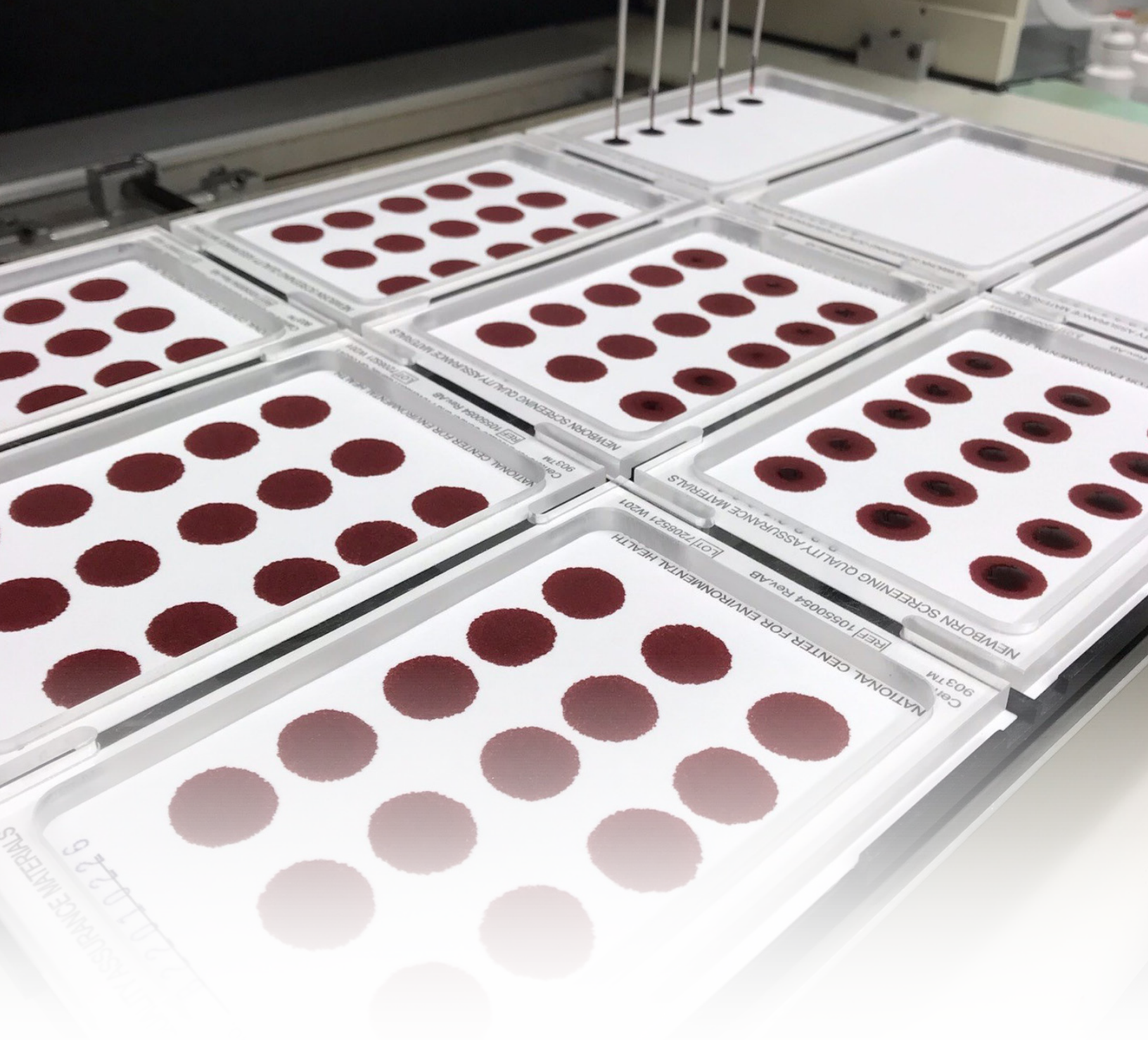


2021 ANNUAL SUMMARY REPORT

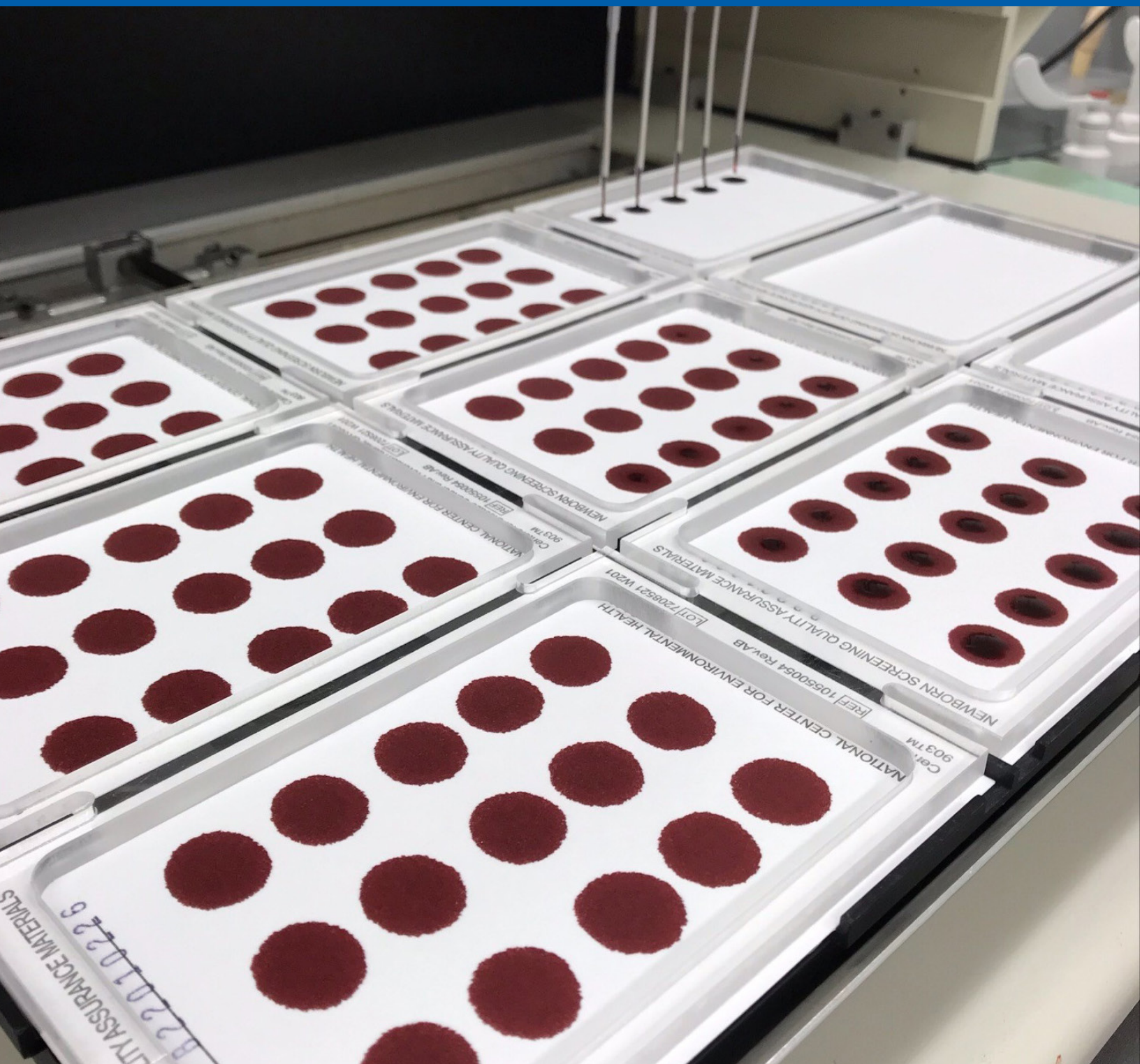
Newborn Screening Quality Assurance Program

Centers for Disease Control and Prevention
National Center for Environmental Health

Newborn Screening Quality Assurance Program

2021 Annual Summary Report, Volume 39a

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 Figures 2–37 (bias plots) are located in Appendix for Accessibility Descriptions, page 43.

AMENDED REPORT
This amended report replaces the Newborn Screening Quality Assurance Program Annual Summary Report, Volume 39. This amended report corrects the cutoff values for Alpha-L-Iduronidase on Table 13. Summary for lysosomal storage disorder cutoff values for domestic laboratories.

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Acronym Glossary

Notation	Description
17OHP	17 α-hydroxyprogesterone
A2LA	American Association for Laboratory Accreditation
ALD	X-linked adrenoleukodystrophy
AP	Astoria Pacific
BIOT	biotinidase
BMSL	Biochemical Mass Spectrometry Laboratory
CAH	second-tier congenital adrenal hyperplasia
CDC	Centers for Disease Control and Prevention
CFDNA	cystic fibrosis DNA
Chromsys	Chromsystems
CLSI	Clinical Laboratory Standards Institute
Color	Colormetric
DBS	dried blood spot
DER	derivatized tandem mass spectrometry method
ELISA	enzyme linked immunosorbent assay
ENZ	enzymatic
EV	expected value
FDA	Food and Drug Administration
FEIA	fluorescence enzyme immunoassay
FLUOR	floremetric
G6PD	glucose-6-phosphate dehydrogenase
GALT	galactose-1-phosphate uridyltransferase
Hb	sickle cell and other hemoglobinopathies
HIV	anti-human immunodeficiency virus-1 Antibody
HORM	hormone + total galactose

Notation	Description
IEC	International Electrotechnical Commission
IRT	immunoreactive trypsinogen
IS	Interscientifica
ISO	International Organization for Standardization
Labsys	Labsystems
LC	liquid chromatography
LSD	lysosomal storage disorder
MAN	manual
MAP	Molecular Assessment Program
MQIP	Molecular Quality Improvement Program
MS/MS	tandem mass spectrometry
MSMS1	tandem MS 1
NDER	non-derivatized tandem mass spectrometry method
NSQAP	Newborn Screening Quality Assurance Program
PE	PerkinElmer
PT	proficiency testing
QC	quality control
RBC	red blood cells
RUSP	Recommended Uniform Screening Panel
SMA	Spinal Muscular Atrophy
T4	thyroxine
TGAL	total galactose
TOXO	anti-Toxoplasma Antibody
TREC	T-cell receptor excision circle
TSH	thyroid stimulating hormone

Newborn screening is one of the most successful preventative health programs in the United States.

Introduction

Newborn screening is one of the most successful preventive health programs in the United States. Healthcare professionals collect DBS specimens from more than 98% of all U.S. newborns shortly after birth. DBS specimens are screened for certain genetic, metabolic, and endocrine disorders. The Centers for Disease Control and Prevention's NSQAP helps newborn screening laboratories with these testing processes.

NSQAP produces certified DBS materials for PT and QC analysis, works to improve the quality and scope of laboratory services, and provides consultation to laboratories. Every day, state-operated and private newborn screening laboratories process thousands of DBS specimens. 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 is accredited by the A2LA for the ISO/IEC 17043. Accreditation is renewed every four years by a thorough review of Newborn Screening and Molecular Biology Branch's quality management system for the ability to develop and administer specific PT protocols. The branch's Biochemical PT program is included in the A2LA Scope of Accreditation. The accreditation does not include testing for G6PD and NSQAP's disease specific PT programs. Consult A2LA Certificate#4190.01 for a complete list of the 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 quality assurance materials for newborn DBS screening tests and have assisted laboratories with DBS-related testing issues. NSQAP primarily supports U.S. newborn screening laboratories; however, private and international laboratories can enroll in the program. Participation is voluntary. NSQAP provides quality assurance services for the core (primary) and secondary conditions listed in the U.S. Recommended Uniform Screening Panel (RUSP) [1].

In 2021, there was a slight decrease in participation for some programs due to the COVID-19 pandemic; however, overall, the NSQAP continued to grow. In 2021, 667 newborn screening laboratories in 88 countries participated in the program (Figure 1). Of these laboratories, 455 participated in PT (Table 1) and 346 in QC (Table 2). NSQAP distributed DBS materials for 75 newborn screening analytes to the participating laboratories (Tables 1 and 2).

The NSQAP Laboratory provides quality assurance materials for T4, TSH, 17OHP, IRT, Hb, HIV, TOXO, and the second-tier CAH programs.

NSQAP works with the Biochemical Mass Spectrometry Laboratory and the Molecular Quality Improvement Program to produce and distribute more specialized DBS materials. Both BMSL and MQIP are part of the Newborn Screening and Molecular Biology Branch.

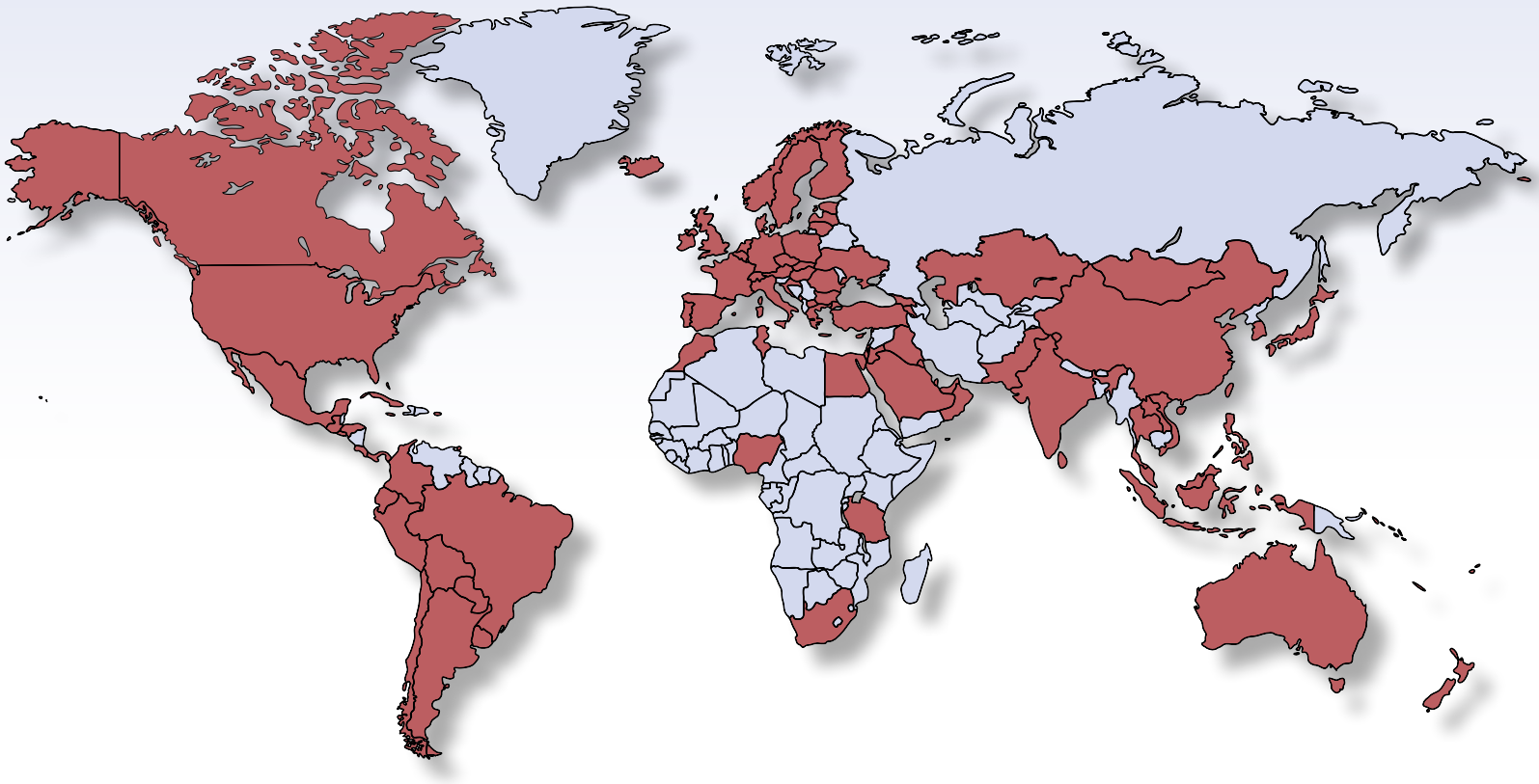
BMSL offers MS/MS quality assurance, education, and research opportunities for newborn screening and oversees the amino acids, acylcarnitines, ALD, BIOT, TGAL, GALT, G6PD, LSD, and filter paper evaluation programs. BMSL also provides second-tier QC programs for maple syrup urine disease/phenylketonuria and homocystinuria.

MQIP oversees the CFDNA PT and TREC PT and provides molecular assay technical assistance to NSQAP participants. In July of 2021, after the completion of a successful pilot program, MQIP launched a new PT program for SMA for laboratories. This program uses DBS to determine the presence or absence of survival motor neuron 1 exon 7. The SMA PT program is offered to qualified domestic and international participants.

MQIP offers the Molecular Assessment Program (MAP) to U.S. newborn screening laboratories. A MAP visit is used to assess components of molecular testing. MAP includes guidance for laboratory-specific needs and assists with evaluating ongoing and future molecular testing procedures. In-person MAP site visits are currently on hold due to COVID-19 pandemic travel restrictions; however, MQIP is offering virtual MAP site visits tailored for specific issues. Contact CGreene@cdc.gov for more information.

