2017 NSQAP ANNUAL SUMMARY REPORT

Newborn Screening
Quality Assurance
Program

Centers for Disease Control and Prevention
National Center for Environmental Health

Newborn Screening Quality Assurance Program
2017 Annual Summary Report

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

Accessible information for all figures is located in

Contents

Effective newborn screening along with follow-up, diagnosis, and intervention, helps prevent developmental delays and premature death caused by inherited diseases.

Introduction

Newborn screening is one of the most successful preventative health programs in the United States. State and public health laboratories or their associated laboratories routinely screen dried blood spot (DBS) specimens collected from newborns shortly after birth for certain genetic, metabolic, and endocrine disorders. Healthcare professionals collect DBS specimens from more than 98% of all newborns in the United States. The Centers for Disease Control and Prevention (CDC) Newborn screening Quality Assurance Program (NSQAP) assists 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 Elecrotechnical Commission (IEC) 17043 accreditation by the American Association for Laboratory Accreditation (A2LA). Accreditation was achieved after a thorough review of its quality management system and competence to develop and administer specific PT protocols. The branch's NSQAP web-based PT programs are included in the A2LA Scope of Accreditation. Testing for Glucose-6-phosphate Dehydrogenase (G6PD) and NSQAP non-web-based PT programs are not included in the scope of accreditation. Please consult A2LA Certificate #4190.01 for a list of accredited NSMBB PT programs.

About NSQAP

For more than 35 years, NSQAP and its cosponsor the Association of Public Health Laboratories, have researched the development of DBS screening test materials and have assisted laboratories with DBS-related quality assurance. NSQAP primarily supports U.S. newborn screening laboratories. Private and international laboratories may also 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 2017, active program participants included 686 newborn screening laboratories in 83 countries (at least one laboratory per country) (Figure 1). Of these laboratories, 603 participated in PT (Figure 2) and 551 in QC (Figure 3). The program distributed DBS materials for 73 analytes to participating laboratories (Figures 2 and 3).

To offer more specialized services, NSQAP works with other departments in the Newborn Screening and Molecular Biology Branch: the Biochemical Mass Spectrometry Laboratory (BMSL), the Newborn Screening Translation Research Initiative (NSTRI), and the Molecular Quality Improvement Program (MQIP).

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

MQIP oversees the cystic fibrosis DNA (CFDNA) PT program and assists newborn screening laboratories with molecular testing. It also offers the Molecular Assessment Program (MAP) which conducts site visits to 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.

NSTRI administers the T-cell Receptor Excision Circle (TREC) and Lysosomal Storage Disorders (LSD) programs. NSTRI is an ongoing collaboration between the CDC Foundation and the Newborn Screening and Molecular Biology Branch [2].
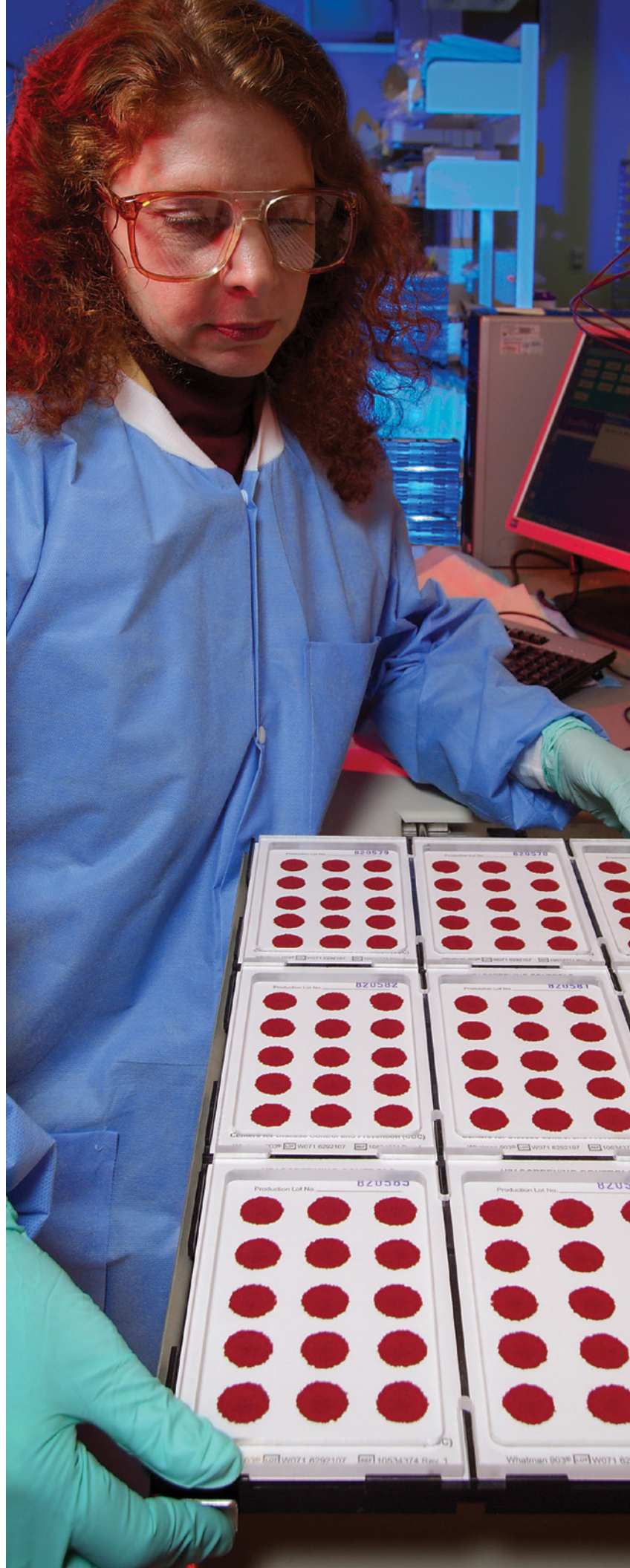
Figure 1. Eighty-three Countries Participated in NSQAP in 2017

Countries Participating in NSQAP During 2017
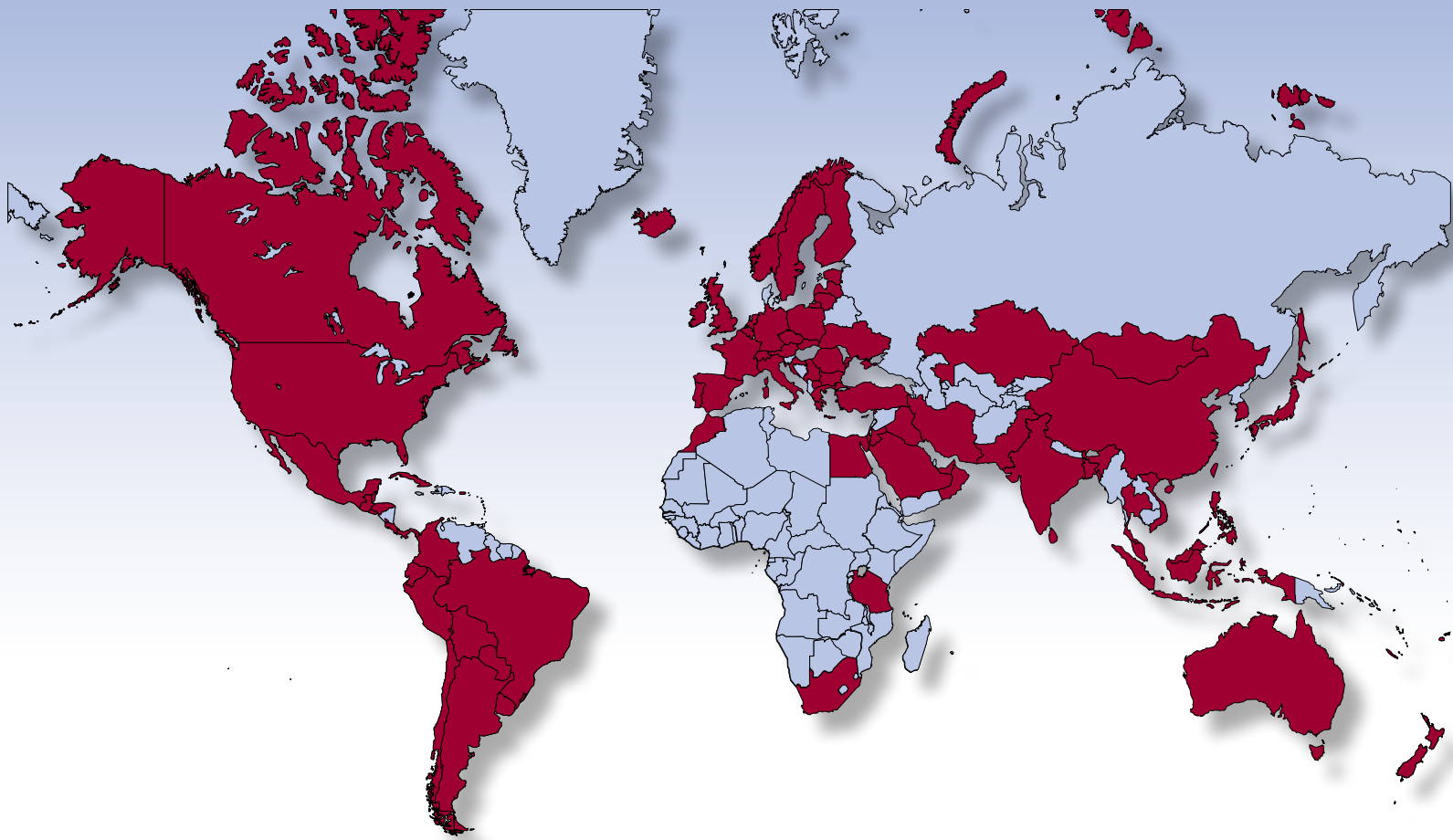
Argentina	Croatia	Hungary	Luxembourg	Peru	Sweden
Armenia	Cuba	Iceland	Macedonia	Philippines	Switzerland
Australia	Czech Republic	India	Malaysia	Poland	Taiwan
Austria	Denmark	Indonesia	Malta	Portugal	Tanzania
Bahrain	Ecuador	Iraq	Mexico	Qatar	Thailand
Belgium	Egypt	Ireland	Mongolia	Romania	Turkey
Bolivia	El Salvador	Israel	Morocco	Saudi Arabia	Ukraine
Brazil	Estonia	Italy	Netherlands	Singapore	United Arab
Bulgaria	Finland	Japan	New Zealand	Slovak Republic	Emirates
Canada	France	Jordan	Norway	Slovenia	United Kingdom
Chile	Germany	Kazakhstan	Oman	South Africa	United States
China	Greece	Kuwait	Pakistan	South Korea	Uruguay
Colombia	Guatemala	Latvia	Panama	Spain	Vietnam
Costa Rica	Honduras	Lithuania	Paraguay	Sri Lanka	

Figure 2. Number of Participants in **Proficiency Testing Program**, 2017 Total—603

Analyte	Total PT Participants in 2016	Additional PT Participants in 2017	TOTAL PT Participation in 2017
17OHP	281	10	291
T4	94	0	88
TSH	355	6	361
TGal	188	0	184
Bio	189	18	207
GALT	138	3	141
IRT	224	5	229
G6PD	56	41	97
CFDNA	60	13	73
HGB	72	5	77
Anti-HIV-1	27	2	29
TOXO	14	3	17
TREC	53	7	60
Arg	272	19	291
Cit	296	18	314
Leu	324	23	347
Met	313	18	331
Phe	438	18	456
SUAC	133	12	145
Tyr	332	18	350
Val	291	17	308
C0(L)	318	21	339
C3	312	22	334
C3DC	143	7	150
C3DC+C4OH	115	19	134
C4	293	25	318
C4OH	135	5	140
C5	323	23	346
C5:1	286	20	306
C5DC	314	16	330
C5OH	289	16	305
C6	301	23	324
C8	326	21	347
C10	315	20	335
C10:1	280	20	300
C10:2	191	19	210
C14	294	25	319
C14:1	303	22	325
C16	309	23	332
C16OH	306	22	328
C18	290	23	313
C18:1	275	22	297
C18OH	248	20	268
17OHP2	20	1	21
4AD2	20	1	21
CORT2	20	1	21
11D2	11	2	13
21D2	11	2	13
LSD	8	6	14
GALC	7	2	9
GAA	8	6	14
IDUA	8	5	13
24-LPC	7	5	12
26-LPC	8	6	14

Figure 3. Number of Participants in **Quality Control Program**, 2017 Total—551

Analyte	Total QC Participants 2016	Additional QC Participants in 2017	TOTAL QC Participation in 2017
17OHP	260	2	262
T4	97	0	91
TSH	343	0	337
TGal	198	0	187
GALT	94	4	98
IRT	223	0	216
Ala	254	26	280
Arg	279	15	294
Cit	300	8	308
Gly	0	235	235
Leu	315	2	317
Met	307	6	313
Orn	0	243	243
Phe	373	0	366
SUAC	154	0	152
Tyr	313	8	321
Val	296	10	306
C0	310	3	313
C2	303	5	308
C3	310	3	313
C3DC	167	3	170
C3DC+C4OH	141	1	142
C4	303	9	312
C4OH	164	0	158
C5	314	6	320
C5DC	306	1	307
C5OH	289	3	292
C6	309	5	314
C8	318	3	321
C10	312	7	319
C12	296	8	304
C14	305	7	312
C16	309	6	315
C16OH	305	91	396
C18	304	3	307
C18OH	266	12	278
17OHP2	23	0	22
4AD2	23	0	22
CORT2	23	0	22
11D2	15	0	15
21D2	14	2	16
GALC	0	14	14
GAA	0	23	23
IDUA	0	20	20
GLA	0	22	22
ABG	0	19	19
ASM	0	12	12
24-LPC	5	6	11
26-LPC	5	7	12
GAA2	10	0	7
CRE2	10	0	6
ALE2	21	1	22
ILE2	20	2	22
LEU2	20	2	22
PHE2	15	5	20
TYR2	15	5	20
VAL2	22	0	22
MMA2	23	3	26
EMA2	12	0	9
MCA2	13	3	16
tHCY2	18	5	23

Filter Paper

NSQAP evaluates absorption characteristics of all filter paper lots that have Food and Drug Administration (FDA) approval 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 is 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 (T_4) contained within a 3.2-mm disk with the serum absorption volume of the disks made from washed, intact red blood cells (RBCs). The latest version of the 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 1 and 2 show serum absorption volumes from 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 of washed intact RBCs [3]. The testing results in Tables 1 and 2 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 Whatman 903 filter paper lots W141, W152, and W161 for the production of QC and PT specimens distributed in 2017.

Table 1. Perkin Elmer 226 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 inch) Punch Avg (StDev)	Absorption Time (sec) Avg (StDev)	Spot Diameter (mm) Avg (StDev)
111064	Jul 2017	1.47 (0.20)	8.2 (1.0)	15.7 (0.5)
110092	Jul 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	Mar 2015	1.56 (0.10)	10.1 (2.1)	15.9 (0.7)
103649	Mar 2014	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)
102277	Dec 2012	1.47 (0.11)	13.0 (4.9)	15.8 (0.6)
101535	Apr 2012	1.49 (0.08)	14.7 (3.1)	15.7 (0.5)

Table 2. Whatman 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 inch) Punch Avg (StDev)	Absorption Time (sec) Avg (StDev)	Spot Diameter (mm) Avg (StDev)
W171	Apr 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	Apr 2015	1.46 (0.08)	11.0 (2.2)	16.0 (0.7)
W141	Mar 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)
W122	May 2013	1.41 (0.11)	14.8 (2.9)	16.3 (0.5)
W121	Jan 2013	1.49 (0.09)	13.7 (3.8)	16.0 (0.6)

Proficiency Testing

NSQAP distributes PT materials at least three times per year. PT panels consist of five blind-coded 75µL DBS 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 ADICS
- arginine (Arg)
- citrulline (Cit)
- leucine (Leu)
- methionine (Met)
- phenylalanine (Phe)
- succinylacetone (SUAC)
- tyrosine (Tyr)
- valine (Val)

ACYLCARNITINES
- low free carnitine (C0(L))
- propionylcarnitine (C3)
- malonylcarnitine (C3DC)
- butyrylcarnitine (C4)
- hydroxybutyrylcarnitine (C4OH)
- isovalerylcarnitine (C5)
- tiglylcarnitine (C5:1)
- glutarylcarnitine (C5DC)
- hydroxyisovalerylcarnitine (C5OH)
- hexanoylcarnitine (C6)
- octanoylcarnitine (C8)
- decanoylcarnitine (C10)
- decenoylcarnitine (C10:1)
- decadienoylcarnitine (C10:2)
- myristoylcarnitine (C14)
- tetradecenoylcarnitine (C14:1)
- palmitoylcarnitine (C16)
- hydroxypalmitoylcarnitine (C16OH)
- stearoylcarnitine (C18)
- oleoylcarnitine (C18:1)

OTHER ANALYTES
- 17 α-hydroxyprogesterone (17OHP)
- 24:0-lysophosphatidylcholine (24LPC)
- 26:0-lysophosphatidylcholine (26LPC)
- acid-α-glucosidase (GAA)
- α-L-iduronida
- biotinidase (BIOT)
- cystic fibrosis DNA (CFDNA)
- galactose-1-phosphate (GALT)
- galactocerebrosidase (GALC)
- glucose-6-sphosphate dehydrogenase (G6PD)
- immunoreactive trypsinogen (IRT)
- hydroxystearoylcarnitine (C18OH)
- 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)
- thyroxine (T$_4$)
- thyroid stimulating hormone (TSH)
- total galactose (TGal)
- *Toxoplasma gondii* 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 unaltered donor blood or by enriching a single donor blood unit with analytes.

Purified analytes are used for PT enrichments. Enrichments made with purchased or custom-synthesized acylcarnitines are based on weight quantities. 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 T_4 standard after reconstituting washed RBCs with purchased T_4-depleted charcoal-stripped serum.

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

Biotinidase PT pools 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.

Low free carnitine (C0[L]) materials are produced by washing fresh RBCs at least six times then combining with charcoal-stripped serum.

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

Hemoglobin specimens are made from individual umbilical cord blood units.

T-cell 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 specimens are prepared from human blood, including cord blood from unaffected persons and leukodepleted adult blood restored with lymphoblast cells from patients with LSD.

Toxoplasma immunoglobulin G and M 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 assessment through the NSQAP data reporting website or use an Excel data reporting form downloaded from the NSQAP section of the CDC website at https://www.cdc.gov/labstandards/nsqap_resources.html.

