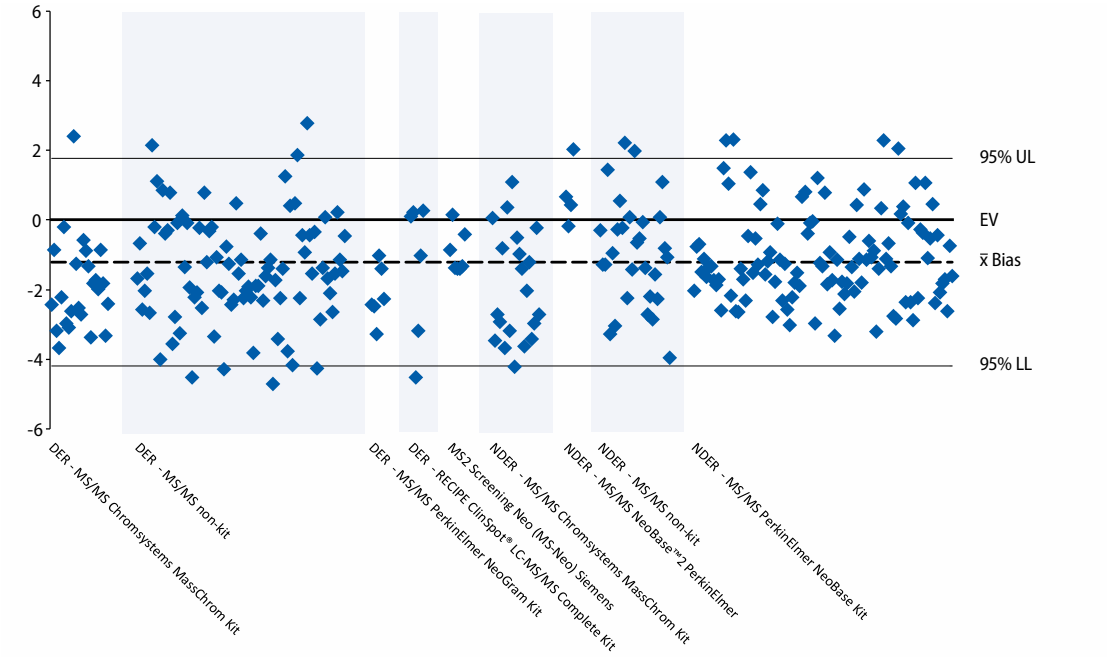
C16 µmol/L blood

Enriched: 12.21

CDC Assayed: 11.99

Participant Mean: 11.62

Participant Bias: -1.20



The C16 bias plot shows units of measure on the y-axis ranging from 6 µmol/L blood to -6 µmol/L blood. The mean bias for this plot is -1.20 µmol/L blood. All methods show a significantly negative bias.

Figure 35. Reproducibility of Results: Bias Plot of Hydroxypalmitoylcarnitine (C16OH) Values by Method Quarter 4, Specimen 41963 Expected Value (EV) = 1.01 µmol/L blood