Figure 1. Countries participating in the Newborn Screening Quality Assurance Program.

NSQAP Participants



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
Georgia
Germany
Greece
Guatemala
Honduras
Hong Kong
Hungary
Iceland
India
Indonesia
Iraq
Ireland
Israel
Italy
Japan
Jordan
Kazakhstan
Kuwait
Laos
Latvia
Lebanon
Lithuania
Luxembourg
Macedonia
Malaysia
Malta
Mexico
Mongolia
Morocco
Netherlands
New Zealand
Nigeria
Norway
Oman
Pakistan
Panama
Paraguay
Peru
Philippines
Poland
Portugal
Qatar
Romania
Saudi Arabia
Singapore
Slovak Republic
Slovenia
South Africa
South Korea
Spain
Sri Lanka
Sweden
Switzerland
Taiwan
Tanzania
Thailand
Tunisia
Turkey
Ukraine
United Arab Emirates
United Kingdom
United States
Uruguay
Vietnam

Table 1. Number of participants reporting proficiency testing analytes. (N = 455)

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

Analyte	Total PT Participation in 2021
17OHP	283
T4	81
TSH	344
TGAL	181
BIOT	213
GALT	147
IRT	239
G6PD	99
CFDNA	74
Hb	82
anti-HIV-1	19
TOXO	12
TREC	84
SMA	28
ARG	263
CIT	289
LEU	317
MET	303
PHE	399
SUAC	181
TYR	319
VAL	284
C0(L)	307
C2(L)	237
C3	308
C3DC	105
C3DC+C4OH	146
C4	290
C4OH	96
C5	315
C5:1	285
C5DC	304
C5OH	275
C6	293
C8	321
C10	309
C10:1	277
C10:2	202
C14	292
C14:1	302
C16	299
C16OH	299
C18	284
C18:1	278
C18OH	250
17OHP2	29
4AD2	29
CORT2	29
11D2	19
21D2	17
GALC	26
GAA	13
IDUA	54
C24-LPC	20
C26-LPC	36

Table 2. Number of participants reporting quality control analytes, 2021 (N = 346)

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

Analyte	Total QC participation in 2021
17OHP	201
T4	47
TSH	264
TGAL	123
GALT	72
IRT	161
ALA	176
ARG	191
CIT	206
GLY	158
LEU	222
MET	213
ORN	161
PHE	278
SUAC	121
TYR	220
VAL	207
C0	216
C2	210
C3	216
C3DC	64
C3DC+C4OH	123
C4	209
C4OH	60
C5	219
C5:1	200
C5DC	208
C5OH	187
C6	213
C8	227
C10	223
C12	203
C14	216
C14:1	207
C16	215
C16OH	215
C18	208
C18OH	183
17OHP2	29
4AD2	28
CORT2	28
11D2	21
21D2	21
GALC	25
GAA	47
IDUA	49
GLA	35
ABG	33
ASM	22
C20-LPC	24
C22-LPC	24
C24-LPC	40
C26-LPC	48
GUAC	12
ALE2	19
CRE2	9
CRN2	5
ILE2	19
LEU2	21
PHE2	23
TYR2	22
VAL2	24
MMA2	29
EMA2	11
MCA2	23
MA2	2
tHCY2	29

Filter Paper

NSQAP evaluates absorption characteristics of all filter paper lots approved by the FDA as a newborn screening collection device [2]. Filter paper manufacturers must establish their own equivalent evaluation. NSQAP's evaluations are an impartial and voluntary service offered as a function of our QC program. The evaluations do not constitute endorsement of any product.

For there to be meaningful comparability in analyte concentration results among NBS specimens, the collection matrix must be highly uniform—both among and within production lots. NSQAP uses an isotopic method developed at CDC to evaluate and compare filter paper lots. Briefly, the method consists of adding radioisotope-labeled T4 to a pool of blood with washed, intact red cells and uses this radioactive blood to create DBS. To calculate serum absorption volumes, radiation emitted by 3.2mm disks punched from the DBS is compared to the radioactivity in a known volume of liquid blood from the same pool. The latest version of CLSI Standard NBS01-Ed7, Blood Collection on Filter Paper for Newborn Screening Programs, describes the isotopic method for filter paper evaluation.

PerkinElmer Health Sciences and Cytiva Life Sciences are FDA-approved, newborn screening filter paper manufacturers. They provided NSQAP with statistically valid sample sets of unprinted filter paper from each production lot. Tables 3 and 4 show serum absorption volumes from the 10 most recent lots from both manufacturers. Using blood with washed intact RBCs, the published, standardized acceptable serum absorption volume per 3.2-mm disk (mean value and 95% confidence interval) is 1.44 ± 0.20 µL. [2] 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 W171, W181, and W191 to produce the QC and PT specimens distributed in 2021.

Table 3. PerkinElmer 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 Punch Average (StDev)	Absorption Time (sec) Average (StDev)	Spot Diameter (mm) Average (StDev)
114691	Aug 2021	1.46 (0.09)	12.3 (2.0)	15.8 (0.7)
114068	Aug 2020	1.44 (0.09)	13.2 (3.8)	16.1 (0.4)
112911	June 2019	1.49 (0.16)	8.4 (1.1)	15.8 (0.7)
112147	Sept 2018	1.49 (0.11)	7.9 (0.9)	15.8 (0.6)
111064	July 2017	1.47 (0.20)	8.2 (1.0)	15.7 (0.5)
110092	July 2016	1.45 (0.09)	9.0 (1.2)	16.0 (0.7)
105617	May 2016	1.46 (0.08)	8.3 (1.8)	15.8 (0.5)
105616	Jan 2016	1.56 (0.11)	10.6 (2.0)	15.6 (0.5)
105178	Aug 2015	1.46 (0.09)	7.8 (1.1)	15.9 (0.6)
104568	March 2015	1.56 (0.10)	10.1 (2.1)	15.9 (0.7)

Table 4. Cytiva Life Sciences 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 Punch Average (StDev)	Absorption Time (sec) Average (StDev)	Spot Diameter (mm) Average (StDev)
W201	Aug 2020	1.40 (0.09)	14.6 (2.8)	16.1 (0.6)
W191	Oct 2019	1.43 (0.18)	12.2 (2.2)	16.0 (0.7)
W181	Sept 2018	1.42 (0.12)	16.1 (3.3)	16.2 (0.6)
W171	April 2017	1.39 (0.10)	19.7 (4.7)	16.0 (0.7)
W162	Jan 2017	1.43 (0.08)	12.9 (2.7)	16.0 (0.7)
W161	May 2016	1.41 (0.08)	14.8 (3.7)	16.2 (0.8)
W152	Aug 2015	1.37 (0.09)	15.8 (2.4)	16.2 (0.6)
W151	Aug 2015	1.39 (0.08)	15.2 (2.6)	16.2 (0.8)
W142	April 2015	1.46 (0.08)	11.0 (2.2)	16.0 (0.7)
W141	March 2014	1.53 (0.10)	13.8 (3.6)	15.9 (0.6)

Proficiency Testing

In 2021, three PT events were conducted. PT panels consisted of five blind-coded specimens. Instructions for analysis and reporting data can be found online in the NSQAP participant portal at https://nbs.dynamics365portals.us/. Specimen sets were packaged in a zip-closed, metalized plastic bag with desiccant. These specimens provided 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))
- low acetylcarnitine (C2(L))
- propionylcarnitine (C3)
- malonylcarnitine [derivatized] (C3DC)
- C3DC+C4OH [non-derivatized]
- butyrylcarnitine (C4)
- hydroxybutyrylcarnitine [derivatized] (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 (C16OH)
- stearoylcarnitine (C18)
- oleoylcarnitine (C18:1)
- hydroxystearoylcarnitine (C18OH)

OTHER ANALYTES

- 17 α-hydroxyprogesterone (17OHP)
- 24:0-lysophosphatidylcholine (C24-LPC)
- 26:0-lysophosphatidylcholine (C26-LPC)
- acid α-glucosidase (GAA)
- α-L-iduronidase (IDUA)
- anti-HIV-1 antibodies (HIV)
- anti-toxoplasma antibodies (TOXO)
- biotinidase (BIOT)
- cystic fibrosis DNA variant detection (CFDNA)
- galactoceramidase (GALC)
- galactose-1-phosphate uridyltransferase (GALT)
- glucose-6-phosphate dehydrogenase (G6PD)
- immunoreactive trypsinogen (IRT)
- second-tier 11-deoxycortisol (11D2)
- second-tier 17 α-hydroxyprogesterone (17OHP2)
- second-tier 21-deoxycortisol (21D2)
- second-tier 4-androstenedione (4AD2)
- second-tier cortisol (CORT2)
- sickle cell disease and other hemoglobinopathies (Hb)
- Spinal Muscular Atrophy (SMAPT)
- T-cell receptor excision circle (TREC)
- thyroid-stimulating hormone (TSH)
- thyroxine (T4)
- total galactose (TGAL)

Proficiency Testing Materials and Methods

For each PT event, NSQAP certified that specimens are homogenous, accurate, stable, and suitable for newborn screening assays. PT materials were produced from unaltered donor blood, enriched or depleted single blood units, or pooled blood units. Most PT specimens were prepared from whole blood of 50% hematocrit.

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

C0(L) and C2(L) PT specimens were produced by washing fresh RBCs at least six times then combining with charcoal-stripped serum.

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

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

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

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

GALT and G6PD deficient PT specimens were made using a 50/50 saline/serum solution combined with compatible washed RBCs. Mixing was followed by heat treatment.

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

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

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

LSD PT specimens were prepared from human blood, including cord blood from unaffected persons and leuko-depleted adult blood restored with lymphoblast cell lines derived from patients with LSD.

SMA PT specimens were prepared from human blood, including leukocyte-depleted blood, and leukocyte-depleted blood containing EBV transduced lymphocytes from anonymous SMA patients, carriers, or unaffected individuals.

TREC PT specimens were prepared from human blood, including leukocyte-depleted blood, cord blood from unaffected persons, and leukocyte-depleted blood containing EBV transduced lymphocytes that do not contain TRECs.

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

Proficiency Testing Data Handling

Participants submitted PT data and clinical assessments using the NSQAP Participant Portal. Laboratories that submitted results before the data reporting deadline received an individual laboratory evaluation and their data were included in the data summary report.

Proficiency Testing Errors and Challenges

Specimens were evaluated as "Acceptable" or "Unacceptable." For each analyte and specimen to achieve an "Acceptable" evaluation, the participating laboratory's presumptive clinical assessment must match the CDC-certified clinical assessment. When clinical assessments differ, the evaluation is "Unacceptable." NSQAP did not identify "Unacceptable" results as "false negative" or "false positive." Instead, the participating laboratory must categorize "Unacceptable" results according to their protocols and policies.

If less than 10 U.S. laboratories reported results for any one specimen, all submitted results were evaluated. If 10 or more U.S. laboratories reported results, a consensus of 80% of the U.S. laboratories must be reached for a specimen to be evaluated. NSQAP occasionally challenges cutoff levels by enriching samples in the cutoff range. Samples in the cutoff range are closely reviewed by the NSQAP PT committee. Specimens that were not evaluated were considered educational.

Tables 5–8 show the 2021 analyte and disorder assessments that were reported as "Unacceptable" by domestic and international laboratories. The rates for unacceptable assessments were based on the total number of specimens tested. Specimens that were not evaluated were not included in the error calculations.

The CFDNA PT program provided evaluations based on allele identification and clinical assessment. Allele identification depended on the method used. Table 9 summarizes the CFDNA variant challenges distributed in 2021.

Table 10 shows the challenges distributed in 2021 for sickle cell disease and other hemoglobinopathies. Participants were evaluated on reported hemoglobin phenotypes and their ability to provide correct clinical assessments.

Table 5. Summary of disease specific and non-MSMS proficiency testing errors by domestic laboratories

Analyte/ Disorder	Specimens Assayed (N)	Unacceptable Assessments (%)
24:0 Lysophosphatidylcholine	75	0.0%
26:0 Lysophosphatidylcholine	245	0.0%
anti-*Toxoplama* Antibodies	30	0.0%
Biotinidase Deficiency	600	0.0%
Congenital Adrenal Hyperplasia	600	0.0%
Congenital Hypothyroidism	615	0.0%
Cystic Fibrosis DNA Variant Clinical Assessment Errors	505	0.4%
G6PD Deficiency	30	0.0%
GALT Deficiency	615	0.0%
Total Galactose Screen	295	0.0%
Human Immunodeficiency Virus	80	0.0%
Immunoreactive Trypsinogen	630	0.2%
Lysosomal Storage Disorder Krabbe	165	0.0%
Lysosomal Storage Disorder Pompe	355	0.0%
Lysosomal Storage Disorder Mucopolysaccharidosis Type 1	370	0.0%
T-Cell Receptor Excision Circle	605	1.7%
Second-tier Congenital Adrenal Hyperplasia	105	6.7%
Sickle Cell and Other Hemoglobinopathies Phenotype Errors	630	0.2%
Sickle Cell and Other Hemoglobinopathies Clinical Assessment Errors	630	0.0%
Spinal Muscular Atrophy	260	0.4%

Table 6. Summary of disease specific and non-MSMS proficiency testing errors by international laboratories

Analyte/ Disorders	Specimens Assayed (N)	Unacceptable Assessments (%)
24:0 Lysophosphatidylcholine	130	1.5%
26:0 Lysophosphatidylcholine	180	2.8%
anti-Toxoplama Antibodies	230	8.3%
Biotinidase Deficiency	2150	0.7%
Congenital Adrenal Hyperplasia	3015	0.5%
Congenital Hypothyroidism	3725	1.1%
Cystic Fibrosis DNA Variant Clinical Assessment Errors	470	3.0%
G6PD Deficiency	1180	1.4%
GALT Deficiency	1360	1.7%
Total Galactose Screen	2000	1.3%
Human Immunodeficiency Virus	130	0.0%
Immunoreactive Trypsinogen	2480	1.8%
Human Immunodeficiency Virus	130	0.0%
T-Cell Receptor Excision Circle	555	2.9%
Second-tier Congenital Adrenal Hyperplasia	280	8.6%
Sickle Cell and Other Hemoglobinopathies Phenotype Errors	475	1.7%
Sickle Cell and Other Hemoglobinopathies Clinical Assessment Errors	475	1.7%

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

Analyte	Specimens Assayed (N)	Unacceptable Assessments (%)
Arginine Screen	515	0.6%
Citrulline Screen	630	0.6%
Leucine Screen	640	0.9%
Methionine Screen	625	0.0%
Phenylalanine Screen	750	0.0%
Succinylacetone Screen	570	0.0%
Tyrosine Screen	685	0.0%
Valine Screen	440	0.0%
C0(L) Screen	665	0.0%
C2(L) Screen	340	0.6%
C3 Screen	680	0.0%
C3DC Screen	185	0.0%
C3DC+C4OH Screen	385	0.0%
C4 Screen	615	0.0%
C4OH Screen	160	1.3%
C5 Screen	680	0.1%
C5:1 Screen	660	0.6%
C5DC Screen	665	0.2%
C5OH Screen	665	0.2%
C6 Screen	610	0.3%
C8 Screen	680	0.1%
C10 Screen	610	0.3%
C10:1 Screen	565	0.0%
C10:2 Screen	380	0.5%
C14 Screen	590	1.0%
C14:1 Screen	680	0.3%
C16 Screen	640	0.3%
C16OH Screen	680	0.1%
C18 Screen	545	2.4%
C18:1 Screen	565	0.4%
C18OH Screen	510	0.2%

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

Analyte	Specimens Assayed (N)	Unacceptable Assessments (%)
Arginine Screen	2740	1.2%
Citrulline Screen	3010	3.0%
Leucine Screen	3380	1.6%
Methionine Screen	3220	2.6%
Phenylalanine Screen	4305	1.3%
Succinylacetone Screen	1720	1.6%
Tyrosine Screen	3360	0.9%
Valine Screen	3160	0.9%
C0(L) Screen	3270	2.0%
C2(L) Screen	2575	5.4%
C3 Screen	3265	1.5%
C3DC Screen	955	2.6%
C3DC+C4OH Screen	1405	1.1%
C4 Screen	3045	1.1%
C4OH Screen	905	3.5%
C5 Screen	3355	1.0%
C5:1 Screen	2945	0.8%
C5DC Screen	3205	2.0%
C5OH Screen	2850	5.4%
C6 Screen	3105	1.4%
C8 Screen	3445	0.9%
C10 Screen	3330	1.8%
C10:1 Screen	2935	1.0%
C10:2 Screen	2100	1.0%
C14 Screen	3120	1.6%
C14:1 Screen	3185	1.0%
C16 Screen	3165	1.1%
C16OH Screen	3185	0.6%
C18 Screen	3035	2.5%
C18:1 Screen	2930	0.5%
C18OH Screen	2640	0.8%

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

Variant (Legacy Name)	Variant (HGVS Nomenclature)	Variants Sent
F508del	p.Phe508del	8
1677delTA	p.Tyr515X	1
2307insA	p.Glu726ArgfsX4	1
3120+1G>A	c.2988+1G>A	1
3272-26A>G	c.3140-26A>G	1
3876delA	p.Lys1250ArgfsX9	1
CFTRdele17a-18	c.(2988+1_2989- 1)_ (3468+1_3469-1)del	1
G551D	p.Gly551Asp	1
Q493X	p.Gln493X	1
R1162X	p.Arg1162X	1
R117H	p.Arg117His	1
R553X	p.Arg553X	1
S549N	p.Ser549Asn	1
Wild type	-	10

Table 10. Hemoglobinopathies accepted presumptive phenotype distributed

Quarter	Specimen 1	Specimen 2	Specimen 3	Specimen 4	Specimen 5
Quarter 1	FA	FAS	FAC	FAS	FAC
Quarter 3	FS	FA	FAC	FAS	Bart's
Quarter 4	FAC	FAS	FAC	FA	FAC

Proficiency Testing Cutoff Values

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

Tables 11–15 summarize the reported cutoff values for domestic and international laboratories. The tables show summary statistics for each analyte. Tables 16–18 summarize domestic cutoff statistics by method.