Laboratories that submit results before the data-reporting deadline will 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 3–5 show the PT errors reported in 2017 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 4). The rates for false-positive misclassifications were based on the number of negative specimens tested, and the rates for false-negative misclassifications on the number of positive 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 3. Summary of non-MS/MS Proficiency Test Errors For Domestic and International Laboratories

Domestic

Disorder	Positive Specimens Assayed (N)	False Negative Errors (%)	Negative Specimens Assayed (N)	False Positive Errors (%)
Congenital Adrenal Hyperplasia	212	0.0%	423	0.0%
Biotinidase Deficiency	218	0.5%	432	2.5%
G6PD Deficiency	16	0.0%	24	0.0%
GALT Deficiency	260	0.0%	390	0.0%
Immunoreactive Trypsinogen	266	1.9%	399	0.3%
Congenital Hypothyroidism	86	0.0%	564	0.0%
Galactosemia	71	0.0%	284	0.4%

International

Disorder	Positive Specimens Assayed (N)	False Negative Errors (%)	Negative Specimens Assayed (N)	False Positive Errors (%)
Congenital Adrenal Hyperplasia	992	1.0%	1978	0.3%
Biotinidase Deficiency	670	1.5%	1325	0.4%
G6PD Deficiency	384	2.3%	576	1.0%
GALT Deficiency	510	1.8%	765	0.8%
Immunoreactive Trypsinogen	942	1.0%	1413	0.4%
Congenital Hypothyroidism	513	5.1%	3377	0.1%
Galactosemia	376	3.2%	1504	0.2%

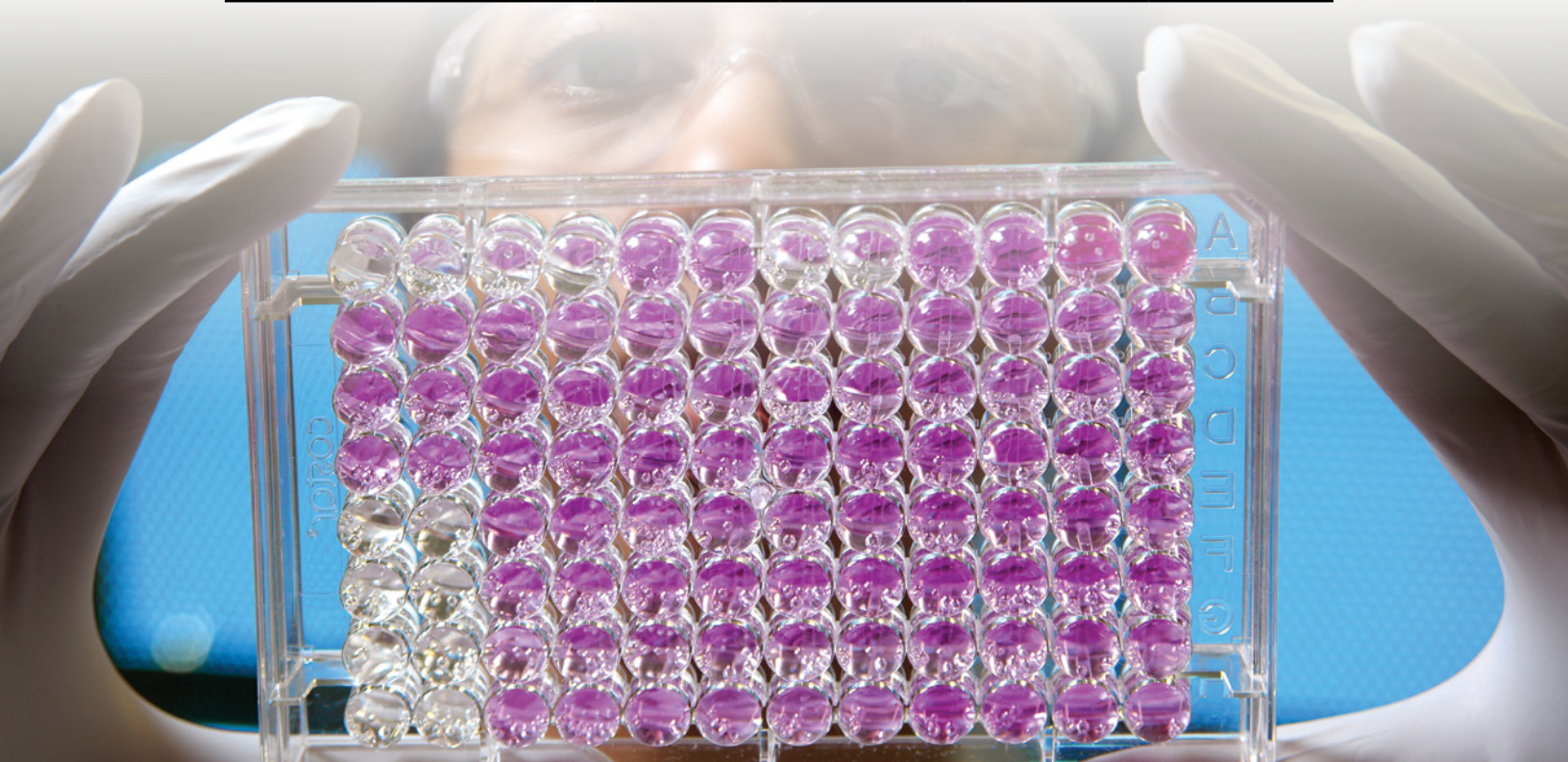**Table 4.** Summary of Amino Acid and Acylcarnitine Proficiency Test Errors by **Domestic** Laboratories

Analyte	Positive Specimens Assayed (N)	False Negative Errors (%)	Negative Specimens Assayed (N)	False Positive Errors (%)
Arginine Screen	72	0.0%	468	0.2%
Citrulline Screen	90	0.0%	585	0.2%
Leucine Screen	137	0.0%	548	1.5%
Methionine Screen	135	0.7%	540	0.0%
Phenylalanine Screen	117	0.9%	748	0.5%
Succinylacetone Screen	102	2.0%	408	0.0%
Tyrosine Screen	106	0.9%	679	0.0%
Valine Screen	95	1.1%	380	0.0%
C0(L) Screen	96	0.0%	619	0.2%
C3 Screen	146	0.0%	584	0.0%
C3DC Screen	40	0.0%	250	0.4%
C3DC+C4OH Screen	86	9.3%	239	0.0%
C4 Screen	90	4.4%	580	0.0%
C4OH Screen	38	2.6%	242	0.0%
C5 Screen	147	0.0%	583	0.0%
C5:1 Screen	96	0.0%	619	0.0%
C5DC Screen	143	0.0%	572	0.2%
C5OH Screen	95	0.0%	615	0.0%
C6 Screen	137	4.4%	548	0.0%
C8 Screen	146	0.7%	584	0.0%
C10 Screen	134	2.2%	536	0.2%
C10:1 Screen	127	3.1%	508	0.0%
C10:2 Screen	56	0.0%	359	0.0%
C14 Screen	134	4.5%	536	0.0%
C14:1 Screen	146	4.1%	584	0.2%
C16 Screen	92	3.3%	593	0.0%
C16OH Screen	98	0.0%	632	0.0%
C18 Screen	168	0.0%	457	0.0%
C18:1 Screen	84	7.1%	541	0.2%
C18OH Screen	76	1.3%	489	0.4%

Table 5. Summary of Amino Acid and Acylcarnitine Proficiency Test Errors by **International** Laboratories

Analyte	Positive Specimens Assayed (N)	False Negative Errors (%)	Negative Specimens Assayed (N)	False Positive Errors (%)
Arginine Screen	431	3.0%	2799	0.1%
Citrulline Screen	462	2.8%	2988	0.1%
Leucine Screen	764	1.6%	3056	0.1%
Methionine Screen	737	1.6%	2948	0.1%
Phenylalanine Screen	674	1.9%	4331	0.0%
Succinylacetone Screen	267	4.5%	1068	0.3%
Tyrosine Screen	507	2.6%	3283	0.1%
Valine Screen	704	1.7%	2816	0.1%
C0(L) Screen	512	2.5%	3273	0.1%
C3 Screen	739	1.6%	2956	0.1%
C3DC Screen	227	5.7%	1408	0.1%
C3DC+C4OH Screen	346	3.2%	964	0.4%
C4 Screen	470	2.8%	3025	0.1%
C4OH Screen	204	6.4%	1301	0.2%
C5 Screen	793	1.5%	3087	0.1%
C5:1 Screen	444	2.9%	2871	0.1%
C5DC Screen	737	1.6%	2948	0.1%
C5OH Screen	449	2.9%	2851	0.1%
C6 Screen	719	1.7%	2876	0.1%
C8 Screen	779	1.5%	3116	0.1%
C10 Screen	757	1.6%	3028	0.1%
C10:1 Screen	660	1.8%	2640	0.1%
C10:2 Screen	304	4.3%	1966	0.1%
C14 Screen	711	1.7%	2844	0.1%
C14:1 Screen	721	1.7%	2884	0.1%
C16 Screen	498	2.6%	3202	0.1%
C16OH Screen	486	2.7%	3114	0.1%
C18 Screen	938	1.2%	2547	0.2%
C18:1 Screen	439	3.0%	2841	0.1%
C18OH Screen	394	3.3%	2531	0.1%

Non-Web Reported Analytes

Table 6 shows a summary of PT errors for programs not reported on the NSQAP database website. Those include the Sickle Cell and Other Hemoglobinopathies, CFDNA Variant Detection, Lysosomal Storage Disorders, T-Cell Receptor Excision Circle, Anti-Toxoplasma Antibodies, X-Linked Adrenoleukodystrophy (XALD), and Second-Tier Congenital Adrenal Hyperplasia programs.

The CFDNA PT program provides evaluations based on allele identification and clinical assessment. Allele detection is dependent on the method used. Table 7 summarizes the CF variant challenges distributed in 2017.

Table 8 shows the challenges distributed in 2017 for sickle cell disease and other hemoglobinopathies. Participants are evaluated on hemoglobin phenotypes and ability to provide correct clinical assessments.

Table 6. Summary of Non-Web Based Analyte Proficiency Test Errors

Sickle Cell and Other Hemoglobinopathies

Proficiency Test	Domestic	International
Specimens Assayed	676	403
Phenotype Errors	1.9%	7.4%
Clinical Assessment Errors	1.8%	5.0%

Cystic Fibrosis DNA Variant

Proficiency Test	Domestic	International
Specimens Assayed	595	711
Allele Errors	0.7%	1.1%
Clinical Assessment Errors	0.2%	0.6%

Lysosomal Storage Disorders
Krabbe

Proficiency Test	Domestic	International
Specimens Assayed	130	n/a
Clinical Assessment Errors	0.8%	n/a

Pompe

Proficiency Test	Domestic	International
Specimens Assayed	165	n/a
Clinical Assessment Errors	0.6%	n/a

MPS-1

Proficiency Test	Domestic	International
Specimens Assayed	165	n/a
Clinical Assessment Errors	0.0%	n/a

T-cell Receptor Excision Circle

Proficiency Test	Domestic	International
Total Specimens Assayed	549	205
Clinical Assessment Errors	0.9%	4.4%

anti-Toxoplasma Antibodies
Screening Results (IgG and IgM)

Proficiency Test	Domestic	International
Total Specimens Assayed	20	145
Clinical Assessment Errors	0.0%	4.1%

Confirmatory Results (IgG and IgM)

Proficiency Test	Domestic	International
Total Specimens Assayed	20	30
Clinical Assessment Errors	0.0%	13.3%

Second-tier Congenital Adrenal Hyperplasia

Proficiency Test	Domestic	International
Specimens Assayed	60	255
Clinical Assessment Errors	5.0%	11.4%

X-linked Adrenoleukodystrophy
24:0 Lysophosphatidylcholine

Proficiency Test	Domestic	International
Specimens Assayed	19	7
Clinical Assessment Errors	10.5%	0.0%

26:0 Lysophosphatidylcholine

Proficiency Test	Domestic	International
Specimens Assayed	27	11
Clinical Assessment Errors	3.7%	0.0%

Table 7. Cystic Fibrosis DNA Variant (CTFR gene) Challenges Distributed in 2017

Variant (Legacy Name)	Variant (HGVS Nomenclature)	Variants Sent
F508del	(c.1521_1523delCTT)	13
2055del9>A	(c.1923_1931del9insA)	1
2184delA	(c.2052delA)	1
3272-26A>G	(c.3140-26A>G)	1
3905insT	(c.3773dupT)	1
394delTT	(c.262_263delTT)	1
621+1G>T	(c.489+1G>T)	1
A559T	(c.1675G>A)	1
G551D	(c.1652G>A)	1
L206W	(c.617T>G)	1
N1303K	(c.3909C>G)	1
R1066C	(c.3196C>T)	1
R553X	(c.1657C>T)	1
S549N	(c.1646G>A)	1

Table 8. Hemoglobinopathies Accepted Presumptive Phenotype Distribution

Panels	Specimen 1	Specimen 2	Specimen 3	Specimen 4	Specimen 5
Panel 1	FS, FSU	FAE, FAV, FAU	FAC, FAV, FAU	FAS	FA
Panel 2	FS, FSU	FS, FSU	FA	FA	FAS
Panel 3	FAS	FA	FAS	FA	FS, FSU

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. Cutoff values vary among participating laboratories because each laboratory establishes its own cutoff level. 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 working cutoff value, which is based on the domestic mean cutoff value. (Figure 4)

Tables 9–11 summarize the reported cutoff values for domestic and international laboratories. The tables show the values for mean, median, and mode for each analyte. Tables 12–14 summarize the mean, median, mode, and minimum/maximum for reported domestic cutoff values, by method.

Table 9. 2017 Summary of non-MS/MS Cutoff Values for Domestic and International Laboratories

Domestic

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	43	34.2	33.0	25.0	17.8	65.0
IRT (ng/mL blood)	44	66.3	60.8	60.0	39.9	125.3
T_4 (µg/dL serum)	23	7.2	6.0	5.0	4.0	27.6
TGal (mg/dL blood)	24	11.1	10.0	10.0	6.0	20.0
TSH (µIU/mL serum)	44	29.7	25.0	20.0	8.5	58.0
Tyr (µmol/L blood)	3	218.3	138.8	N/A	116.0	400.0
Phe (µmol/L blood)	7	154.2	150.0	150.0	121.0	188.0

International

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	200	26.1	20.9	19.8	3.0	120.0
IRT (ng/mL blood)	158	67.1	65.0	70.0	15.0	100.0
T_4 (µg/dL serum)	38	8.1	6.4	6.0	3.1	22.0
TGal (mg/dL blood)	128	12.9	10.0	10.0	3.1	30.0
TSH (µIU/mL serum)	263	22.2	20.0	20.0	5.3	55.0
Phe (µmol/L blood)	90	161.7	151.5	120.0	96.8	345.0

Table 10. 2017 Summary of MS/MS Cutoff Values for Domestic Laboratories (µmol/L blood)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine	36	70.9	60.0	100.0	20.0	125.0
Citrulline	45	54.4	55.0	50.0	18.0	100.0
Leucine	46	288.8	288.5	250.0	175.0	400.0
Methionine	45	74.1	75.0	100.0	35.0	100.0
Phenylalanine	50	140.5	145.0	130.0	70.0	182.0
Succinylacetone	34	2.5	2.0	4.5	0.5	5.4
Tyrosine	49	395.1	360.0	300.0	92.0	850.0
Valine	32	296.7	291.0	250.0	175.0	530.0
C0(L)	48	8.18	7.50	6.00	5.00	24.00
C3	49	5.67	6.00	6.30	2.82	8.50
C3DC	20	0.20	0.20	0.20	0.10	0.43
C3DC+ C4OH	21	0.55	0.40	0.38	0.25	3.03
C4	45	1.26	1.30	1.30	0.49	1.90
C4OH	19	0.60	0.65	0.70	0.27	1.00
C5	49	0.70	0.66	0.60	0.38	1.20
C5:1	48	0.20	0.15	0.10	0.03	0.50
C5DC	48	0.36	0.35	0.50	0.05	0.80
C5OH	47	0.78	0.80	0.80	0.25	1.36
C6	46	0.38	0.28	0.25	0.14	0.95
C8	49	0.44	0.40	0.35	0.25	0.73
C10	45	0.43	0.40	0.30	0.22	0.80
C10:1	43	0.28	0.25	0.25	0.14	0.45
C10:2	28	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	0.60	0.65	0.60	0.17	0.80
C16	46	7.60	7.80	8.00	2.14	10.00
C16OH	49	0.12	0.11	0.10	0.06	0.25
C18	41	2.32	2.21	3.50	0.70	3.50
C18:1	42	3.51	3.00	3.00	2.00	7.00
C18OH	38	0.09	0.10	0.10	0.03	0.16

Table 11. 2017 Summary of MS/MS Cutoff Values for International Laboratories (µmol/L blood)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine	217	56.8	51.8	50.0	10.0	150.0
Citrulline	230	52.1	46.9	55.0	20.0	200.0
Leucine	256	312.2	300.0	300.0	147.0	650.0
Methionine	248	55.5	50.0	50.0	20.0	146.0
Phenylalanine	248	133.8	122.9	120.0	48.0	240.0
Succinylacetone	86	2.2	1.6	2.0	0.3	10.0
Tyrosine	256	295.1	270.0	400.0	79.9	600.0
Valine	239	270.2	265.0	300.0	150.0	700.0
C0(L)	253	11.46	8.80	10.00	3.00	90.00
C3	248	5.19	5.00	6.00	1.50	11.00
C3DC	109	0.31	0.25	0.30	0.04	3.30
C3DC+ C4OH	89	0.48	0.44	0.45	0.16	2.13
C4	236	0.95	0.93	1.30	0.16	1.80
C4OH	97	0.56	0.54	0.50	0.05	1.40
C5	263	0.69	0.60	1.00	0.20	2.00
C5:1	223	0.15	0.12	0.25	0.02	0.80
C5DC	249	0.34	0.30	0.35	0.07	1.00
C5OH	223	0.74	0.72	1.00	0.19	2.20
C6	238	0.29	0.23	0.20	0.04	1.00
C8	261	0.34	0.30	0.50	0.05	1.50
C10	250	0.37	0.36	0.30	0.07	1.20
C10:1	220	0.27	0.25	0.30	0.05	1.00
C10:2	150	0.15	0.12	0.15	0.02	2.00
C14	235	0.61	0.55	0.80	0.10	1.50
C14:1	242	0.45	0.40	0.60	0.04	2.50
C16	247	6.54	6.67	7.50	0.13	14.00
C16OH	243	0.12	0.10	0.10	0.02	0.60
C18	235	2.12	2.00	2.50	0.17	4.10
C18:1	220	2.94	3.00	3.50	0.10	5.80
C18OH	193	0.11	0.09	0.10	0.01	2.00

Table 12. 2017 Domestic non-MS/MS Cutoff Summary by Analyte (ng/mL serum) and Method *(Methods N < 2 not shown)*

17OHP µg/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**34.2**	**33.0**	**25.0**	**17.8**	**65.0**
AutoDelfia	7	39.1	40.0	35.0	17.8	60.0
AutoDelfia Neonatal 17-OHP (B024)	13	32.6	33.0	33.0	25.0	50.0
PerkinElmer GSP Neonatal	23	33.6	30.0	25.0	25.0	65.0

TSH µIU/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**29.7**	**25.0**	**20.0**	**8.5**	**58.0**
AutoDelfia	21	35.1	30.0	20.0	12.6	58.0
PerkinElmer GSP Neonatal	22	25.0	25.0	25.0	8.5	36.0

T$_4$ µg/dL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**23**	**7.2**	**6.0**	**5.0**	**4.0**	**27.6**
AutoDelfia	7	9.3	6.5	6.5	4.0	27.6
PerkinElmer GSP Neonatal	15	6.2	6.0	5.0	5.0	8.3

TGal mg/dL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**24**	**11.1**	**10.0**	**10.0**	**6.0**	**20.0**
Astoria-Pacific 50 Hour Reagent Kit	6	11.0	10.0	10.0	10.0	15.0
Fluorometric manual (e.g. Hill or Misuma)	3	14.7	14.0	0	10.0	20.0
PerkinElmer GSP Neonatal	8	11.2	11.0	10.0	7.3	14.0