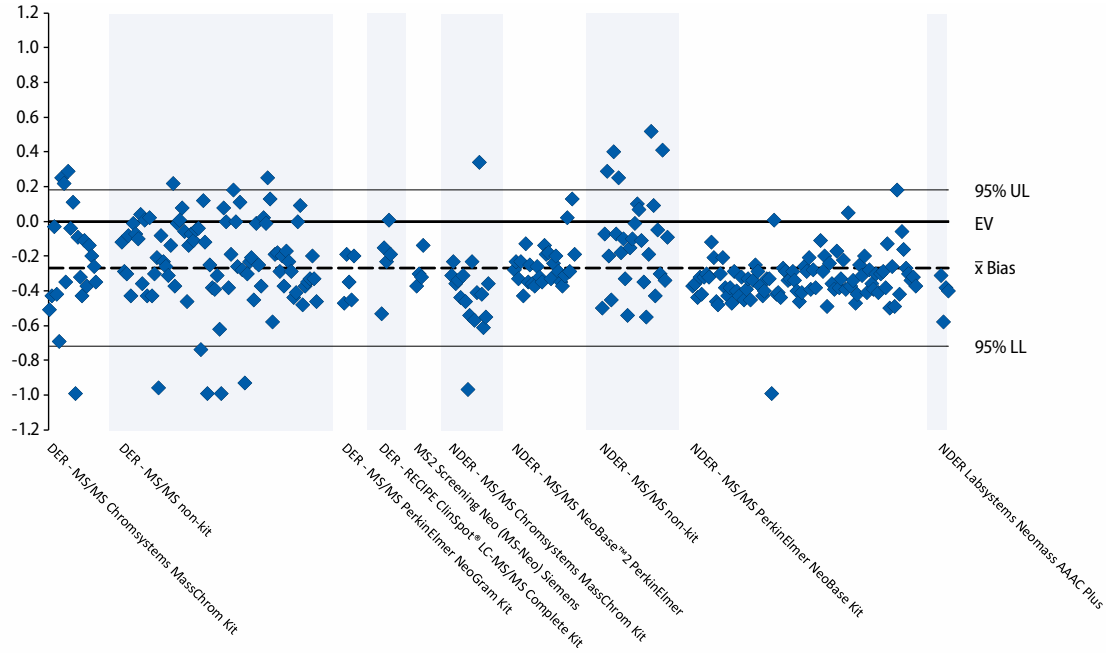
C16OH µmol/L blood

Enriched: 1.00

CDC Assayed: 0.97

Participant Mean: 0.74

Participant Bias: -0.27



The C16OH bias plot shows units of measure on the y-axis ranging from 1.2 µmol/L blood to -1.2 µmol/L blood. The mean bias for this plot is -0.38 µmol/L blood . All methods show a significantly negative bias.

Figure 36. Reproducibility of Results: Bias Plot of Stearoylcarnitine (C18) Values by Method Quarter 3, Specimen 31965 Expected Value (EV) = 5.35 µmol/L blood

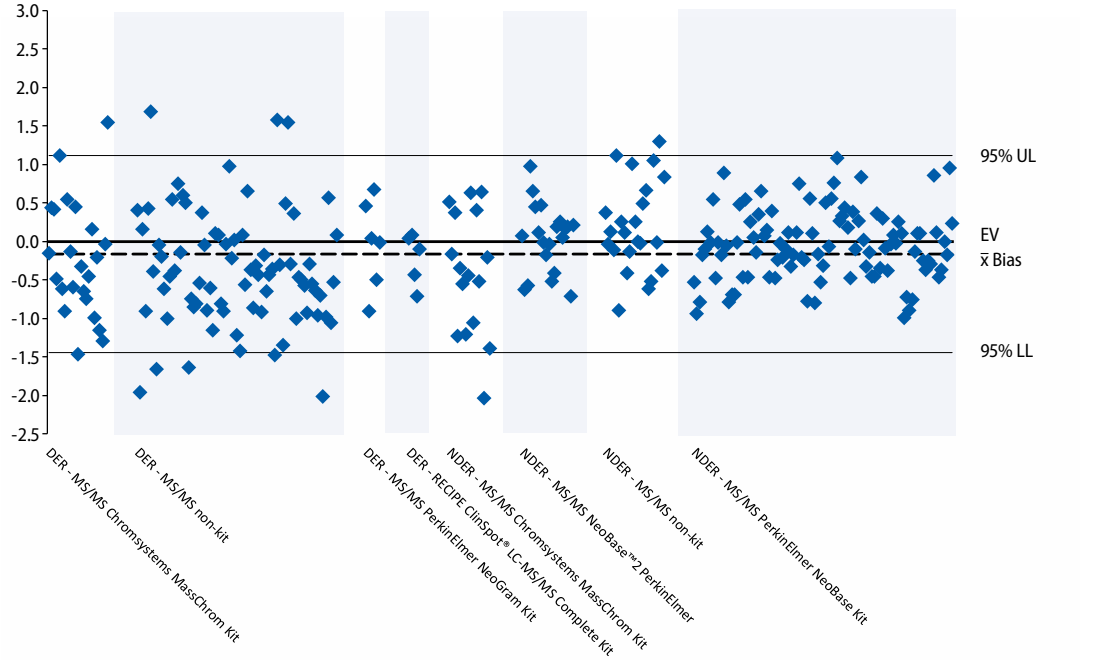
C18 µmol/L blood

Enriched: 5.00

CDC Assayed: 5.37

Participant Mean: 5.19

Participant Bias: -0.16



The C18 bias plot shows units of measure on the y-axis ranging from 3.0 µmol/L blood to -3.0 µmol/L blood. The mean bias for this plot is -0.16 µmol/L blood . All methods show an even scatter across the EV.