Table 11. Summary of non-MS/MS cutoff values for domestic laboratories

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	41	37.3	33.0	33.0	20.0	80.0
IRT (ng/mL blood)	43	61.9	58.0	60.0	45.0	120.0
T4 (µg/dL serum)	19	6.3	6.0	5.0	4.0	8.0
TGal (mg/dL blood)	19	11.4	10.0	10.0	6.0	20.0
TSH (µIU/mL serum)	42	30.8	26.3	20.0	13.0	58.0

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

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	199	23.9	19.8	30.0	6.0	103.5
IRT (ng/mL blood)	161	66.1	65.0	70.0	25.0	150.0
T4 (µg/dL serum)	44	7.3	6.0	6.0	3.0	34.2
TGal (mg/dL blood)	130	12.4	10.0	10.0	2.7	30.0
TSH (µIU/mL serum)	245	21.3	20.0	20.0	5.0	49.8
Phe (µmol/L blood)	48	155.2	141.7	121.2	103.0	242.4

Table 13. Summary of lysosomal storage disorder cutoff values for domestic laboratories

Flow Injection Analysis (FIA)-MS/MS multiplexed enzyme reaction (µmol/hr/L)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Galactoceramidase	4	0.66	0.60	n/a	0.40	1.05
Acid Alpha-Glucosidase	7	1.88	1.97	n/a	1.10	2.12
Alpha-L-Iduronidase	7	1.16	1.19	n/a	0.57	1.80

Digital Microfluidic Fluorescence (µmol/hr/L)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Acid Alpha-Glucosidase	7	8.56	8.70	n/a	6.60	10.00
Alpha-L-Iduronidase	7	4.79	4.90	5.00	3.94	5.77

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

Analyte	N	Mean	Median	Mode	Minimum	Maximum
24:0-Lysophosphatidylcholine – First-tier	8	0.6	0.5	n/a	0.2	1.0
24:0-Lysophosphatidylcholine – Second-tier	3	0.3	0.2	n/a	0.2	0.4
26:0-Lysophosphatidylcholine – First-tier	21	0.4	0.4	0.5	0.1	1.1
26:0-Lysophosphatidylcholine – Second-tier	9	0.2	0.2	NA	0.1	0.3
Arginine	36	75.9	77.0	50.0	27.0	125.0
Citrulline	43	54.0	54.8	60.0	34.0	75.0
Leucine	44	290.3	275.0	250.0	145.0	400.0
Methionine	43	73.5	74.0	100.0	40.0	130.0
Phenylalanine	50	140.0	139.5	130.0	74.0	182.0
Succinylacetone	39	2.3	2.0	1.0	0.8	5.4
Tyrosine	48	389.9	352.5	300.0	27.6	850.0
Valine	30	293.1	300.0	300.0	180.0	530.0
C0(L)	46	7.90	7.00	6.00	5.00	19.00
C2(L)	22	6.98	7.40	9.00	2.00	10.00
C3	47	5.76	6.00	5.00	3.10	9.00
C3DC	13	0.18	0.19	0.20	0.10	0.30
C3DC+ C4OH	26	0.55	0.41	0.38	0.25	3.03
C4	43	1.26	1.30	1.20	0.49	1.90
C4OH	11	0.58	0.65	0.75	0.20	0.80
C5	47	0.71	0.66	0.60	0.34	1.20
C5:1	45	0.19	0.11	0.10	0.03	0.51
C5DC	46	0.38	0.45	0.50	0.05	0.80
C5OH	46	0.85	0.85	0.85	0.36	1.50
C6	42	0.37	0.26	0.24	0.14	0.95
C8	47	0.43	0.43	0.60	0.12	0.70
C10	42	0.44	0.40	0.30	0.22	0.70
C10:1	39	0.27	0.25	0.25	0.12	0.45
C10:2	26	0.14	0.10	0.10	0.04	0.38
C14	41	0.72	0.70	0.70	0.27	1.20
C14:1	47	0.60	0.60	0.60	0.17	0.80
C16	44	7.83	7.95	10.00	2.14	10.36
C16OH	47	0.12	0.10	0.10	0.07	0.25
C18	37	2.33	2.20	2.00	0.70	3.50
C18:1	39	3.58	3.00	2.50	2.00	7.00
C18OH	36	0.09	0.10	0.10	0.03	0.16

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

Analyte	N	Mean	Median	Mode	Minimum	Maximum
24:0-Lysophosphatidylcholine – First-tier	8	0.79	0.81	n/a	0.32	1.20
26:0-Lysophosphatidylcholine – First-tier	11	0.50	0.43	0.40	0.14	0.92
Arginine	182	56.2	55.0	70.0	10.0	150.0
Citrulline	199	49.1	48.1	55.0	6.2	100.0
Leucine	223	309.9	296.4	300.0	100.0	686.7
Methionine	213	55.4	50.0	75.0	22.0	140.0
Phenylalanine	238	131.7	120.0	120.0	45.9	360.0
Succinylacetone	110	2.1	1.6	2.0	0.3	10.0
Tyrosine	217	304.0	299.1	350.0	87.0	800.0
Valine	209	269.2	265.0	300.0	132.0	470.0
C0(L)	217	13.21	8.00	8.00	1.70	125.00
C2(L)	164	17.37	7.65	7.00	0.00	98.00
C3	217	5.33	5.20	5.00	0.44	11.00
C3DC	61	0.24	0.25	0.25	0.04	0.69
C3DC+ C4OH	93	0.51	0.45	0.45	0.08	3.00
C4	202	0.95	0.91	1.30	0.34	3.80
C4OH	60	0.56	0.57	0.50	0.04	1.20
C5	223	0.67	0.60	1.00	0.09	2.00
C5:1	197	0.14	0.10	0.25	0.01	0.90
C5DC	212	0.35	0.30	0.35	0.01	2.99
C5OH	190	0.70	0.68	1.00	0.09	1.50
C6	204	0.27	0.20	0.40	0.07	1.30
C8	229	0.34	0.30	0.50	0.06	1.30
C10	219	0.36	0.32	0.45	0.06	1.10
C10:1	195	0.23	0.20	0.30	0.03	1.00
C10:2	139	0.16	0.10	0.15	0.01	3.66
C14	205	0.61	0.55	0.75	0.11	1.30
C14:1	210	0.46	0.40	0.60	0.07	2.50
C16	209	6.91	7.00	7.50	0.41	14.00
C16OH	212	0.11	0.10	0.10	0.02	0.75
C18	199	2.08	2.00	2.30	0.17	4.00
C18:1	194	3.12	3.00	3.50	0.34	7.00
C18OH	176	0.08	0.07	0.10	0.01	0.50

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

17 α-Hydroxyprogesterone ng/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**41**	**37.3**	**33.0**	**33.0**	**20.0**	**80.0**
AutoDELFIA® Neonatal 17OHP PerkinElmer	13	37.5	33.0	33.0	25.0	70.0
GSP® 17OHP Neonatal PerkinElmer	28	37.2	34.0	30.0	20.0	80.0

Immunoreactive Trypsinogen ng/mL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**61.9**	**58.0**	**60.0**	**45.0**	**120.0**
AutoDELFIA® Neonatal IRT PerkinElmer	17	66.9	69.0	69.0	51.0	90.0
GSP® IRT Neonatal PerkinElmer, ng/mL blood	26	58.7	54.5	50.0	45.0	120.0

Thyroxine µg/dL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**19**	**6.3**	**6.0**	**5.0**	**4.0**	**8.0**
AutoDELFIA® Neonatal T4 PerkinElmer	3	6.4	6.5	n/a	6.0	6.6
GSP® T4 Neonatal PerkinElmer	15	6.3	6.0	5.0	4.0	8.0

Thyroid-Stimulating Hormone µIU/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**30.8**	**26.3**	**20.0**	**13.0**	**58.0**
AutoDELFIA® Neonatal hTSH PerkinElmer	13	41.1	40.0	58.0	20.0	58.0
GSP® hTSH Neonatal PerkinElmer	28	26.4	25.0	20.0	13.0	40.0

Total Galactose mg/dL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**19**	**11.4**	**10.0**	**10.0**	**6.0**	**20.0**
50hr Reagent Kit Spotcheck® TGal Astoria-Pacific	4	11.3	10.5	n/a	9.1	15.0
GSP® TGal Neonatal PerkinElmer	11	11.1	10.0	10.0	7.3	14.0

Biotinidase

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**n/a**	**n/a**	**n/a**	**n/a**	**n/a**	**n/a**
50hr Reagent Kit Spotcheck® BIOT Astoria-Pacific, ERU (1µmol/dL/90min)	8	15.7	10.0	10.0	10.0	49.5
GSP® BIOT Neonatal PerkinElmer, U/dL	15	53.3	55.0	50.0	16.0	80.0

Galactose-1-phosphate Uridyltransferase

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**n/a**	**n/a**	**n/a**	**n/a**	**n/a**	**n/a**
50hr Reagent Kit Spotcheck® GALT Astoria-Pacific, µmol/L blood	8	42.9	50.0	50.0	3.1	50.0
Fluorescence GALT Neonatal PerkinElmer, U/g Hb	10	3.2	3.1	3.0	2.4	4.0
GSP® GALT Neonatal PerkinElmer, U/dL blood	17	3.5	3.5	3.5	2.0	5.5
Microplate Reagent Kit Spotcheck® GALT Astoria-Pacific, U/g Hb	3	2.1	2.0	2.0	2.0	2.2

Table 17. Domestic cutoff summary by analyte and method—X-Linked Adrenoleukodystrophy (µmol/L blood) (methods N < 3 not shown)

24:0-Lysophosphatidylcholine

Method	N	Mean	Median	Mode	Min	Max
First-tier ALL METHODS	**8**	**0.6**	**0.5**	**n/a**	**0.2**	**1.0**
Flow Injection Analysis (FIA) - MS/MS non-derivitized non-kit	3	0.4	0.4	n/a	0.4	0.5
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	3	0.9	0.8	n/a	0.8	1.0
Second-tier ALL METHODS	**3**	**0.3**	**0.2**	**n/a**	**0.2**	**0.4**

26:0-Lysophosphatidylcholine

Method	N	Mean	Median	Mode	Min	Max
First-tier ALL METHODS	**21**	**0.4**	**0.4**	**0.5**	**0.1**	**1.1**
Flow Injection Analysis (FIA) - MS/MS non-derivitized non-kit	6	0.6	0.5	n/a	0.4	1.1
LC-MS/MS negative ion mode	7	0.2	0.2	n/a	0.1	0.2
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	0.5	0.5	0.5	0.4	0.6
Second-tier ALL METHODS	**9**	**0.2**	**0.2**	**n/a**	**0.1**	**0.3**
LC-MS/MS positive ion mode	4	0.2	0.2	n/a	0.2	0.3
LC-MS/MS negative ion mode	5	0.2	0.2	n/a	0.1	0.3

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

Arginine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**36**	**75.9**	**77.0**	**50.0**	**27.0**	**125.0**
Derivatized - MS/MS non-kit	7	65.4	60.0	n/a	27.0	125.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	15	76.9	80.0	50.0	48.0	120.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	10	84.0	94.5	100.0	50.0	105.0

Citrulline

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**43**	**54.0**	**54.8**	**60.0**	**34.0**	**75.0**
Derivatized - MS/MS non-kit	8	53.8	55.0	55.0	34.0	75.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	58.5	60.0	60.0	40.0	75.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	49.2	50.0	50.0	45.0	56.0
Non-derivatized - MS/MS non-kit	3	49.7	49.0	n/a	45.0	55.0

Leucine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**44**	**290.3**	**275.0**	**250.0**	**145.0**	**400.0**
Derivatized - MS/MS non-kit	8	275.1	269.5	220.0	220.0	350.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	293.8	270.0	250.0	225.0	400.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	303.2	350.0	350.0	145.0	400.0
Non-derivatized - MS/MS non-kit	3	285.0	300.0	n/a	250.0	305.0

Methionine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**43**	**73.5**	**74.0**	**100.0**	**40.0**	**130.0**
Derivatized - MS/MS non-kit	8	57.7	57.9	50.0	44.0	70.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	81.6	85.0	100.0	50.0	100.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	76.7	75.0	75.0	45.0	130.0
Non-derivatized - MS/MS non-kit	3	51.7	55.0	n/a	40.0	60.0

Phenylalanine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**50**	**140.0**	**139.5**	**130.0**	**74.0**	**182.0**
Derivatized - MS/MS non-kit	10	138.0	139.5	n/a	80.0	182.0
LC-MS/MS non-kit	3	105.0	120.0	n/a	74.0	121.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	149.3	160.0	165.0	120.0	180.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	138.4	150.0	120.0	100.0	160.0
Non-derivatized - MS/MS non-kit	4	127.5	130.0	130.0	100.0	150.0

Succinylacetone

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**39**	**2.3**	**2.0**	**1.0**	**0.8**	**5.4**
Derivatized - MS/MS non-kit	7	2.8	2.2	2.0	1.9	5.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	18	2.6	2.0	4.5	1.0	4.5
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	1.4	1.0	1.0	0.8	2.8
Non-derivatized - MS/MS non-kit	3	3.1	2.0	n/a	1.8	5.4

Tyrosine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**48**	**389.9**	**352.5**	**300.0**	**27.6**	**850.0**
Derivatized - MS/MS non-kit	10	314.6	327.5	300.0	99.0	500.0
LC-MS/MS non-kit	3	172.9	91.0	n/a	27.6	400.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	520.6	400.0	850.0	175.0	850.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	381.1	375.0	350.0	243.0	500.0
Non-derivatized - MS/MS non-kit	4	265.0	290.0	290.0	120.0	360.0

Valine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**30**	**293.1**	**300.0**	**300.0**	**180.0**	**530.0**
Derivatized - MS/MS non-kit	6	271.7	240.0	240.0	180.0	420.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	8	332.1	300.0	300.0	250.0	530.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	10	274.7	287.5	180.0	180.0	360.0
Non-derivatized - MS/MS non-kit	3	253.3	250.0	n/a	210.0	300.0

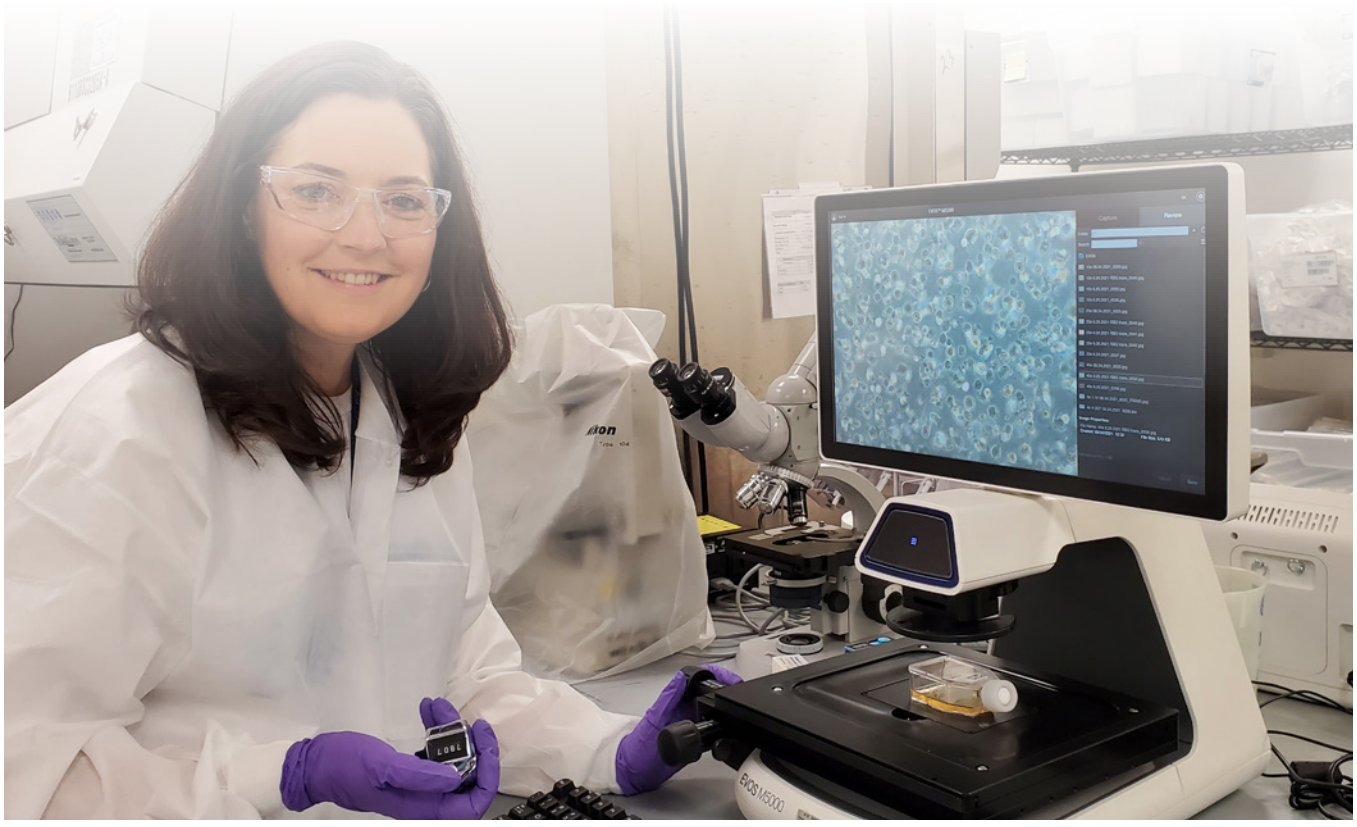


Table 19. Domestic cutoff summary by analyte and method—acylcarnitines (µmol/L blood) (methods N < 3 not shown)