IRT ng/mL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**66.3**	**60.8**	**60.0**	**39.9**	**125.3**
Auto Delfia	23	72.1	67.0	67.0	55.0	125.3
PerkinElmer GSP Neonatal	21	59.9	55.0	55.0	39.9	100.0

Table 13. 2017 Domestic Cutoff Summary by Analyte (ng/mL blood) and Method—Amino Acids (µmol/L blood)

Arginine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**36**	**70.9**	**60.0**	**100.0**	**20.0**	**125.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	82.5	85.0	100.0	60.0	100.0
Derivatized - MS/MS non-kit	13	52.1	45.0	60.0	20.0	125.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	19	81.4	100.0	50.0	50.0	120.0

Continued

Citrulline

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**45**	**54.4**	**55.0**	**50.0**	**18.0**	**100.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	62.5	55.0	N/A	40.0	100.0
Derivatized - MS/MS non-kit	15	47.8	50.0	50.0	18.0	75.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	56.9	60.0	60.0	40.2	75.0

Leucine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**46**	**288.8**	**288.5**	**250.0**	**175.0**	**400.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	281.3	275.0	275.0	250.0	325.0
Derivatized - MS/MS non-kit	15	265.7	250.0	300.0	200.0	350.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	301.6	290.0	250.0	175.0	400.0

Methionine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**45**	**74.1**	**75.0**	**100.0**	**35.0**	**100.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	75.0	75.0	75.0	70.0	80.0
Derivatized - MS/MS non-kit	15	62.3	60.0	50.0	35.0	100.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	81.5	85.0	100.0	54.5	100.0

Phenylalanine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**50**	**140.5**	**145.0**	**130.0**	**70.0**	**182.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	136.3	132.5	130.0	130.0	150.0
Derivatized - MS/MS non-kit	19	132.7	130.0	182.0	70.0	182.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	150.6	160.0	165.0	120.0	180.0
Non-derivatized - MS/MS non-kit	3	115.0	120.0	N/A	75.0	150.0

Succinylacetone

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**34**	**2.5**	**2.0**	**4.5**	**0.5**	**5.4**
Derivatized - MS/MS non-kit	11	2.3	2.0	.	0.5	5.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	2.4	2.0	4.5	0.7	4.5

Tyrosine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**49**	**395.1**	**360.0**	**300.0**	**92.0**	**850.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	282.5	290.0	300.0	250.0	300.0
Derivatized - MS/MS non-kit	18	287.1	280.0	300.0	99.0	500.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	508.8	435.3	850.0	300.0	850.0
Non-derivatized - MS/MS non-kit	3	284.0	360.0	.	92.0	400.0

Continued

Valine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**32**	**296.7**	**291.0**	**250.0**	**175.0**	**530.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	316.7	300.0	.	250.0	400.0
Derivatized - MS/MS non-kit	11	265.0	255.0	200.0	175.0	420.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	16	315.6	312.5	250.0	250.0	530.0

Table 14. 2017 Domestic Cutoff Summary by Analyte (µmol/L blood) and Method—Acylcarnitines (µmol/L blood) *(Methods N < 2 not shown)*

C0(L)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**8.18**	**7.50**	**6.00**	**5.00**	**24.00**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	11.12	11.23	.	9.00	13.00
Derivatized - MS/MS non-kit	18	9.78	8.50	8.00	5.00	24.00
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	6.56	6.00	6.00	5.00	10.00

C3

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**49**	**5.67**	**6.00**	**6.30**	**2.82**	**8.50**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	5.54	5.57	.	5.00	6.00
Derivatized - MS/MS non-kit	19	5.25	5.00	5.00	2.82	8.50
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	5.95	6.30	6.30	4.00	7.50

C3DC

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**20**	**0.20**	**0.20**	**0.20**	**0.10**	**0.43**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.25	0.26	0.30	0.19	0.30
Derivatized - MS/MS non-kit	16	0.19	0.17	0.20	0.10	0.43

C3DC + C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**21**	**0.55**	**0.40**	**0.38**	**0.25**	**3.03**
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	20	0.43	0.39	0.38	0.25	0.85

C4

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**1.26**	**1.30**	**1.30**	**0.49**	**1.90**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	1.00	0.95	.	0.81	1.30
Derivatized - MS/MS non-kit	17	1.14	1.20	1.40	0.49	1.90
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	1.39	1.30	1.70	1.10	1.70

Continued

C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**19**	**0.60**	**0.65**	**0.70**	**0.27**	**1.00**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.73	0.68	.	0.55	1.00
Derivatized - MS/MS non-kit	15	0.57	0.65	0.70	0.27	1.00

C5

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**49**	**0.70**	**0.66**	**0.60**	**0.38**	**1.20**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.66	0.70	0.70	0.54	0.70
Derivatized - MS/MS non-kit	19	0.66	0.60	0.50	0.38	1.20
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.74	0.70	1.00	0.50	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	4	0.20	0.20	0.15	0.15	0.25
Derivatized - MS/MS non-kit	19	0.17	0.14	0.08	0.05	0.50
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	0.22	0.17	0.50	0.03	0.50

C5DC

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**0.36**	**0.35**	**0.50**	**0.05**	**0.80**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.28	0.28	.	0.24	0.32
Derivatized - MS/MS non-kit	19	0.19	0.18	0.21	0.05	0.35
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	0.51	0.50	0.50	0.32	0.80

C5OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**0.78**	**0.80**	**0.80**	**0.25**	**1.36**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.69	0.66	.	0.60	0.83
Derivatized - MS/MS non-kit	19	0.76	0.80	0.80	0.25	1.36
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	0.80	0.80	0.85	0.60	1.05

C6

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**46**	**0.38**	**0.28**	**0.25**	**0.14**	**0.95**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.26	0.25	0.25	0.24	0.30
Derivatized - MS/MS non-kit	18	0.31	0.30	0.22	0.14	0.63
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	0.45	0.26	0.95	0.16	0.95

Continued

C8

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**49**	**0.44**	**0.40**	**0.35**	**0.25**	**0.73**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.37	0.37	0.35	0.35	0.40
Derivatized - MS/MS non-kit	19	0.39	0.35	0.50	0.25	0.73
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.49	0.46	0.60	0.30	0.70

C10

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.43**	**0.40**	**0.30**	**0.22**	**0.80**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.36	0.33	.	0.27	0.50
Derivatized - MS/MS non-kit	17	0.40	0.40	0.40	0.22	0.80
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	0.47	0.43	0.65	0.22	0.70

C10:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**0.28**	**0.25**	**0.25**	**0.14**	**0.45**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.29	0.30	0.30	0.25	0.30
Derivatized - MS/MS non-kit	16	0.25	0.23	0.17	0.17	0.38
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	0.29	0.25	0.45	0.14	0.45

C10:2

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**28**	**0.15**	**0.12**	**0.10**	**0.04**	**0.39**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	0.17	0.15	0.15	0.15	0.20
Derivatized - MS/MS non-kit	14	0.17	0.13	0.10	0.06	0.39
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	10	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	4	0.63	0.65	0.70	0.52	0.70
Derivatized - MS/MS non-kit	17	0.67	0.70	0.70	0.26	0.96
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	0.82	0.71	1.20	0.46	1.20

C14:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**49**	**0.60**	**0.65**	**0.60**	**0.17**	**0.80**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.55	0.55	.	0.40	0.70
Derivatized - MS/MS non-kit	19	0.54	0.60	0.60	0.17	0.75
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.66	0.68	0.80	0.37	0.80

Continued

C16

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	46	7.60	7.80	8.00	2.14	10.00
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	7.04	6.93	.	6.50	7.80
Derivatized - MS/MS non-kit	18	6.73	7.40	8.00	2.14	9.00
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	8.34	8.00	10.00	6.00	10.00

C16OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	49	0.12	0.11	0.10	0.06	0.25
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.15	0.15	.	0.12	0.18
Derivatized - MS/MS non-kit	19	0.13	0.13	0.10	0.06	0.25
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.11	0.10	0.10	0.06	0.20

C18

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	41	2.32	2.21	3.50	0.70	3.50
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	2.17	2.15	.	1.89	2.50
Derivatized - MS/MS non-kit	14	1.87	1.83	1.50	0.70	2.80
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	2.62	2.50	3.50	1.55	3.50

C18:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	42	3.51	3.00	3.00	2.00	7.00
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	3.14	3.43	.	2.50	3.50
Derivatized - MS/MS non-kit	16	2.71	2.68	3.00	2.00	3.50
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	4.14	3.13	7.00	2.27	7.00

C18OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	38	0.09	0.10	0.10	0.03	0.16
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.12	0.11	0.10	0.10	0.16
Derivatized - MS/MS non-kit	13	0.09	0.10	0.10	0.03	0.16
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 4. NSQAP's Grading Algorithm Flow chart
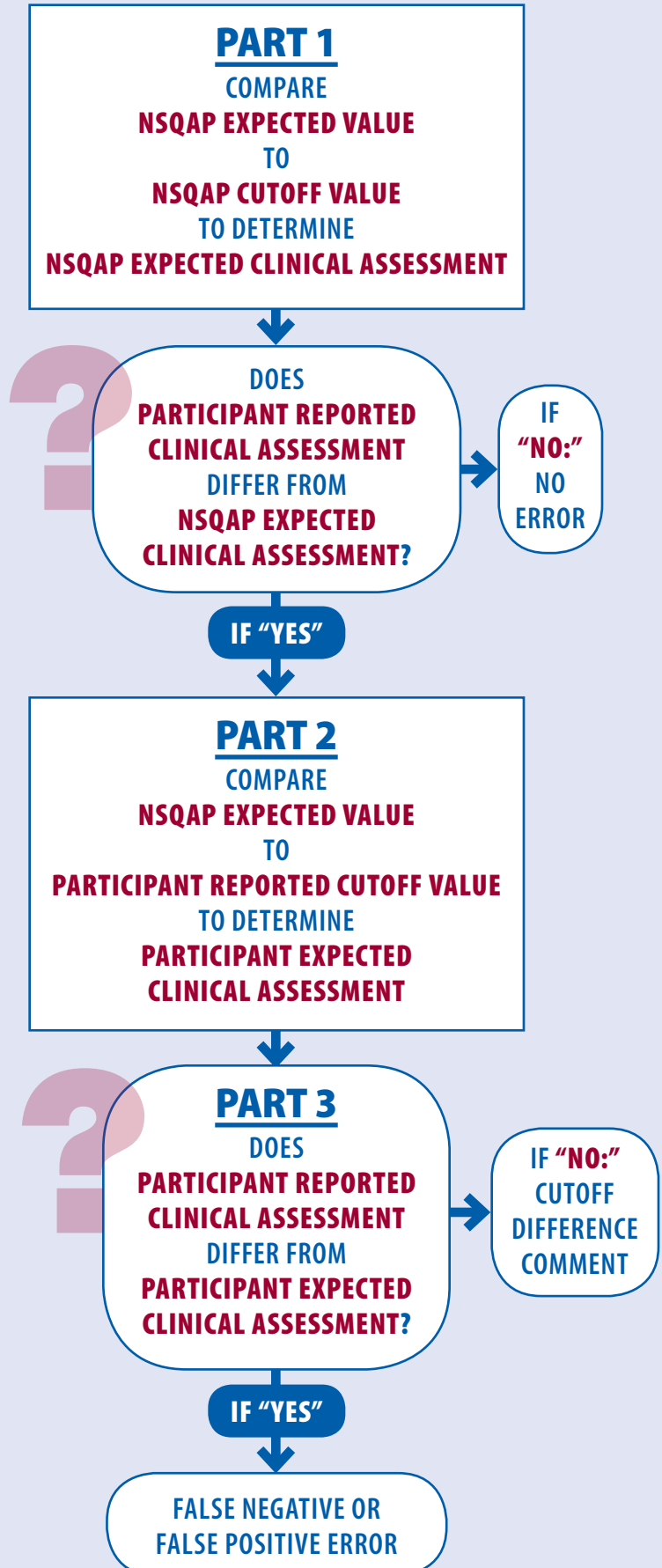
2017 Bias Plots

Proficiency Testing Bias Plots

Figures 5–41 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. GALT, G6PD, and C0(L) use CDC-assayed values due to production methods for deficient analytes. Immunoreactive Trypsinogen (IRT) standard cannot be fully recovered by any IRT analytical method; therefore, IRT PT uses CDC-assayed values.

Non-derivatized MS/MS method 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% CI 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.
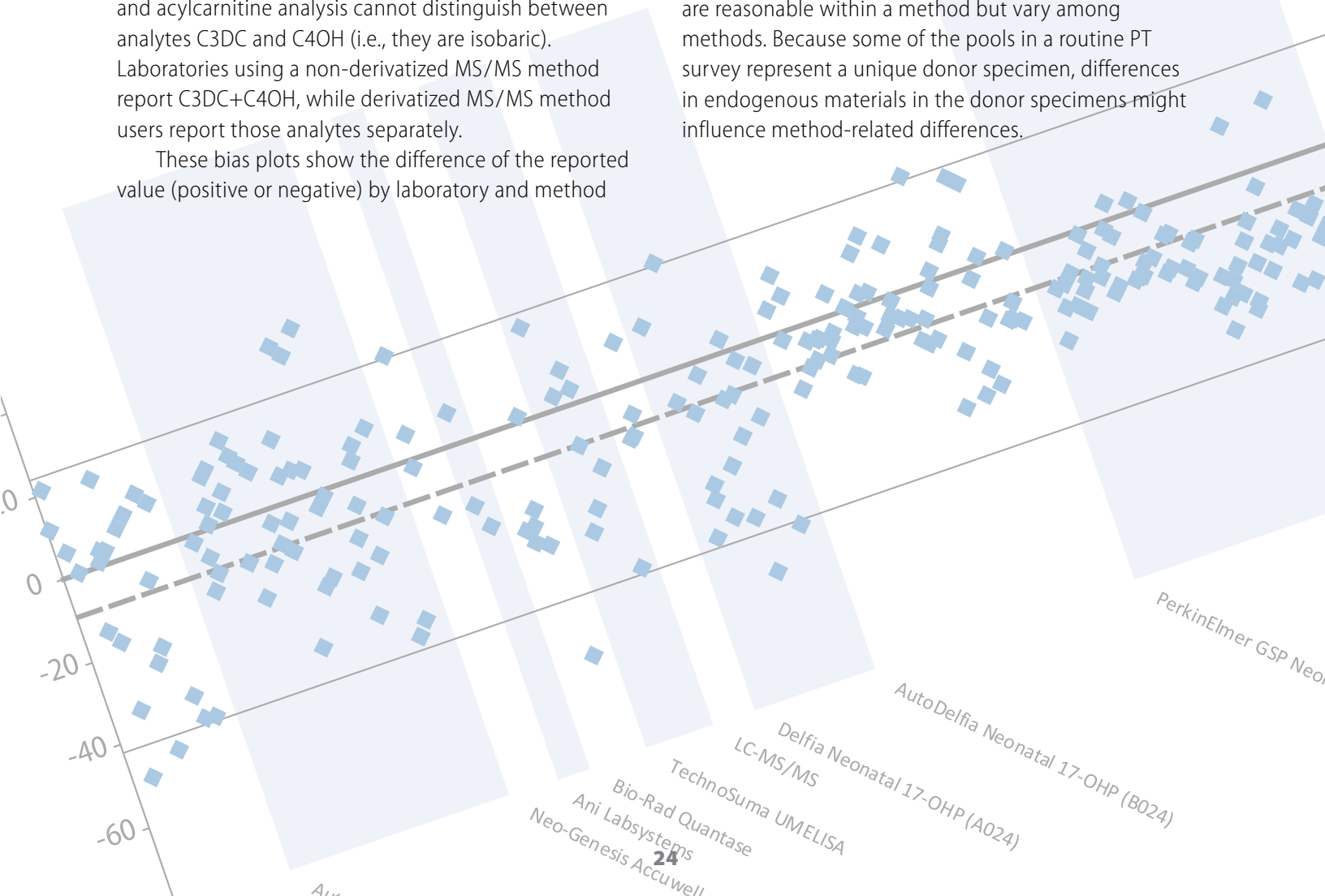
Figure5. Reproducibility of Results:
Bias Plot of 17 α-Hydroxyprogesterone (17OHP) Values by Method
Quarter 3, Specimen 31715
Expected Value (EV) = 86.0 ng / mL serum

17OHP ng / mL serum

Quarter 3
Specimen 31715

Enriched—85.0

CDC Assayed—71.4

Participant Mean—76.9

Participant Bias— -9.1
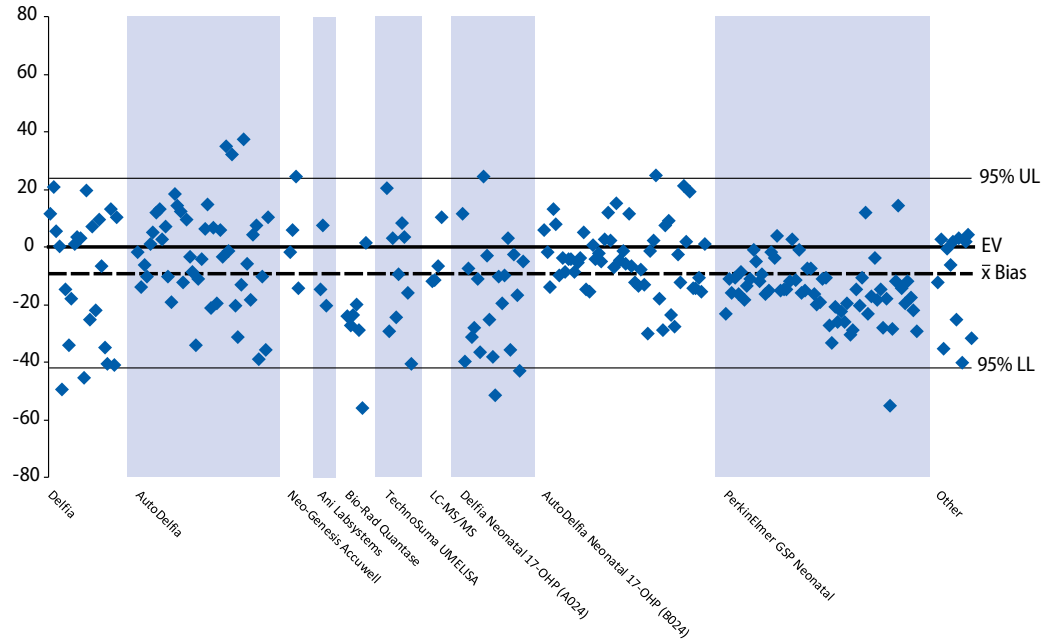
The 17OHP bias plot shows units of measure on the y-axis ranging from 80 ng / mL serum to -80 ng / mL serum. The bias for this plot is -9.1 ng / mL serum below zero. The data on this plot shows a tight scatter among all participants.

