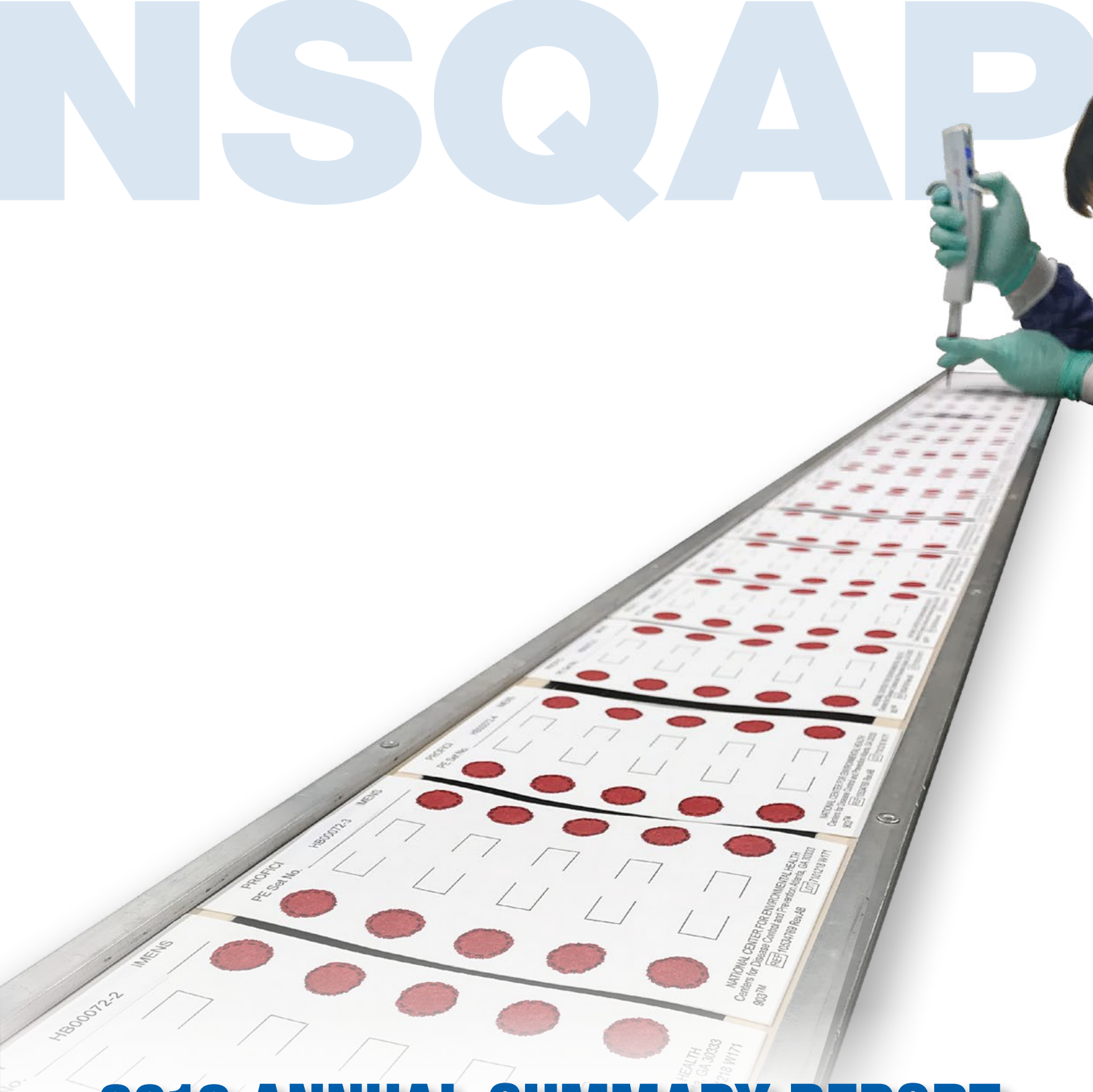
NSQAP



2018 ANNUAL SUMMARY REPORT

Newborn Screening Quality Assurance Program

Centers for Disease Control and Prevention
National Center for Environmental Health

Newborn Screening Quality Assurance Program

2018 Annual Summary Report, Volume 36

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 3–36 (bias plots) are located in Appendix for Accessibility Descriptions, page 42.

Contents

NSQAP helps newborn screening laboratories ensure that testing accurately detects disorders, does not delay diagnoses, minimizes false-positive reports, and sustains high-quality performance.

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 newborns shortly after birth in the United States. State and public health laboratories or their associated laboratories routinely screen these DBS specimens for certain genetic, metabolic, and endocrine disorders. The Centers for Disease Control and Prevention (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 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. The scope of 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. 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 2018, active program participants included 663 newborn screening laboratories in 85 countries (at least one laboratory per country) (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 Newborn Screening and Molecular Biology Branch.

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, Lysosomal Storage Disorders (LSD), and the 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 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.

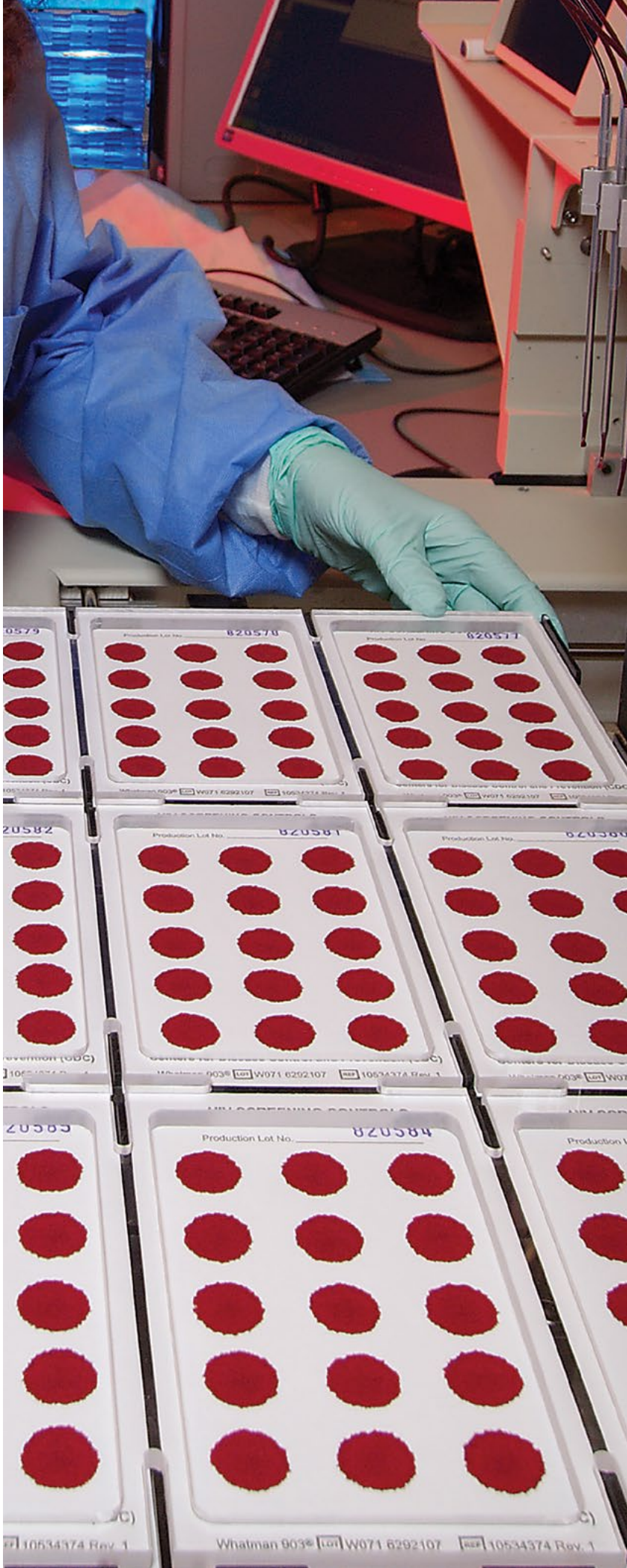
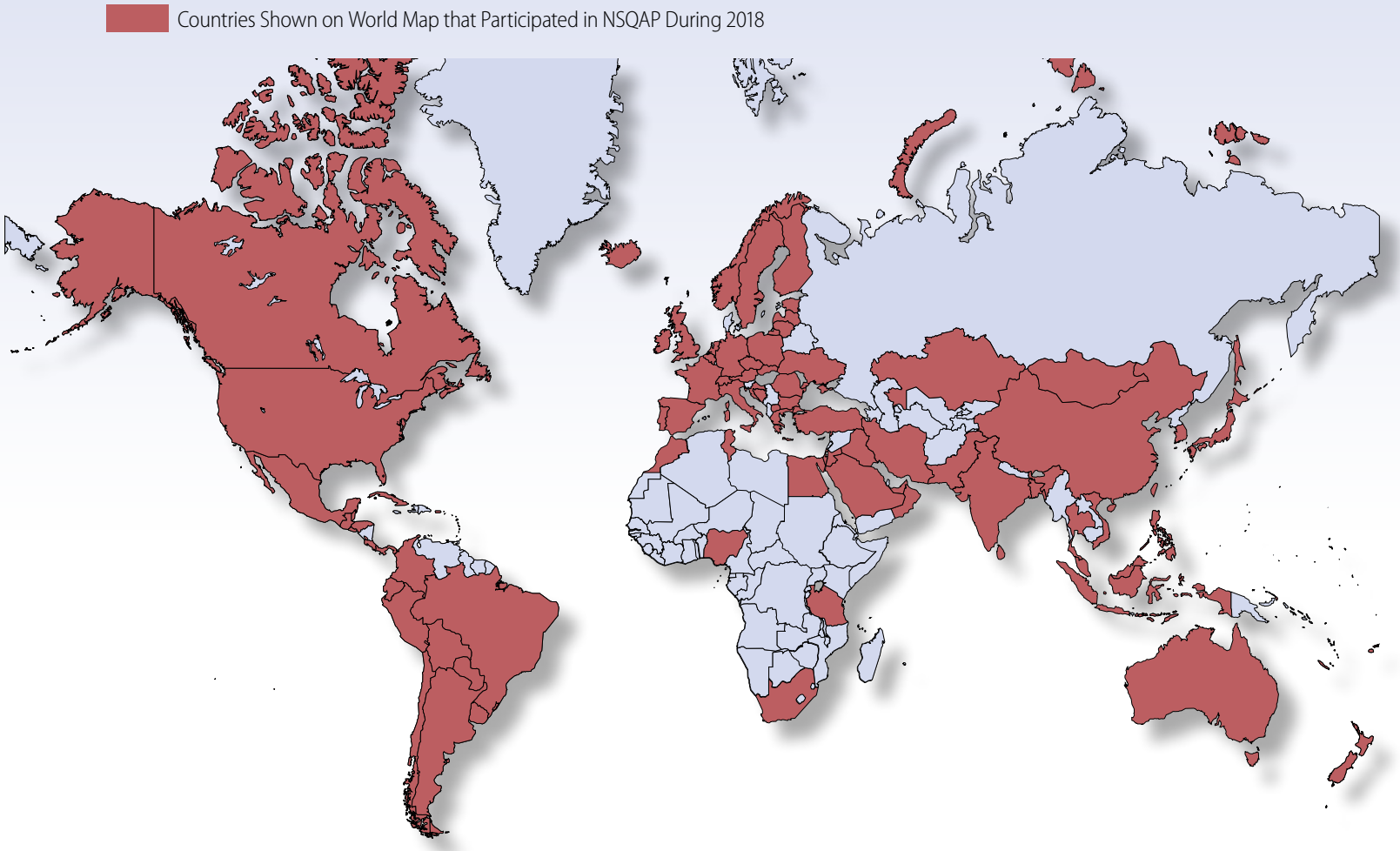


Figure 1. Eighty-five countries participated in the Newborn Screening Quality Assurance Program in 2018.



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
France
Germany
Greece
Guatemala
Honduras
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Iceland
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Kazakhstan
Kuwait
Latvia
Lebanon
Lithuania
Luxembourg
Macedonia
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Oman
Pakistan
Panama
Paraguay
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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**, 2018 (N = 588)

Analyte	Total PT Participation in 2018
17OHP	303
T4	93
TSH	377
TGal	193
BIOT	219
GALT	148
IRT	252
G6PD	101
CFDNA	71
Hb	70
Anti-HIV-1	22
TOXO	18
TREC	62
Arg	304
Cit	327
Leu	358
Met	342
Phe	461
SUAC	163
Tyr	359
Val	321
C0(L)	347
C3	344
C3DC	145
C3DC+C4OH	143
C4	324
C4OH	138
C5	357
C5:1	317
C5DC	340
C5OH	310
C6	332
C8	358
C10	345
C10:1	313
C10:2	224
C14	330
C14:1	338
C16	340
C16OH	337
C18	323
C18:1	311
C18OH	286
17OHP2	24
4AD2	24
CORT2	24
11D2	17
21D2	17
GALC	11
GAA	17
IDUA	15
C24-LPC	17
C26-LPC	20

Table 2. Number of participants reporting **quality control analytes**, 2018 (N = 522)

Analyte	Total QC participation in 2018
17OHP	264
T4	77
TSH	340
TGal	166
GALT	93
IRT	210
Ala	260
Arg	285
Cit	305
Gly	227
Leu	319
Met	313
Orn	231
Phe	389
SUAC	142
Tyr	320
Val	302
C0	308
C2	303
C3	308
C3DC	133
C3DC+C4OH	151
C4	302
C4OH	127
C5	316
C5DC	304
C5OH	280
C6	307
C8	317
C10	313
C12	297
C14	309
C16	310
C16OH	303
C18	302
C18OH	258
17OHP2	23
4AD2	23
CORT2	23
11D2	16
21D2	16
GALC	19
GAA	31
IDUA	28
GLA	27
ABG	26
ASM	14
C20-LPC	7
C22-LPC	7
C24-LPC	15
C26-LPC	19
GAA2	8
CRE2	5
ALE2	20
ILE2	18
LEU2	19
PHE2	22
TYR2	21
VAL2	21
MMA2	22
EMA2	9
MCA2	16
MA2	2
tHCY2	21

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 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 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 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 W152, W161, and W171 to produce the QC and PT specimens distributed in 2018.

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)
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 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)

Table 4. 903™ 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)
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)
W122	May 2013	1.41 (0.11)	14.8 (2.9)	16.3 (0.5)

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 ACIDS

- 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) Hydroxystearoylcarnitine (C18OH)

OTHER ANALYTES

- 17 α-hydroxyprogesterone (17OHP)
- 24:0-lysophosphatidylcholine (C24-LPC)
- 26:0-lysophosphatidylcholine (C26-LPC)
- anti-HIV-1 Antibodies (HIV)
- acid-α-glucosidase (GAA)
- 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: using unaltered donor blood, enriching a single blood unit or pooling 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 materials are enriched with galactose and galactose-1-phosphate, allowing measurement of free galactose (galactose alone) and total galactose (free galactose plus galactose-1-phosphate).

Biotinidase 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.

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 anonymous cystic fibrosis patients, carriers, or unaffected individuals without hematocrit adjustment.

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

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

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.

Lysosomal storage disorder 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.