C0(L)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**46**	**7.90**	**7.00**	**6.00**	**5.00**	**19.00**
Derivatized - MS/MS non-kit	11	9.91	9.20	10.00	5.00	19.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	6.91	6.50	6.00	5.00	10.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	6.76	6.90	7.50	5.50	8.00
Non-derivatized - MS/MS non-kit	3	7.20	7.00	n/a	6.00	8.60

C2(L)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**22**	**6.98**	**7.40**	**9.00**	**2.00**	**10.00**
Derivatized - MS/MS non-kit	6	7.30	8.66	n/a	2.00	10.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	6	7.14	7.50	n/a	4.00	9.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	5	6.70	7.00	9.00	3.50	9.00
Non-derivatized - MS/MS non-kit	3	6.50	6.70	n/a	5.00	7.80

C3

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**5.76**	**6.00**	**5.00**	**3.10**	**9.00**
Derivatized - MS/MS non-kit	12	4.77	4.25	n/a	3.10	7.70
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	6.03	6.10	6.30	5.00	8.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	6.22	6.20	5.00	4.00	9.00
Non-derivatized - MS/MS non-kit	3	6.81	6.92	n/a	6.00	7.50

C3DC

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**13**	**0.18**	**0.19**	**0.20**	**0.10**	**0.30**
Derivatized - MS/MS non-kit	11	0.17	0.18	0.20	0.10	0.30

C3DC + C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**26**	**0.55**	**0.41**	**0.38**	**0.25**	**3.03**
Non-derivatized - MS/MS NeoBase™ PerkinElmer	14	3.07	0.38	0.38	0.25	38.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	10	0.47	0.47	0.41	0.30	0.60
Non-derivatized - MS/MS non-kit	3	1.52	1.20	n/a	0.33	3.03

C4

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**1.26**	**1.30**	**1.20**	**0.49**	**1.90**
Derivatized - MS/MS non-kit	11	1.14	1.20	0.80	0.49	1.90
Non-derivatized - MS/MS NeoBase™ PerkinElmer	16	1.42	1.40	1.70	1.00	1.70
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	1.23	1.30	1.30	0.90	1.40
Non-derivatized - MS/MS non-kit	3	1.27	1.20	n/a	1.10	1.50

C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**11**	**0.58**	**0.65**	**0.75**	**0.20**	**0.80**
Derivatized - MS/MS non-kit	9	0.57	0.65	0.75	0.20	0.80

C5

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**0.71**	**0.66**	**0.60**	**0.34**	**1.20**
Derivatized - MS/MS non-kit	12	0.69	0.64	n/a	0.34	1.20
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	0.76	0.71	1.00	0.45	1.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	0.67	0.60	0.58	0.51	0.87
Non-derivatized - MS/MS non-kit	3	0.60	0.60	n/a	0.50	0.70

C5:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.19**	**0.11**	**0.10**	**0.03**	**0.51**
Derivatized - MS/MS non-kit	12	0.17	0.11	0.08	0.05	0.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	0.27	0.20	0.50	0.03	0.50
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	0.10	0.10	0.10	0.04	0.25
Non-derivatized - MS/MS non-kit	3	0.10	0.08	n/a	0.04	0.19

C5DC

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**46**	**0.38**	**0.45**	**0.50**	**0.05**	**0.80**
Derivatized - MS/MS non-kit	12	0.16	0.14	0.11	0.05	0.30
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	0.51	0.50	0.50	0.30	0.80
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	10	0.40	0.45	0.24	0.24	0.51
Non-derivatized - MS/MS non-kit	3	0.48	0.50	n/a	0.35	0.60

C5OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**46**	**0.85**	**0.85**	**0.85**	**0.36**	**1.50**
Derivatized - MS/MS non-kit	12	0.75	0.76	0.36	0.36	1.25
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	0.82	0.85	0.85	0.60	1.05
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	10	1.01	0.92	1.50	0.78	1.50
Non-derivatized - MS/MS non-kit	3	1.06	1.08	n/a	0.90	1.20

C6

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**0.37**	**0.26**	**0.24**	**0.14**	**0.95**
Derivatized - MS/MS non-kit	11	0.31	0.30	0.24	0.14	0.59
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	0.51	0.30	0.95	0.16	0.95
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	9	0.26	0.25	0.24	0.16	0.40
Non-derivatized - MS/MS non-kit	3	0.20	0.15	0.15	0.15	0.30

C8

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**0.43**	**0.43**	**0.60**	**0.12**	**0.70**
Derivatized - MS/MS non-kit	12	0.36	0.35	0.50	0.12	0.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	0.50	0.50	0.60	0.32	0.70
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	0.43	0.41	0.40	0.29	0.60
Non-derivatized - MS/MS non-kit	3	0.38	0.40	n/a	0.23	0.50

C10

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**0.44**	**0.40**	**0.30**	**0.22**	**0.70**
Derivatized - MS/MS non-kit	11	0.36	0.30	0.30	0.22	0.55
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	0.50	0.43	0.65	0.30	0.70
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	9	0.45	0.45	0.55	0.25	0.60
Non-derivatized - MS/MS non-kit	3	0.43	0.45	n/a	0.34	0.50

C10:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**39**	**0.27**	**0.25**	**0.25**	**0.12**	**0.45**
Derivatized - MS/MS non-kit	10	0.24	0.23	0.25	0.17	0.37
Non-derivatized - MS/MS NeoBase™ PerkinElmer	15	0.32	0.30	0.45	0.15	0.45
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	9	0.21	0.20	0.13	0.12	0.40
Non-derivatized - MS/MS non-kit	3	0.28	0.30	n/a	0.15	0.40

C10:2

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**26**	**0.14**	**0.10**	**0.10**	**0.04**	**0.38**
Derivatized - MS/MS non-kit	8	0.19	0.15	0.10	0.06	0.38
Non-derivatized - MS/MS NeoBase™ PerkinElmer	7	0.11	0.10	0.10	0.10	0.15
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	0.13	0.10	0.10	0.05	0.21

C14

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**41**	**0.72**	**0.70**	**0.70**	**0.27**	**1.20**
Derivatized - MS/MS non-kit	11	0.60	0.70	0.70	0.27	0.80
Non-derivatized - MS/MS NeoBase™ PerkinElmer	16	0.88	0.77	1.20	0.46	1.20
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	9	0.66	0.70	0.60	0.57	0.76
Non-derivatized - MS/MS non-kit	3	0.63	0.60	n/a	0.50	0.80

C14:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**0.60**	**0.60**	**0.60**	**0.17**	**0.80**
Derivatized - MS/MS non-kit	12	0.49	0.56	0.60	0.17	0.70
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	0.70	0.68	0.80	0.50	0.80
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	0.61	0.60	0.60	0.51	0.70
Non-derivatized - MS/MS non-kit	3	0.54	0.56	n/a	0.45	0.60

C16

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**7.83**	**7.95**	**10.00**	**2.14**	**10.36**
Derivatized - MS/MS non-kit	11	7.03	7.00	7.00	2.14	10.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	8.49	8.50	10.00	5.00	10.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	7.88	8.60	7.00	3.50	10.36
Non-derivatized - MS/MS non-kit	3	7.47	7.20	n/a	6.50	8.70

C16OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**47**	**0.12**	**0.10**	**0.10**	**0.07**	**0.25**
Derivatized - MS/MS non-kit	12	0.14	0.12	0.10	0.10	0.25
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	0.11	0.10	0.10	0.07	0.20
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	11	0.11	0.10	0.10	0.08	0.16
Non-derivatized - MS/MS non-kit	3	0.19	0.20	n/a	0.11	0.25

C18

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**37**	**2.33**	**2.20**	**2.00**	**0.70**	**3.50**
Derivatized - MS/MS non-kit	8	1.70	1.83	n/a	0.70	2.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	16	2.67	2.50	3.50	1.55	3.50
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	2.45	2.30	2.30	2.00	3.09
Non-derivatized - MS/MS non-kit	3	2.16	2.00	2.00	2.00	2.47

C18:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**39**	**3.58**	**3.00**	**2.50**	**2.00**	**7.00**
Derivatized - MS/MS non-kit	9	2.73	2.60	2.50	2.00	3.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	16	4.60	3.83	7.00	2.00	7.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	9	2.90	2.70	2.50	2.50	3.80
Non-derivatized - MS/MS non-kit	3	3.44	3.53	n/a	2.80	4.00

C18OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**36**	**0.09**	**0.10**	**0.10**	**0.03**	**0.16**
Derivatized - MS/MS non-kit	7	0.10	0.10	0.10	0.03	0.16
Non-derivatized - MS/MS NeoBase™ PerkinElmer	15	0.09	0.10	0.10	0.05	0.16
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	9	0.07	0.06	0.04	0.04	0.13
Non-derivatized - MS/MS non-kit	3	0.09	0.10	n/a	0.04	0.12

2021 Bias Plots

Proficiency Testing Bias Plots

Figures 2–37 were created for PT analytes reported during 2021. For each analyte, bias plots were selected to compare PT results for different methods. The NSQAP expected value of each specimen equals the sum of the enriched value and the endogenous (non-enriched) value. For IRT PT specimens, the CDC-assayed value is reported.

Non-derivatized MS/MS methods for amino acids and acylcarnitines analysis cannot distinguish between analytes C3DC and C4OH (i.e., they are isobaric). Laboratories that use a derivatized MS/MS method are able to identify C3DC and C4OH as individual analytes. Laboratories that use a non-derivatized MS/MS method report combined C3DC+C4OH. The bias plots show the laboratory reported value minus the EV 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 EV 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. A reasonable bias is less than 20% of the EV.

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 may vary between 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 2–37, the bias plot's explanation follows each figure title.

Quarter 1

Specimen: 20211001001

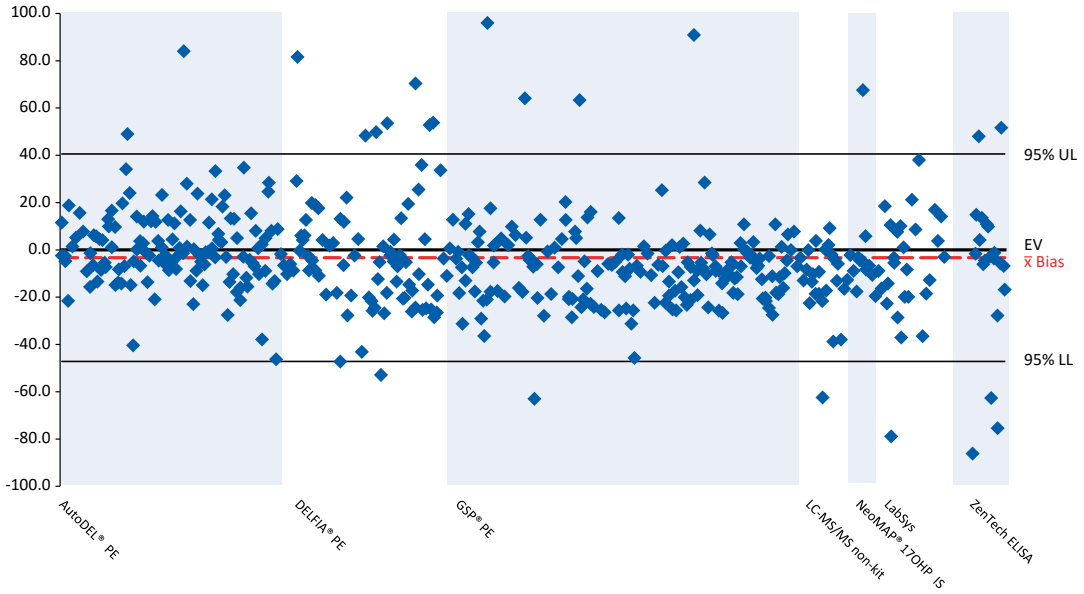
Enriched: 85.0

CDC Assayed: 66.6

Participant Mean: 82.9

Participant Bias: -3.3

Figure 2.
Bias Plot of 17 α-Hydroxyprogesterone (17OHP) Values by Method
Quarter 1 , Specimen 20211001001
Expected Value (EV) = 86.2 mg/mL serum



The 17OHP bias plot shows units of measure on the y-axis ranging from 100.0 mg/mL serum to -100.0 ng/mL serum. The bias for this plot is -3.3 ng/mL serum. The data on this plot shows an even scatter among all participants.

Quarter 1

Specimen: 20211001003

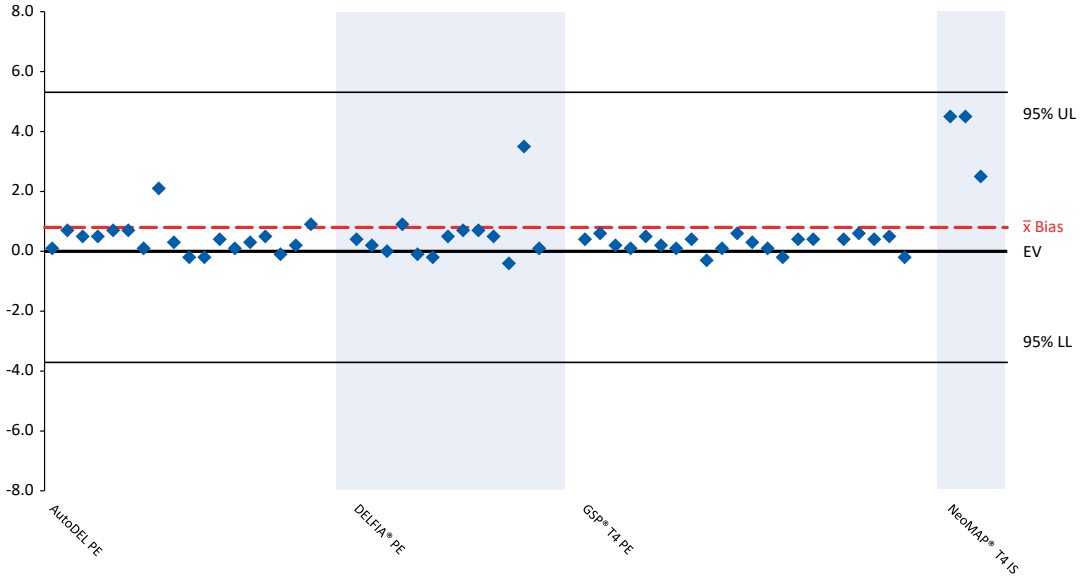
Enriched: 1.5

CDC Assayed: 1.7

Participant Mean: 2.3

Participant Bias: 0.8

Figure 3.
Bias Plot of Thyroxine (T4) Values by Method
Quarter 1, Specimen 20211001003
Expected Value (EV) = 1.5 µg/dL serum



The T4 bias plot shows units of measure on the y-axis ranging from 8.0 µg/dL serum to -8.0 µg/dL serum. The bias for this plot is 0.8. One method demonstrated a slightly higher bias than the others.