Figure 37. Reproducibility of Results: Bias Plot of Oleoylcarnitine (C18:1) Values by Method Quarter 3, Specimen 31965 Expected Value (EV) = 13.80 µmol/L blood

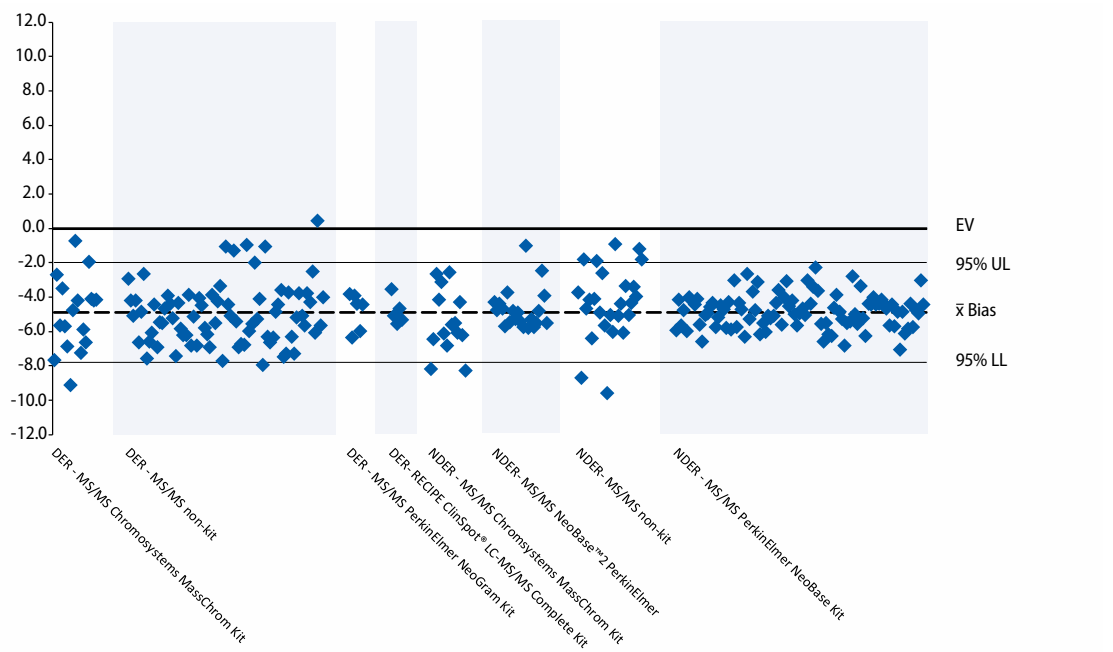
C18:1 µmol/L blood

Enriched: 13.20

CDC Assayed: 9.53

Participant Mean: 8.90

Participant Bias: -4.90



The C18:1 bias plot shows units of measure on the y-axis ranging from 12 µmol/L blood to -12 µmol/L blood. The mean bias for this plot is -4.90 µmol/L blood . All methods show a significantly negative bias.

C18OH

Figure 38. Reproducibility of Results: Bias Plot of Hydroxystearoylcarnitine (C18OH) Values by Method Quarter 4, Specimen 41963 Expected Value (EV)[1] = 0.80 µmol/L blood