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 5–7 show the PT errors reported in 2018 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-positive misclassifications were based on the number of negative specimens tested. The rates for false-negative misclassifications were based 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 5. Summary of non-MS/MS proficiency test errors by domestic and international laboratories

Domestic

Analyte	Positive specimens assayed (N)	False negative errors (%)	Negative specimens assayed (N)	False positive errors (%)
Congenital adrenal hyperplasia	126	0.0%	504	0.0%
Biotinidase deficiency	215	1.4%	430	1.9%
G6PD deficiency	15	0.0%	30	3.3%
GALT deficiency	258	0.0%	387	0.0%
Immunoreactive trypsinogen	262	1.1%	393	0.0%
Congenital hypothyroidism	215	0.0%	430	0.2%
Galactosemia	92	0.0%	253	0.0%

International

Analyte	Positive specimens assayed (N)	False negative errors (%)	Negative specimens assayed (N)	False positive errors (%)
Congenital adrenal hyperplasia	658	1.7%	2637	0.7%
Biotinidase deficiency	752	1.7%	1493	2.0%
G6PD deficiency	404	2.5%	836	1.2%
GALT deficiency	548	2.4%	822	1.1%
Immunoreactive trypsinogen	1038	1.3%	1557	6.3%
Congenital hypothyroidism	1408	0.7%	2797	0.6%
Galactosemia	560	2.0%	1550	0.3%

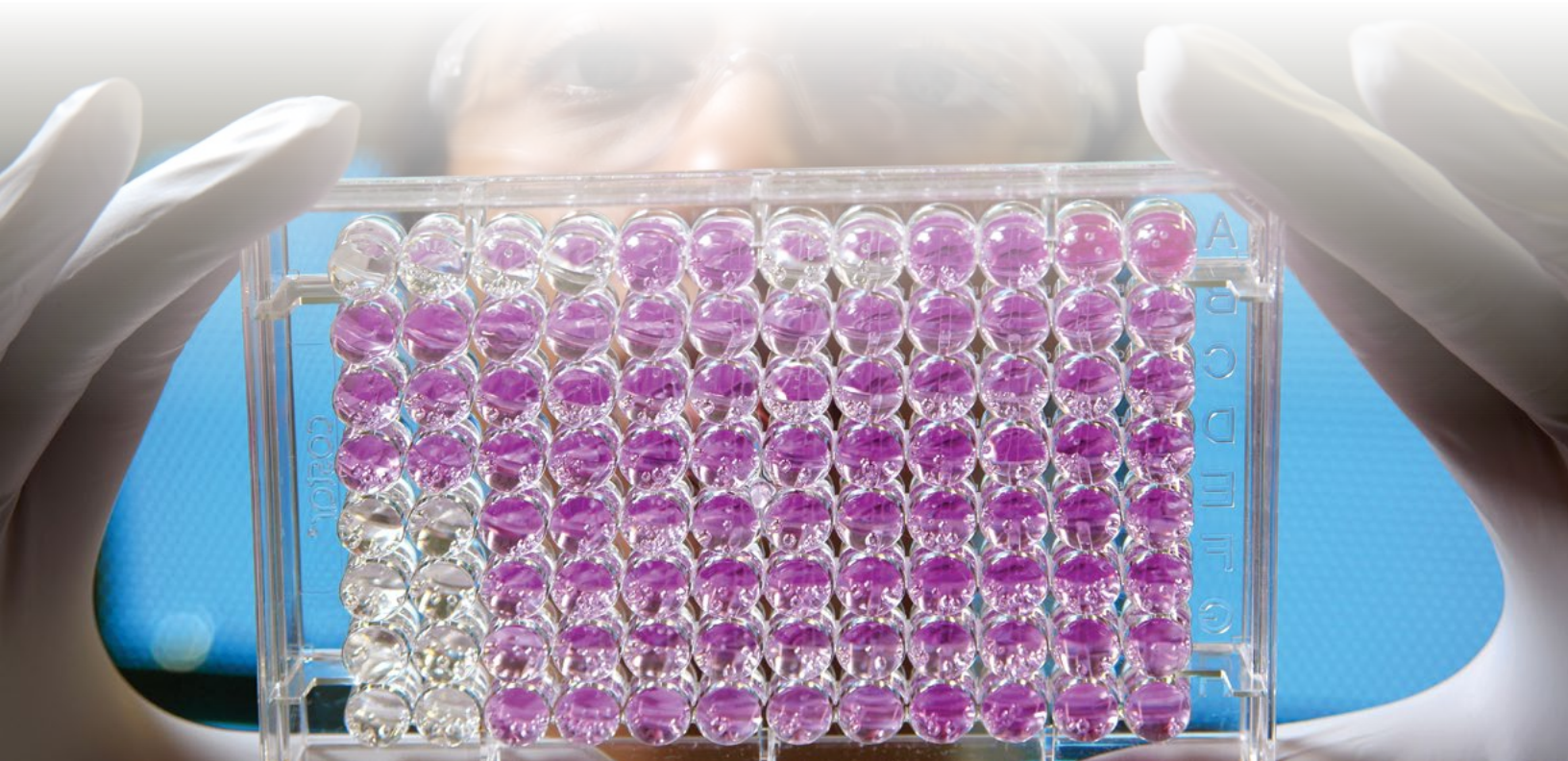


Table 6. Summary of amino acid and acylcarnitine proficiency test errors by **Domestic** laboratories

Analyte	Positive specimens assayed (N)	False negative errors (%)	Negative specimens assayed (N)	False positive errors (%)
Arginine screen	36	0.0%	504	0.0%
Citrulline screen	132	0.0%	528	0.0%
Leucine screen	89	0.0%	581	0.0%
Methionine screen	176	0.0%	484	0.0%
Phenylalanine screen	164	1.2%	656	1.2%
Succinylacetone screen	34	0.0%	486	0.0%
Tyrosine screen	100	0.0%	635	0.3%
Valine screen	90	3.3%	365	1.4%
C0(L) screen	0	0.0%	700	0.4%
C3 screen	96	1.0%	619	0.0%
C3DC screen	0	0.0%	280	0.0%
C3DC+C4OH screen	0	0.0%	320	0.0%
C4 screen	0	0.0%	645	0.5%
C4OH Screen	0	0.0%	270	0.0%
C5 screen	48	0.0%	667	0.0%
C5:1 screen	0	0.0%	700	0.1%
C5DC screen	93	1.1%	607	0.0%
C5OH screen	47	2.1%	653	0.3%
C6 screen	134	0.7%	536	0.0%
C8 screen	96	0.0%	619	0.2%
C10 screen	88	4.5%	567	0.0%
C10:1 screen	83	7.2%	532	0.0%
C10:2 screen	0	0.0%	405	0.0%
C14 screen	130	5.4%	525	0.0%
C14:1 screen	140	0.0%	570	0.0%
C16 screen	0	0.0%	675	0.0%
C16OH screen	47	0.0%	668	0.0%
C18 screen	0	0.0%	630	0.0%
C18:1 screen	0	0.0%	610	0.0%
C18OH screen	0	0.0%	545	0.2%

Table 7. 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	219	2.3%	3196	0.3%
Citrulline screen	733	1.9%	2932	0.6%
Leucine screen	554	2.7%	3486	0.4%
Methionine screen	1034	1.8%	2826	0.8%
Phenylalanine screen	1057	2.4%	4228	1.4%
Succinylacetone screen	91	0.0%	1424	0.4%
Tyrosine screen	508	0.8%	3492	1.9%
Valine screen	772	4.8%	2968	1.3%
C0(L) screen	0	0.0%	3950	1.4%
C3 screen	515	1.7%	3380	0.4%
C3DC screen	0	0.0%	1590	2.5%
C3DC+C4OH screen	0	0.0%	1465	0.5%
C4 screen	0	0.0%	3645	1.3%
C4OH screen	0	0.0%	1490	0.8%
C5 screen	281	6.4%	3784	0.1%
C5:1 screen	0	0.0%	3485	1.7%
C5DC screen	503	0.4%	3332	1.1%
C5OH screen	232	6.0%	3173	2.6%
C6 screen	750	0.9%	3000	0.8%
C8 screen	543	0.7%	3552	1.3%
C10 screen	526	4.2%	3439	0.8%
C10:1 screen	461	8.0%	3029	0.8%
C10:2 screen	0	0.0%	2455	0.6%
C14 screen	741	5.7%	2979	0.6%
C14:1 screen	759	1.3%	3041	0.4%
C16 screen	0	0.0%	3825	0.8%
C16OH screen	257	1.6%	3528	0.8%
C18 screen	0	0.0%	3640	0.3%
C18:1 screen	0	0.0%	3480	0.3%
C18OH screen	0	0.0%	3150	1.3%

Non-Web Reported Analytes

Table 8 shows a summary of PT errors for programs not reported on the NSQAP database website. Those include the Hb, CFDNA Variant Detection, LSD, TREC, Anti-*Toxoplasma* Antibodies, X-linked Adrenoleukodystrophy (XALD), and Second-tier Congenital Adrenal Hyperplasia (CAH) programs.

The CFDNA PT program provides evaluations based on allele identification and clinical assessment. Allele detection is dependent on the method used. Table 9 summarizes the CF variant challenges distributed in 2018.

Table 10 shows the challenges distributed in 2018 for sickle cell disease and other hemoglobinopathies. Participants are evaluated on hemoglobin phenotypes and ability to provide correct clinical assessments.

Table 8. Summary of non-web based analyte proficiency test errors

Sickle Cell and Other Hemoglobinopathies

Proficiency Test	Domestic	International
Specimens Assayed	665	370
Phenotype Errors	0.2%	2.7%
Clinical Assessment Errors	0.0%	2.4%

Cystic Fibrosis DNA Variant

Proficiency Test	Domestic	International
Specimens Assayed	638	700
Allele Errors	0.5%	1.7%
Clinical Assessment Errors	0.2%	0.6%

Lysosomal Storage Disorders

Krabbe

Proficiency Test	Domestic	International
Specimens Assayed	155	n/a
Clinical Assessment Errors	1.3%	n/a

Pompe

Proficiency Test	Domestic	International
Specimens Assayed	235	n/a
Clinical Assessment Errors	0.9%	n/a

Mucopolysaccharidosis Type I

Proficiency Test	Domestic	International
Specimens Assayed	205	n/a
Clinical Assessment Errors	0.0%	n/a

T-cell Receptor Excision Circle

Proficiency Test	Domestic	International
Total Specimens Assayed	1466	580
Clinical Assessment Errors	0.7%	3.3%

Second-tier Congenital Adrenal Hyperplasia

Proficiency Test	Domestic	International
Specimens Assayed	75	300
Clinical Assessment Errors	5.3%	9.7%

X-linked Adrenoleukodystrophy

24:0 Lysophosphatidylcholine

Proficiency Test	Domestic	International
Specimens Assayed	165	60
Clinical Assessment Errors	1.2%	0.0%

26:0 Lysophosphatidylcholine

Proficiency Test	Domestic	International
Specimens Assayed	165	75
Clinical Assessment Errors	1.2%	0.0%

Table 9. Cystic Fibrosis DNA variant (CTFR gene) challenges distributed in 2018

Variant (Legacy name)	Variant (HGVS nomenclature)	Variants sent
F508del	(c.1521_1523delCTT)	10
W1204X	(c.3612G>A)	2
R1066C	(c.3196C>T)	1
G551D	(c.1652G>A)	1
2789+5G>A	(c.2657+5G>A)	1
3876delA	(c.3744delA)	1
R334W	(c.1000C>T)	1
Y1092X	(c.3276C>A)	1
1898+G>A	(c.1766+1G>A)	1
3120+1G>A	(c.2988+1G>A)	1
Q890X	(c.2668C>T)	1
E60X	(c.178G>T)	1
G542X	(c.1624G>T)	1
3849+10kbC>T	(c.3717+12191C>T)	1
2183AA>G	(c.2051_2052delAAinsG)	1

Table 10. Hemoglobinopathies accepted presumptive phenotype distribution

Quarter	Specimen 1	Specimen 2	Specimen 3	Specimen 4	Specimen 5
Quarter 1	FAS	FA	FAC	Alpha Thal—Silent Carrier, FA	FA
Quarter 3	FAS	FAC	FA	FS, FSU	FA
Quarter 4	FS	FA	FAC	FAS	FA

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. CDC does not test newborns; therefore, 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 11–13 summarize the reported cutoff values for domestic and international laboratories. The tables show the values for mean, median, and mode for each analyte. Tables 14–16 summarize the mean, median, mode, and minimum/maximum for reported domestic cutoff values, by method.

Table 11. Summary of non-MS/MS cutoff values for domestic and international laboratories, 2018

Domestic

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	41	33.7	33.0	30.0	17.8	65.0
IRT (ng/mL blood)	42	68.3	63.4	60.0	46.3	160.0
T4 (µg/dL serum)	21	6.4	6.0	5.0	5.0	8.5
TGal (mg/dL blood)	23	11.2	10.0	10.0	6.0	20.0
TSH (µIU/mL serum)	42	30.7	25.0	20.0	19.0	58.0
Phe (µmol/L blood)	3	168.9	181.8	n/a	137.0	188.0

International

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	217	25.2	20.0	19.8	2.6	100.0
IRT (ng/mL blood)	169	67.1	65.0	70.0	40.0	140.5
T4 (µg/dL serum)	49	6.5	6.0	6.0	2.4	12.8
TGal (mg/dL blood)	139	12.2	10.0	10.0	3.0	30.0
TSH (µIU/mL serum)	275	22.5	20.0	20.0	6.0	55.0
Phe (µmol/L blood)	27	159.7	180.0	121.2	96.8	242.4

Table 12. Summary of MS/MS cutoff values for domestic laboratories (µmol/L blood), 2018

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine	36	71.7	63.0	50.0	20.0	120.0
Citrulline	44	54.2	55.0	60.0	18.0	75.0
Leucine	44	287.9	281.5	250.0	175.0	400.0
Methionine	44	73.7	75.0	100.0	30.0	100.0
Phenylalanine	51	143.2	150.0	130.0	70.0	188.0
Succinylacetone	35	2.5	2.0	4.5	0.7	5.4
Tyrosine	48	391.6	357.5	300.0	91.0	850.0
Valine	30	302.0	300.0	250.0	175.0	530.0
C0(L)	47	8.12	7.50	6.00	4.50	24.00
C3	48	5.56	5.97	5.00	2.82	7.50
C3DC	19	0.21	0.20	0.14	0.10	0.45
C3DC+ C4OH	21	0.52	0.38	0.38	0.25	3.03
C4	43	1.25	1.30	1.30	0.49	1.90
C4OH	18	0.64	0.65	0.65	0.30	1.00
C5	48	0.73	0.69	0.60	0.39	1.20
C5:1	47	0.20	0.15	0.10	0.03	0.50
C5DC	47	0.37	0.39	0.50	0.05	0.80
C5OH	47	0.80	0.80	0.80	0.25	1.36
C6	45	0.38	0.29	0.25	0.14	0.95
C8	48	0.45	0.40	0.35	0.20	0.73
C10	44	0.43	0.40	0.30	0.22	0.70
C10:1	41	0.28	0.25	0.25	0.11	0.45
C10:2	27	0.15	0.13	0.10	0.04	0.39
C14	44	0.74	0.70	0.70	0.26	1.20
C14:1	48	0.61	0.65	0.70	0.17	0.80
C16	45	7.59	7.80	10.00	2.14	10.00
C16OH	48	0.12	0.11	0.10	0.06	0.25
C18	41	2.31	2.20	3.50	0.70	3.50
C18:1	41	3.52	3.00	2.50	2.00	7.00
C18OH	37	0.09	0.10	0.10	0.03	0.18

Table 13. Summary of MS/MS cutoff values for international laboratories (µmol/L blood), 2018

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine	229	57.0	55.0	70.0	10.0	150.0
Citrulline	248	51.5	50.0	55.0	20.0	200.0
Leucine	272	304.3	294.5	300.0	145.0	600.0
Methionine	261	55.8	50.0	75.0	20.0	120.0
Phenylalanine	325	138.3	129.0	120.0	1.8	250.0
Succinylacetone	102	2.1	1.5	2.0	0.4	8.0
Tyrosine	269	293.6	280.0	350.0	79.9	600.0
Valine	254	268.3	265.0	300.0	44.0	470.0
C0(L)	262	16.47	9.00	10.00	2.00	100.00
C3	262	5.44	5.40	5.65	0.20	70.00
C3DC	105	0.28	0.25	0.25	0.04	1.82
C3DC+ C4OH	100	0.49	0.44	0.45	0.15	3.07
C4	245	0.96	0.92	1.30	0.29	3.80
C4OH	100	0.57	0.57	0.65	0.05	1.40
C5	271	0.68	0.60	0.70	0.20	2.00
C5:1	232	0.15	0.12	0.25	0.01	0.97
C5DC	256	0.33	0.30	0.35	0.07	0.90
C5OH	226	0.76	0.79	1.00	0.19	2.50
C6	247	0.29	0.25	0.20	0.05	1.00
C8	276	0.35	0.30	0.50	0.07	1.00
C10	261	0.47	0.37	0.45	0.07	25.00
C10:1	227	0.35	0.25	0.30	0.05	20.00
C10:2	158	0.15	0.12	0.15	0.01	2.00
C14	245	0.60	0.57	0.50	0.08	1.30
C14:1	251	0.45	0.40	0.60	0.04	2.50
C16	251	6.81	7.00	7.50	0.52	14.00
C16OH	251	0.30	0.10	0.10	0.02	48.00
C18	243	2.10	2.00	2.30	0.20	4.00
C18:1	230	3.01	3.00	3.50	0.16	8.00
C18OH	208	0.10	0.08	0.10	0.01	2.00

Table 14. Domestic cutoff summary by analyte and method—hormones, galactose, and immunoreative trypsinogen, 2018 (Methods N < 3 not shown)

17 α-Hydroxyprogesterone ng/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**41**	**33.7**	**33.0**	**30.0**	**17.8**	**65.0**
AutoDelfia	6	39.6	37.5	35.0	17.8	60.0
AutoDelfia eNonatal 17-OHP (B024)	12	31.1	33.0	33.0	25.0	35.0
PerkinElmer GSP Neonatal	23	33.5	30.0	30.0	25.0	65.0