Quarter 1

Specimen: 20211001002

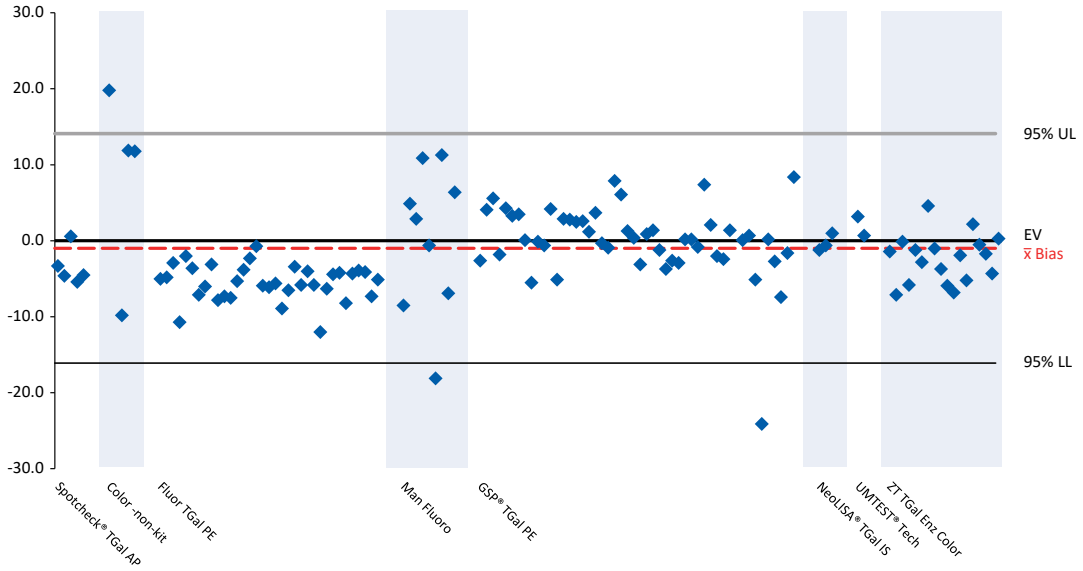
Enriched: 25.0

CDC Assayed: 21.1

Participant Mean: 24.1

Participant Bias: -1.0

Figure 4.
Bias Plot of Total Galactose (TGal) Values by Method
Quarter 1, Specimen 20211001002
Expected Value (EV) = 25.1 mg/dL blood



The TGal bias plot shows units of measure on the y-axis ranging from 30.0 mg/dL blood to -30.0 mg/dL blood. The bias for this plot is -1.0. One method demonstrates a slightly lower bias than others.

Quarter 4

Specimen: 20214001003

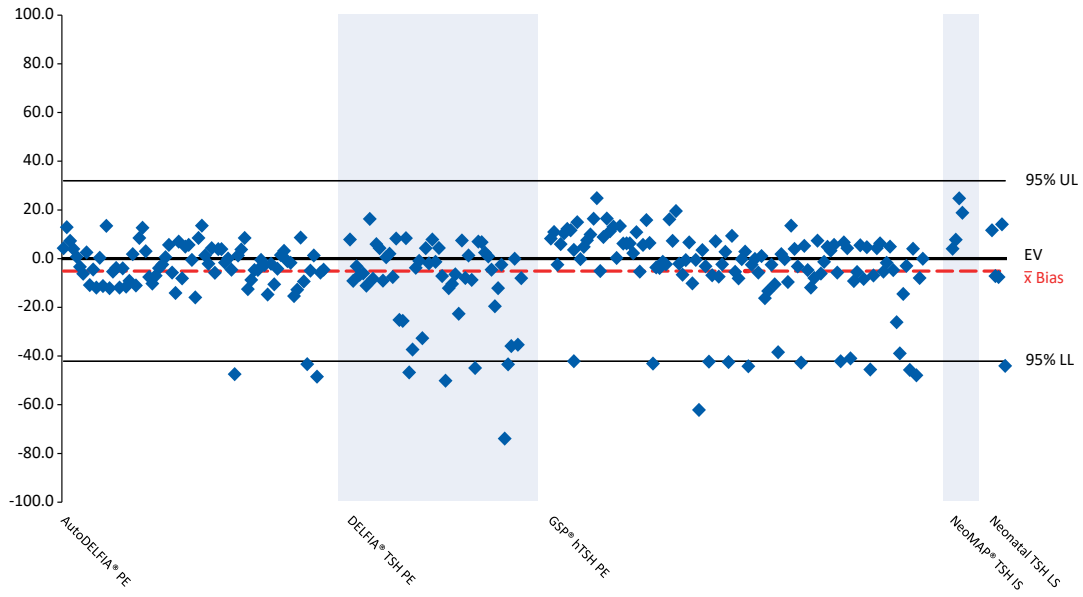
Enriched: 80.0

CDC Assayed: 90.7

Participant Mean: 75.0

Participant Bias: -5.1

Figure 5.
Bias Plot of Thyroid-Stimulating Hormone (TSH) Values by Method
Quarter 4, Specimen 20214001003
Expected Value (EV) = 80.1 µIU/mL serum



The TSH bias plot shows units of measure on the y-axis ranging from 100.0 µIU/mL serum to -100.0 µIU/mL serum. The bias for this plot is -5.1. The data show an even bias scatter across methods.

Figure 6.
Bias Plot of Immunoreactive Trypsinogen (IRT) Values by Method
Quarter 1, Specimen 20211008001
Assayed Value (AV) = 143.5 ng/mL blood

Quarter 1

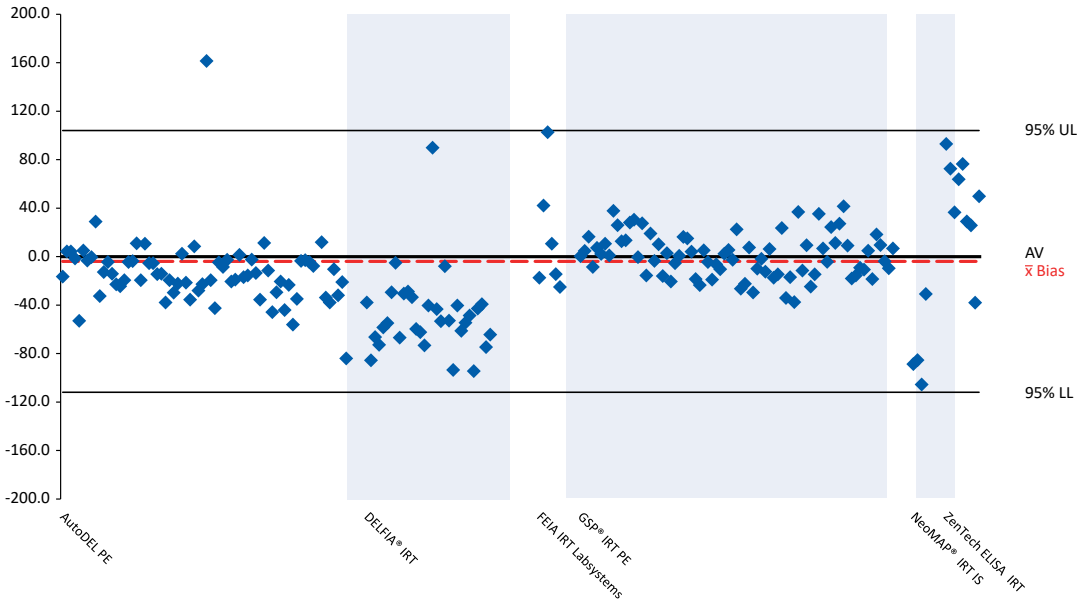
Specimen: 20211008001

Enriched: 250.0

CDC Assayed: 142.4

Participant Mean: 139.6

Participant Bias: -3.9



The IRT bias plot shows units of measure on the y-axis ranging from 200.0 µg/dL serum to -200.0 mg/dL blood. The bias for this plot is -3.9. Two methods showed a moderately lower bias than others.

Figure 7.
Bias Plot of Arginine (Arg) Values by Method
Quarter 1, Specimen 20211005001
Expected Value (EV) = 216.6 µmol/L blood

Quarter 1

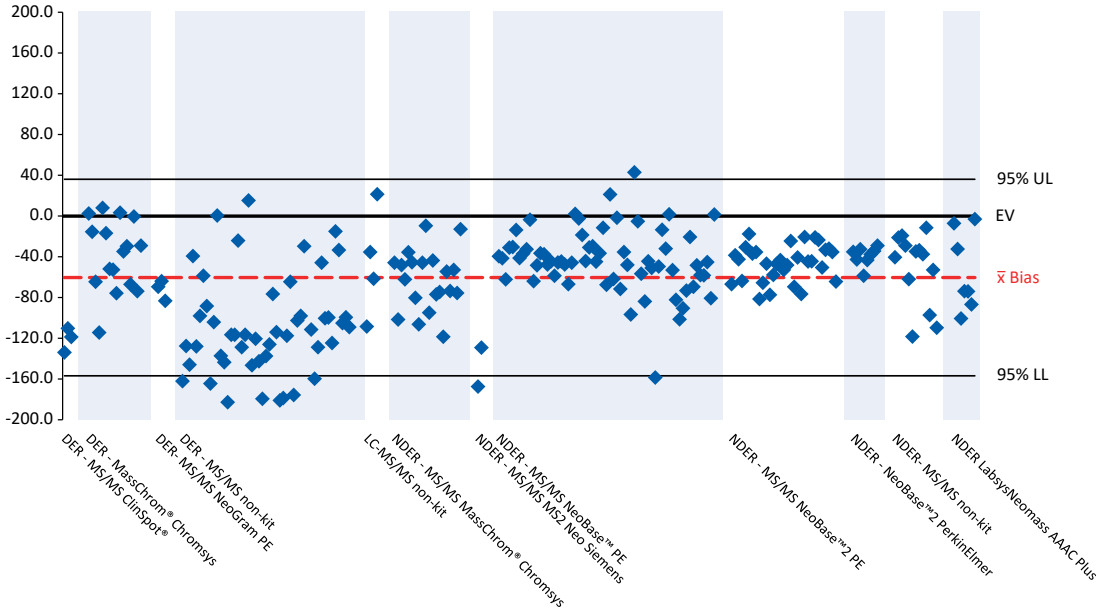
Specimen: 20211005001

Enriched: 200.0

CDC Assayed: 136.7

Participant Mean: 156.3

Participant Bias: -60.3



The Arg bias plot shows units of measure on the y-axis ranging from 200.0 µmol/L blood to -200.0 µmol/L blood. The bias for this plot is -60.3. This plot shows all methods demonstrated a low bias.

Quarter 1

Specimen: 20211005001

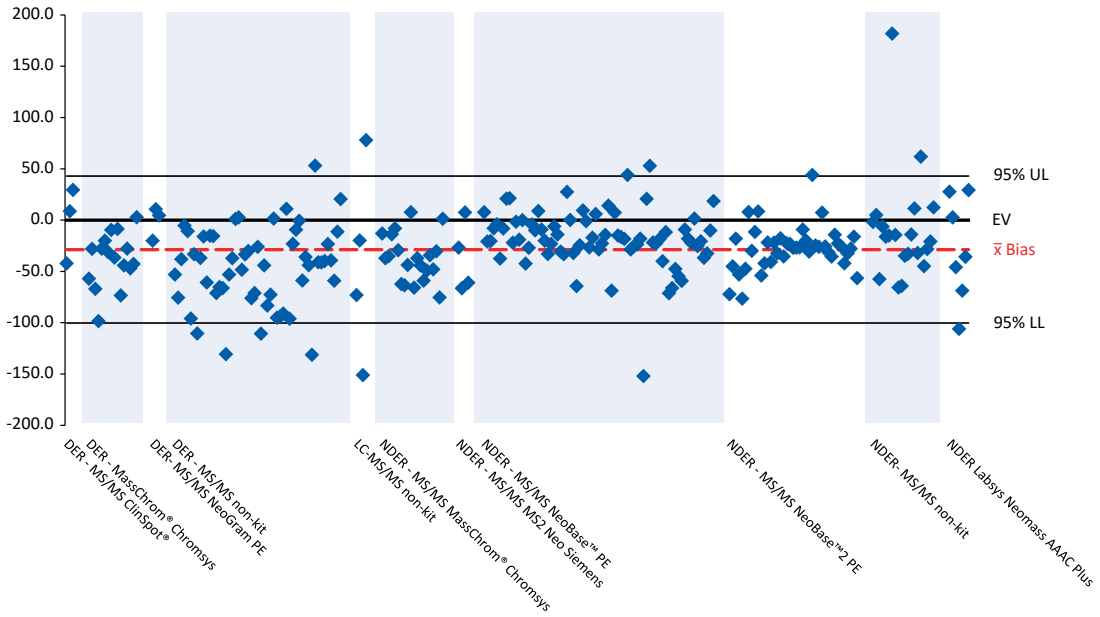
Enriched: 180.0

CDC Assayed: 159.1

Participant Mean: 188.3

Participant Bias: -28.7

Figure 8.
Bias Plot of Citrulline (Cit) Values by Method
Quarter 1, Specimen 20211005001
Expected Value (EV) = 217.0 µmol/L blood



The Cit bias plot shows units of measure on the y-axis ranging from 200.0 µmol/L blood to -200.0 µmol/L blood. The bias for this plot is -28.7. This plot shows a moderately negative bias across methods.

Quarter 3

Specimen: 20213005004

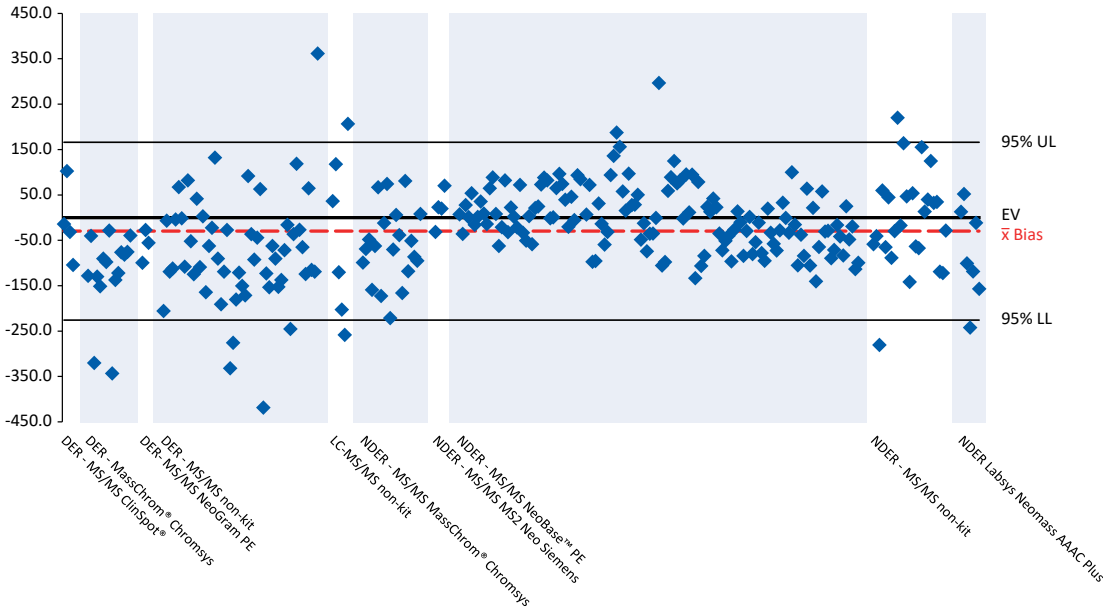
Enriched: 450.0

CDC Assayed: 580.7

Participant Mean: 604.5

Participant Bias: -29.8

Figure 9.
Bias Plot of Leucine (Leu) Values by Method
Quarter 3, Specimen 20213005004
Expected Value (EV) = 634.3 µmol/L blood



The Leu bias plot shows units of measure on the y-axis ranging from 450.0 µmol/L blood to -450.0 µmol/L blood. The bias for this plot is -29.8. This plot shows an even scatter across methods.

Figure 10.
Bias Plot of Methionine (Met) Values by Method
Quarter 1, Specimen 20211005003
Expected Value (EV) = 211.1 µmol/L blood

Quarter 1

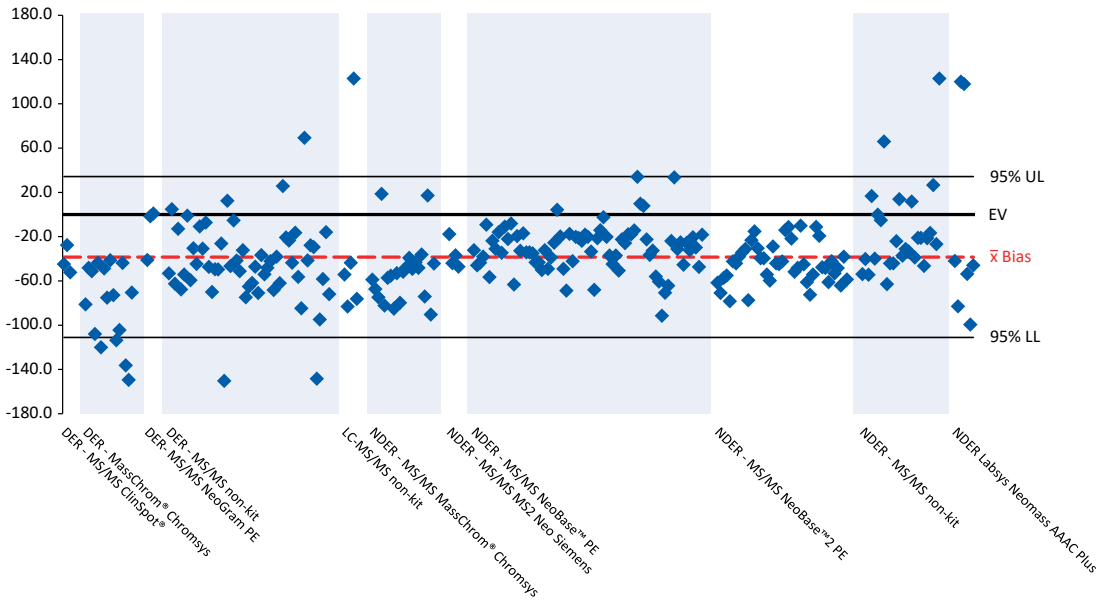
Specimen: 20211005003

Enriched: 180.0

CDC Assayed: 189.0

Participant Mean: 172.7

Participant Bias: -38.4



The Met bias plot shows units of measure on the y-axis ranging from 180.0 µmol/L blood to -180.0 µmol/L blood. The bias for this plot is -38.4. This plot shows a moderately negative bias across most methods.