Figure 6. Reproducibility of Results:
Bias Plot of Thyroxine (T$_4$) Values by Method
Quarter 1, Specimen 11711
Expected Value (EV) = 1.6 µg/dL serum

T$_4$ µg / dL serum

Quarter 1
Specimen 11711

Enriched—1.5

CDC Assayed—1.7

Participant Mean—1.6

Participant Bias— 0.0
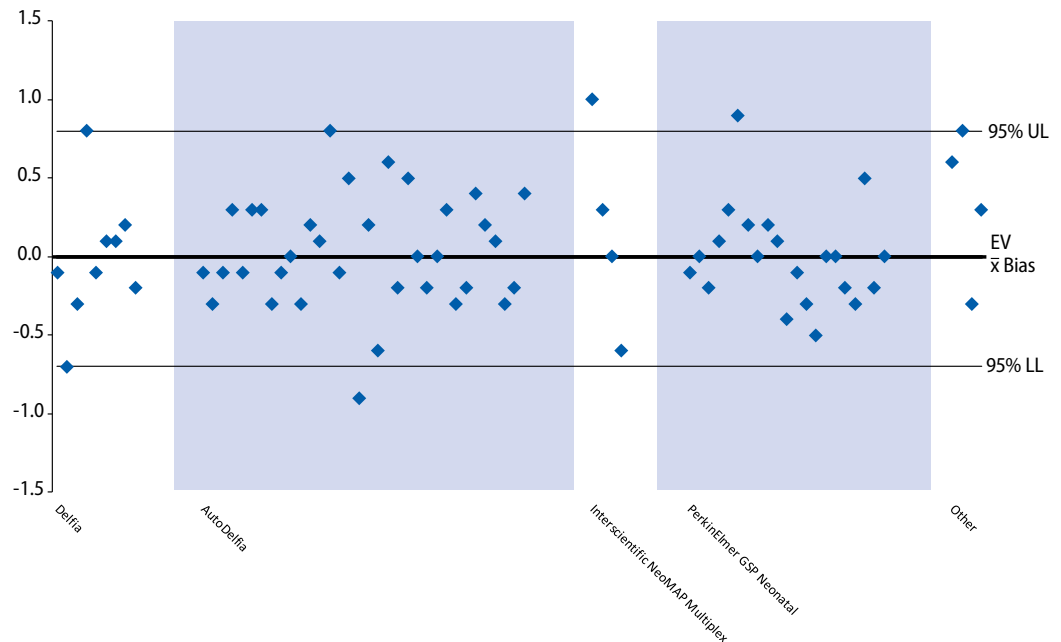
The T$_4$ bias plot shows units of measure on the y-axis ranging from 1.5 µg/dL serum to -1.5 µg/dL serum. The bias for this plot is 0.0 µg/dL serum. This plot shows participant bias is equal to the expected value and with good agreement among all participants.

Figure 7. Reproducibility of Results:
Bias Plot of Thyroid-Stimulating Hormone (TSH) Values by Method
Quarter 1, Specimen 11711
Expected Value (EV) = 80.6 µIU/mL serum

TSH µIU/mL serum

Quarter 1
Specimen 11711

Enriched — 80.0

CDC Assayed — 80.0

Participant Mean — 88.7

Participant Bias — 8.1
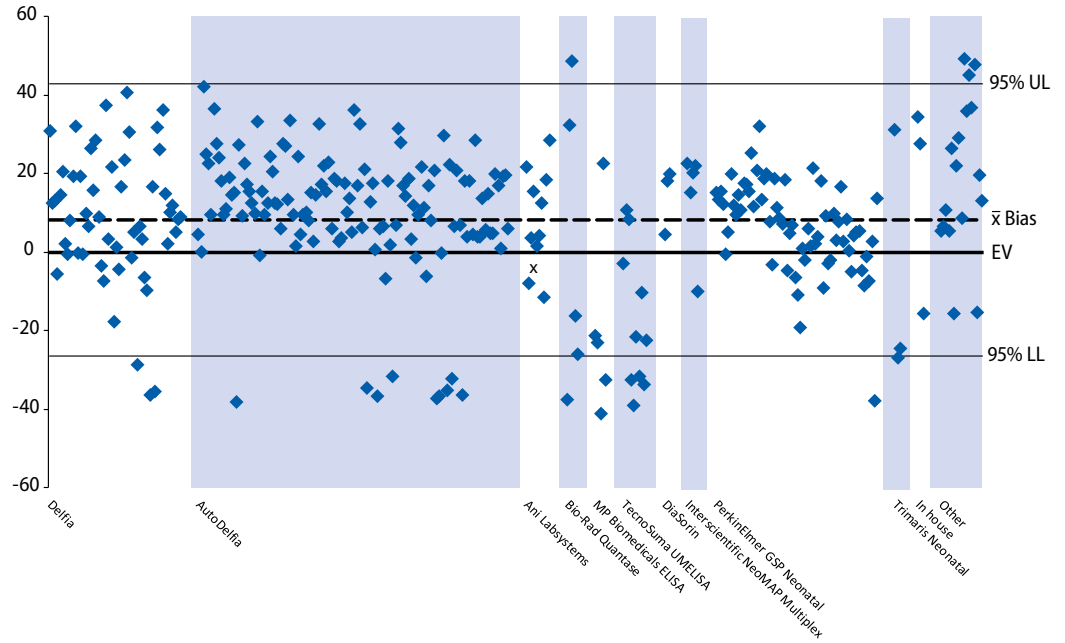
The TSH bias plot shows units of measure on the y-axis ranging from 60 µIU/mL serum to -60 µIU/mL serum. The bias for this plot is 8.1 µIU/mL serum above zero. This plot shows a positive bias compared to the CDC-expected value. All methods show a tight scatter with most participants clustering in a positive bias.

Figure 8. Reproducibility of Results:
Bias Plot of Total Galactose (TGal) Values by Method
Quarter 1, Specimen 11715
Expected Value (EV) = 25.4 mg/dL blood
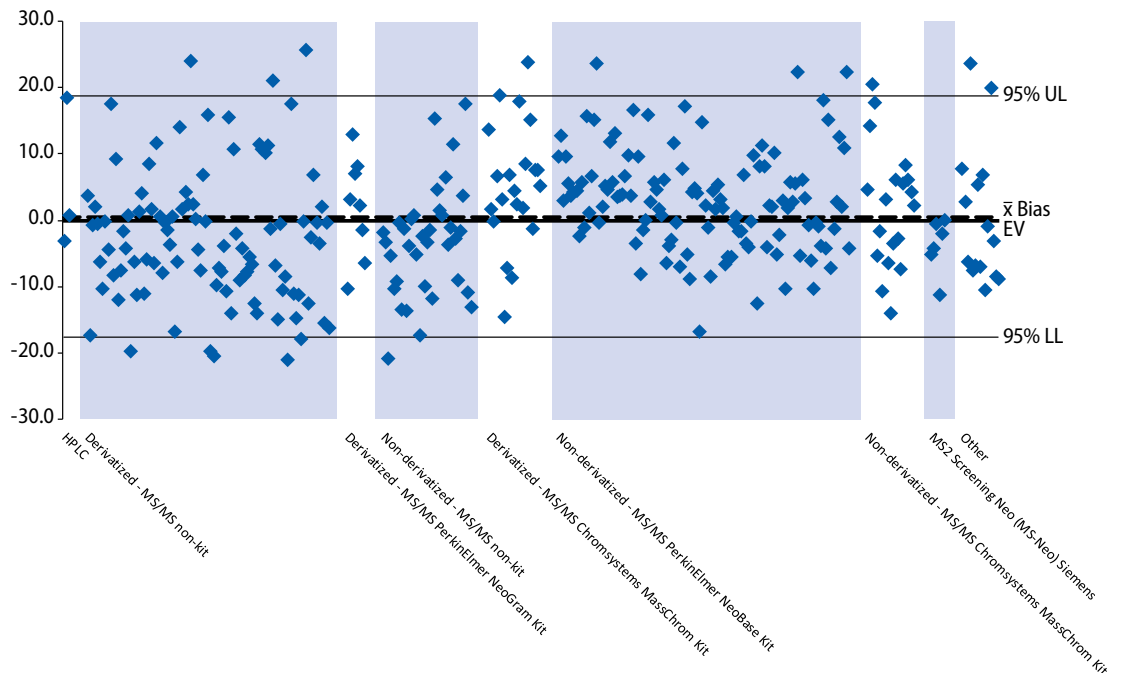
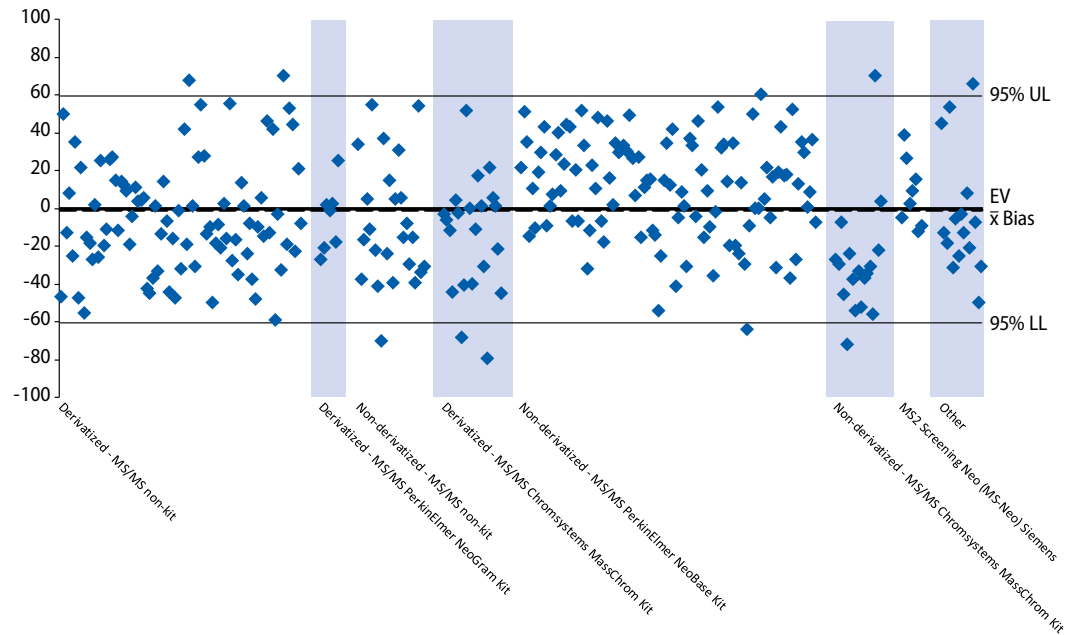**TGal** mg/dL blood

Quarter 1
Specimen 11715

Enriched — 25.0

CDC Assayed — 20.2

Participant Mean — 26.0

Participant Bias — 0.6
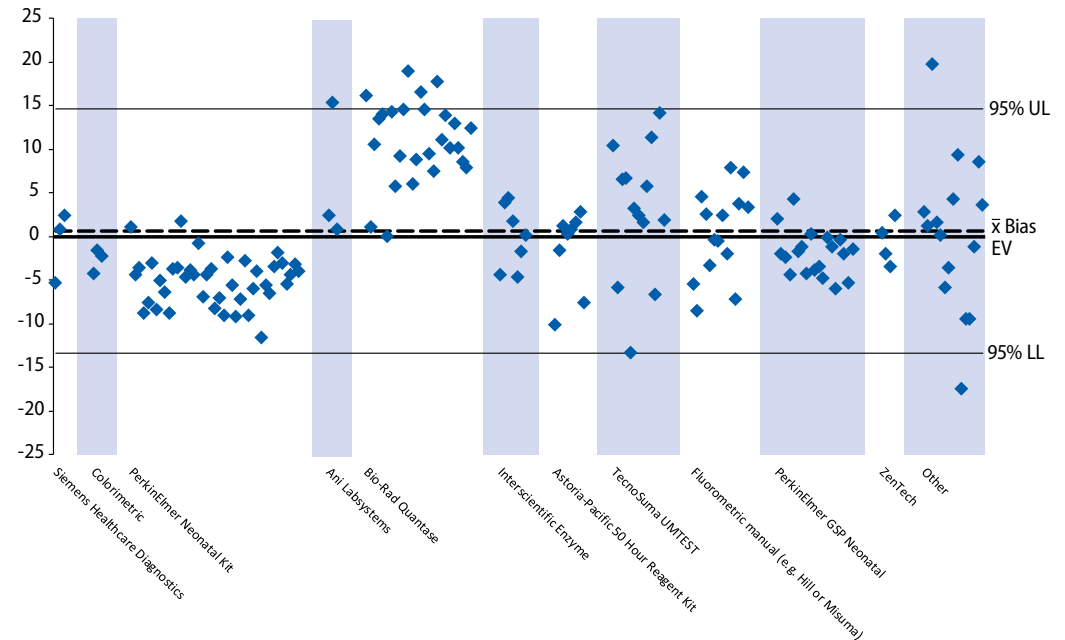
The TGal bias plot shows units of measure on the y-axis ranging from 25 mg/dL blood to -25 mg/dL blood. The bias for this plot is 0.6 mg/dL blood above zero. The TGal bias plot shows distinct differences between methods but a tight scatter within each method.

Figure 9. Reproducibility of Results:
Bias Plot of Total Immunoreactive Trypsinogen (IRT) Values by Method
Quarter 1, Specimen 11785
Expected Value (EV) = 207.7 ng/mL blood

IRT ng/mL blood

Quarter 1
Specimen 11785

Enriched — 350.0

CDC Assayed — 207.7

Participant Mean — 192.8

Participant Bias — -14.9
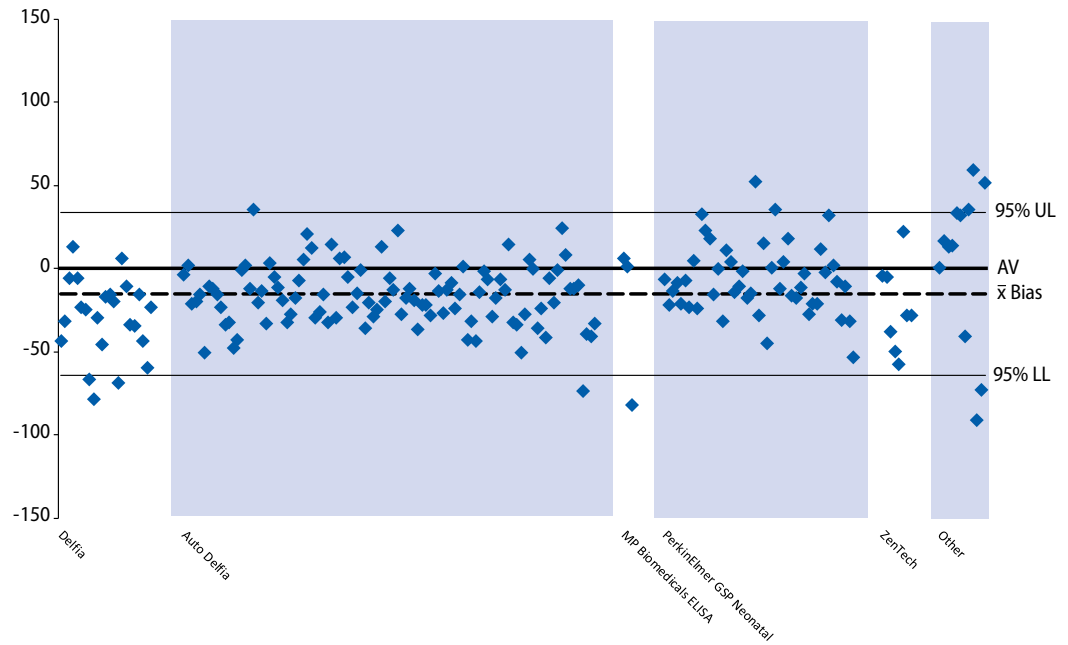
The IRT bias plot shows units of measure on the y-axis ranging from 150 ng/mL blood to -150 ng/mL blood. The bias for this plot is -14.9 ng/mL blood below zero. The IRT bias plot shows a slightly negative bias with consistent scatter among users and methods.

Figure 10. Reproducibility of Results:
Bias Plot of Arginine (Arg) Values by Method
Quarter 1, Specimen 11752
Expected Value (EV) = 12.0 μmol/L blood

Arg μmol/L blood

Quarter 1
Specimen 11752

Enriched — 0.0

CDC Assayed — 11.2

Participant Mean — 10.7

Participant Bias — -1.3
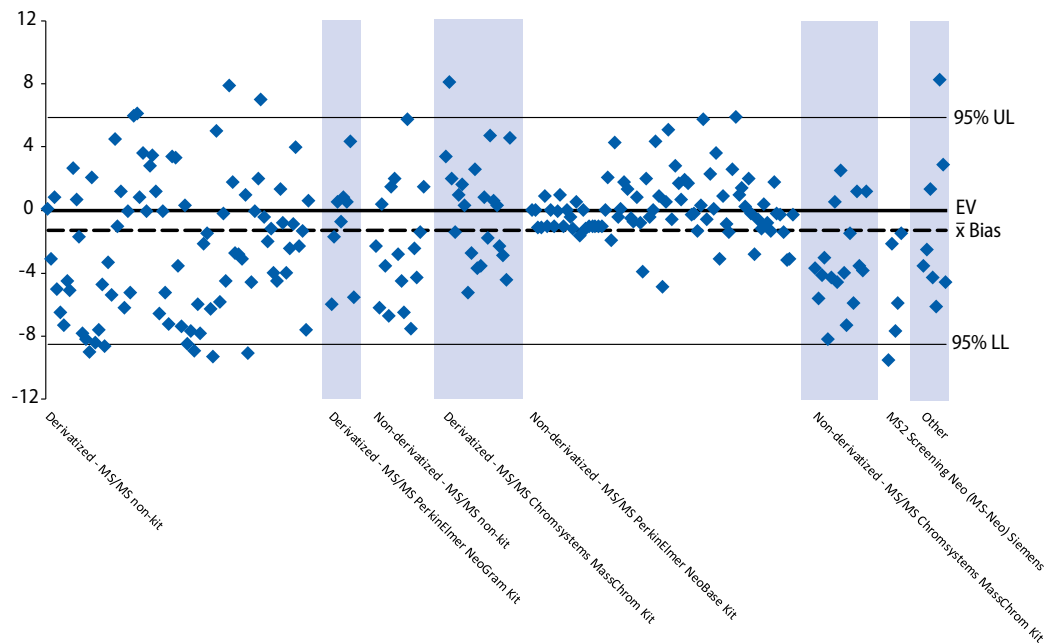
The Arg bias plot shows units of measure on the y-axis ranging from 12 μmol/L blood to -12 μmol/L blood. The bias for this plot is -1.3 μmol/L blood below zero. The Arg bias plot shows a slight negative bias with a tight scatter around the bias for most methods. One method, Non-derivatized-MS/MS PerkinElmer NeoBase Kit, shows a higher recovery among all participants for all users.