Thyroxine µg/dL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**21**	**6.4**	**6.0**	**5.0**	**5.0**	**8.5**
AutoDelfia	6	6.7	6.6	n/a	5.5	8.0
PerkinElmer GSP Neonatal	14	6.3	6.0	5.0	5.0	8.5

Thyroid-Stimulating Hormone µIU/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**30.7**	**25.0**	**20.0**	**19.0**	**58.0**
AutoDelfia	18	36.1	29.3	20.0	20.0	58.0
PerkinElmer GSP Neonatal	23	27.0	25.0	25.0	19.0	54.0

Total Galactose mg/dL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**23**	**11.2**	**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	10.8	10.0	10.0	7.0	14.0

Immunoreactive Trypsinogen ng/mL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**68.3**	**63.4**	**60.0**	**46.3**	**160.0**
AutoDelfia	21	72.5	66.0	65.0	52.0	115.6
PerkinElmer GSP Neonatal	21	64.1	58.0	60.0	46.3	160.0

Table 15. Domestic cutoff summary by analyte and method—amino acids (µmol/L blood), 2018 (Methods N < 3 not shown)

Arginine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**36**	**71.7**	**63.0**	**50.0**	**30.0**	**120.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	82.5	85.0	100.0	60.0	100.0
Derivatized - MS/MS non-kit	11	53.6	46.0	n/a.	20.0	115.0
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	**44**	**54.2**	**55.0**	**60.0**	**18.0**	**75.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	53.8	55.0	n/a	40.0	65.0
Derivatized - MS/MS non-kit	13	49.2	50.0	40.0	18.0	75.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	57.3	60.0	60.0	40.2	75.0

Leucine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**44**	**287.9**	**281.5**	**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	13	264.6	250.0	300.0	200.0	350.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	303.0	300.0	250.0	175.0	400.0

Methionine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**44**	**73.7**	**75.0**	**100.0**	**30.0**	**100.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	75.0	75.0	75.0	70.0	80.0
Derivatized - MS/MS non-kit	13	61.3	60.0	50.0	30.0	100.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	81.1	80.6	100.0	54.5	100.0

Phenylalanine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**51**	**143.2**	**150.0**	**130.0**	**70.0**	**188.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	136.3	132.5	130.0	130.0	150.0
Derivatized - MS/MS non-kit	17	136.7	139.0	130.0	70.0	182.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	150.0	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	**35**	**2.5**	**2.0**	**4.5**	**0.7**	**5.4**
Derivatized - MS/MS non-kit	10	2.5	2.3	2.0	0.9	5.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	2.4	2.0	4.5	0.7	4.5

Tyrosine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**48**	**391.6**	**357.5**	**300.0**	**91.0**	**850.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	282.5	290.0	300.0	250.0	300.0
Derivatized - MS/MS non-kit	16	291.9	290.0	300.0	99.0	500.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	521.3	450.0	850.0	300.0	850.0

Continued

Valine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**30**	**302.0**	**300.0**	**250.0**	**175.0**	**530.0**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	316.7	300.0	n/a	250.0	400.0
Derivatized - MS/MS non-kit	10	268.5	260.0	200.0	175.0	420.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	15	328.1	330.0	250.0	250.0	530.0

Table 16. Domestic cutoff summary by analyte and method—acylcarnitines (µmol/L blood), 2018 (Methods N < 3 not shown)

C0(L)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**8.12**	**7.50**	**6.00**	**4.50**	**24.00**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	11.12	11.23	n/a	9.00	13.00
Derivatized - MS/MS non-kit	16	9.88	8.85	10.00	5.00	24.00
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	6.48	6.00	6.00	4.50	10.00

C3

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**5.56**	**5.97**	**5.00**	**2.82**	**7.50**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	5.54	5.57	n/a	5.00	6.00
Derivatized - MS/MS non-kit	17	4.86	5.00	5.00	2.82	7.30
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	5.96	6.30	6.30	3.09	7.50

C3DC

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**19**	**0.21**	**0.20**	**0.14**	**0.10**	**0.45**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.25	0.26	0.30	0.19	0.30
Derivatized - MS/MS non-kit	15	0.19	0.18	0.14	0.10	0.45

C3DC + C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**21**	**0.52**	**0.38**	**0.38**	**0.25**	**3.03**
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	19	0.40	0.38	0.38	0.25	0.60

C4

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**1.25**	**1.30**	**1.30**	**0.49**	**1.90**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	1.00	0.95	n/a	0.81	1.30
Derivatized - MS/MS non-kit	15	1.14	1.20	1.40	0.49	1.90
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	1.39	1.32	1.70	1.06	1.70

Continued

C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**18**	**0.64**	**0.65**	**0.65**	**0.30**	**1.00**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.73	0.68	n/a	0.55	1.00
Derivatized - MS/MS non-kit	14	0.61	0.65	0.40	0.30	1.00

C5

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**0.73**	**0.69**	**0.60**	**0.39**	**1.20**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.66	0.70	0.70	0.54	0.70
Derivatized - MS/MS non-kit	17	0.74	0.68	0.50	0.39	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	**47**	**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	17	0.19	0.15	0.07	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	**47**	**0.37**	**0.39**	**0.50**	**0.05**	**0.80**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.28	0.28	n/a	0.24	0.32
Derivatized - MS/MS non-kit	17	0.19	0.18	0.21	0.05	0.30
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	0.51	0.50	0.50	0.35	0.80

C5OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**0.80**	**0.80**	**0.80**	**0.25**	**1.36**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.69	0.66	n/a	0.60	0.83
Derivatized - MS/MS non-kit	17	0.79	0.80	0.80	0.25	1.36
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	24	0.81	0.83	0.85	0.60	1.05

C6

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.38**	**0.29**	**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	16	0.33	0.31	0.24	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	**48**	**0.45**	**0.40**	**0.35**	**0.20**	**0.73**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.37	0.37	0.35	0.35	0.40
Derivatized - MS/MS non-kit	17	0.41	0.35	0.35	0.20	0.73
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.49	0.46	0.60	0.35	0.70

C10

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**0.43**	**0.40**	**0.30**	**0.22**	**0.70**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.36	0.33	n/a	0.27	0.50
Derivatized - MS/MS non-kit	15	0.38	0.40	0.30	0.22	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	**41**	**0.28**	**0.25**	**0.25**	**0.11**	**0.45**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.29	0.30	0.30	0.25	0.30
Derivatized - MS/MS non-kit	14	0.26	0.25	0.21	0.11	0.42
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	21	0.29	0.25	0.45	0.14	0.45

C10:2

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**27**	**0.15**	**0.13**	**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	12	0.17	0.15	0.10	0.06	0.39
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	11	0.13	0.10	0.10	0.04	0.30

C14

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**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	16	0.66	0.72	0.80	0.26	0.96
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	0.83	0.73	1.20	0.46	1.20

C14:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**0.61**	**0.65**	**0.70**	**0.17**	**0.80**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.55	0.55	n/a	0.40	0.70
Derivatized - MS/MS non-kit	17	0.54	0.65	0.70	0.17	0.77
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	25	0.68	0.68	0.80	0.50	0.80

Continued

C16

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**7.59**	**7.80**	**10.00**	**2.14**	**10.00**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	7.04	6.93	n/a	6.50	7.80
Derivatized - MS/MS non-kit	16	6.69	7.40	8.00	2.14	9.00
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	23	8.25	8.00	10.00	5.00	10.00

C16OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**48**	**0.12**	**0.11**	**0.10**	**0.06**	**0.25**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.15	0.15	n/a	0.12	0.18
Derivatized - MS/MS non-kit	17	0.14	0.14	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**	**2.31**	**2.20**	**3.50**	**0.70**	**3.50**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	2.17	2.15	n/a	1.89	2.50
Derivatized - MS/MS non-kit	13	1.87	1.85	1.50	0.70	2.80
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	2.59	2.48	3.50	1.55	3.50

C18:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**41**	**3.52**	**3.00**	**2.50**	**2.00**	**7.00**
Derivatized - MS/MS PerkinElmer NeoGram Kit	3	3.14	3.43	n/a	2.50	3.50
Derivatized - MS/MS non-kit	14	2.68	2.54	2.50	2.00	3.50
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	22	4.14	3.33	7.00	2.00	7.00

C18OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**37**	**0.09**	**0.10**	**0.10**	**0.03**	**0.18**
Derivatized - MS/MS PerkinElmer NeoGram Kit	4	0.12	0.11	0.10	0.10	0.16
Derivatized - MS/MS non-kit	11	0.10	0.10	0.10	0.03	0.18
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**.

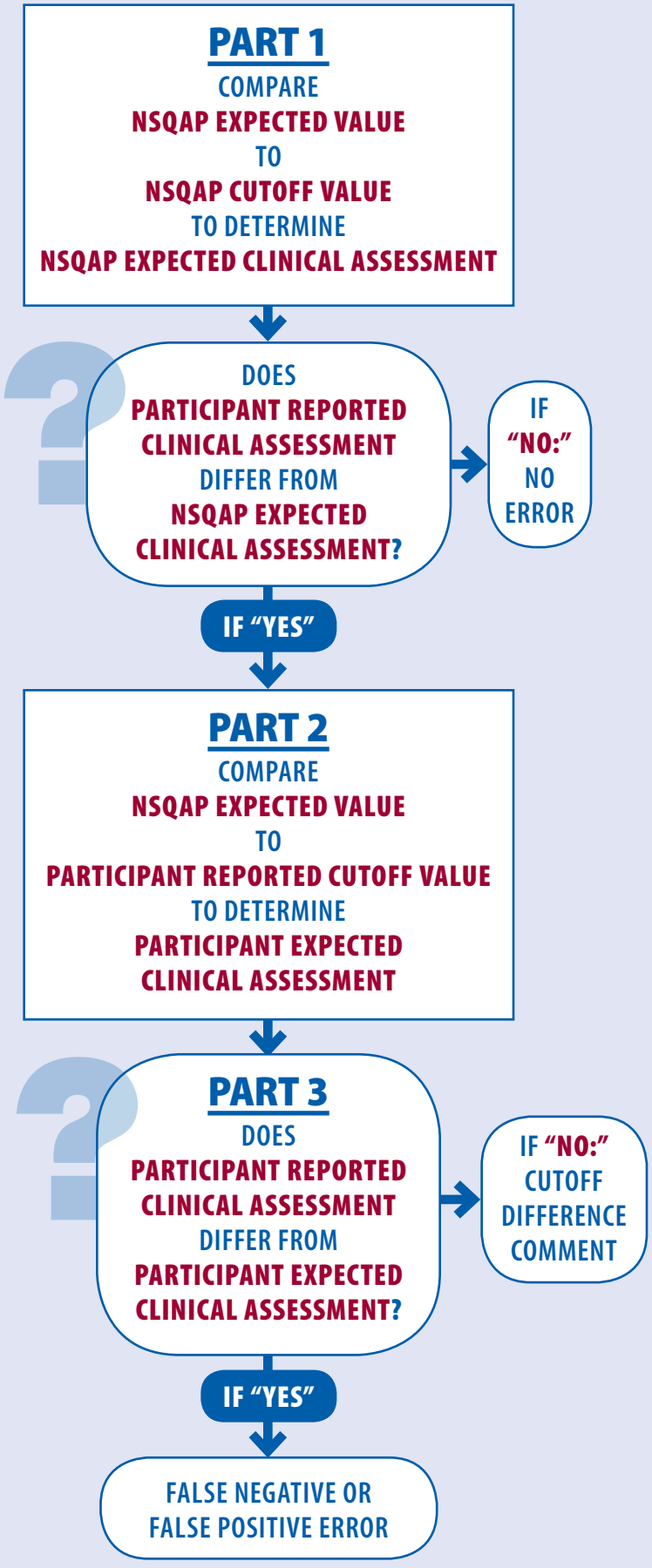
Clinical assessments are reported as "within normal limits" or "outside normal limits." The NSQAP expected value is the sum of the endogenous value plus the enrichment value for an individual analyte. The NSQAP cutoff value is determined annually using the mean of all domestic laboratories' reported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



2018 Bias Plots

Proficiency Testing Bias Plots

Figures 3–36 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. Immunoreactive trypsinogen (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 3–36, the bias plot's explanation follows each figure title.

17OHP ng/mL serum

Quarter 1

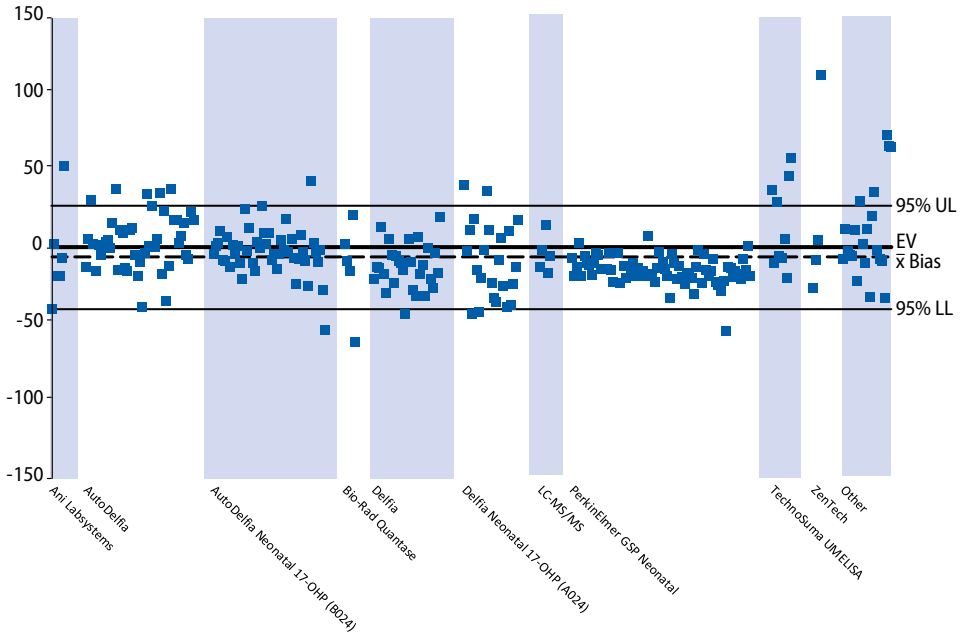
Enriched—85.0

CDC Assayed—71.4

Participant Mean—79.3

Participant Bias—-6.7

Figure 3. Reproducibility of Results: Bias Plot of 17 α-Hydroxyprogesterone (17OHP) Values by Method Quarter 1, Specimen 11815 Expected Value (EV) = 86.0 ng/mL serum



The 17OHP bias plot shows units of measure on the y-axis ranging from 150 ng/mL serum to -150 ng/mL serum. The mean bias for this plot is -6.7 ng/mL serum. The data on this plot shows a tight scatter among all participants.

T4 µg/dL serum

Quarter 1

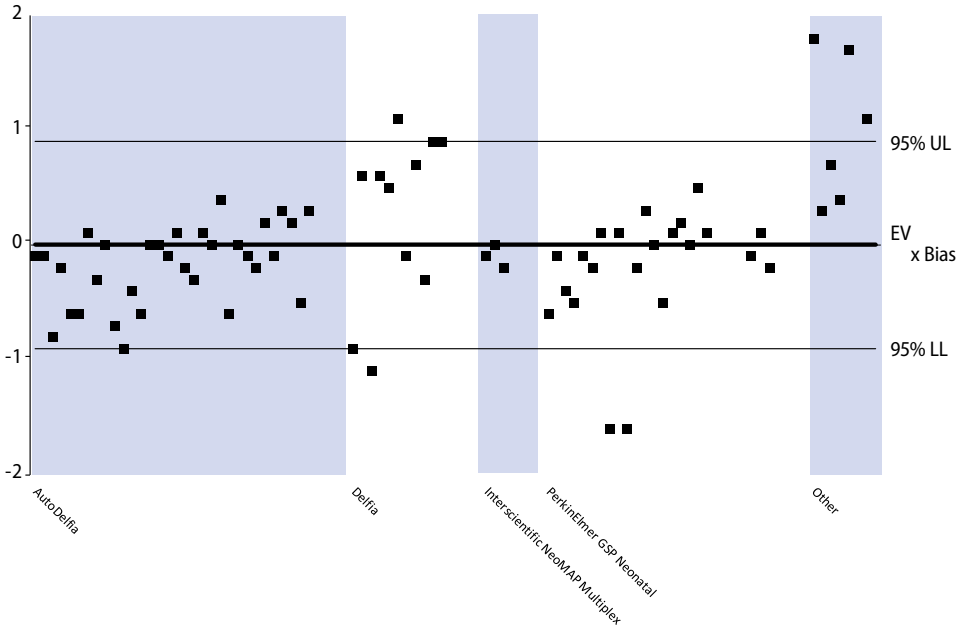
Enriched—1.5

CDC Assayed—1.5

Participant Mean—1.6

Participant Bias—0.0

Figure 4. Reproducibility of Results: Thyroxine (T4) Values by Method Quarter 1, Specimen 11811 Expected Value (EV) = 1.6 µg/dL serum



The T4 bias plot shows units of measure on the y-axis ranging from 2 µg/dL serum to -2 µg/dL serum. The mean bias for this plot is zero. The data on this plot shows a good agreement among participants.