Figure 11.
Bias Plot of Phenylalanine (Phe) Values by Method
Quarter 1, Specimen 20211005002
Expected Value (EV) = 295.6 µmol/L blood

Quarter 1

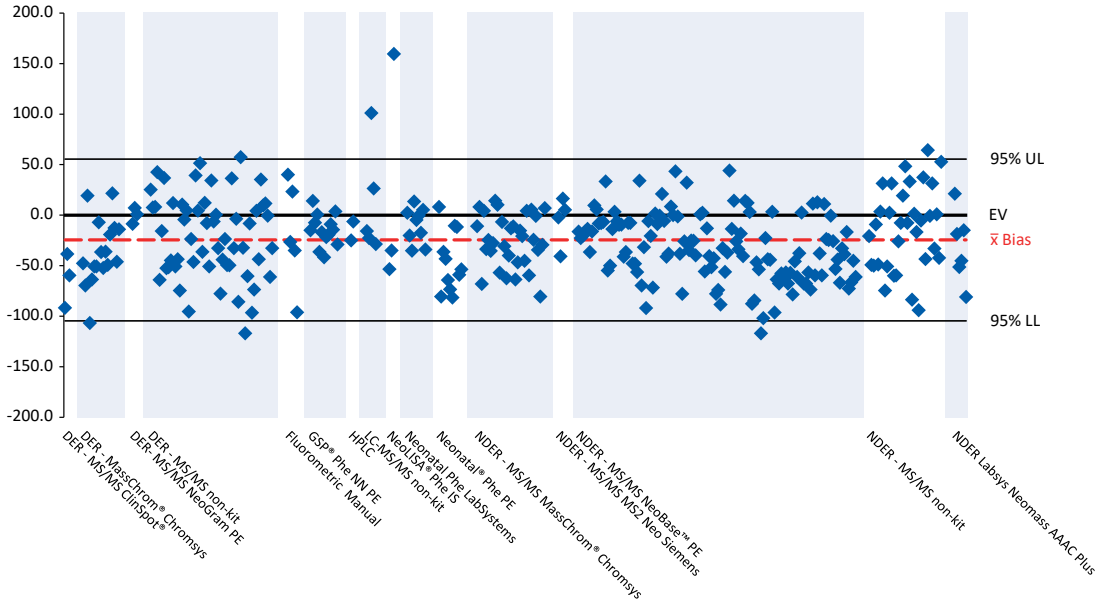
Specimen: 20211005002

Enriched: 230.0

CDC Assayed: 268.3

Participant Mean: 271.1

Participant Bias: -24.5



The Phe bias plot shows units of measure on the y-axis ranging from 200.0 µmol/L blood to -200.0 µmol/L blood. The bias for this plot is -24.5. This plot shows an even scatter across acorss the expected value for most methods.

Figure 12.
Bias Plot of Succinylacetone (SUAC) Values by Method
Quarter 1, Specimen 20211005005
Expected Value (EV) = 25.5 µmol/L blood

Quarter 1

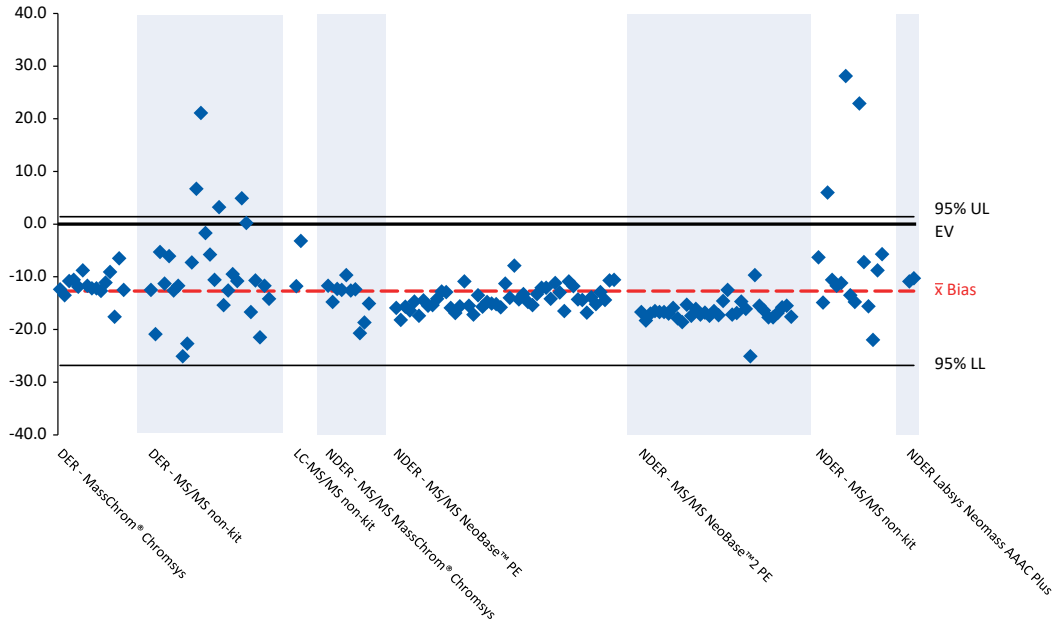
Specimen: 20211005005

Enriched: 25.0

CDC Assayed: 15.8

Participant Mean: 12.8

Participant Bias: -12.7



The SUAC bias plot shows units of measure on the y-axis ranging from 40.0 µmol/L blood to -40.0 µmol/L blood. The bias for this plot is -12.7. This plot shows a strongly negative bias across methods, which is historical for this analyte.

Figure 13.
Bias Plot of Tyrosine (Tyr) Values by Method
Quarter 1, Specimen 20211005005
Expected Value (EV) = 906.6 µmol/L blood

Quarter 1

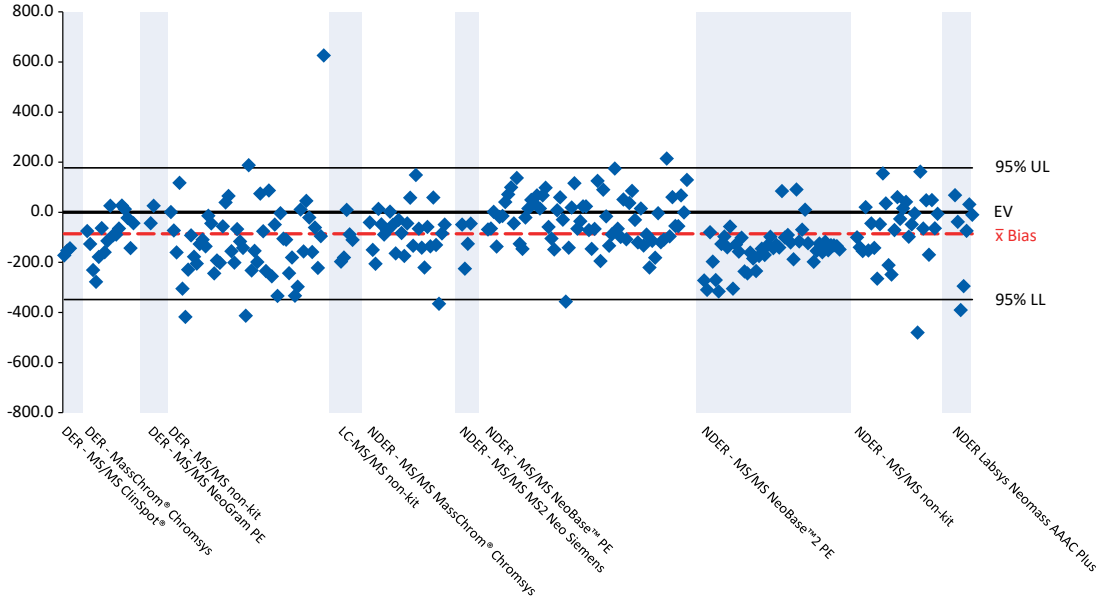
Specimen: 20211005005

Enriched: 800.0

CDC Assayed: 850.8

Participant Mean: 821.1

Participant Bias: -85.5



The Tyr bias plot shows units of measure on the y-axis ranging from 800.0 µmol/L blood to -800.0 µmol/L blood. The bias for this plot is -85.5. This plot shows a slightly negative bias across methods.

Figure 14.
Bias Plot of Valine (Val) Values by Method
Quarter 3, Specimen 20213005004
Expected Value (EV) = 644.1 µmol/L blood

Quarter 3

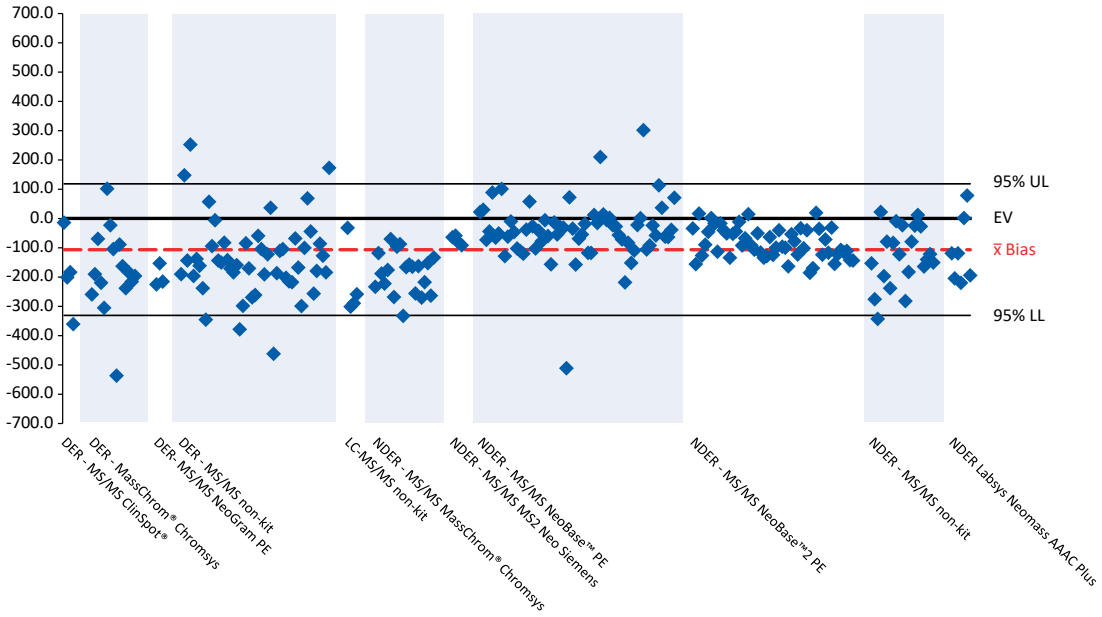
Specimen: 20213005004

Enriched: 430.0

CDC Assayed: 610.7

Participant Mean: 537.6

Participant Bias: -106.5



The Val bias plot shows units of measure on the y-axis ranging from 700.0 µmol/L blood to -700.0 µmol/L blood. The bias for this plot is -106.5. This plot shows a moderately negative bias across methods

Figure 15.
Bias Plot of Low Free Carnitine (C0(L)) Values by Method
Quarter 3, Specimen 20213006001
Expected Value (EV) = 5.09 µmol/L blood

Quarter 3

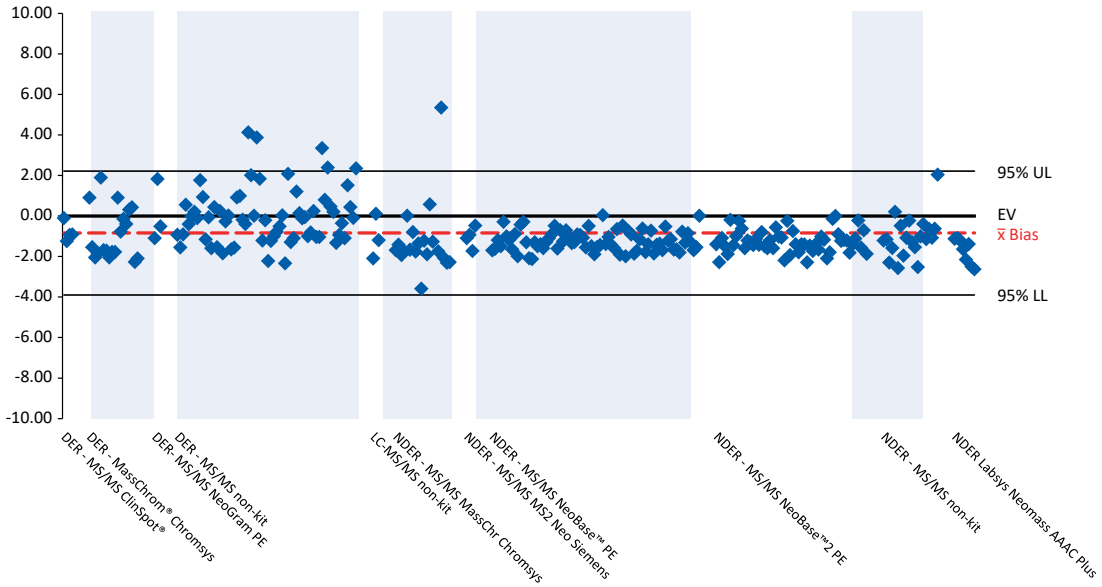
Specimen: 20213006001

Enriched: 0.00

CDC Assayed: 5.45

Participant Mean: 4.25

Participant Bias: -0.84



The C0(L) bias plot shows units of measure on the y-axis ranging from 10.00 µmol/L blood to -10.00 µmol/L blood. The bias for this plot is -0.84. This plot shows a slightly negative bias across methods

Quarter 3

Specimen: 20213006001

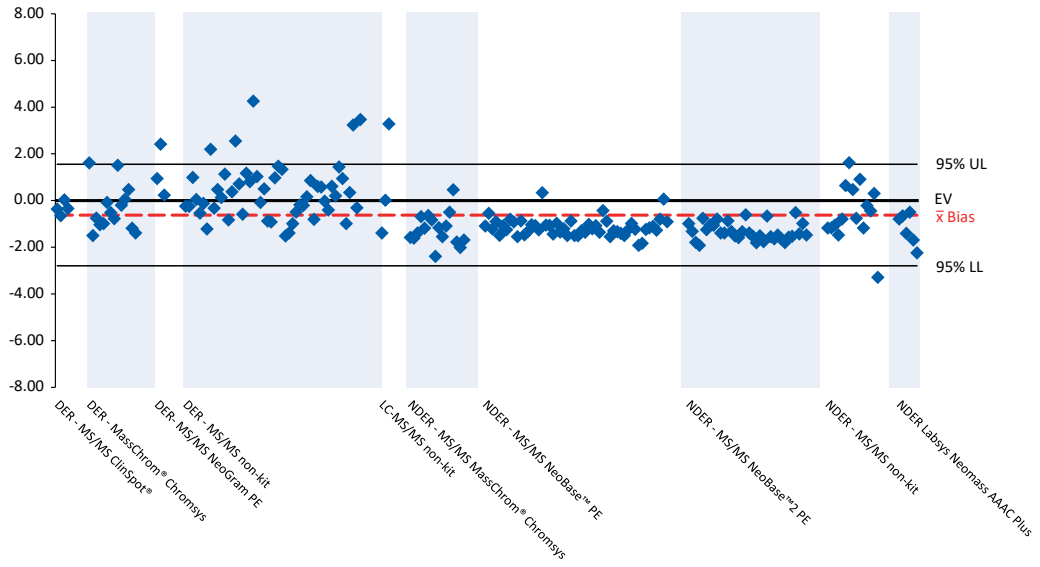
Enriched: 0.00

CDC Assayed: 4.23

Participant Mean: 3.77

Participant Bias: -0.62

Figure 16. Reproducibility of Results: Bias Plot of Low Acetylcarnitine (C2(L)) Values by Method Quarter 3, Specimen 20213006001 Expected Value (EV) = 4.39 µmol/L blood



The C2(L) bias plot shows units of measure on the y-axis ranging from 8.00 µmol/L blood to -8.00 µmol/L blood. The bias for this plot is -0.62. This plot shows three methods with a slightly more negative bias than the others

Quarter 1

Specimen: 20211006003

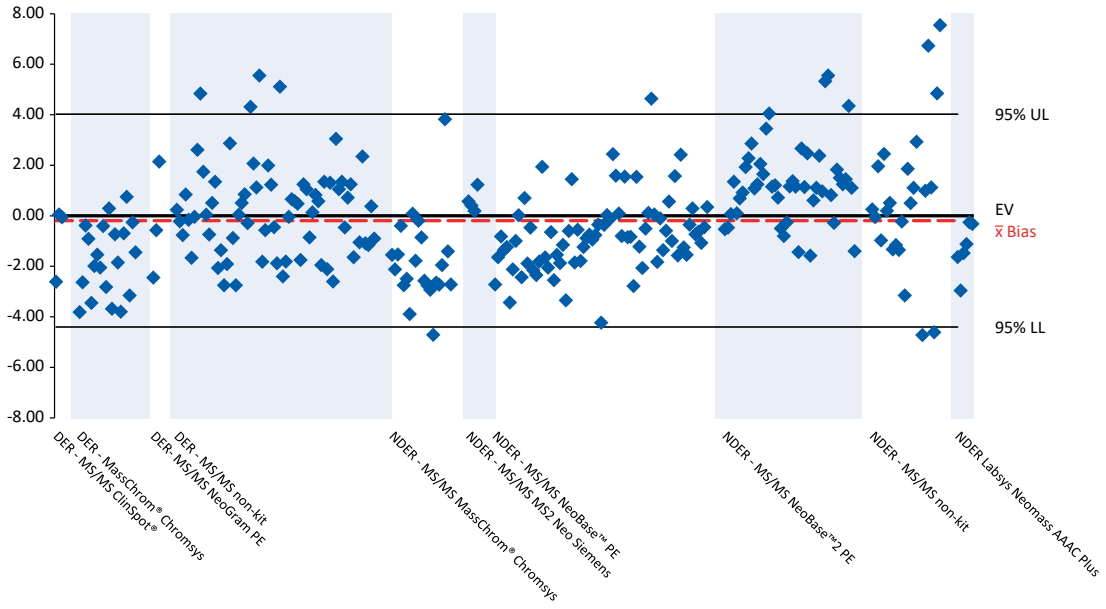
Enriched: 12.00

CDC Assayed: 14.71

Participant Mean: 12.96

Participant Bias: -0.19

Figure 17. Bias Plot of Propionylcarnitine (C3) Values by Method Quarter 1, Specimen 20211006003 Expected Value (EV) = 13.15 µmol/L blood



The C3 bias plot shows units of measure on the y-axis ranging from 8.00 µmol/L blood to -8.00 µmol/L blood. The bias for this plot is -0.19. This plot shows an even scatter across methods.