Figure 11. Reproducibility of Results:
Bias Plot of Citrulline (Cit) Values by Method
Quarter 1, Specimen 11753
Expected Value (EV) = 149.7 μmol/L blood

Cit μmol/L blood

Quarter 1
Specimen 11753

Enriched — 125.0

CDC Assayed — 124.5

Participant Mean — 142.9

Participant Bias — -6.8
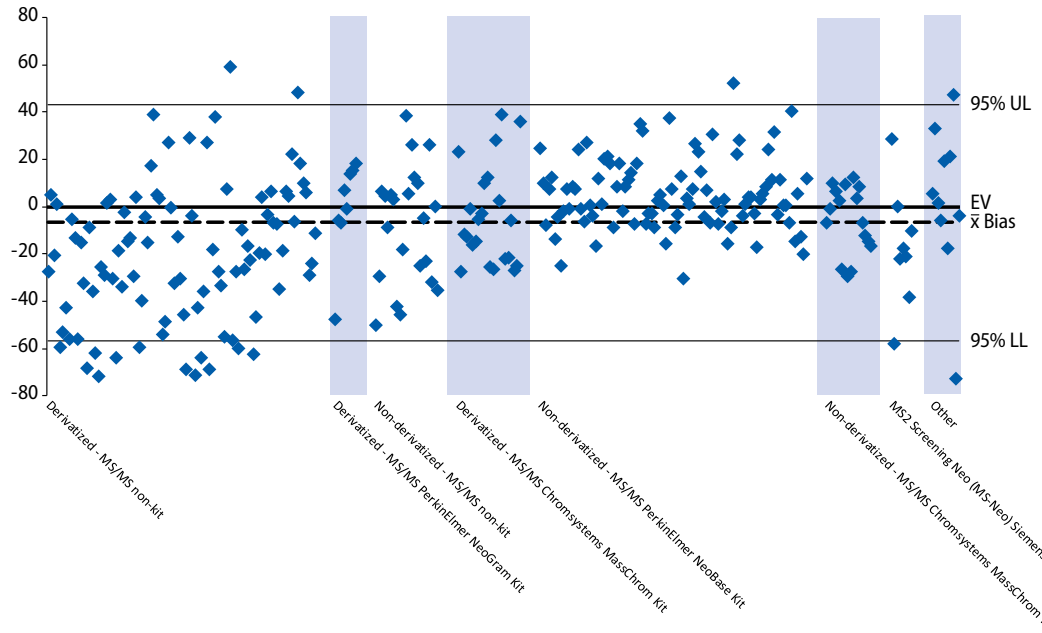
The Cit bias plot shows units of measure on the y-axis ranging from 80 μmol/L blood to -80 μmol/L blood. The bias for this plot is -6.8 μmol/L blood below zero. The Cit bias plot shows some methods with a tight cluster of values but with distinct differences between nonkit and kit methods.

Figure 12. Reproducibility of Results:
Bias Plot of Leucine (Leu) Values by Method
Quarter 3, Specimen 31753
Expected Value (EV) = 161.4 μmol/L blood

Leu μmol/L blood

Quarter 3
Specimen 31753

Enriched — 0.0

CDC Assayed — 157.5

Participant Mean — 146.1

Participant Bias — -15.3
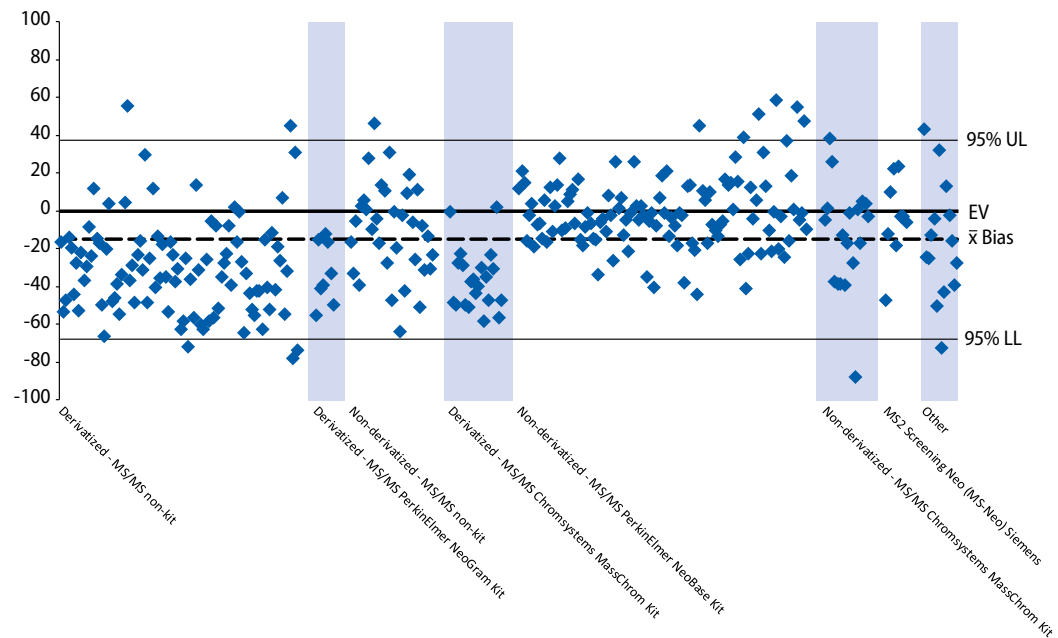
The Leu bias plot shows units of measure on the y-axis ranging from 100 μmol/L blood to -100 μmol/L blood. The bias for this plot is -15.3 μmol/L blood below zero. The Leu bias plot shows a negative bias with values scattered above and below the bias. One method, Non-derivatized-MS/MS PerkinElmer NeoBase Kit, shows most participants above the bias.

Figure 13. Reproducibility of Results:
Bias Plot of Methionine (Met) Values by Method
Quarter 1, Specimen 11752
Expected Value (EV) = 224.1 μmol/L blood

Met μmol/L blood

Quarter 1
Specimen 11752

Enriched — 200.0

CDC Assayed — 197.0

Participant Mean — 190.0

Participant Bias — -34.1
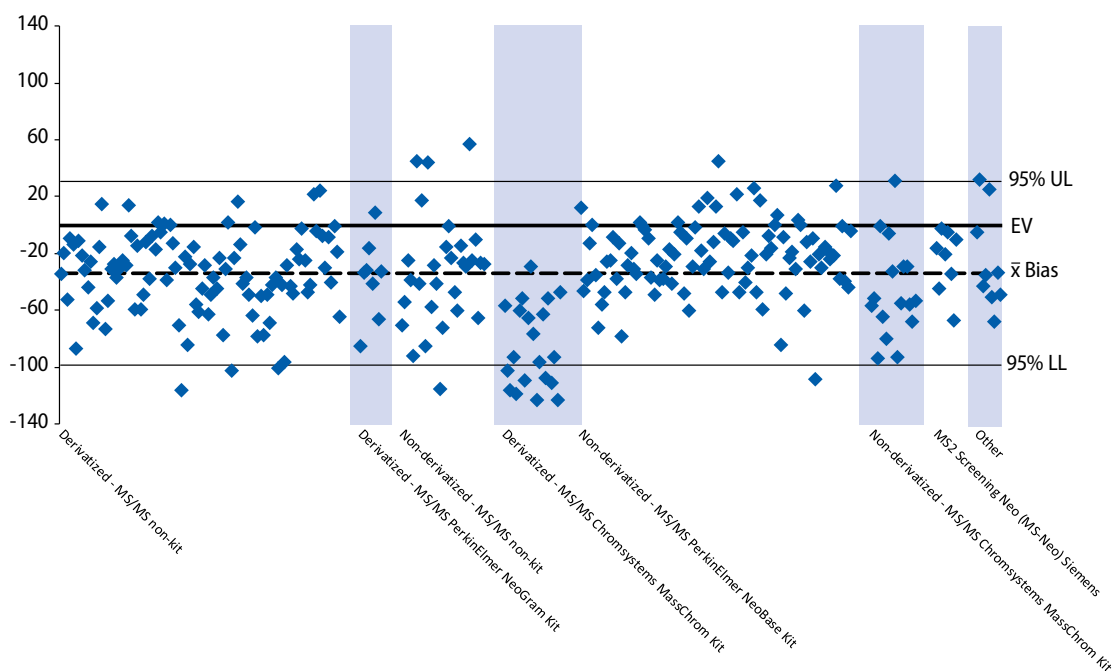
The Met bias plot shows units of measure on the y-axis ranging from 140 μmol/L blood to -140 μmol/L blood. The bias for this plot is -34.1 μmol/L blood below zero. The Leu bias plot shows a negative bias with values scattered above and below the bias. The Methionine bias plot shows a negative bias with a good scatter among users and methods.

Figure 14. Reproducibility of Results:
Bias Plot of Phenylalanine (Phe) Values by Method
Quarter 3, Specimen 31751
Expected Value (EV) = 49.6 μmol/L blood

Phe μmol/L blood

Quarter 3
Specimen 31751

Enriched — 0.0

CDC Assayed — 48.4

Participant Mean — 54.4

Participant Bias — 4.8
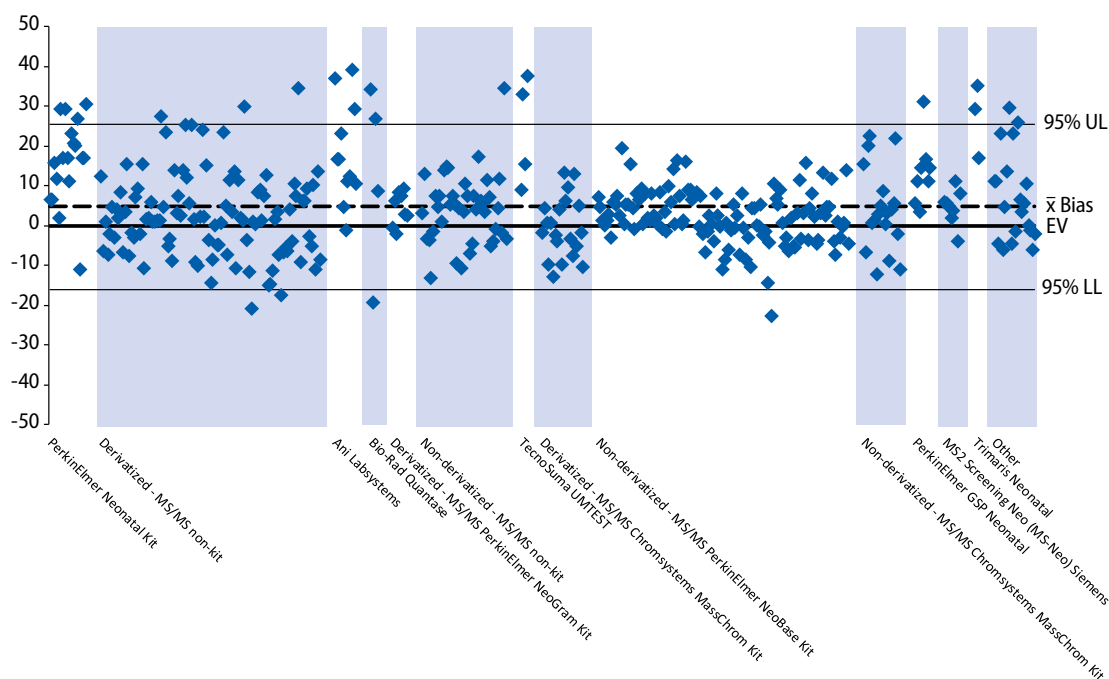
The Phe bias plot shows units of measure on the y-axis ranging from 50 μmol/L blood to -50 μmol/L blood. The bias for this plot is 4.8 μmol/L blood above zero. The Phe bias plot shows good agreement between laboratories and among methods and has a small participant bias when compared to the EV.

Figure 15. Reproducibility of Results:
Bias Plot of Succinylacetone (SUAC) Values by Method
Quarter 3, Specimen 31752
Expected Value (EV) = 20.4 μmol/L blood

SUAC μmol/L blood

Quarter 3
Specimen 31752

Enriched— 20.0

CDC Assayed— 6.6

Participant Mean— 7.8

Participant Bias— -12.6
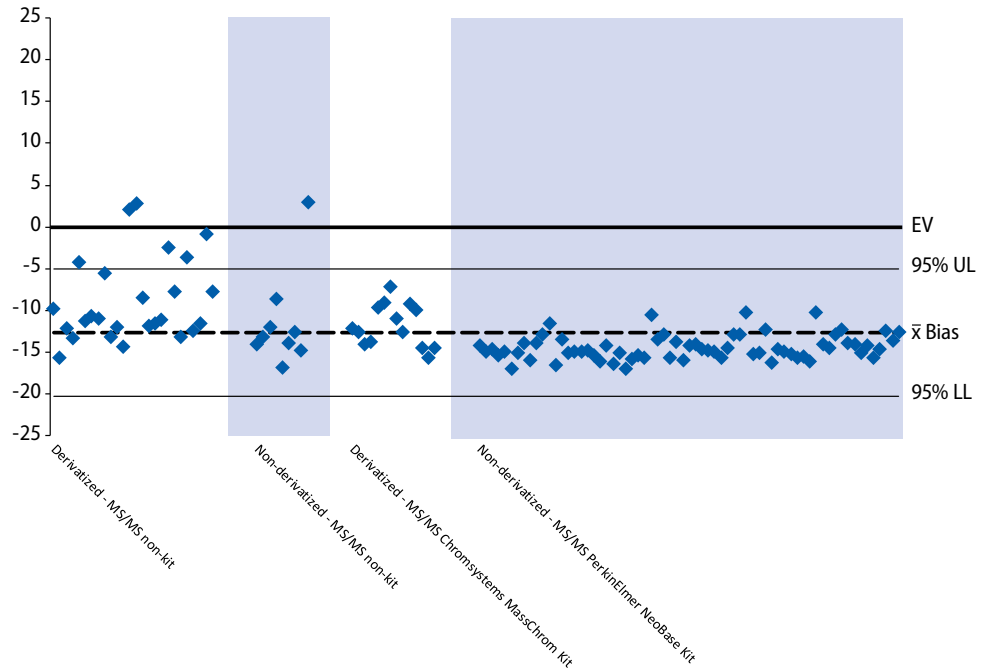
The SUAC bias plot shows units of measure on the y-axis ranging from 25 μmol/L blood to –25 μmol/L blood. The bias for this plot is –12.6 μmol/L blood below zero. The SUAC bias plot show a strong negative bias with consistent scatter among users and methods clustered around the bias result. However, few SUAC methods show good recoveries relative to the EV.

Figure 16. Reproducibility of Results:
Bias Plot of Tyrosine (Tyr) Values by Method
Quarter 3, Specimen 31753
Expected Value (EV) = 58.3 μmol/L blood

Tyr μmol/L blood

Quarter 3
Specimen 31753

Enriched— 0.0

CDC Assayed— 53.6

Participant Mean— 58.8

Participant Bias— 0.5

The Tyr bias plot shows units of measure on the y-axis ranging from 30 μmol/L blood to –30 μmol/L blood. The bias for this plot is 0.5 μmol/L blood above zero. The Tyr bias plot shows almost no bias from the CDC expected value. The plot shows good scatter among participants and methods.

Figure 17. Reproducibility of Results:
Bias Plot of Valine (Val) Values by Method
Quarter 3, Specimen 31751
Expected Value (EV) = 161.0 μmol/L blood

Val μmol/L blood

Quarter 3
Specimen 31751

Enriched— 0.0

CDC Assayed— 148.6

Participant Mean— 160.4

Participant Bias— -0.6

The Val bias plot shows units of measure on the y-axis ranging from 100 μmol/L blood to –100 μmol/L blood. The bias for this plot is -0.6 μmol/L blood below zero. There is almost no bias between the CDC expected value for Val. The plot shows good scatter among participants and methods.

Figure 18. Reproducibility of Results:
Bias Plot of Free Carnitine (C0(L)) Values by Method
Quarter 3, Specimen 31761
Assayed Value = 12.92 μmol/L blood

C0(L) μmol/L blood

Quarter 3
Specimen 31761

Enriched— 0.00

CDC Assayed— 17.10

Participant Mean— 14.17

Participant Bias— 1.25
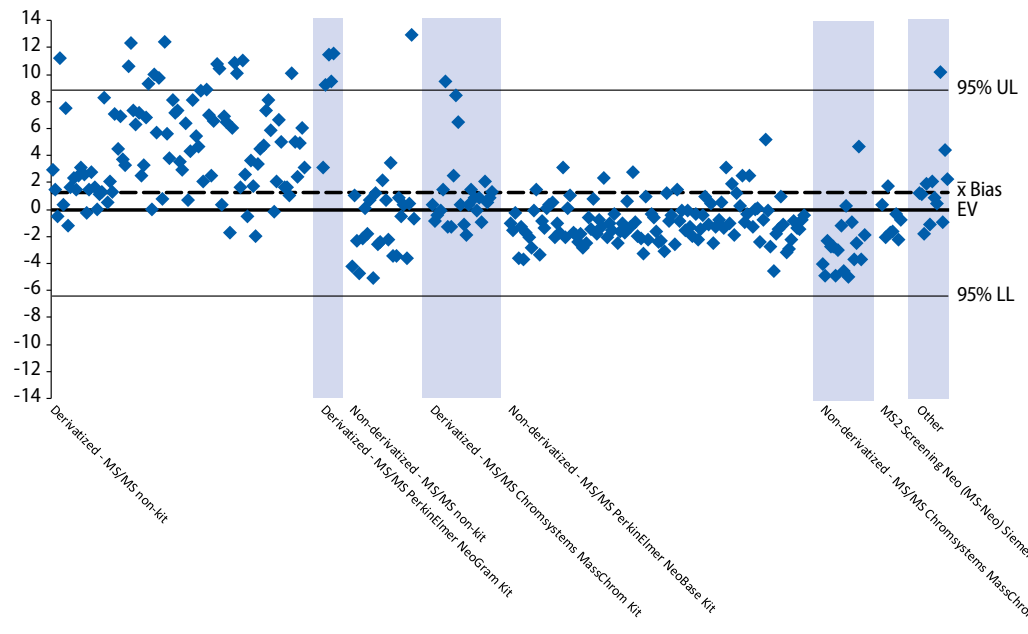
The C0(L) bias plot shows units of measure on the y-axis ranging from 14 μmol/L blood to –14 μmol/L blood. The bias for this plot is -1.25 μmol/L blood below zero. The C0 (L) bias plot shows a slight positive bias for most methods with the exception of one method showing a negative bias for all users.

Figure 19. Reproducibility of Results:
Bias Plot of Propionylcarnitine (C3) Values by Method
Quarter 3, Specimen 31761
Expected Value (EV) = 12.72 μmol/L blood

C3 μmol/L blood

Quarter 3
Specimen 31761

Enriched — 12.00

CDC Assayed — 14.97

Participant Mean — 12.63

Participant Bias — -0.09
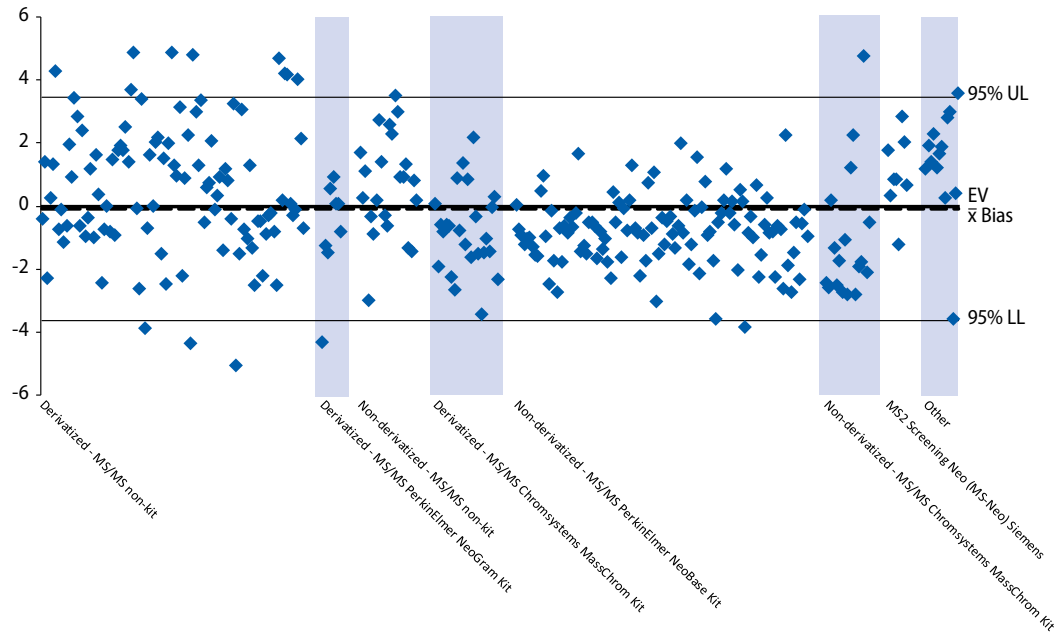
The C3 bias plot shows units of measure on the y-axis ranging from 6 μmol/L blood to –6 μmol/L blood. The bias for this plot is –0.09 μmol/L blood below zero. The C3 data show good agreement between the expected value and bias and show a tight scatter among all participants.