Figure 5. Reproducibility of Results: Bias Plot for Thyroid-Stimulating Hormone (TSH) Values by Method Quarter 1, Specimen 11811 Expected Value (EV) = 85.6 µIU/mL serum

TSH µIU/mL serum

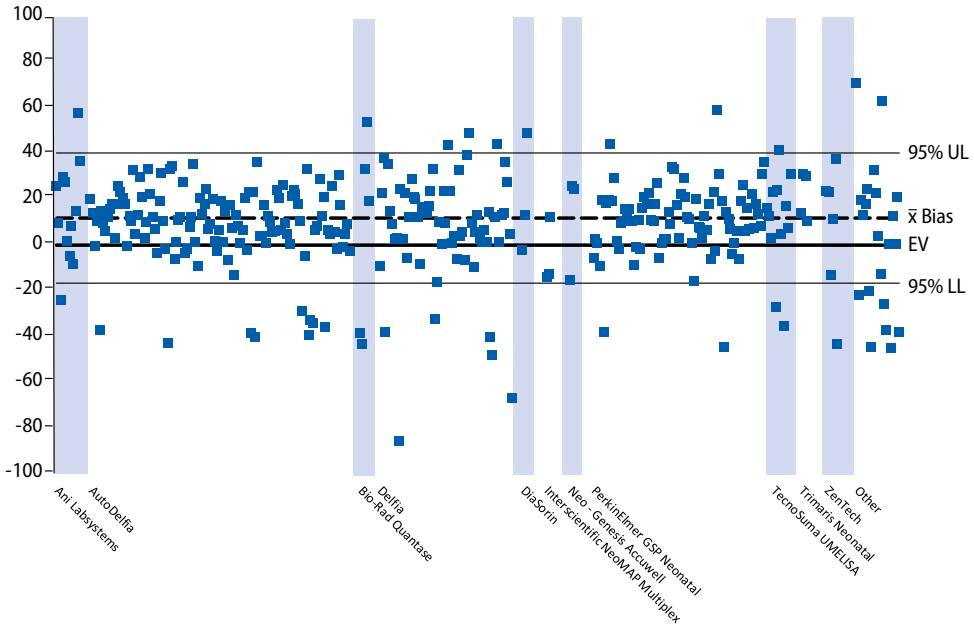
Quarter 1

Enriched—85.0

CDC Assayed—104.9

Participant Mean—97.7

Participant Bias—12.1



The TSH bias plot shows units of measure on the y-axis ranging from 100 µIU/mL serum to -100 µIU/mL serum. The mean bias for this plot is 12.1 µg/dL. This plot shows a positive bias comparted to the CDC-expected value. All methods show a tight scatter with most participants clustering in a positive bias.

Figure 6. Reproducibility of Results: Bias Plot for Total Galactose (TGal) Values by Method Quarter 1, Specimen 11814 Expected Value (EV) = 25.4 mg/dL blood

TGal mg/dL blood

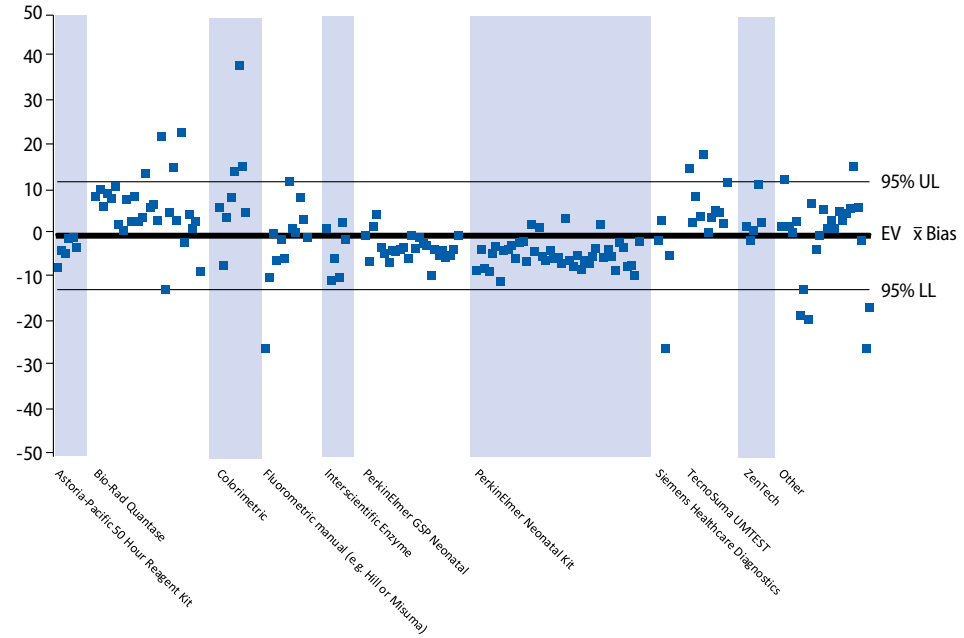
Quarter 1

Enriched—25.0

CDC Assayed—20.3

Participant Mean—25.7

Participant Bias—0.3



The TGal bias plot shows units of measure on the y-axis ranging from 50 mg/dL blood to -50 mg/dL blood. This plot shows a slight positive bias compared to the CDC-expected value. There is good agreement within each method however, some methods show a positive bias while other methods show a negative bias.

Figure 7. Reproducibility of Results: Bias Plot for Immunoreactive Trypsinogen (IRT) Values by Method Quarter 1, Specimen 11882 Expected Value (EV) = 256.5 ng/mL blood

IRT ng/mL blood

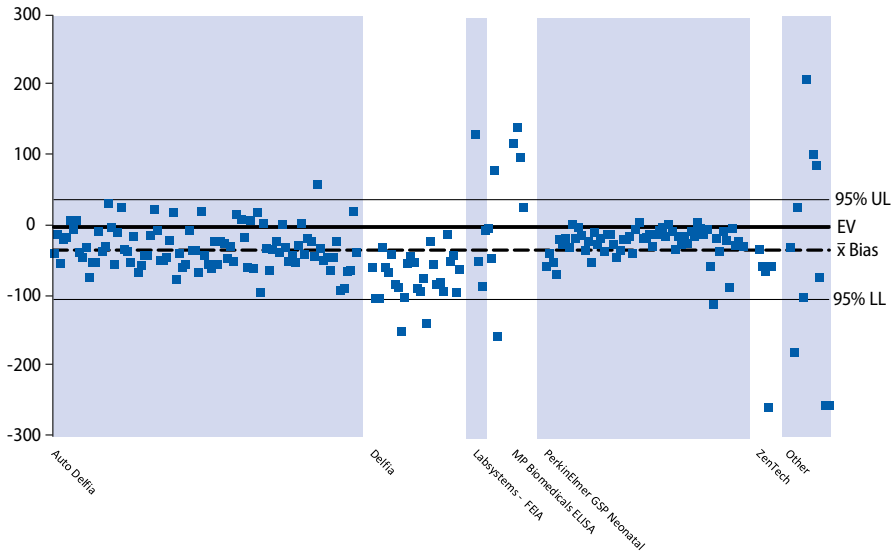
Quarter 1

Enriched—400.0

CDC Assayed—256.5

Participant Mean—224.1

Participant Bias—-32.4



The IRT bias plot shows units of measure on the y-axis ranging from 300 ng/mL blood to -300 ng/mL blood. The mean bias for this plot is -32.4 ng/mL blood. There is tight scatter with all except for the other method category which shows a wide range of results.

Figure 8. Reproducibility of Results: Bias Plot of Arginine (Arg) Values by Method Quarter 1, Specimen 11853 Expected Value (EV) = 258.6 µmol/L blood

Arg µmol/L blood

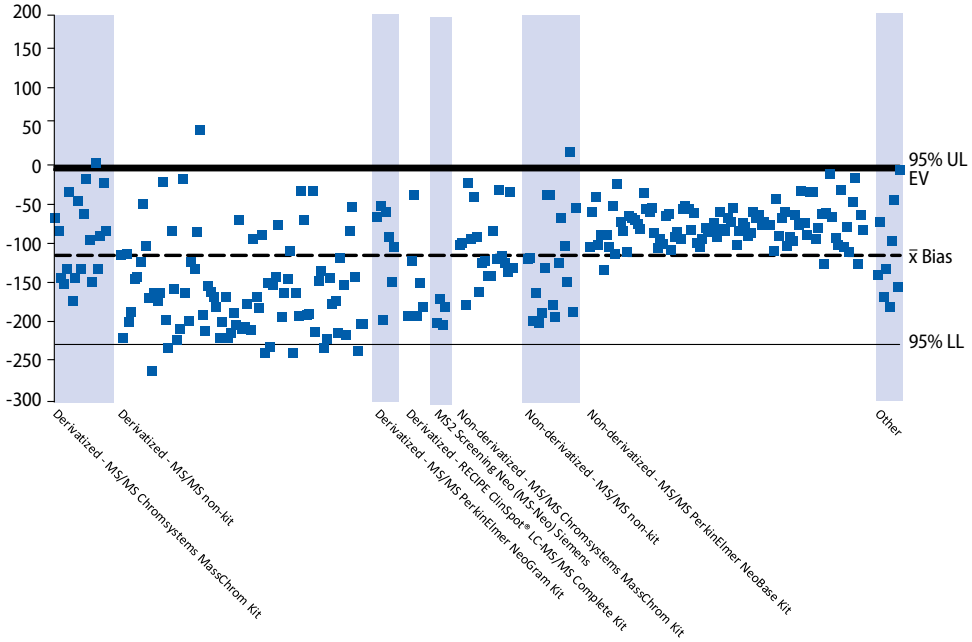
Quarter 1

Enriched—250.0

CDC Assayed—198.7

Participant Mean—148.5

Participant Bias—-110.1



The Arg bias plot shows units of measure on the y-axis ranging from 200 µmol/L blood to -300 µmol/L blood. The mean bias for this plot is -110.1 µmol/L blood. When compared to the CDC expected value, this plot shows a negative bias for all methods.

Figure 9. Reproducibility of Results: Bias Plot for Citrulline (Cit) Values by Method Quarter 3, Specimen 31852 Expected Value (EV) = 251.2 µmol/L blood

Cit µmol/L blood

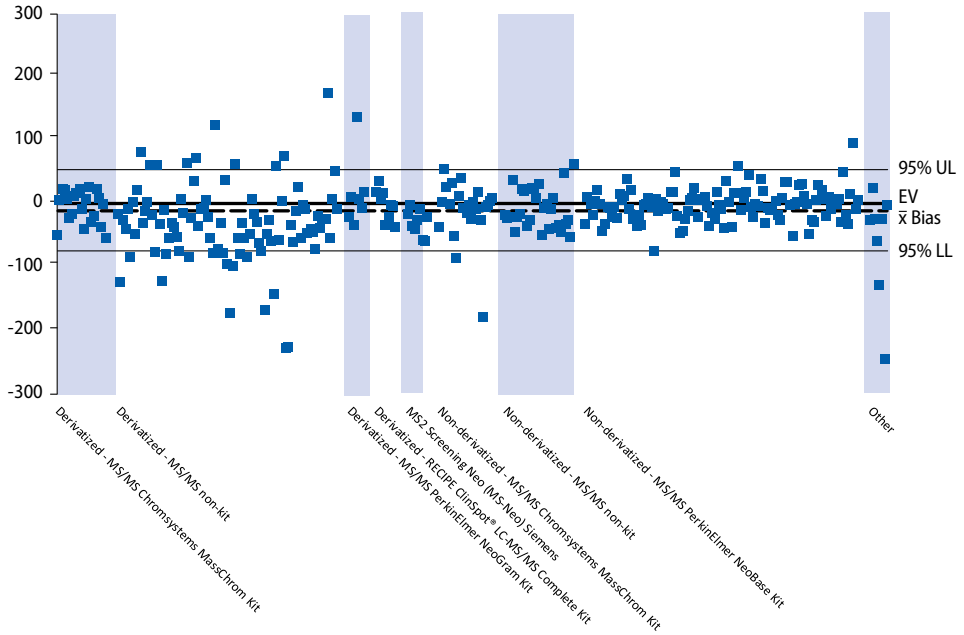
Quarter 3

Enriched—239.2

CDC Assayed—230.3

Participant Mean—240.8

Participant Bias—-10.39



The Cit bias plot shows units of measure on the y-axis ranging from 300 µmol/L blood to -300 µmol/L blood. The mean bias for this plot is -10.39 µmol/L blood. The Cit bias plot shows a good agreement amoung methods.

Figure 10. Reproducibility of Results: Bias Plot for Leucine (Leu) Values by Method Quarter 3, Specimen 31854 Expected Value (EV) = 773.8 µmol/L blood

Leu µmol/L blood

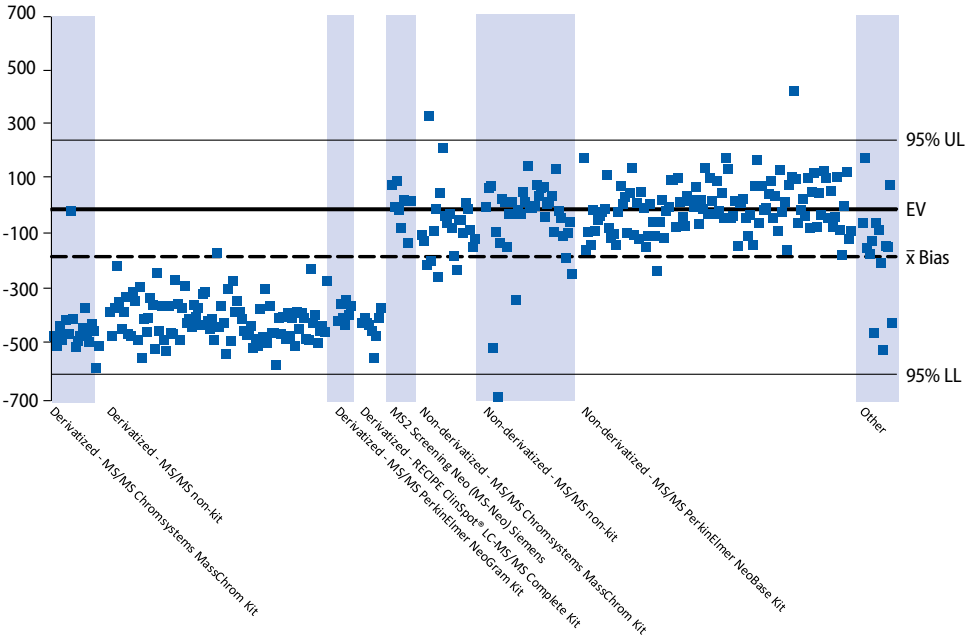
Quarter 3

Enriched—748.8

CDC Assayed—770.3

Participant Mean—601.3

Participant Bias—- 172.5



The Leu bias plot shows units of measure on the y-axis ranging from 700 µmol/L blood to -700 µmol/L blood. The mean bias for this plot is -172.5 µmol/L blood. The bias plot shows distinct differences between methods with some methods below the bias and some above.