Quarter 3

Specimen: 20213006003

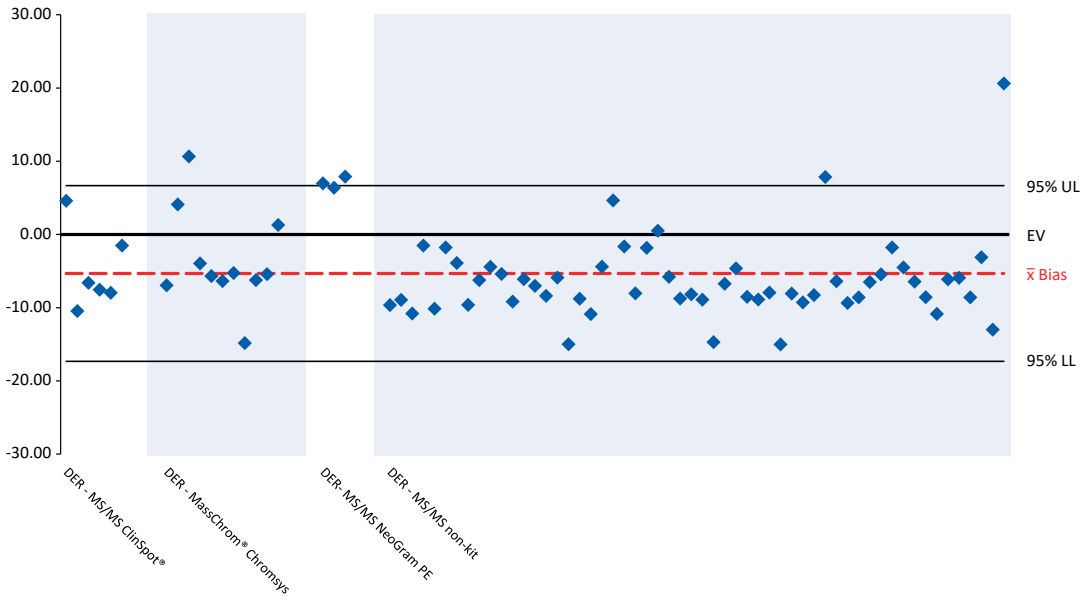
Enriched: 15.00

CDC Assayed: 12.45

Participant Mean: 9.70

Participant Bias: -5.32

Figure 18.
Bias Plot of Malonylcarnitine (C3DC) Values by Method
Quarter 3, Specimen 20213006003
Expected Value (EV) = 15.02 µmol/L blood



The C3DC bias plot shows units of measure on the y-axis ranging from 30.00 µmol/L blood to -30.00 µmol/L blood. The bias for this plot is -5.4. This plot shows a slightly negative bias across methods.

Quarter 3

Specimen: 20213006003

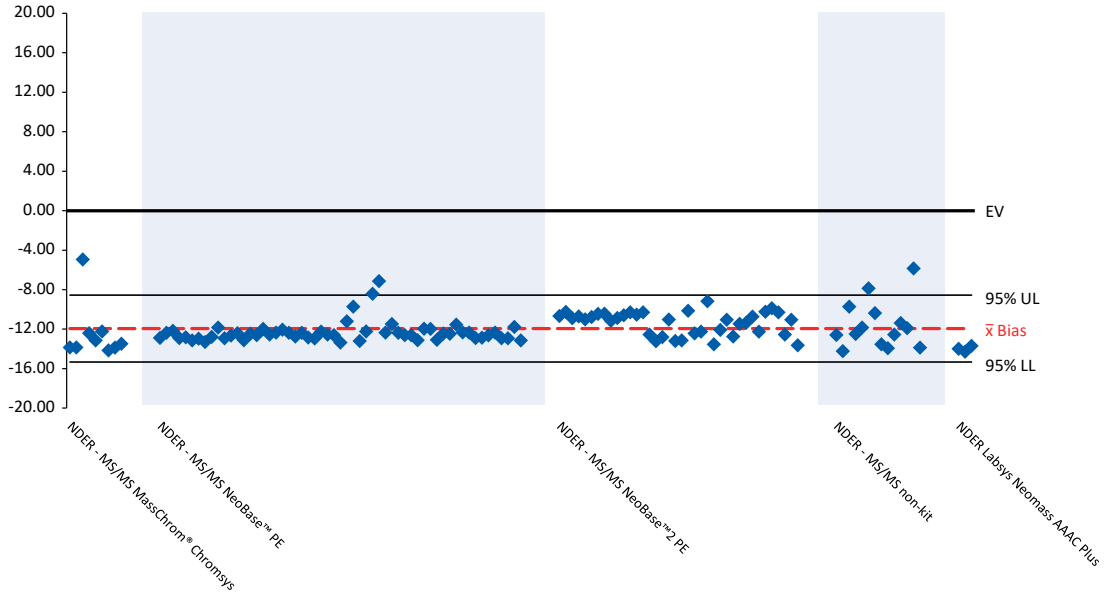
Enriched: 15.00

CDC Assayed: 1.28

Participant Mean: 3.09

Participant Bias: -11.95

Figure 19.
Bias Plot of C3DC+C4OH Non-derivatized Values by Method
Quarter 3, Specimen 20213006003
Expected Value (EV) = 15.04 µmol/L blood



The C3DC+C4OH bias plot shows units of measure on the y-axis ranging from 20.00 µmol/L blood to -20.00 µmol/L blood. The bias for this plot is -11.95. This plot shows a strongly negative bias across methods as historically observed.

Figure 20. Reproducibility of Results: Bias Plot of Butyrylcarnitine (C4) Values by Method Quarter 1, Specimen 20211006001 Expected Value (EV) = 0.13 µmol/L blood

Quarter 1

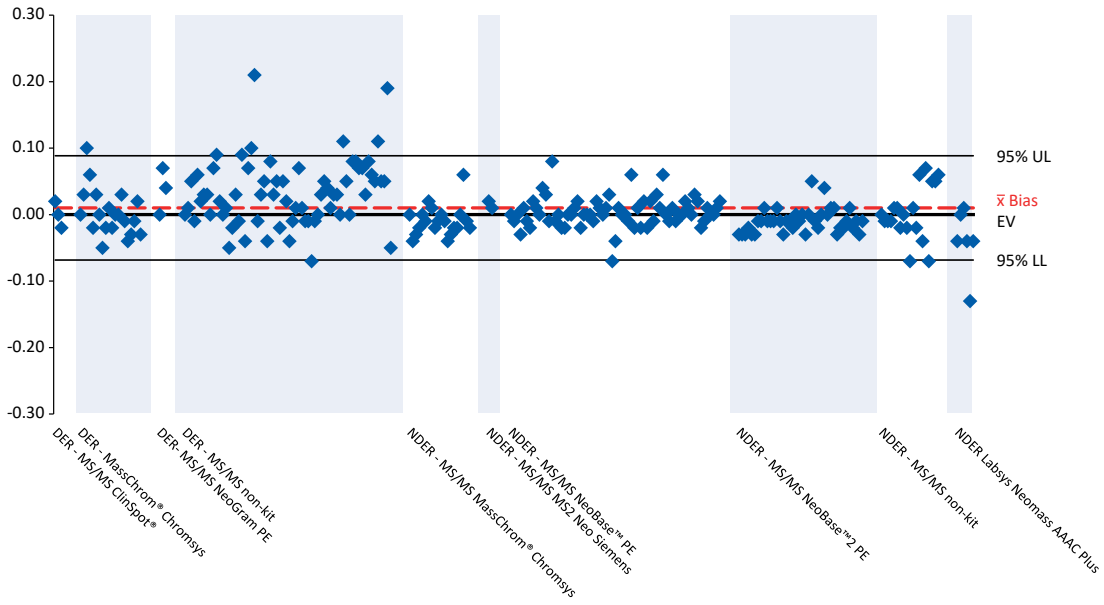
Specimen: 20211006001

Enriched: 0.00

CDC Assayed: 0.14

Participant Mean: 0.14

Participant Bias: 0.01



The C4 bias plot shows units of measure on the y-axis ranging from 0.30 µmol/L blood to -0.30 µmol/L blood. The bias for this plot is 0.01. This plot shows a moderately negative bias across methods.

Figure 21. Bias Plot of Hydroxybutyrylcarnitine (C4OH) Values by Method Quarter 1, Specimen 20211006003 Expected Value (EV) = 0.07 µmol/L blood

Quarter 1

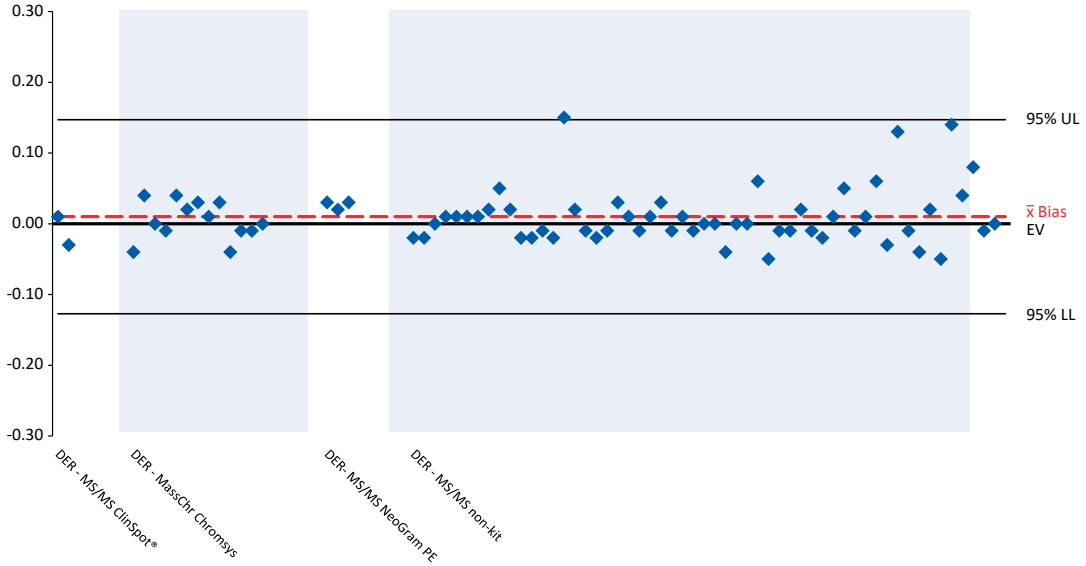
Specimen: 20211006003

Enriched: 0.00

CDC Assayed: 0.07

Participant Mean: 0.08

Participant Bias: 0.01



The C4OH bias plot shows units of measure on the y-axis ranging from 0.30 µmol/L blood to -0.30 µmol/L blood. The bias for this plot is 0.01. This plot shows a negligible bias across methods.

Figure 22.
Bias Plot of Isovalerylcarnitine (C5) Values by Method
Quarter 1, Specimen 20211006001
Expected Value (EV) = 0.08 µmol/L blood

Quarter 1

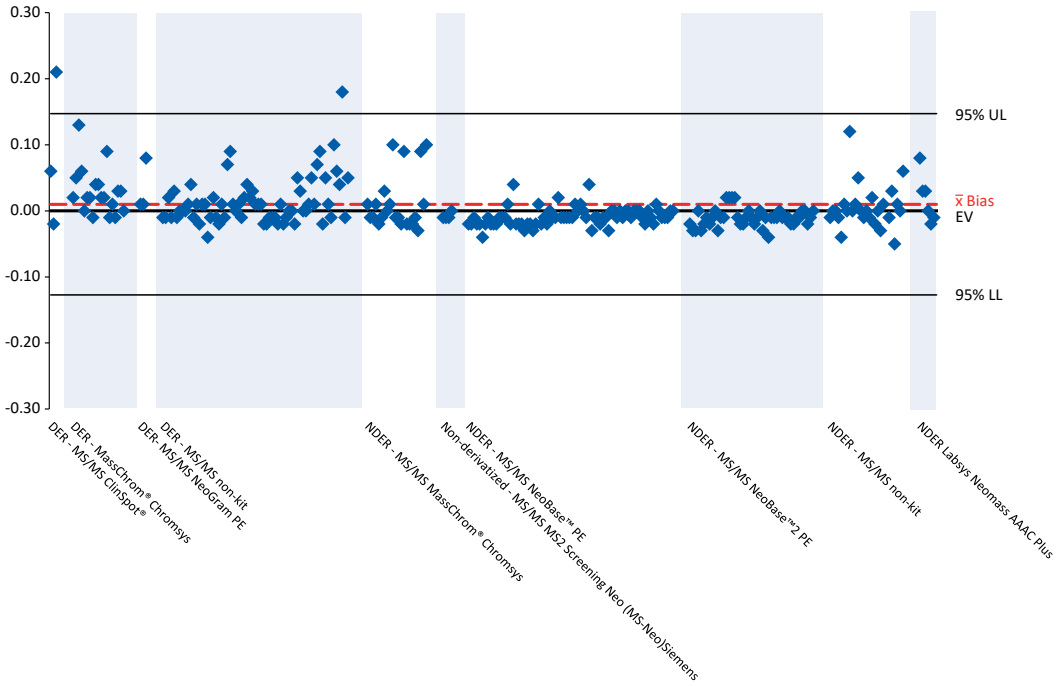
Specimen: 20211006001

Enriched: 0.00

CDC Assayed: 0.07

Participant Mean: 0.09

Participant Bias: 0.01



The C5 bias plot shows units of measure on the y-axis ranging from 0.30 µmol/L blood to -0.30 µmol/L blood. The bias for this plot is 0.01. This plot shows a negligible bias across methods.