Figure 20. Reproducibility of Results:
Bias Plot of Malonylcarnitine (C3DC) Values by Method
Quarter 3, Specimen 31761
Expected Value (EV) = 3.52 μmol/L blood

C3DC μmol/L blood

Quarter 3
Specimen 31761

Enriched — 3.50

CDC Assayed — 2.75

Participant Mean — 2.18

Participant Bias — -1.34
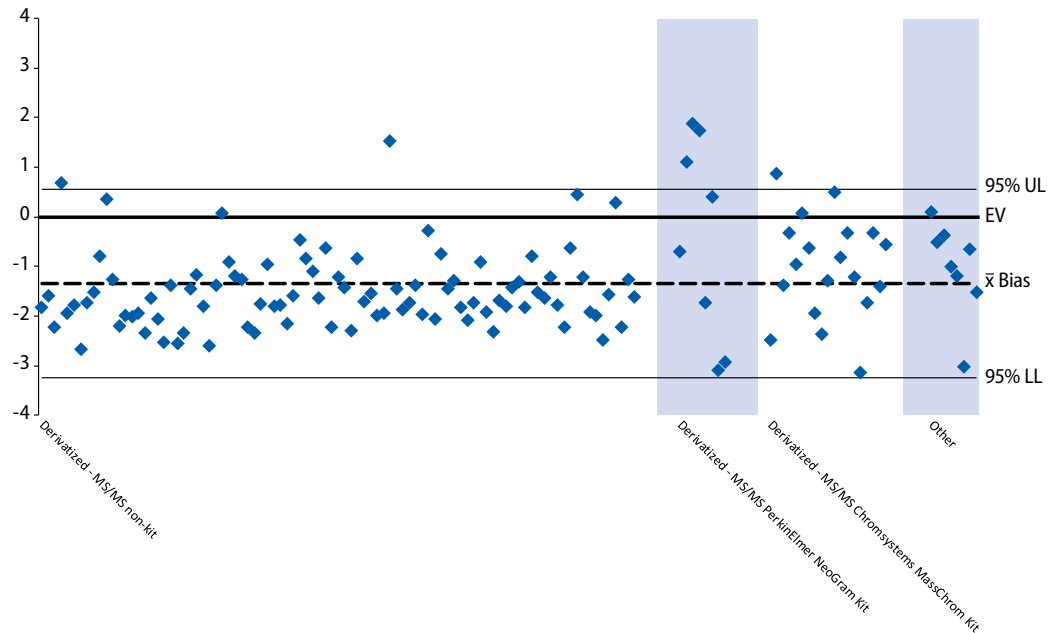
The C3DC bias plot shows units of measure on the y-axis ranging from 4 μmol/L blood to –4 μmol/L blood. The bias for this plot is –1.34 μmol/L blood below zero. The C3DC bias plot shows a negative bias among most participants across all methods.

Figure 21. Reproducibility of Results: Bias Plot of Malonylcarnitine + Hydroxybutyrylcarnitine (C3DC+C4OH) Values by Method
Quarter 3, Specimen 31761
Expected Value (EV) = 3.54 μmol/L blood

C3DC+C4OH
μmol/L blood

Quarter 3
Specimen 31761

Enriched — 3.50

CDC Assayed — 0.27

Participant Mean — 0.62

Participant Bias — -2.92
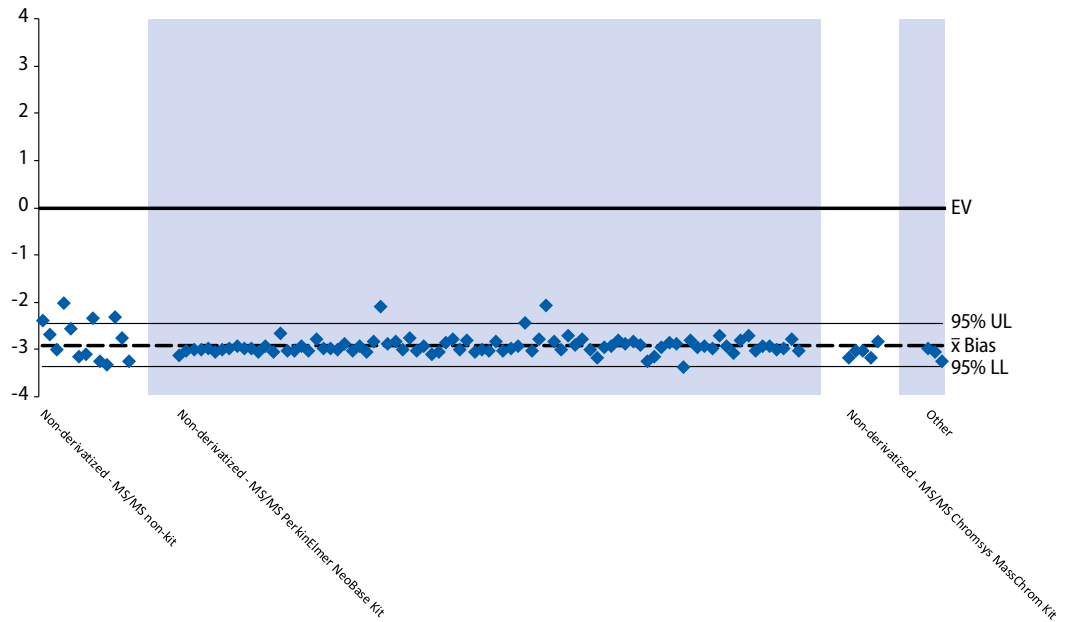
The C3DC+C4OH bias plot shows units of measure on the y-axis ranging from 4.00 μmol/L blood to -4.00 μmol/L blood. The bias for this plot is -2.92 μmol/L blood below zero. The C3DC+C4OH bias plot shows a strong negative bias with tight scatter around the bias among all methods.

Figure 22. Reproducibility of Results: Bias Plot of Butylcarnitine (C4) Values by Method
Quarter 3, Specimen 31762
Expected Value (EV) = 0.20 μmol/L blood

C4 μmol/L blood

Quarter 3
Specimen 31752

Enriched — 0.00

CDC Assayed — 0.21

Participant Mean — 0.21

Participant Bias — 0.01
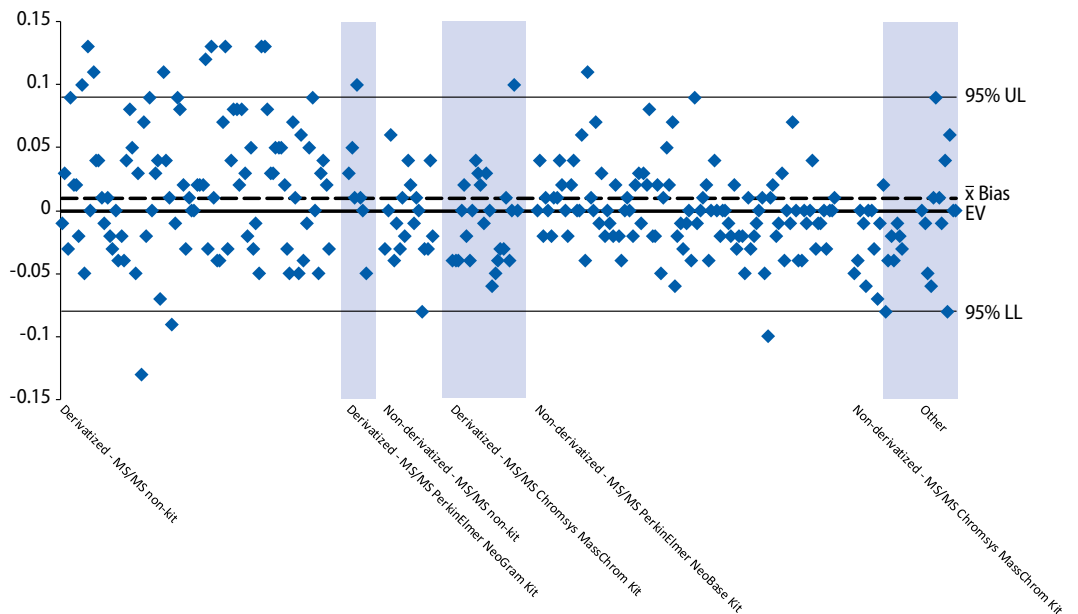
The C4 bias plot shows units of measure on the y-axis ranging from 0.15 μmol/L blood to -0.15 μmol/L blood. The bias for this plot is -0.01 μmol/L blood below zero. The C4 bias plot shows a slight positive bias with consistent scatter across all methods.

Figure 23. Reproducibility of Results:
Bias Plot of Hydroxybutyrylcarnitine (C4OH) Values by Method
Quarter 3, Specimen 31762
Expected Value (EV) = 0.11 μmol/L blood

C4OH μmol/L blood

Quarter 3
Specimen 31762

Enriched—0.00

CDC Assayed—0.15

Participant Mean—0.15

Participant Bias— 0.04
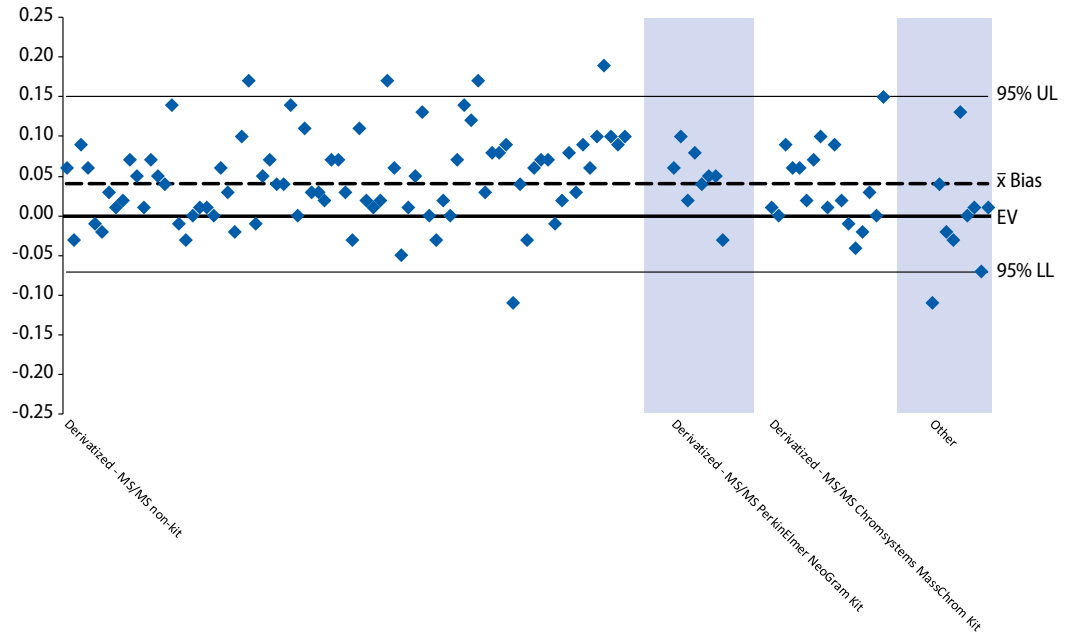
The C4OH bias plot shows units of measure on the y-axis ranging from 0.25 μmol/L blood to -0.25 μmol/L blood. The bias for this plot is 0.04 μmol/L blood above zero. The C4OH bias plot shows a positive bias with most methods clustered around the bias line above the EV.

Figure 24. Reproducibility of Results:
Bias Plot of Isovalerylcarnitine (C5) Values by Method
Quarter 3, Specimen 31763
Expected Value (EV) = 1.63 μmol/L blood

C5 μmol/L blood

Quarter 3
Specimen 31763

Enriched—1.50

CDC Assayed—1.61

Participant Mean—1.47

Participant Bias— -0.16
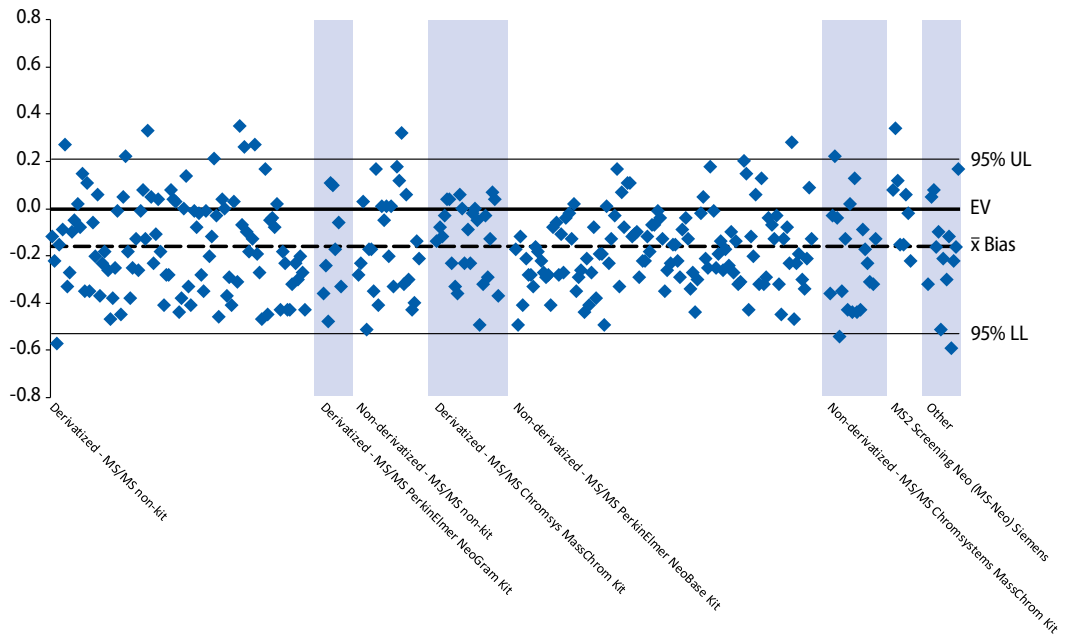
The C5 bias plot shows units of measure on the y-axis ranging from 0.8 μmol/L blood to -0.8μmol/L blood. The bias for this plot is -0.16 μmol/L blood below zero. The C5 bias plots show values that are minimally scattered around the slightly negative bias.

Figure 25. Reproducibility of Results:
Bias Plot of Tiglylcarnitine (C5:1) Values by Method
Quarter 3, Specimen 31762
Expected Value (EV) = 1.02 μmol/L blood

C5:1 μmol/L blood

Quarter 3
Specimen 31762

Enriched — 1.00

CDC Assayed — 1.12

Participant Mean — 1.00

Participant Bias — -0.02
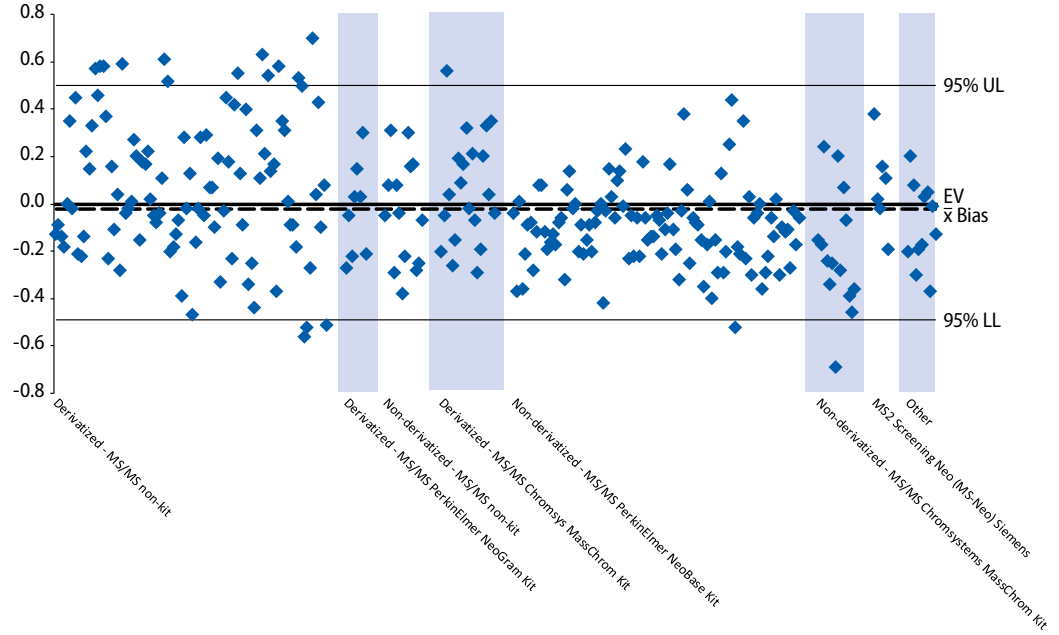
The C5:1 bias plot shows units of measure on the y-axis ranging from 0.8 μmol/L blood to -0.8 μmol/L blood. The bias for this plot is -0.02 μmol/L blood below zero. The C5:1 bias plot shows good agreement with the EV and good scatter among participants and methods.