Figure 11. Reproducibility of Results: Bias Plot for Methionine (Met) Values by Method Quarter 3, Specimen 31851 Expected Value (EV) =204.4 µmol/L blood

Met µmol/L blood

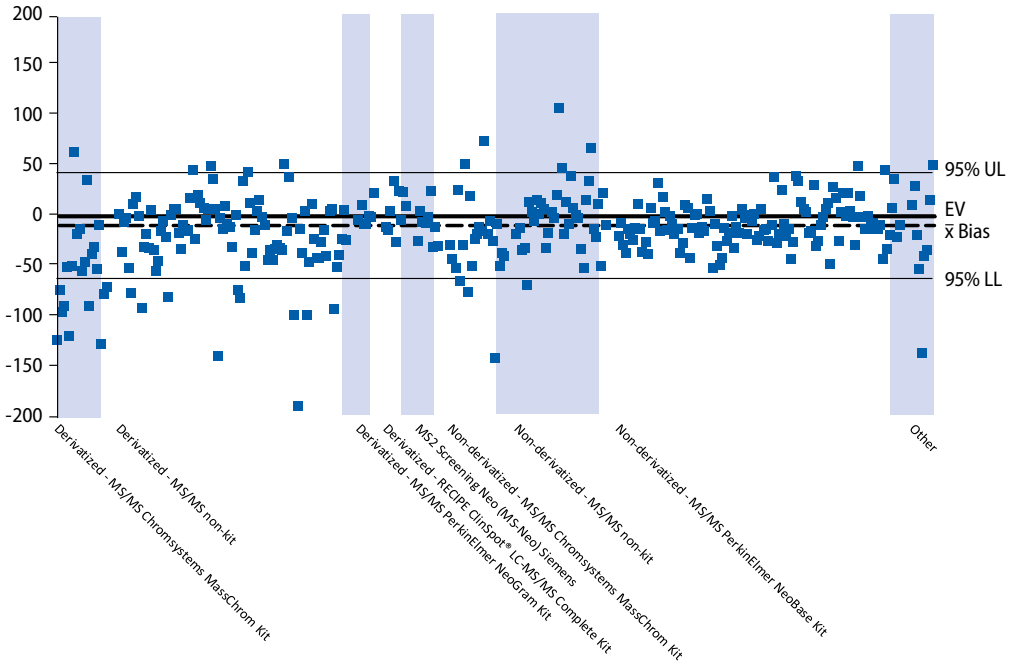
Quarter 3

Enriched—200.4

CDC Assayed—195.6

Participant Mean—194.8

Participant Bias—- 9.6



The Met 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 - 9.6 µmol/L blood. The data shows good scatter among all methods.

Figure 12. Reproducibility of Results: Phenylalanine (Phe) Values by Method Quarter 1, Specimen 11851 Expected Value (EV) = 285.0 µmol/L blood

Phe µmol/L blood

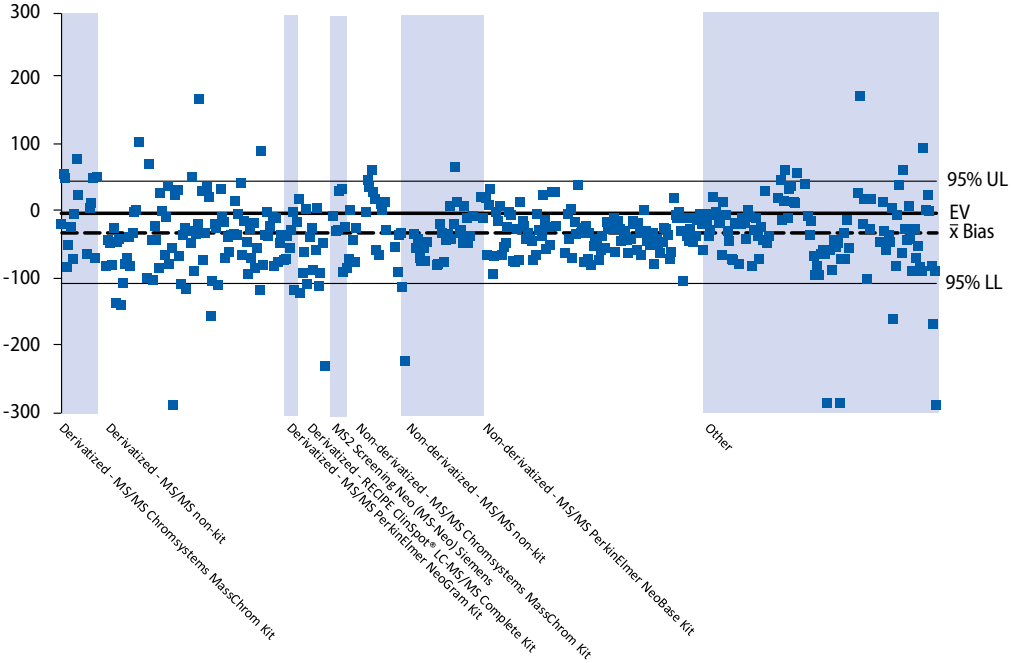
Quarter 1

Enriched—225.0

CDC Assayed—250.9

Participant Mean—257.0

Participant Bias—- 28.0



The Phe bias plot shows units of measure on the y-axis ranging from 300 µmol/L blood to -300 µmol/L blood. The bias for this plot is - 28.0 µmol/L blood. The Phe bias plot shows good agreement between and among methods.

Figure 13. Reproducibility of Results: Succinylacetone (SUAC) Values by Method Quarter 1, Specimen 11854 Expected Value (EV) = 15.4 µmol/L blood

SUAC µmol/L blood

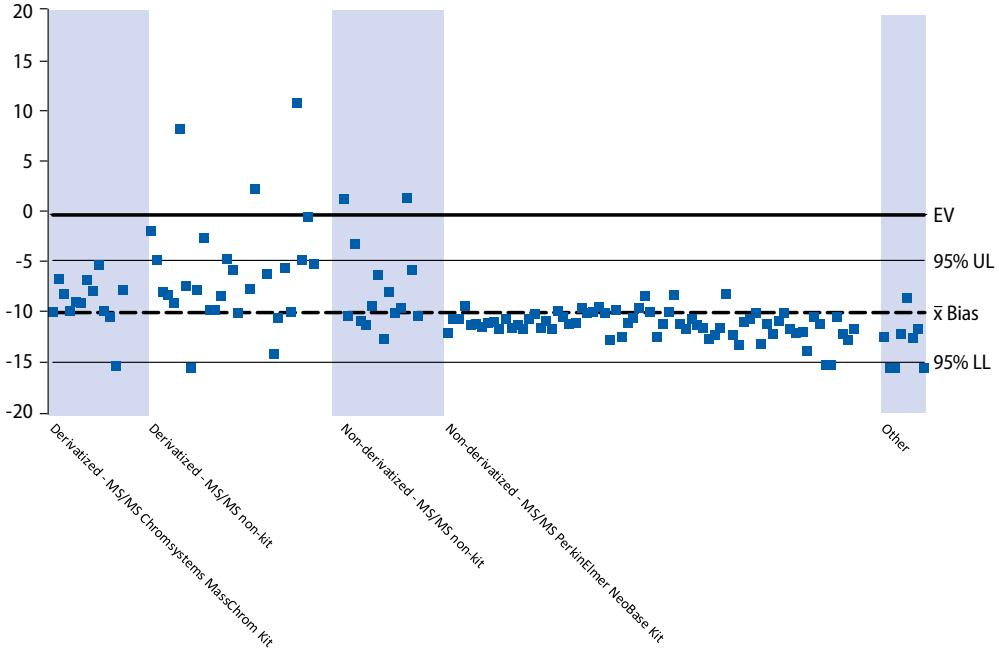
Quarter 1

Enriched—15.0

CDC Assayed—6.3

Participant Mean—5.7

Participant Bias—- 9.7



The SUAC 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 - 9.7 µmol/L blood. The SUAC bias plot shows a very tight scatter among methods with only a few outliers.

Figure 14. Reproducibility of Results: Bias Plot for Tyrosine (Tyr) Values by Method Quarter 1, Specimen 11854 Expected Value (EV) = 731.8 µmol/L blood

Tyr µmol/L blood

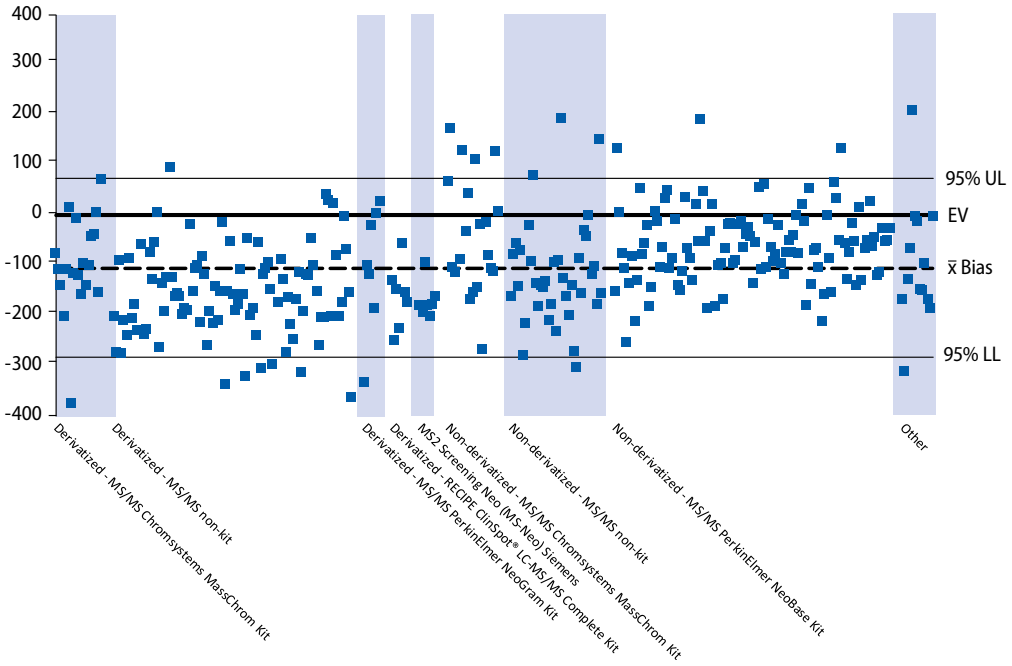
Quarter 1

Enriched—675.0

CDC Assayed—617.6

Participant Mean—626.5

Participant Bias—-105.3



The Tyr 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 - 105.3 µmol/L blood. The bias plot shows good scatter among participants and methods.

Figure 15. Reproducibility of Results: Bias Plot for Valine (Val) Values by Method Quarter 3, Specimen 31854 Expected Value (EV) = 629.1 µmol/L blood

Val µmol/L blood

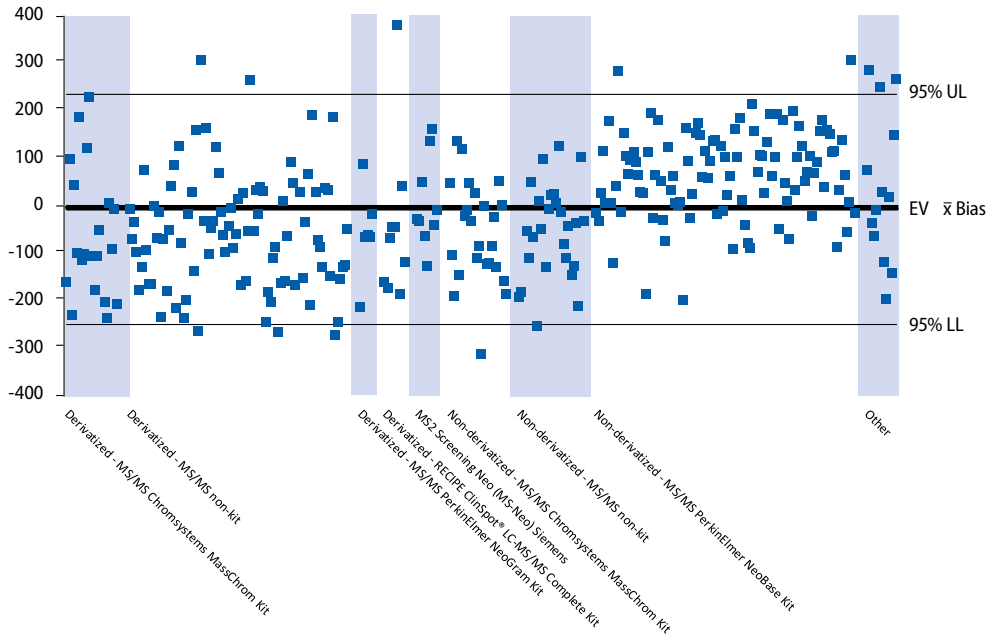
Quarter 3

Enriched—604.1

CDC Assayed—646.3

Participant Mean—624.5

Participant Bias—- 4.61



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 -4.61 µmol/L blood. The Val bias plot shows good scatter among all participants and methods.

Figure 16. Reproducibility of Results: Bias Plot of Free Carnitine(C0(L)) Values by Method Quarter 3, Specimen 31865 Expected Value (EV) = 41.51 µmol/L blood

C0(L) µmol/L blood

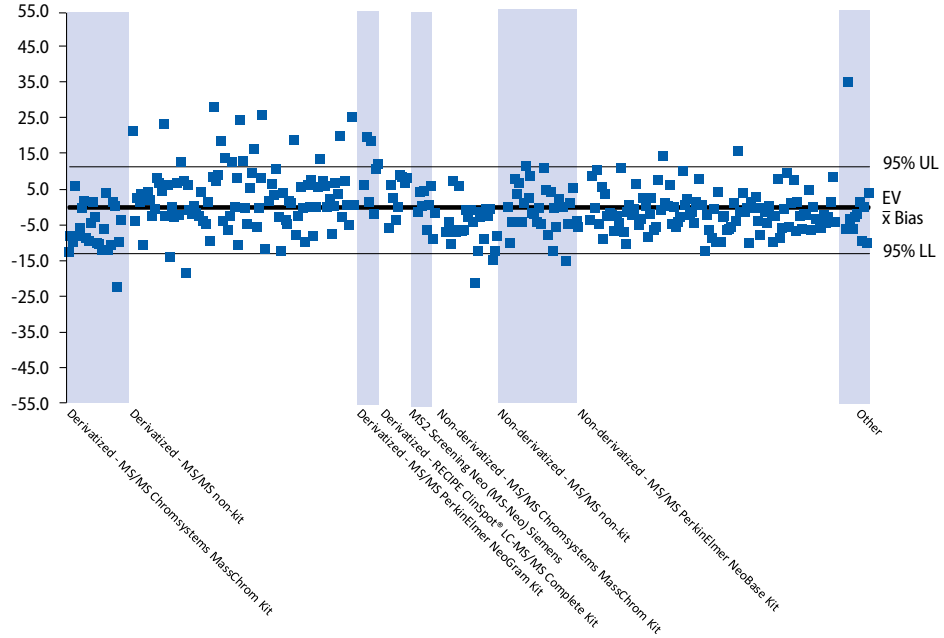
Quarter 3

Enriched—31.56

CDC Assayed—46.16

Participant Mean—40.97

Participant Bias—-0.54



The C0(L) bias plot shows units of measure on the y-axis ranging from 55 µmol/L blood to -55 µmol/L blood. The mean bias for this plot is - 0.54 µmol/L blood. The bias for this specimen is very close the to the CDC expected value and there is tight scatter among all methods.

Figure 17. Reproducibility of Results: Bias Plot of Propionylcarnitine (C3) Values by Method Quarter 1, Specimen 11865 Expected Value (EV) = 11.69 µmol/L blood

C3 µmol/L blood

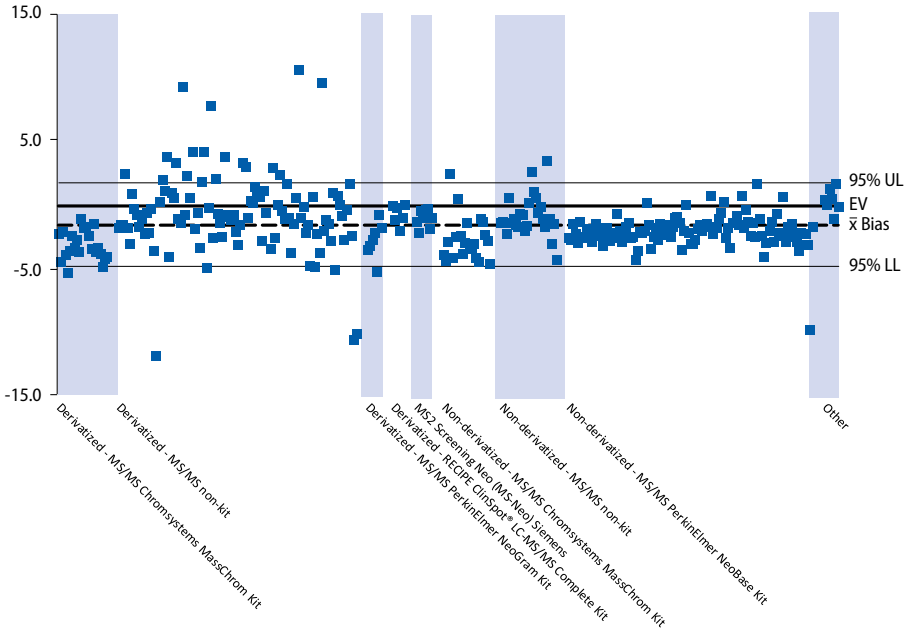
Quarter 1

Enriched—11.00

CDC Assayed—12.80

Participant Mean—10.22

Participant Bias—-1.47



The C3 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 –1.47 µmol/L blood. The bias plot shows good scatter around the bias.