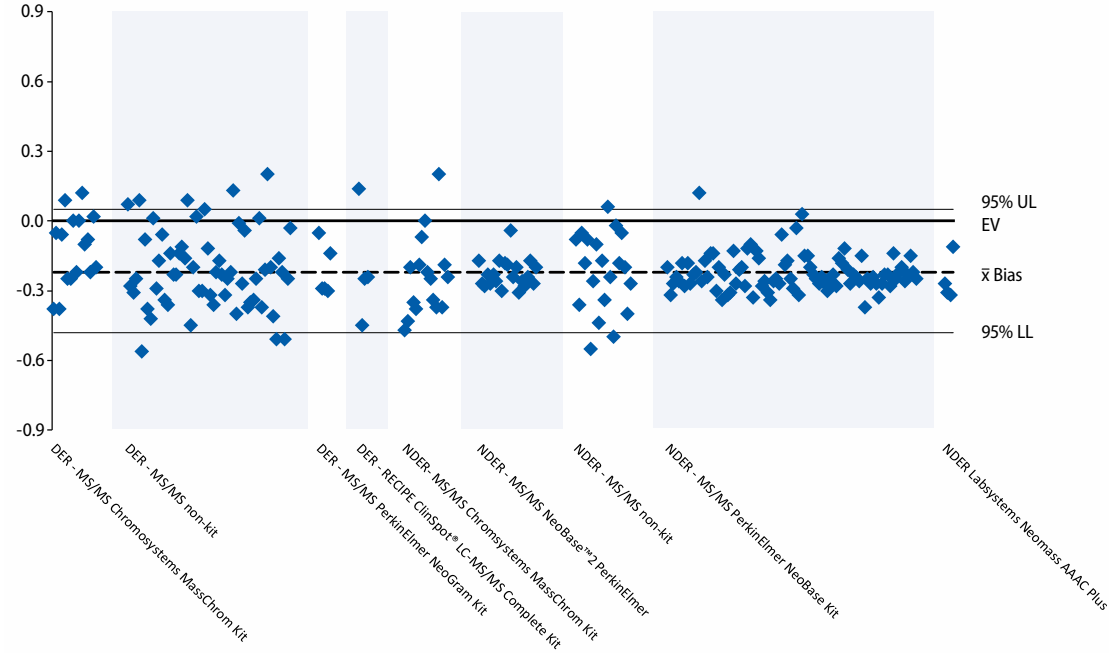
C18OH µmol/L blood

Enriched: 0.80

CDC Assayed: 0.55

Participant Mean: 0.58

Participant Bias: -0.22



The C18OH bias plot shows units of measure on the y-axis ranging from 0.9 µmol/L blood to -0.9 µmol/L blood. The mean bias for this plot is -0.22 µmol/L blood . All methods show a significantly negative bias.

Appendix for Accessibility Descriptions

Figure 2: NSQAP's Grading Algorithm Flow chart.

1. PART 1 is in a square box and makes the statement, "COMPARE NSQAP EXPECTED VALUE TO NSQAP CUTOFF VALUE TO DETERMINE NSQAP EXPECTED CLINICAL ASSESSMENT."
2. A down arrow points to an oval shape and asks the question, "DOES PARTICIPANT REPORTED CLINICAL ASSESSMENT DIFFER FROM NSQAP EXPECTED CLINICAL ASSESSMENT?"
3. A right-side arrow from the oval points to a smaller oval with the statement, "IF 'NO': NO ERROR"
4. A down arrow from the oval contains a solid oval and the words, "IF 'YES.'" The down arrow points to PART 2 in a square box that says, "PART 2 COMPARE NSQAP EXPECTED VALUE TO PARTICIPANT REPORTED CUTOFF VALUE TO DETERMINE PARTICIPANT EXPECTED CLINICAL ASSESSMENT."
5. A down arrow points to PART 3 in an oval shape and asks the question, "DOES PARTICIPANT REPORTED CLINICAL ASSESSMENT DIFFER FROM PARTICIPANT EXPECTED CLINICAL ASSESSMENT?"
6. A right-side arrow from the oval points to a smaller oval with the statement, "IF 'NO': CUTOFF DIFFERENCE COMMENT."

Figures 5–38, Bias Plots: Bias plots, which compare two measurements of the same variable, have been created to show a wide range of PT challenge specimens. The bias, which is calculated by subtracting the participant mean value from the CDC Expected Value (EV), is represented by the broken line. Expected Value is the sum of the endogenous plus the enrichment values. The solid line represents perfect agreement with the EV or zero bias. When comparing data scatter among figures, the scale (y-axis) might differ. We included the 95% confidence interval for the mean participant bias. A tight scatter within this interval indicates good performance for a method or a group of methods. To illustrate any method-related differences in analyte recoveries, we group the PT quantitative results by kit or method. Because some of the pools in a routine PT survey represent a unique donor specimen, differences in endogenous materials in the donor specimens might influence method-related differences. We show representative bias plots for all those analytes distributed in PT challenges that required a quantitative measurement to determine the presumptive clinical assessments.

References

[1]Newborn Screening: Towards a Uniform Screening Panel and System." Genetic Medicine 2006;8(5) Suppl: S12–S252, as authored by the American College of Medical Genetics and commissioned by the Health Resources and Services Administration.

[2] De Jesús VR, Mei JV, Cordovado SK, Cuthbert CD. The Newborn Screening Quality Assurance Program at the Centers for Disease Control and Prevention: Thirty-Five Year Experience Assuring Newborn Screening Laboratory Quality. International Journal of Newborn Screening 2015,1; 13-26.

[3]Clinical and Laboratory Standards Institute. Blood collection on filter paper for newborn screening programs: Approved Standard—Sixth Edition. CLSI Document NBS01-A6. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

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