Figure 26. Reproducibility of Results:
Bias Plot of Glutarylcarnitine (C5DC) Values by Method
Quarter 3, Specimen 31761
Expected Value (EV) = 1.31 μmol/L blood

C5DC μmol/L blood

Quarter 3
Specimen 31761

Enriched — 1.30

CDC Assayed — 1.28

Participant Mean — 1.30

Participant Bias — -0.01
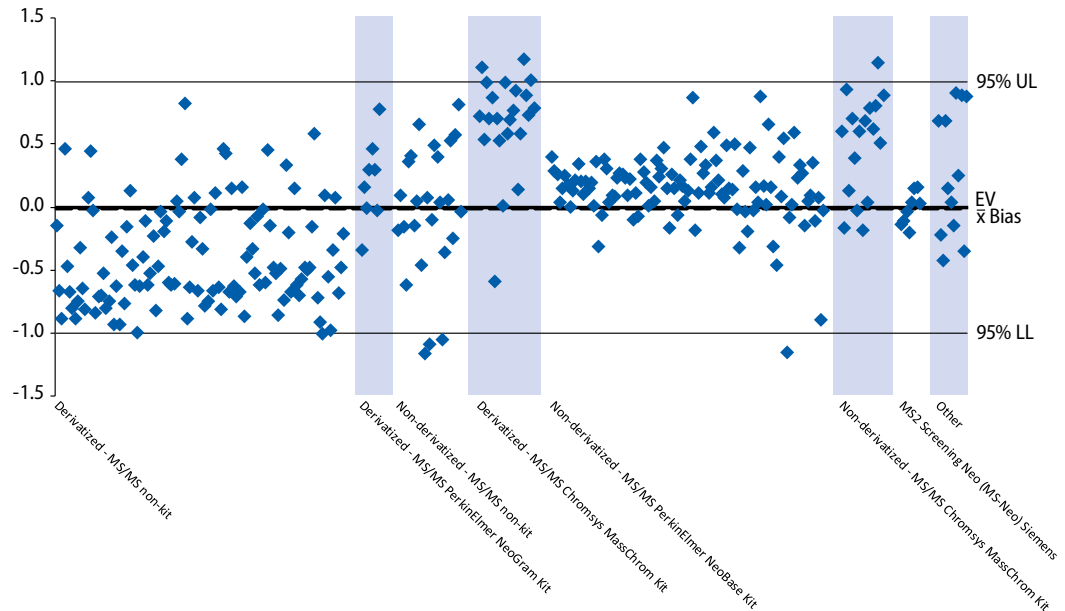
The C5DC bias plot shows units of measure on the y-axis ranging from 1.5 μmol/L blood to -1.5 μmol/L blood. The bias for this plot is -0.01 μmol/L blood below zero. The C5DC bias plot show a tight scatter within each method, with nonkit methods showing a negative bias and most kit methods showing a positive bias.

Figure 27. Reproducibility of Results:
Bias Plot of Hydroxyisovalerylcarnitine (C5OH) Values by Method
Quarter 3, Specimen 31763
Expected Value (EV) = 0.71 μmol/L blood

C5OH μmol/L blood

Quarter 3
Specimen 31763

Enriched—0.0

CDC Assayed—0.72

Participant Mean—0.55

Participant Bias— -0.16
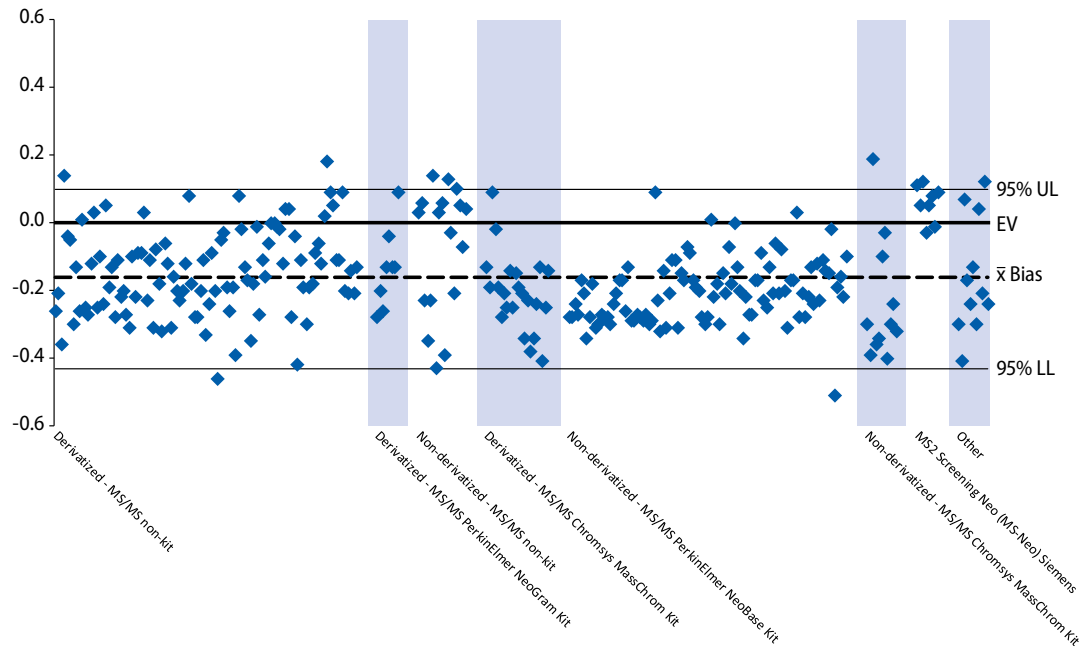
The C5OH bias plot shows units of measure on the y-axis ranging from 0.6 μmol/L blood to -0.6 μmol/L blood. The bias for this plot is -0.16 μmol/L blood below zero. The C5OH bias plot shows a slight negative bias but good scatter among most methods.

Figure 28. Reproducibility of Results:
Bias Plot of Hexanoylcarnitine (C6) Values by Method
Quarter 3, Specimen 31765
Expected Value (EV) = 1.53 μmol/L blood

C6 μmol/L blood

Quarter 3
Specimen 31765

Enriched—1.50

CDC Assayed—1.24

Participant Mean—1.33

Participant Bias— -0.2
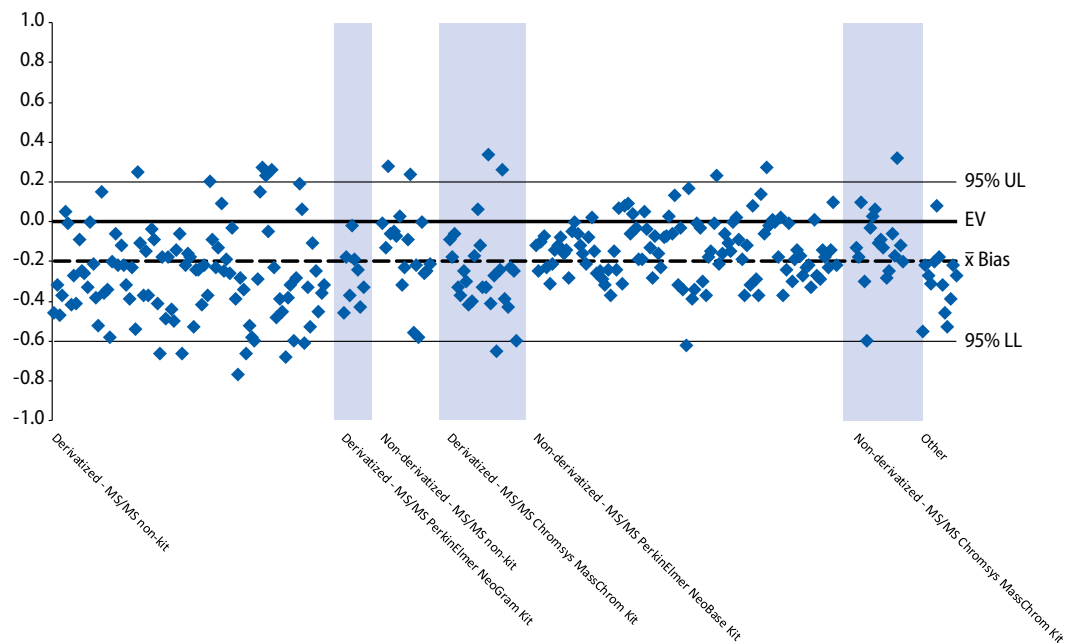
The C6 bias plot shows units of measure on the y-axis ranging from 1.0 μmol/L blood to -1.0 μmol/L blood. The bias for this plot is -0.2 μmol/L blood below zero. The C6 bias plot shows a slight negative participant bias with tight scatter around bias.

Figure 29. Reproducibility of Results:
Bias Plot of Octanylcarnitine (C8) Values by Method
Quarter 3, Specimen 31765
Expected Value (EV) = 1.59 μmol/L blood

C8 μmol/L blood

Quarter 3
Specimen 31765

Enriched— 1.50

CDC Assayed— 1.70

Participant Mean— 1.53

Participant Bias— -0.06
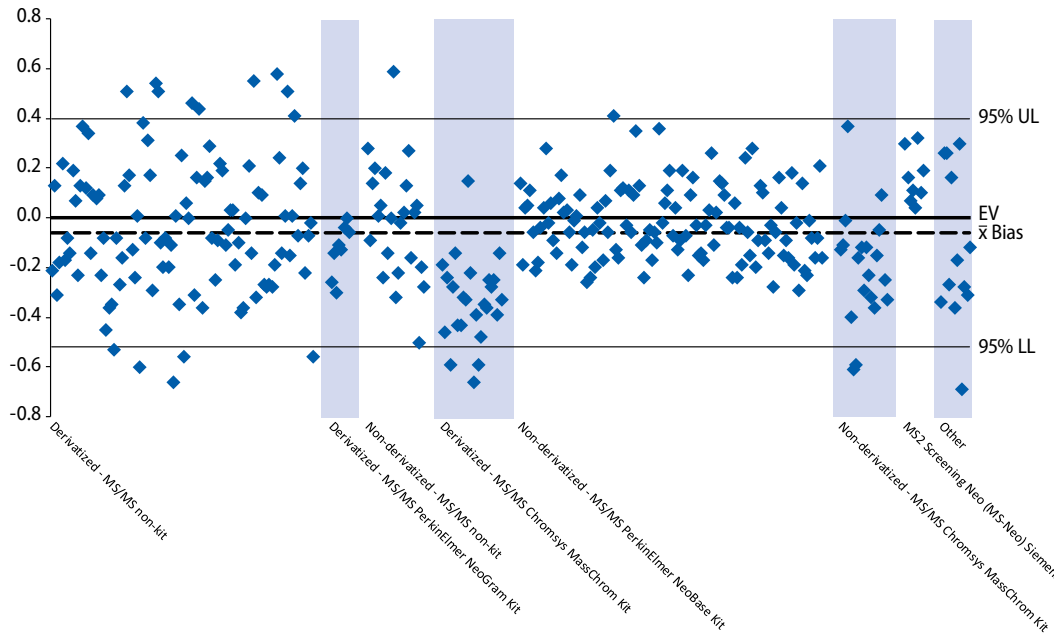
The C8 bias plot shows units of measure on the y-axis ranging from 0.8 μmol/L blood to -0.8 μmol/L blood. The bias for this plot is -0.06 μmol/L blood below zero. The C8 bias plot shows tight scatter around the expected value.

Figure 30. Reproducibility of Results:
Bias Plot of Decanoylcarnitine (C10) Values by Method
Quarter 1, Specimen 11762
Expected Value (EV) = 0.15 μmol/L blood

C10 μmol/L blood

Quarter 1
Specimen 11762

Enriched— 0.00

CDC Assayed— 0.17

Participant Mean— 0.18

Participant Bias— 0.03
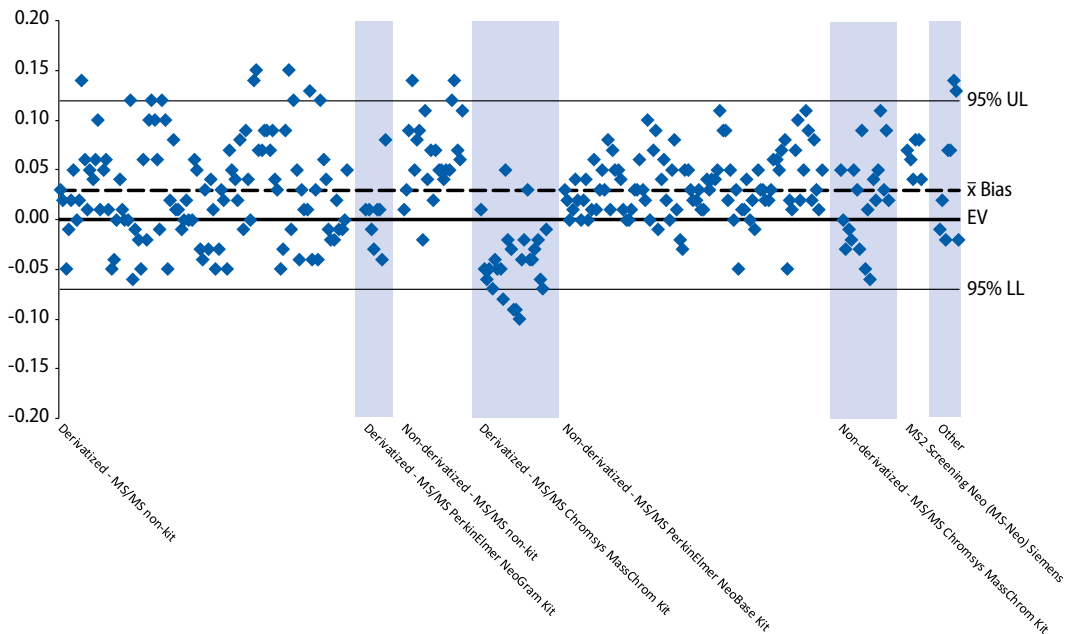
The C10 bias plot shows units of measure on the y-axis ranging from 0.20 μmol/L blood to -0.20 μmol/L blood. The bias for this plot is 0.03 μmol/L blood above zero. The C10 bias plot shows reasonable scatter among all participants and methods around a slightly positive bias.

Figure 31. Reproducibility of Results:
Bias Plot of Decenoylcarnitine (C10:1) Values by Method
Quarter 1, Specimen 11763
Expected Value (EV) = 1.00 µmol/L blood

C10:1 µmol/L blood

Quarter 1
Specimen 11763

Enriched — 1.00

CDC Assayed — 1.25

Participant Mean — 0.94

Participant Bias — -0.06
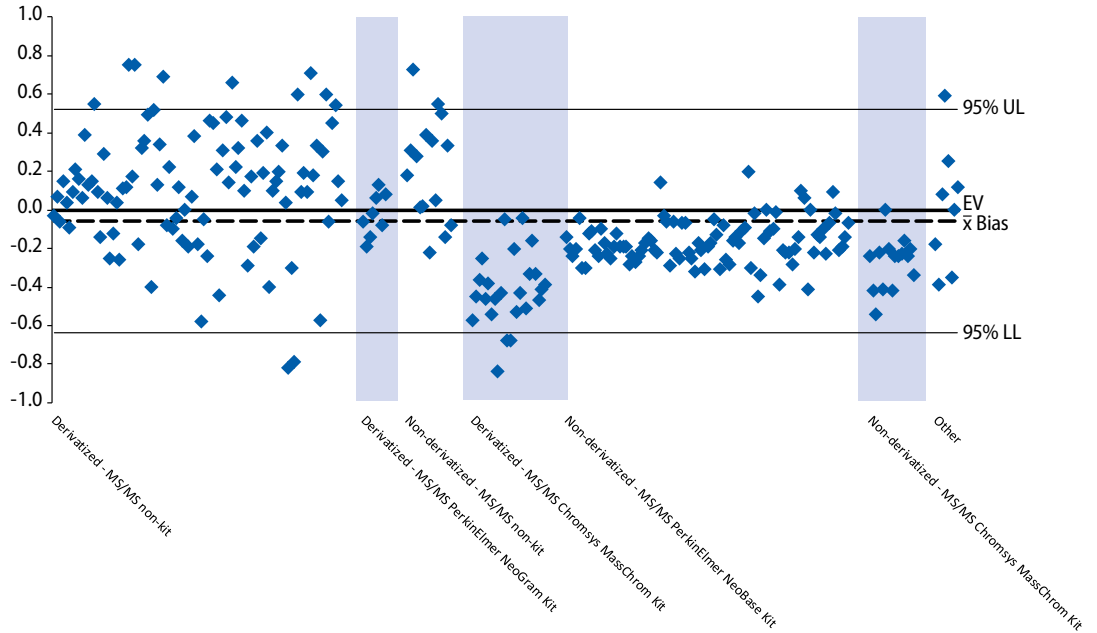
The C10:1 bias plot shows units of measure on the y-axis ranging from 1.0 µmol/L blood to -1.0 µmol/L blood. The bias for this plot is -0.06 µmol/L blood below zero. The C10:1 bias plot shows a slight positive bias among kit methods and a slight negative bias among nonkit methods.

Figure 32. Reproducibility of Results:
Bias Plot of Decadienoylcarnitine (C10:2) Values by Method
Quarter 1, Specimen 11764
Expected Value (EV) = 0.91 µmol/L blood
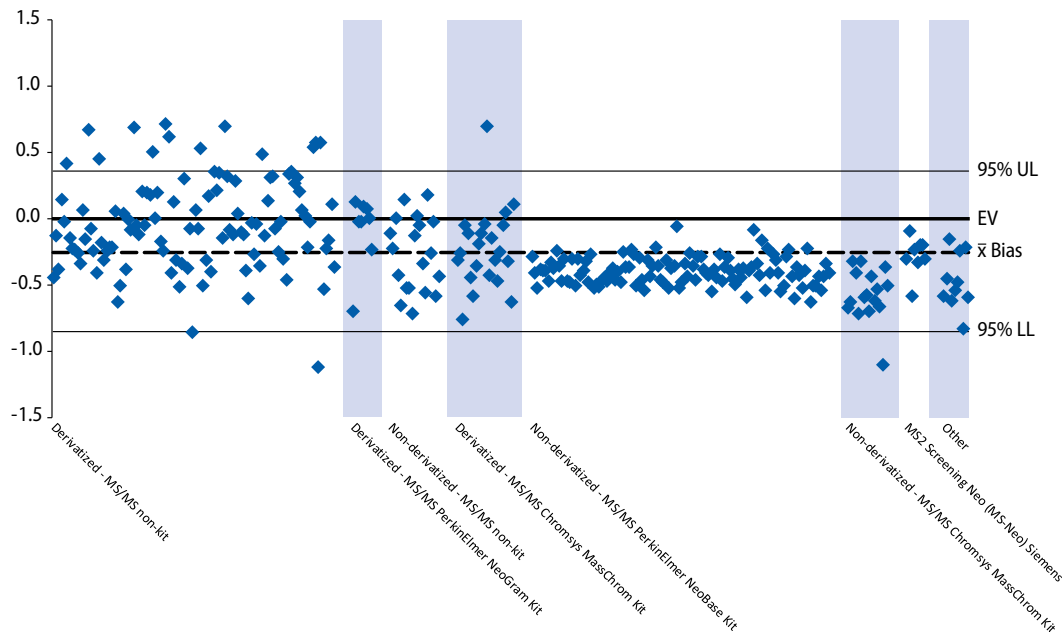
C10:2 µmol/L blood

Quarter 1
Specimen 11764

Enriched — 0.90

CDC Assayed — 1.07

Participant Mean — 0.74

Participant Bias — -0.17
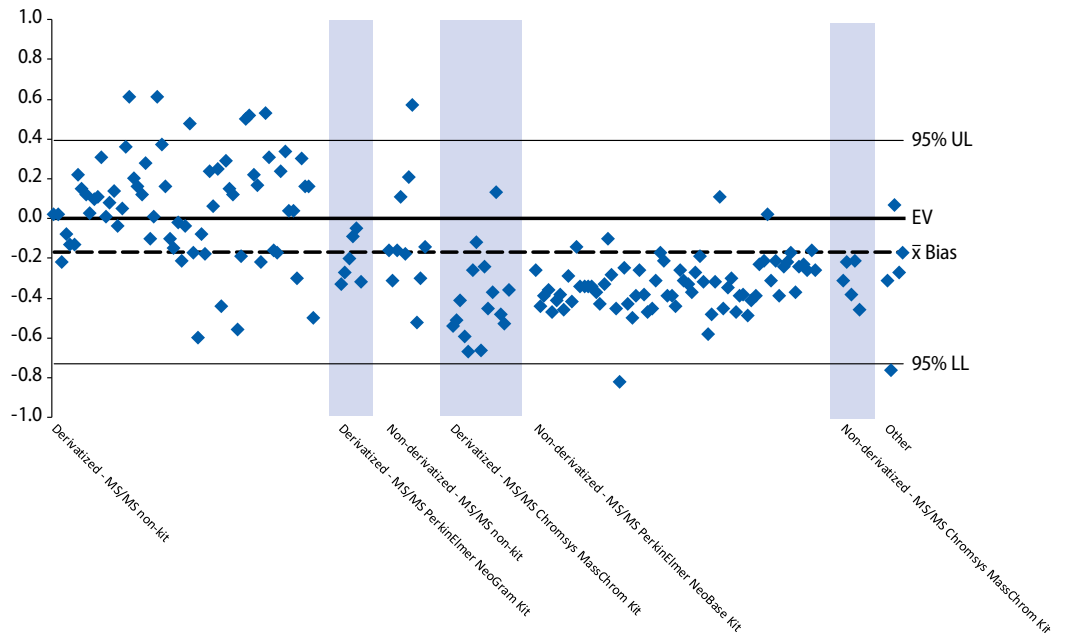
The C10:2 bias plot shows units of measure on the y-axis ranging from 1.0 µmol/L blood to -1.0 µmol/L blood. The bias for this plot is -0.17 µmol/L blood below zero. The C10:2 bias plot shows a slight positive bias among nonkit methods and a slight negative bias among kit methods.