Figure 18. Reproducibility of Results: Bias Plot of Malonylcarnitine (C3DC) Values by Method Quarter 4, Specimen 41862 Expected Value (EV) = 0.03 µmol/L blood

C3DC µmol/L blood

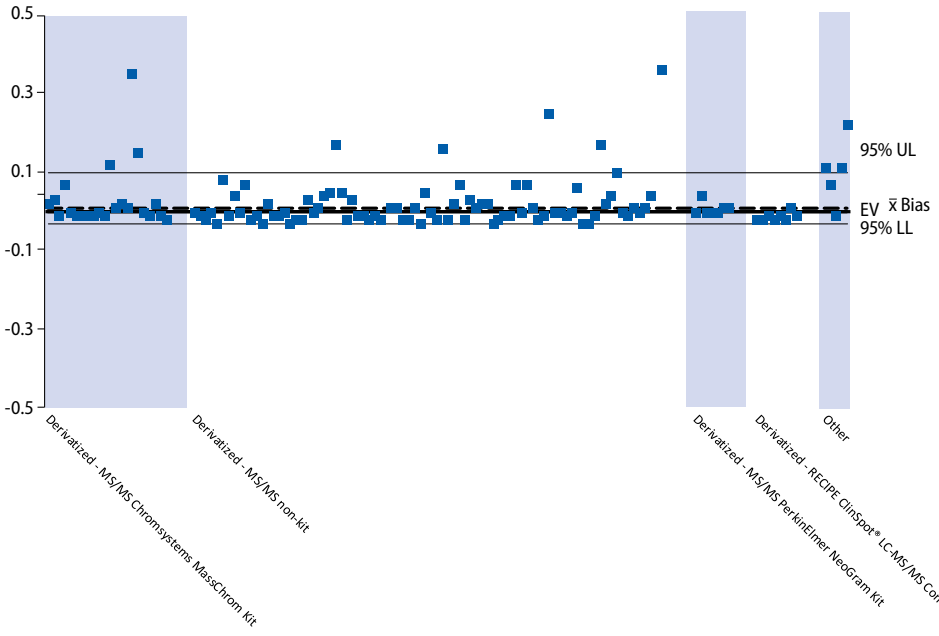
Quarter 4

Enriched—0.00

CDC Assayed—0.03

Participant Mean—0.04

Participant Bias—0.01



The C3DC bias plot shows units of measure on the y-axis ranging from 0.5 µmol/L blood to -0.5 µmol/L blood. The mean bias for this plot is 0.01µmol/L blood. The expected value of this specimen was very close to zero. The participant bias was very close the to expected value and with the exception of a few outliers, all data points are very close to the bias.

Figure 19. Reproducibility of Results: Bias Plot of Butylcarnitine (C4) Values by Method Quarter 1, Specimen 11861 Expected Value (EV) = 0.08 µmol/L blood

C4 µmol/L blood

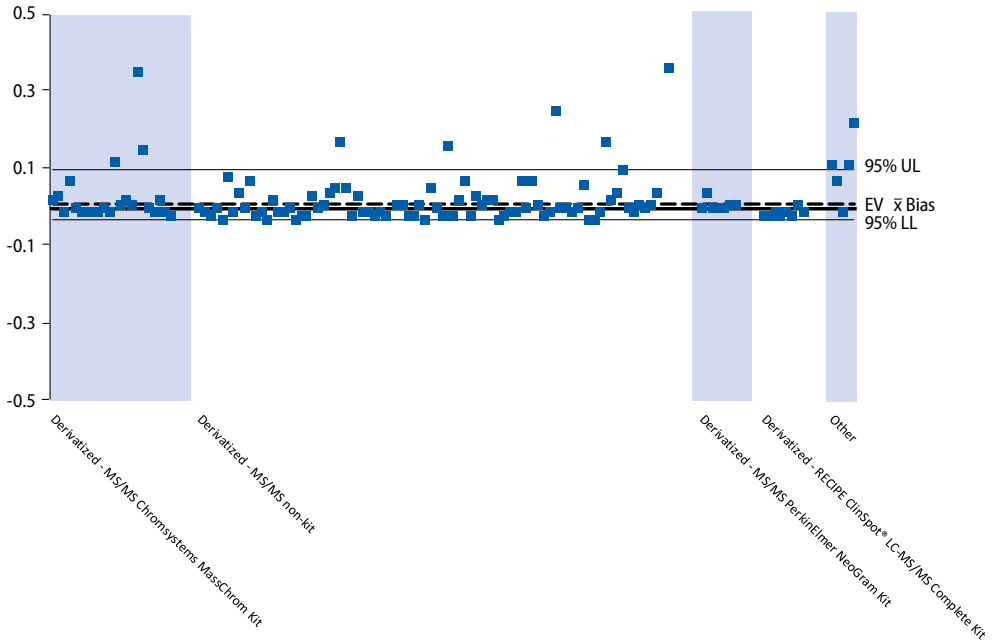
Quarter 1

Enriched—0.00

CDC Assayed—0.09

Participant Mean—0.10

Participant Bias—0.02



The C4 bias plot shows units of measure on the y-axis ranging from 0.5 µmol/L blood to -0.5 µmol/L blood. The mean bias for this plot is 0.02 µmol/L blood. All methods show a very tight scatter very close to the bias.

Figure 20. Reproducibility of Results: Bias Plot for Hydroxybutyrylcarntine (C4OH) Values by Method Quarter 4, Specimen 41862 Expected Value (EV) = 0.20 µmol/L blood

C4OH µmol/L blood

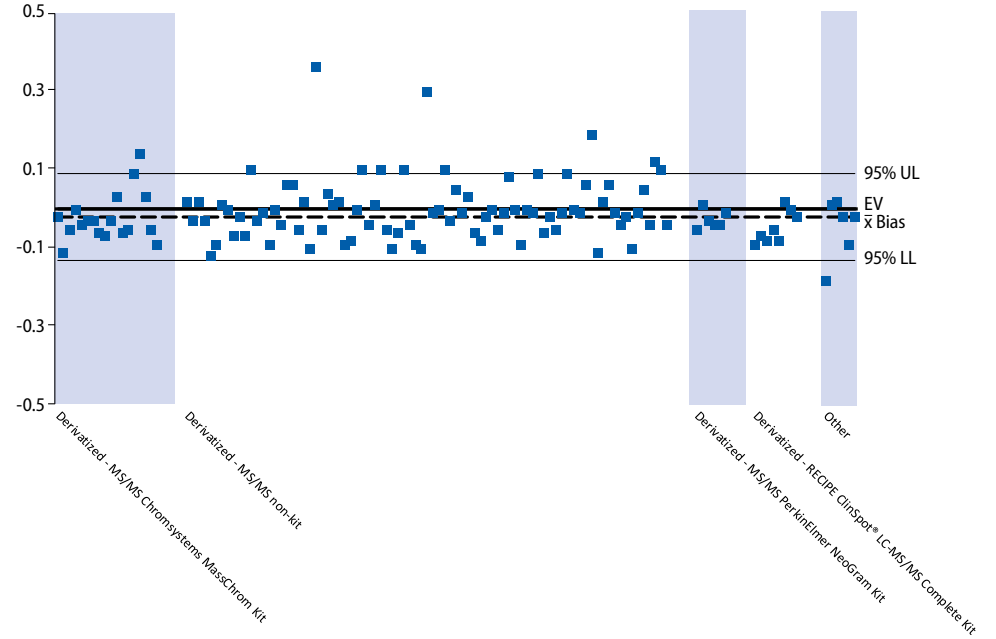
Quarter 4

Enriched—0.00

CDC Assayed—0.20

Participant Mean—0.18

Participant Bias—-0.2



The C4 bias plot shows units of measure on the y-axis ranging from 0.5 µmol/L blood to -0.5 µmol/L blood. The bias for this plot is - 0.02 µmol/L blood. All methods show a very tight scatter very close to the bias.

Figure 21. Reproducibility of Results: Bias Plot for Isovalerylcarnitine (C5) Values by Method Quarter 3, Specimen 31863 Expected Value (EV) = 2.99 µmol/L blood

C5 µmol/L blood

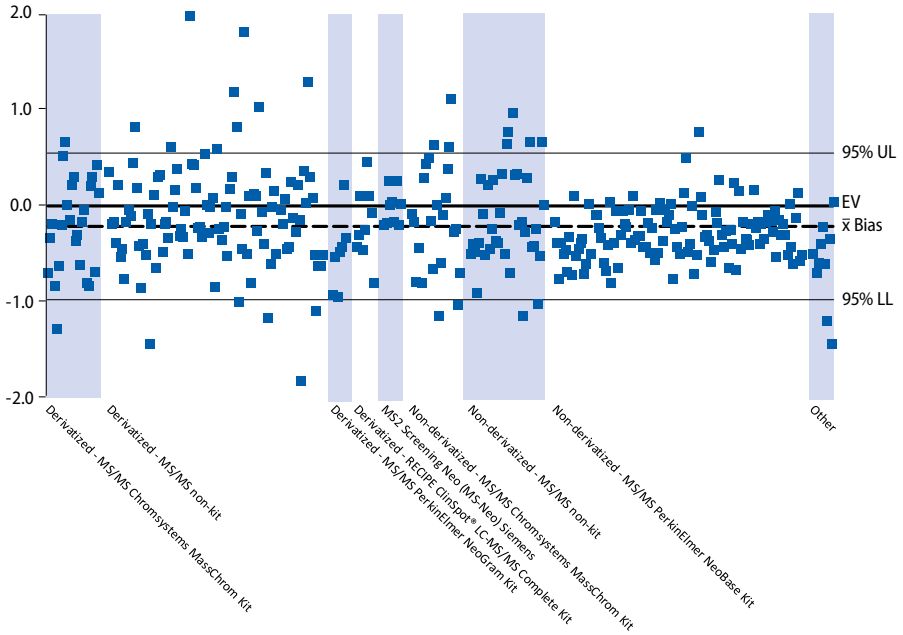
Quarter 3

Enriched—2.92

CDC Assayed—3.13

Participant Mean—2.78

Participant Bias—-0.21



The C5 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 -0.21 µmol/L blood. The C5 plot shows a good scatter close to the bias for all methods.

Figure 22. Reproducibility of Results: Bias Plot for Tiglylcarnitine (C5:1) Values by Method Quarter 1, Specimen 11861 Expected Value (EV) = 0.01 µmol/L blood

C5:1 µmol/L blood

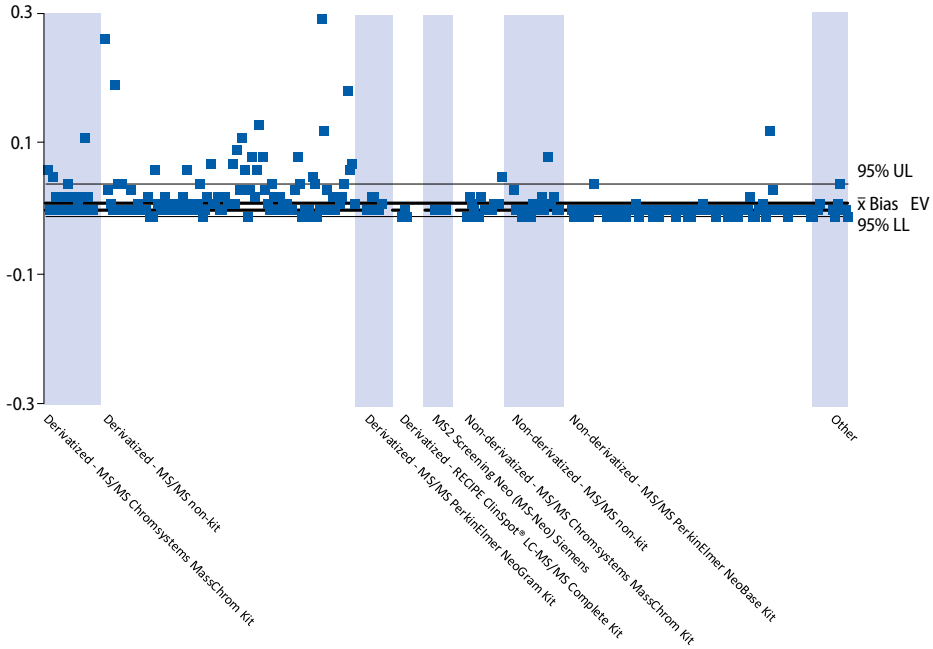
Quarter 1

Enriched—0.00

CDC Assayed—0.01

Participant Mean—0.02

Participant Bias—0.01



The C5:1 bias plot shows units of measure on the y-axis ranging from 0.3 µmol/L blood to -0.3 µmol/L blood. The mean bias for this plot is 0.01 µmol/L blood. The expected value of this specimen was very close to zero. The participant bias was very close the to expected value and with the exception of a few outliers, all data points are very close to the bias.

Figure 23. Reproducibility of Results: Bias Plot for Glutarylcarnitine (C5DC) Values by Method Quarter 1, Specimen 11862 Expected Value (EV) = 1.31 µmol/L blood

C5DC µmol/L blood

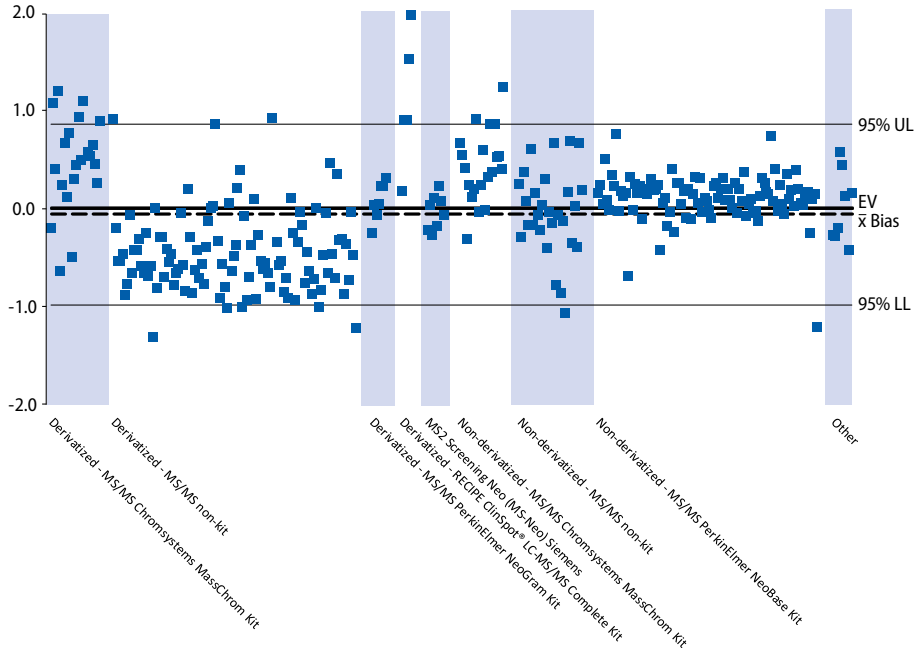
Quarter 1

Enriched—1.30

CDC Assayed—1.30

Participant Mean—1.25

Participant Bias—-0.06



The C5DC 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 -0.06 µmol/L blood. The C5DC plot shows a tight scatter within each method but shows distinctive bias differences between methods.

Figure 24. Reproducibility of Results: Bias Plot for Hydroxyisovalerylcarnitine (C5OH) Values by Method Quarter 3, Specimen 31864 Expected Value (EV) = 1.83 µmol/L blood

C5OH µmol/L blood

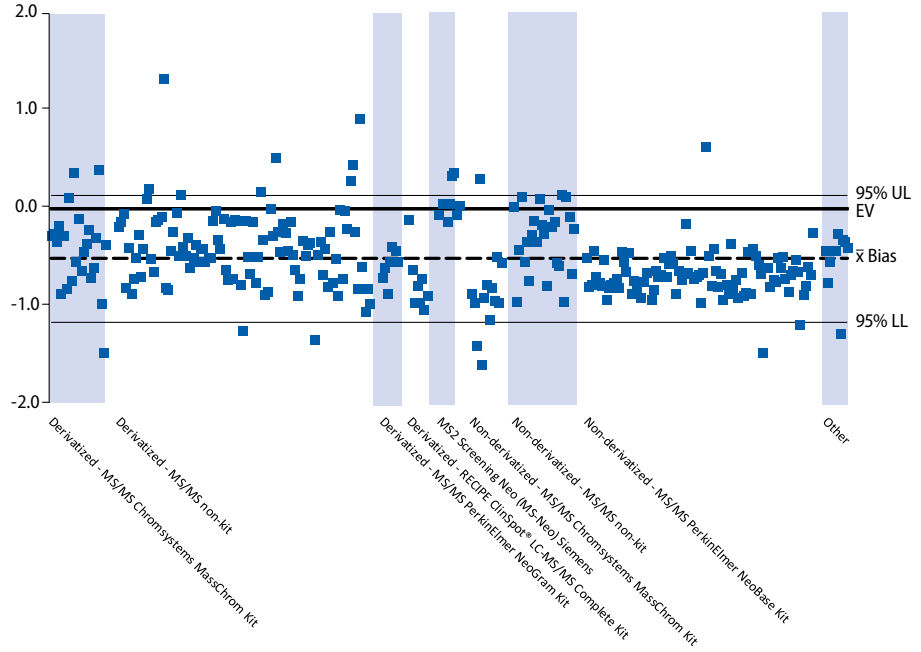
Quarter 3

Enriched—1.29

CDC Assayed—1.53

Participant Mean—1.32

Participant Bias—-0.51



The C5OH bias plot shows units of measure on the y-axis ranging from 2 µmol/L blood to -2 µmol/L blood. The bias for this plot is -0.51 µmol/L blood. The C5DC plot shows a slight negative bias but good scatter among most methods.

Figure 25. Reproducibility of Results: Bias Plot for Hexanoylcarnitine (C6) Values by Method Quarter 3, Specimen 31862 Expected Value (EV) = 1.54 µmol/L blood

C6 µmol/L blood

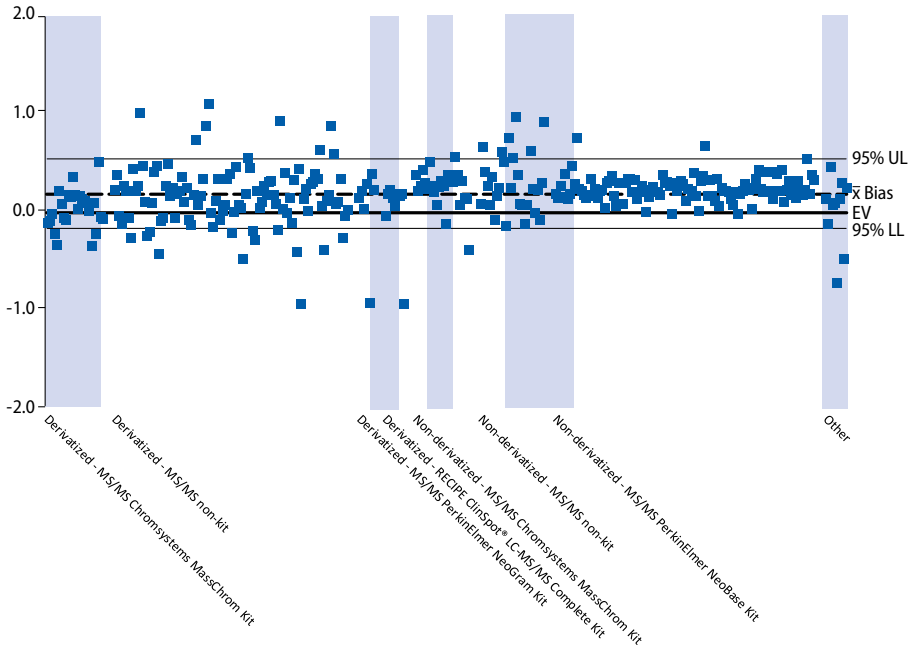
Quarter 3

Enriched—1.53

CDC Assayed—1.33

Participant Mean—1.31

Participant Bias—-0.23



The C6 bias plot shows units of measure on the y-axis ranging from 2 µmol/L blood to -2 µmol/L blood. The bias for this plot is -0.23 µmol/L blood. The plot shows a negative participant bias with good scatter among methods.

Figure 26. Reproducibility of Results: Bias Plot for Octanylcarnitine (C8) Values by Method Quarter 1, Specimen 11861 Expected Value (EV) = 1.63 µmol/L blood

C8 µmol/L blood

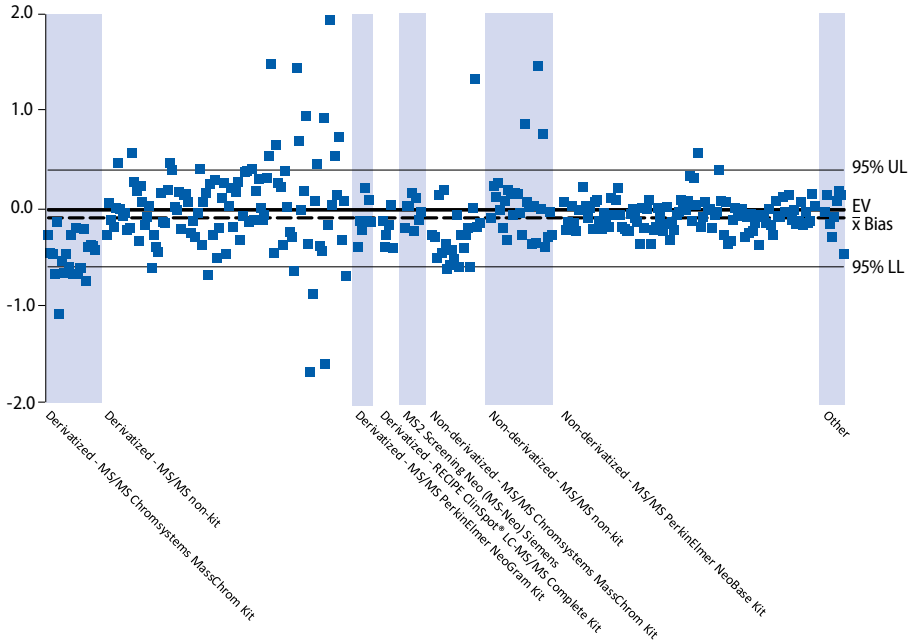
Quarter 1

Enriched—1.60

CDC Assayed—1.66

Participant Mean—1.57

Participant Bias—-0.06



The C8 bias plot shows units of measure on the y-axis ranging from 2 µmol/L blood to -2 µmol/L blood. The bias for this plot is -0.06 µmol/L blood. The participant bias is very close to the CDC expected value and there is good scatter among methods.

Figure 27. Reproducibility of Results: Bias Plot for Decanoylcarnitine (C10) Values by Method Quarter 1, Specimen 11861 Expected Value (EV) = 0.81 µmol/L blood

C10 µmol/L blood

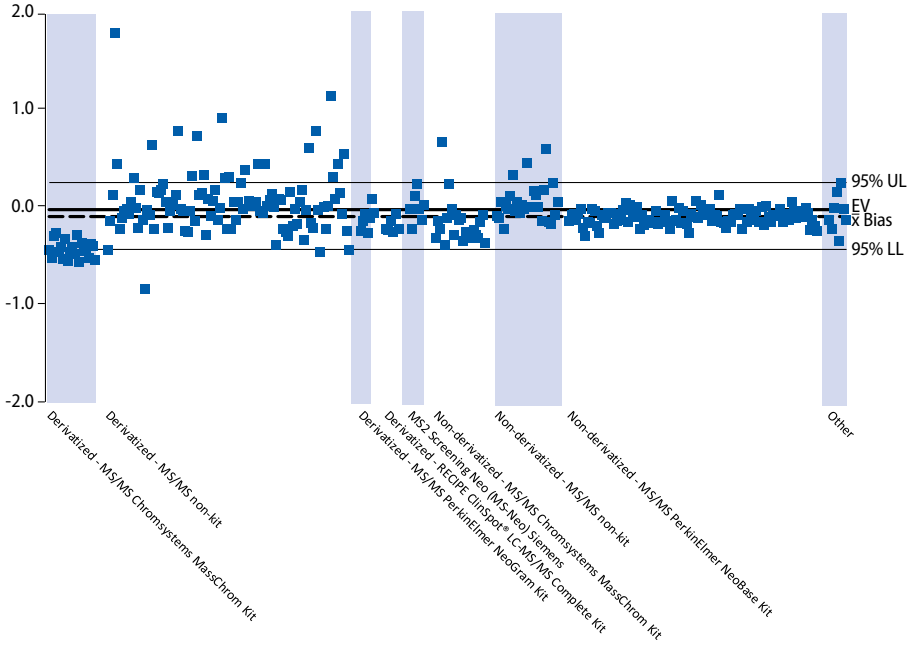
Quarter 1

Enriched—0.00

CDC Assayed—0.80

Participant Mean—0.74

Participant Bias—-0.07



The C10 bias plot shows units of measure on the y-axis ranging from 2 µmol/L blood to -2 µmol/L blood. The bias for this plot is -0.07 µmol/L blood. One method shows a distinct negative bias. The other methods show good scatter around the bias.

Figure 28. Reproducibility of Results: Bias Plot for Decenoylcarnitine (C10:1) Values by Method Quarter 1, Specimen 11861 Expected Value (EV) = 0.52 µmol/L blood

C10:1 µmol/L blood

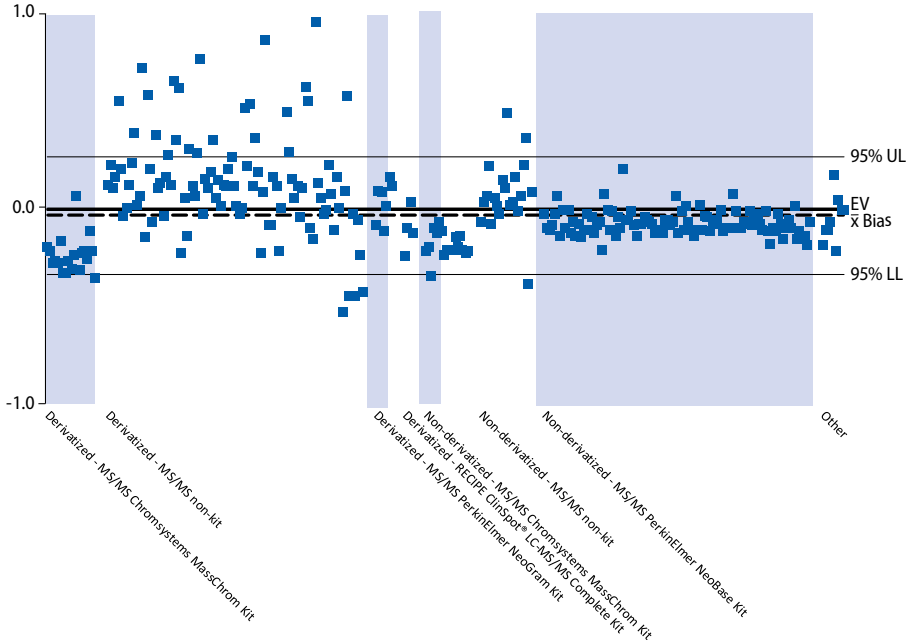
Quarter 1

Enriched—0.50

CDC Assayed—0.58

Participant Mean—0.49

Participant Bias—-0.03



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 29. Reproducibility of Results: Bias Plot of Decadienoylcarnitine (C10:2) Values by Method Quarter 3, Specimen 31862 Expected Value (EV) = 0.00 µmol/L blood

C10:2 µmol/L blood

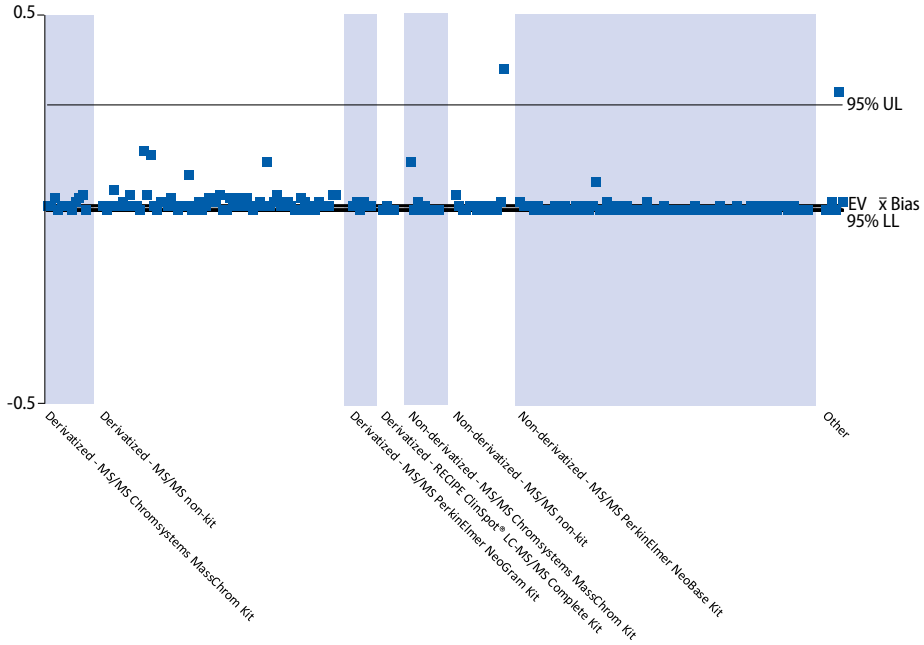
Quarter 3

Enriched—0.00

CDC Assayed—0.00

Participant Mean—0.01

Participant Bias—0.01



The C10:2 bias plot shows units of measure on the y-axis ranging from 0.5 µmol/L blood to -0.5 µmol/L blood. The bias for this plot is 0.01 µmol/L blood. The expected value of this specimen was very close to zero and the participant bias was very close the to expected value. With the exception of a few outliers, all data points are very close to the bias.

Figure 30. Reproducibility of Results: Bias Plot for Myristoylcarnitine (C14) Values by Method Quarter 1, Specimen 11864 Expected Value (EV) = 1.34 µmol/L blood

C14 µmol/L blood

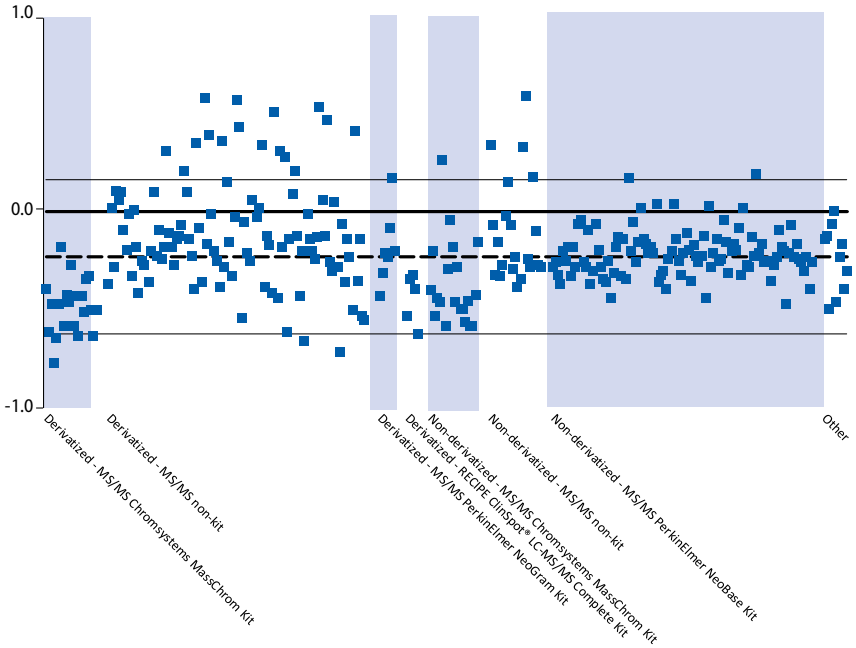
Quarter 1

Enriched—1.30

CDC Assayed—1.18

Participant Mean—1.11

Participant Bias—-0.23



The C14 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 -0.23 µmol/L blood. The C14 plot shows a slight negative bias and the majority of data points are below the bias.