Figure 33. Reproducibility of Results:
Bias Plot of Myristoylcarnitine (C14) Values by Method
Quarter 3, Specimen 31762
Expected Value (EV) = 0.12 µmol/L blood

C14 µmol/L blood

Quarter 3
Specimen 31762

Enriched — 0.00

CDC Assayed — 0.16

Participant Mean — 0.15

Participant Bias — 0.03
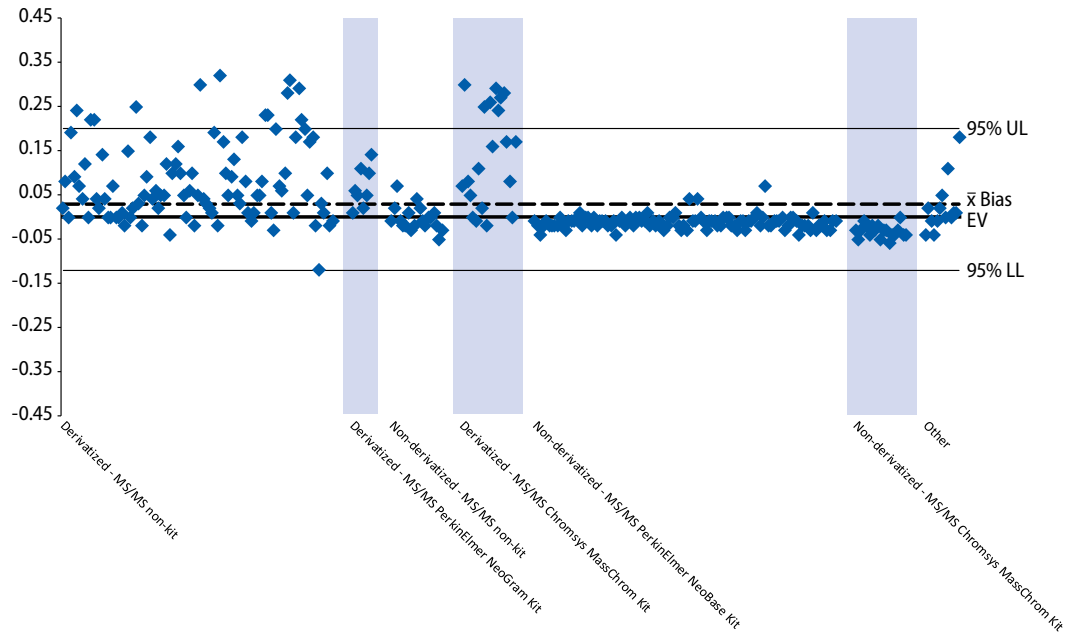
The C14 bias plot shows units of measure on the y-axis ranging from 0.45 µmol/L blood to -0.45 µmol/L blood. The bias for this plot is 0.03 µmol/L blood above zero. The C14 bias plot shows a slight positive bias for nonkit MS/MS methods. The nonkit MS/MS methods show a tight cluster of values slightly below the EV.

Figure 34. Reproducibility of Results:
Bias Plot of Tetradecenoylcarnitine (C14:1) Values by Method
Quarter 3, Specimen 31761
Expected Value (EV) = 1.32 µmol/L blood

C14:1 µmol/L blood

Quarter 3
Specimen 31761

Enriched — 1.30

CDC Assayed — 1.13

Participant Mean — 1.07

Participant Bias — -0.25

The C14:1 bias plot shows units of measure on the y-axis ranging from 1.5 µmol/L blood to -1.5 µmol/L blood. The bias for this plot is -0.25 µmol/L blood below zero. The C14:1 bias plot shows reasonable scatter but two MS/MS kit methods show a negatively clustered bias.

Figure 35. Reproducibility of Results:
Bias Plot of Palmitoylcarnitine (C16) Values by Method
Quarter 3, Specimen 31763
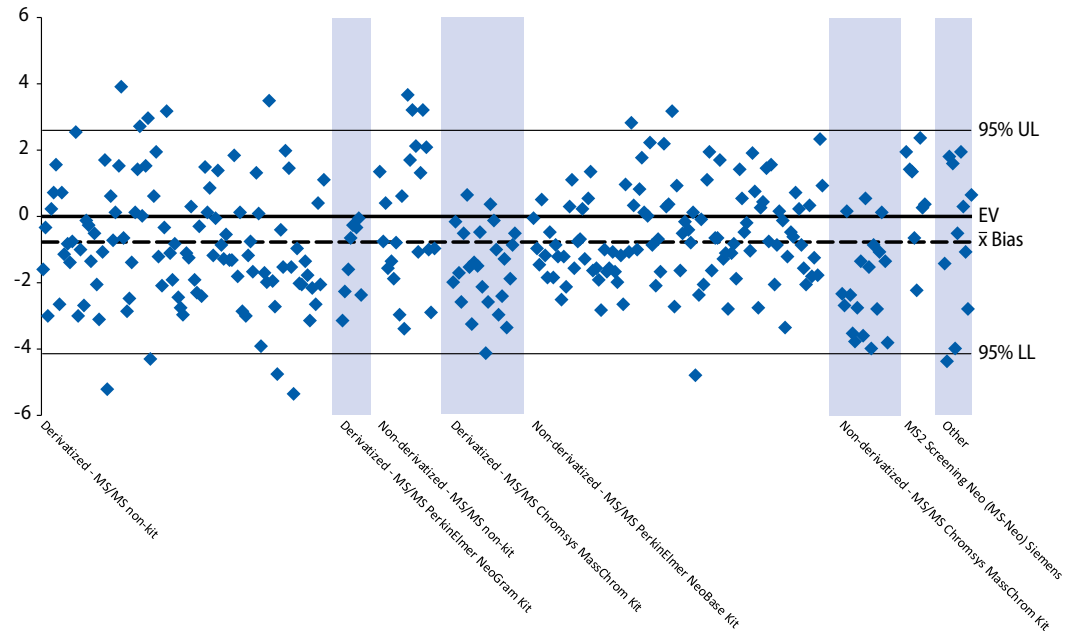## Expected Value (EV) = 12.76 μmol/L blood

C16 μmol/L blood

Quarter 3
Specimen 31763

Enriched — 12.00

CDC Assayed — 13.04

Participant Mean — 11.99

Participant Bias — -0.77

The C16 bias plot shows units of measure on the y-axis ranging from 6 μmol/L blood to -6 μmol/L blood. The bias for this plot is -0.77 μmol/L blood below zero. The C16 bias plot shows a slight negative bias with good scatter among all participants and all methods.

Figure 36. Reproducibility of Results:
Bias Plot of Hydroxypalmitoycarnitine (C16OH) Values by Method
Quarter 3, Specimen 31762
Expected Value (EV) = 0.82 μmol/L blood

C16OH μmol/L blood

Quarter 3
Specimen 31762

Enriched — 0.80

CDC Assayed — 0.94

Participant Mean — 0.56

Participant Bias — -0.26
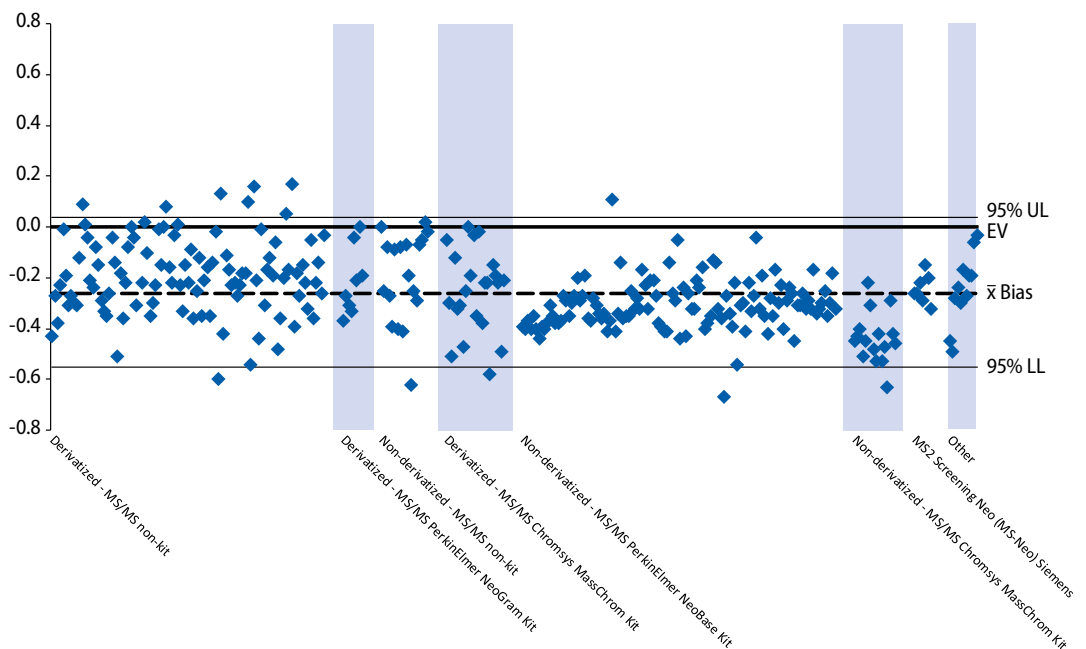
The C16OH bias plot shows units of measure on the y-axis ranging from 0.8 μmol/L blood to -0.8 μmol/L blood. The bias for this plot is -0.26 μmol/L blood below zero. The C16OH bias plot demonstrates consistent scatter among all methods with most laboratories showing a negative bias.

Figure 37. Reproducibility of Results:
Bias Plot of Stearoylcarnitine (C18) Values by Method
Quarter 3, Specimen 31761
Expected Value (EV) = 5.56 μmol/L blood

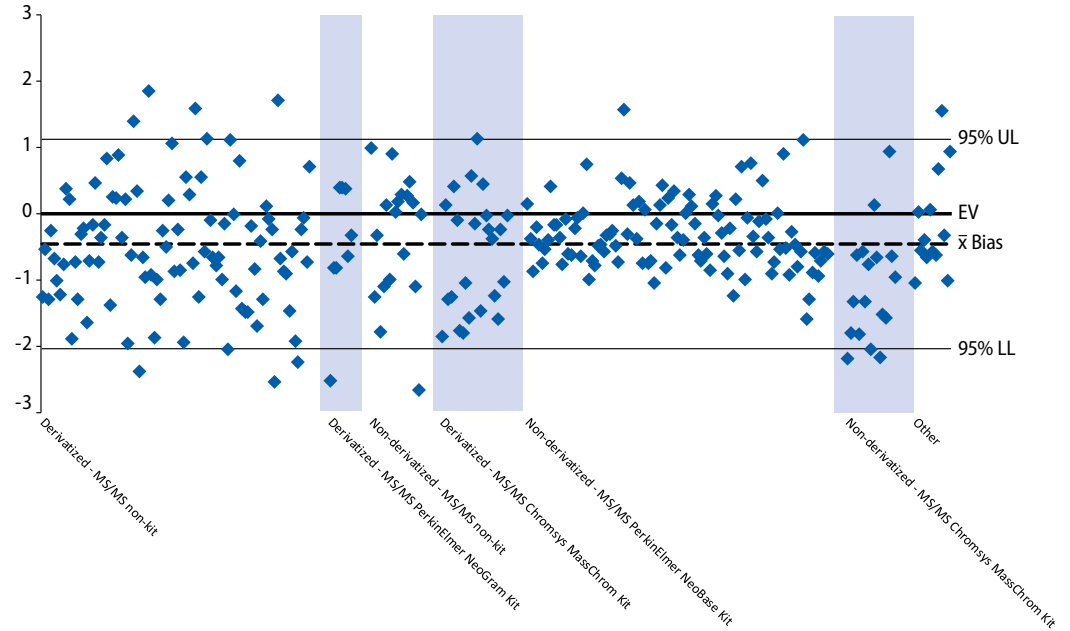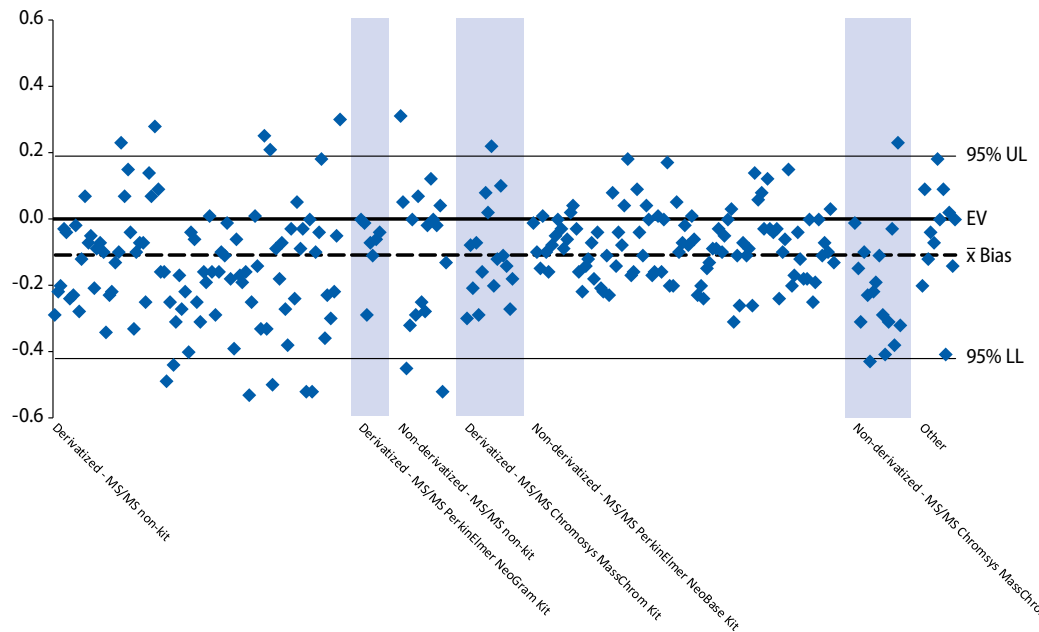**C18** μmol/L blood

Quarter 3
Specimen 31761

  Enriched — 5.00

  CDC Assayed — 5.32

  Participant Mean — 5.11

  Participant Bias — -0.45

The C18 bias plot shows units of measure on the y-axis ranging from 3 μmol/L blood to -3 μmol/L blood. The bias for this plot is -0.45 μmol/L blood below zero. The C18 bias plot illustrates a reasonable scatter of values within and among methods while showing a slight negative bias.

Figure 38. Reproducibility of Results:
Bias Plot of Oleoylcarnitine (C18:1) Values by Method
Quarter 3, Specimen 31765
Expected Value (EV) = 0.92 μmol/L blood

C18:1 μmol/L blood

Quarter 3
Specimen 31765

  Enriched — 0.0

  CDC Assayed — 0.90

  Participant Mean — 0.81

  Participant Bias — -0.11
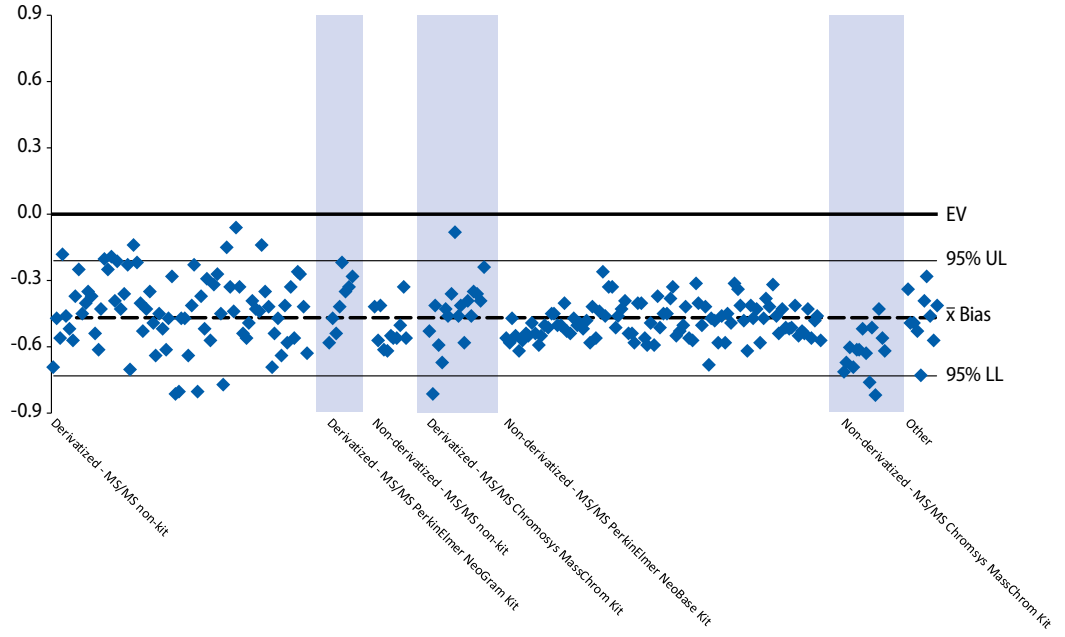

The C18:1 bias plot shows units of measure on the y-axis ranging from 0.6 μmol/L blood to -0.6 μmol/L blood. The bias for this plot is -0.11 μmol/L blood below zero. The C18:1 shows a negative participant bias with good scatter among all methods.

Figure 39. Reproducibility of Results:
Bias Plot of Hydroxystearoylcarnitine (C18OH) Values by Method
Quarter 3, Specimen 31762
Expected Value (EV) = 1.01 μmol/L blood

C18OH μmol/L blood

Quarter 3
Specimen 31762

Enriched — 1.00

CDC Assayed — 0.64

Participant Mean — 0.54

Participant Bias — -0.47

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 bias for this plot is -0.47 μmol/L blood below zero. This C18OH plot shows a negative bias with all methods clustered around the bias.

Appendix for Accessibility Descriptions

Figure 4: 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 within it, 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"
7. A down arrow from the oval contains a solid oval within it, and the words, "IF 'YES'". The down arrow points to a final oval containing the words: FALSE NEGATIVE OR FALSE POSITIVE ERROR

Figures 5–39, 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.

Notes:

CS 290517-A