Figure 31. Reproducibility of Results: Bias Plot of Tetradecenoylcarnitine (C14:1) Values by Method Quarter 4, Specimen 41861 Expected Value (EV) = 1.31 µmol/L blood

C14:1 µmol/L blood

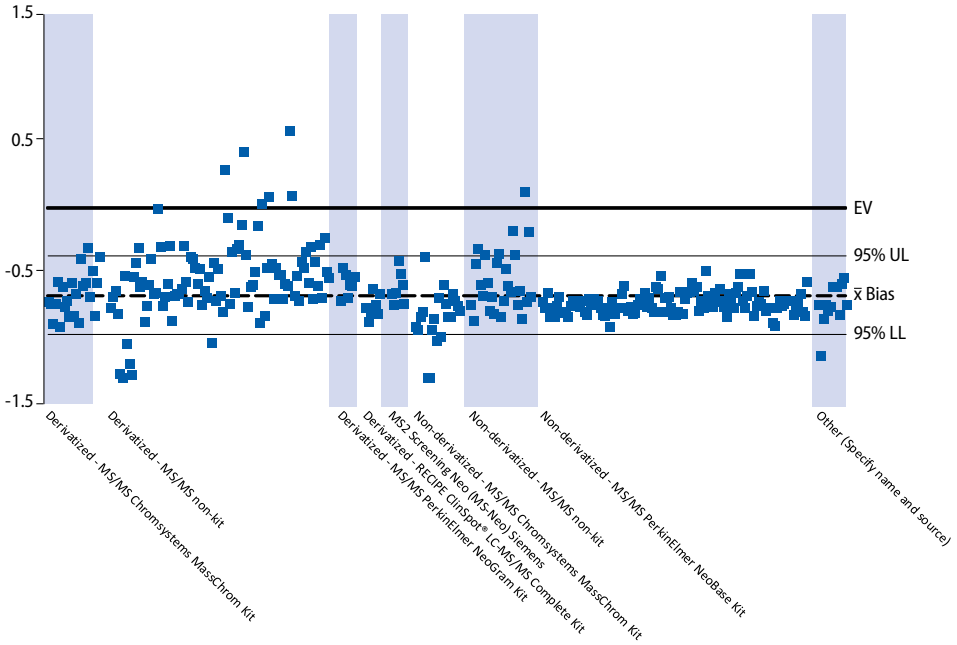
Quarter 4

Enriched—1.28

CDC Assayed—0.78

Participant Mean—0.64

Participant Bias—-0.67



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 - 0.67 µmol/L blood. The non-kit methods show a tight negative cluster around the bias and the kit methods are scatter above and below the bias.

Figure 32. Reproducibility of Results: Palmitoylcarnitine (C16) Values by Method Quarter 3, Specimen 31865 Expected Value (EV) = 3.70 µmol/L blood

C16 µmol/L blood

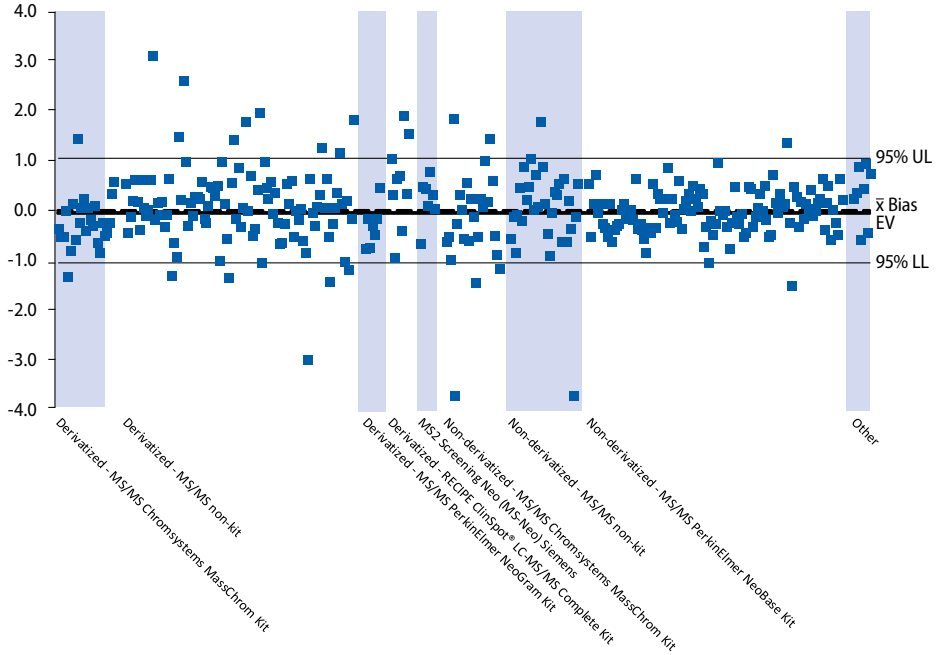
Quarter 3

Enriched—3.24

CDC Assayed—3.75

Participant Mean—3.75

Participant Bias—0.05



The C16 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 0.05 µmol/L blood. The C16 bias shows a bias very close to zero with good scatter among all participants and methods.

Figure 33. Reproducibility of Results: Hydroxypalmitoycarnitine (C16OH) Values by Method Quarter 4, Specimen 41861 Expected Value (EV) = 1.40 µmol/L blood

C16OH µmol/L blood

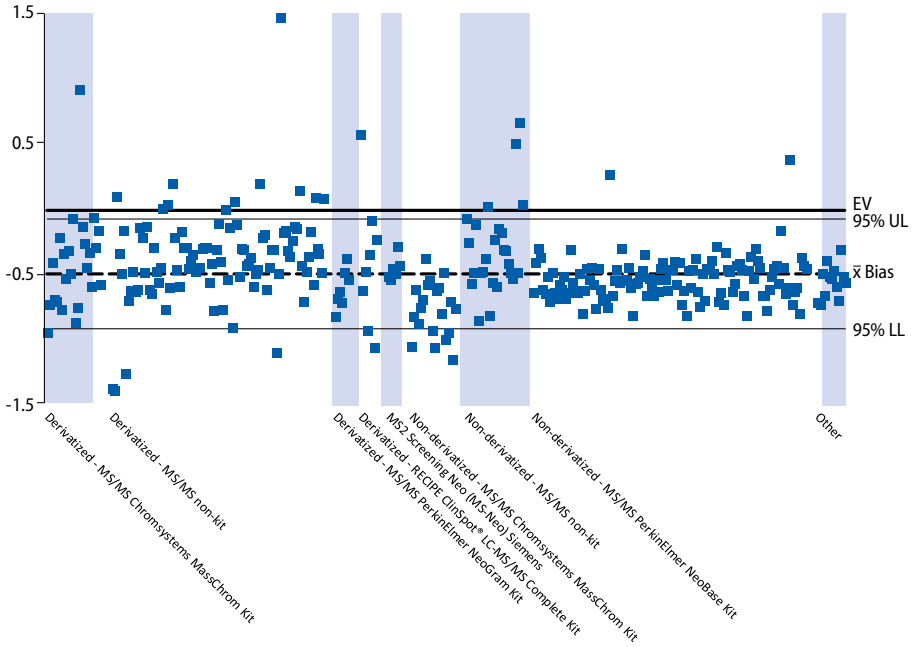
Quarter 4

Enriched—1.39

CDC Assayed—1.39

Participant Mean—0.92

Participant Bias—-0.48



The C16OH 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 - 0.48 µmol/L blood. The C16OH bias plot demonstrates scatter among all methods with most laboratories showing a negative bias.

Figure 34. Reproducibility of Results: Bias Plot for Stearoylcarnitine (C18) Values by Method Quarter 3, Specimen 31865 Expected Value (EV) = 1.73 µmol/L blood

C18 µmol/L blood

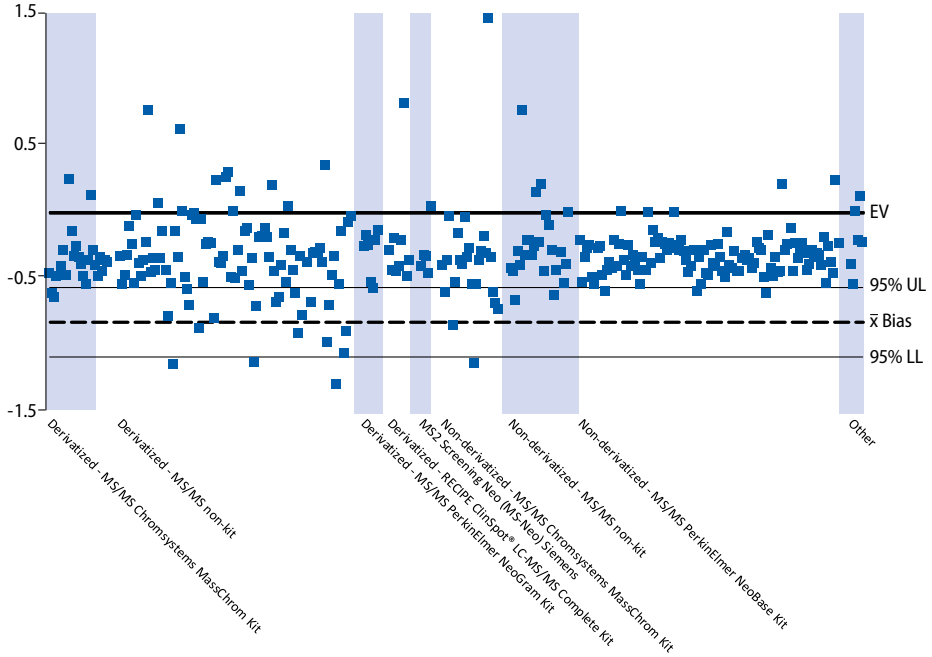
Quarter 3

Enriched—1.29

CDC Assayed—1.37

Participant Mean—1.40

Participant Bias—-0.33



The C18 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 -0.33 µmol/L blood. The C18 bias plot shows reasonable scatter of values within and among methods while showing a slight negative bias.

Figure 35. Reproducibility of Results: Bias Plots for Oleoylcarnitine (C18:1) Values by Method Quarter 1, Specimen 11865 Expected Value (EV) = 0.84 µmol/L blood

C18:1 µmol/L blood

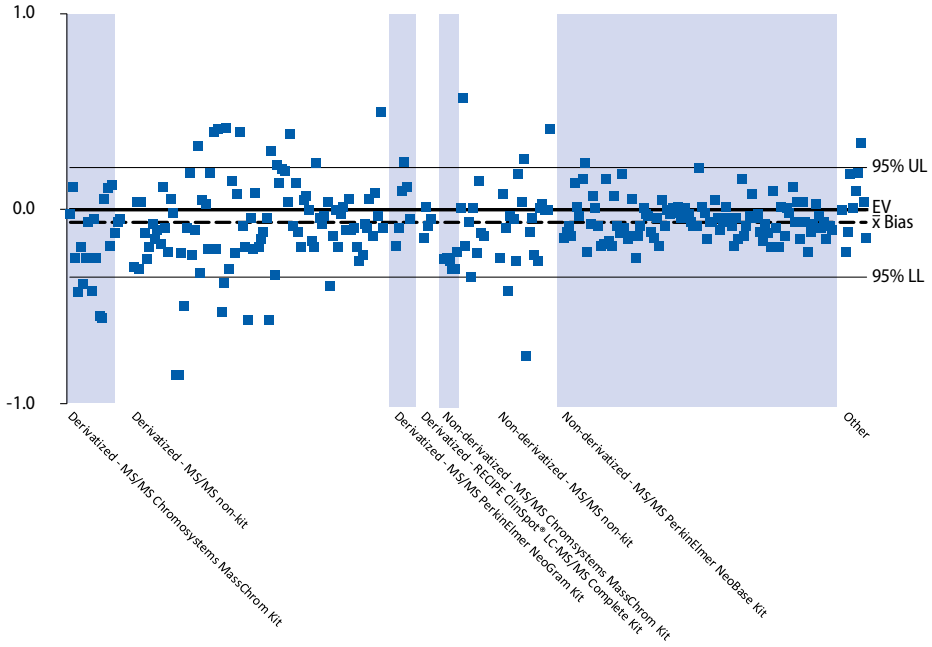
Quarter 1

Enriched—0.00

CDC Assayed—0.85

Participant Mean—0.78

Participant Bias—-0.06



The C18 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 -0.06 µmol/L blood. The C18 bias plot shows reasonable scatter of values within and among methods while showing a slight negative bias.

Figure 36. Reproducibility of Results: Bias Plot of Hydroxystearoylcarnitine (C18OH) Values by Method Quarter 4, Specimen 41861 Expected Value (EV) = 1.47 µmol/L blood

C18OH µmol/L blood

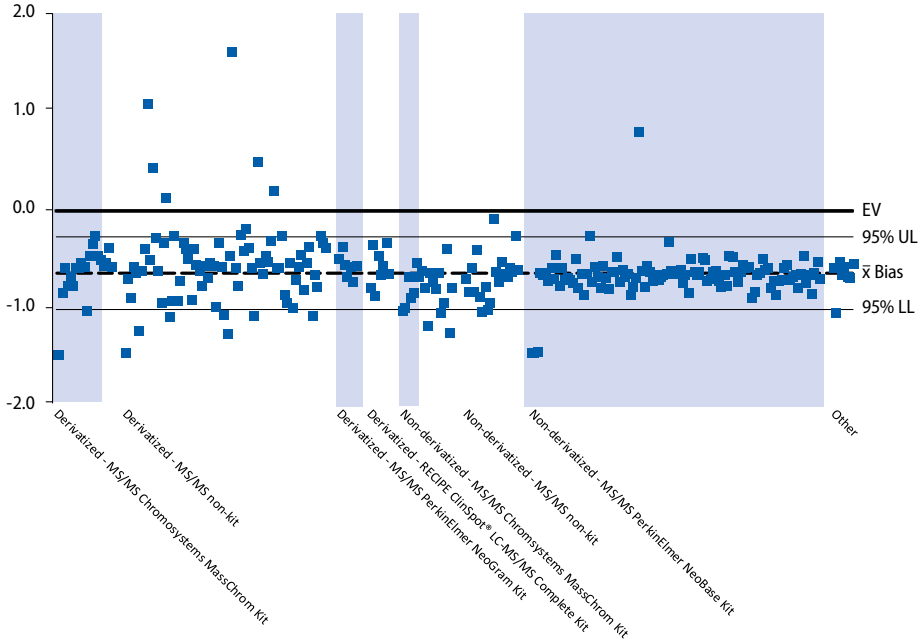
Quarter 4

Enriched—1.46

CDC Assayed—0.85

Participant Mean—0.83

Participant Bias—-0.64



The C18OH bias plot shows units of measure on the y-axis ranging from 2 µmol/L blood to -2 µmol/L blood. The bias for this plot is - 0.64 µmol/L blood. The C18OH plot shows a negative bias with all methods clustered around the 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 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"

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.

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[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.

Acknowlegments

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CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) ATLANTA, GA 30341

Director
Robert R. Redfield, M.D.
Director
National Center for Environmental Health
Patrick Breysse, Ph.D.

Director
Division of Laboratory Sciences
James L. Pirkle, M.D., Ph.D.
Chief
Newborn Screening and Molecular Biology Branch
Carla Cuthbert, Ph.D.

Contributors

Carter Asef, BS
Nicole Baird, Ph.D
John Bernstein, MS
Quan Bui, MS
Suzanne Cordovado, Ph.D
Paul Dantonio, MS
Katherine Duneman, MS
Sharon Flores, MS
Christopher Greene, Ph.D
Elizabeth Hall, BS
Laura Hancock, MS
Christopher Haynes, Ph.D
Jessica Hendricks, MS
Miyono Hendrix, MS
Laura C. Hildreth, BS
Deborah Koontz, Ph.D
Francis Lee, Ph.D
LiXia Li, Ph.D
Tim Lim, Ph.D
Daniel Mandel, Ph.D
Joanne Mei, Ph.D
Kristina Mercer, Ph.D
Stanimila Nikolova, Ph.D
Gyliann Pena, MS
Kostas Petritis, Ph.D
C. Austin Pickens, Ph.D
Blanche Temate, Ph.D
E. Shannon Torres, Ph.D
Robert Vogt, Ph.D
Irene Williams, MS
Sophia Winchester, BS
Golriz Yazdanpanah, MS
Sherri Zobel, BS

Production
Vinay Anumula, MS
Kizzy Stewart
Joy Pressley

ASSOCIATION OF PUBLIC HEALTH LABORATORIES SILVER SPRING, MD 20910

President
Joanne Bartkus, PhD
Chairman, Newborn Screening and Genetics in Public Health Committee
Michele Caggana, Sc.D., FACMG
Chairman, Newborn Screening Quality Assurance Quality Control Subcommittee
Patricia R. Hunt, B.A. and Joseph Orsini, Ph.D.
Chairman, Newborn Screening Molecular Subcommittee
Rachel Lee, Ph.D.

INQUIRIES TO:
Sherri Zobel, Editor
Centers for Disease Control and Prevention (CDC),
Newborn Screening Quality Assurance Program—Mailstop F-19
4770 Buford Highway, N.E., Atlanta, GA 30341-3724
E-mail: NSQAPDMT@cdc.gov

Notes:

For more information please contact
Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 33029-4027
Telephone: 1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348
E-mail: NSQAPDMT@cdc.gov
Web: https://www.cdc.gov/labstandards/nsqap.html
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