Figure 23.
Bias Plot of Tiglylcarnitine (C5:1) Values by Method
Quarter 1, Specimen 20211006002
Expected Value (EV) = 0.03 µmol/L blood

Quarter 1

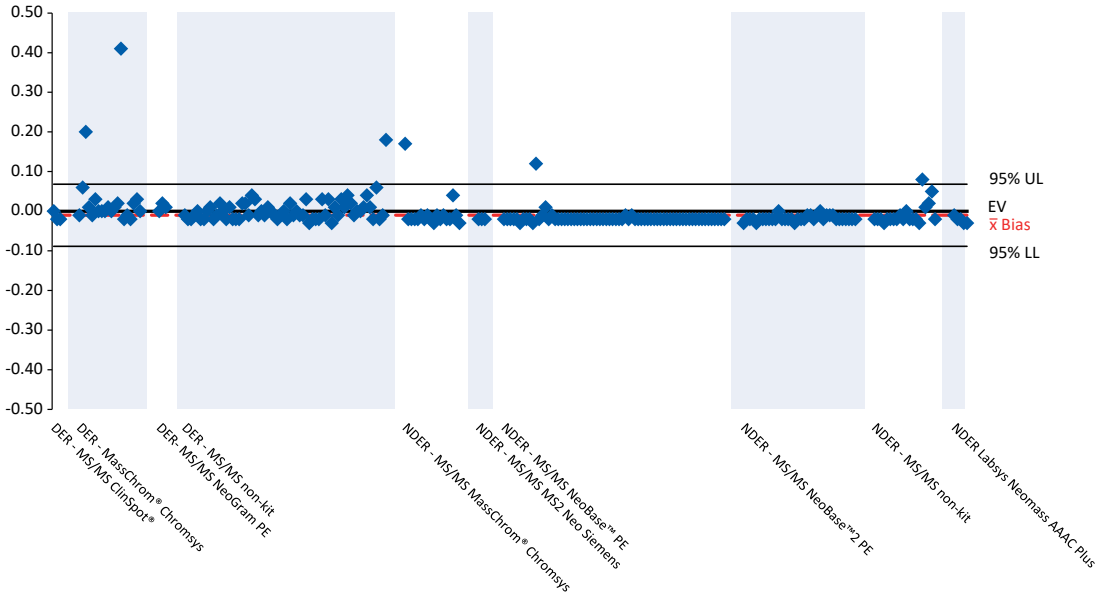
Specimen: 20211006002

Enriched: 0.00

CDC Assayed: 0.03

Participant Mean: 0.02

Participant Bias: -0.01



The C5:1 bias plot shows units of measure on the y-axis ranging from 0.50 µmol/L blood to -0.50 µmol/L blood. The bias for this plot is -0.01. This plot shows a slightly negative bias across most methods

Quarter 1

Specimen: 20211006001

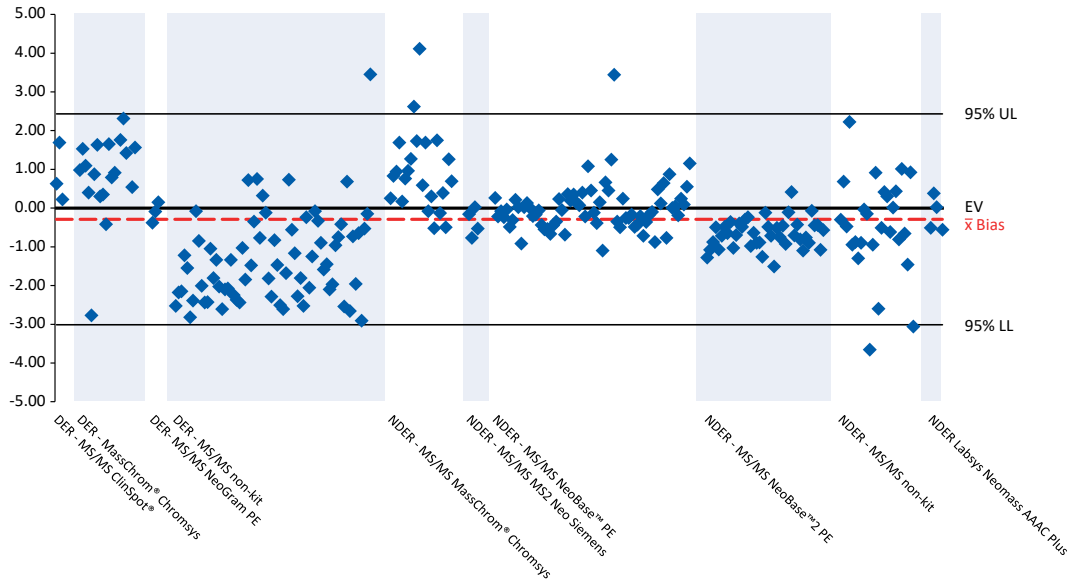
Enriched: 3.70

CDC Assayed: 3.60

Participant Mean: 3.46

Participant Bias: -0.29

Figure 24.
Bias Plot of Glutarylcarnitine (C5DC) Values by Method
Quarter 1, Specimen 20211006001
Expected Value (EV) = 3.75 µmol/L blood



The C5DC bias plot shows units of measure on the y-axis ranging from 5.00 µmol/L blood to -5.00 µmol/L blood. The bias for this plot is -0.29. This plot shows an even scatter for most methods

Quarter 3

Specimen: 20213006004

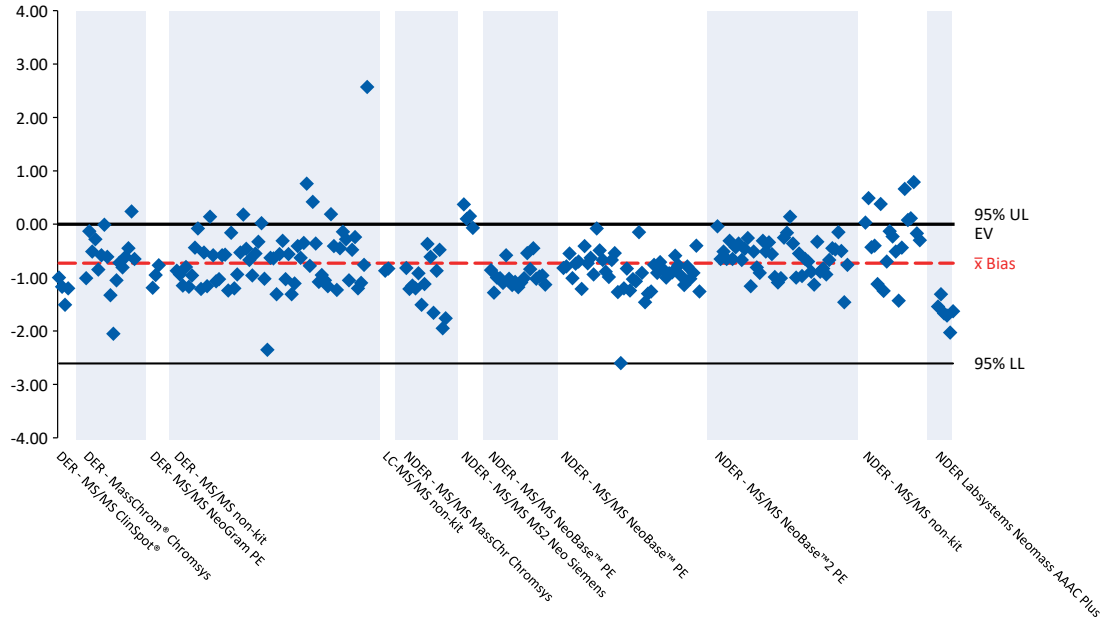
Enriched: 2.00

CDC Assayed: 2.35

Participant Mean: 1.88

Participant Bias: -0.73

Figure 25.
Bias Plot of Hydroxyisovalerylcarnitine (C5OH) Values by Method
Quarter 3, Specimen 20213006004
Expected Value (EV) = 2.61 µmol/L blood



The C5OH 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 -0.73. This plot shows a moderately negative bias across methods

Figure 26. Reproducibility of Results: Bias Plot of Hexanoylcarnitine (C6) Values by Method Quarter 1, Specimen 20211006002 Expected Value (EV) = 1.24 µmol/L blood

Quarter 1

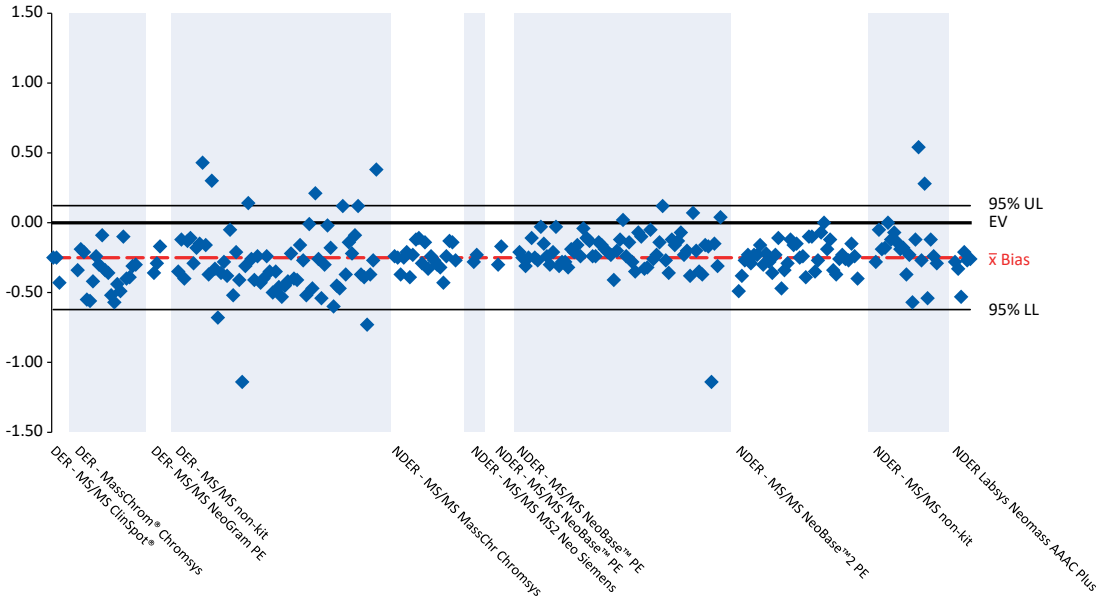
Specimen: 20211006002

Enriched: 1.20

CDC Assayed: 1.05

Participant Mean: 0.99

Participant Bias: -0.25



The C6 bias plot shows units of measure on the y-axis ranging from 1.50 µmol/L blood to -1.50 µmol/L blood. The bias for this plot is -0.25. This plot shows a moderately negative bias across all methods

Figure 27. Bias Plot of Octanoylcarnitine (C8) Values by Method Quarter 1, Specimen 20211006002 Expected Value (EV) = 1.57 µmol/L blood

Quarter 1

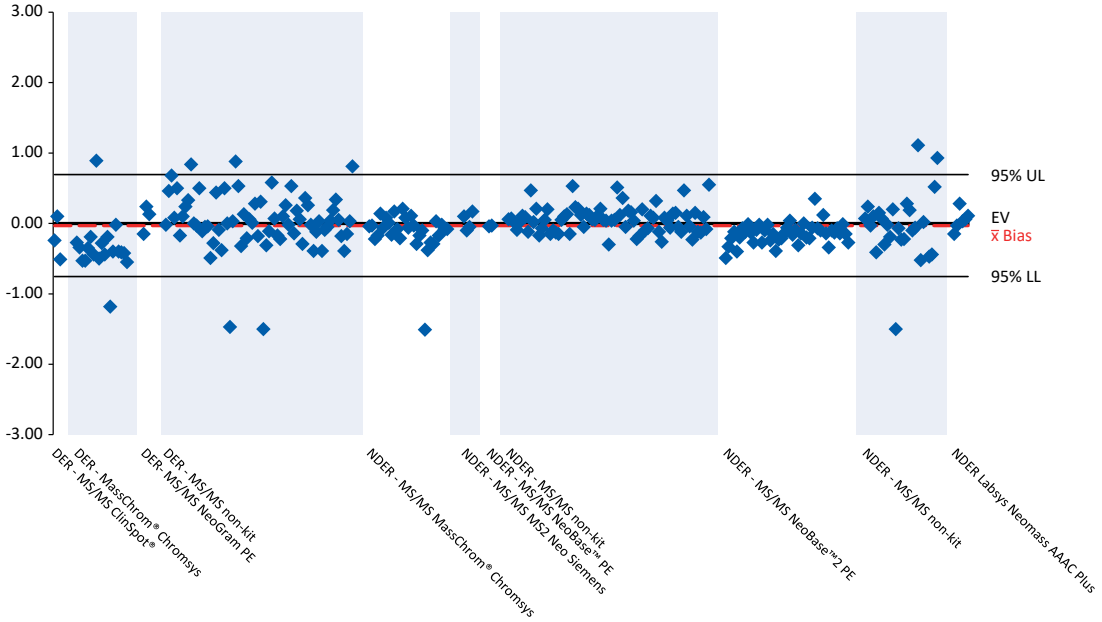
Specimen: 20211006002

Enriched: 1.50

CDC Assayed: 1.68

Participant Mean: 1.54

Participant Bias: -0.03



The C8 bias plot shows units of measure on the y-axis ranging from 3.00 µmol/L blood to -3.00 µmol/L blood. The bias for this plot is -0.03. This plot shows an even scatter across all methods

Figure 28.
Bias Plot of Decanoylcarnitine (C10) Values by Method
Quarter 1, Specimen 20211006002
Expected Value (EV) = 1.10 µmol/L blood

Quarter 1

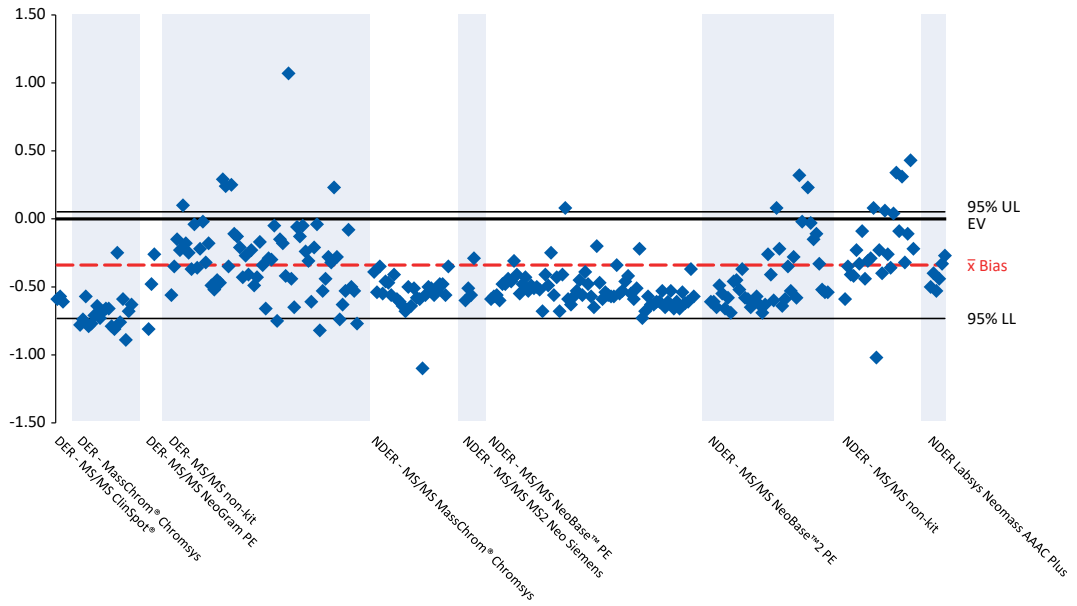
Specimen: 20211006002

Enriched: 1.00

CDC Assayed: 0.80

Participant Mean: 0.76

Participant Bias: -0.34



The C10 bias plot shows units of measure on the y-axis ranging from 1.50 µmol/L blood to -1.50 µmol/L blood. The bias for this plot is -0.34. This plot shows a moderately negative bias across all methods.

Figure 29.
Bias Plot of Decenoylcarnitine (C10:1) Values by Method
Quarter 1, Specimen 20211006002
Expected Value (EV) = 0.98 µmol/L blood

Quarter 1

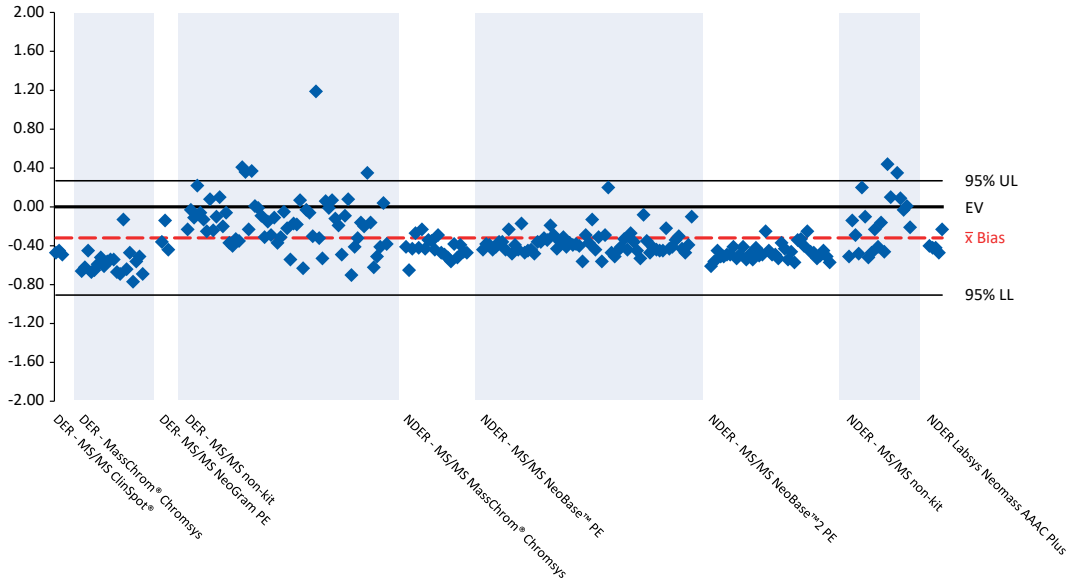
Specimen: 20211006002

Enriched: 0.90

CDC Assayed: 0.80

Participant Mean: 0.66

Participant Bias: -0.32



The C10:1 bias plot shows units of measure on the y-axis ranging from 2.00 µmol/L blood to -2.00 µmol/L blood. The bias for this plot is -0.32. This plot shows the derivitized MassChrom kit as having a slightly more negative bias than other reported methods.

Figure 30. Reproducibility of Results: Bias Plot of Decadienoylcarnitine (C10:2) Values by Method Quarter 1, Specimen 20211006001 Expected Value (EV) = 0.02 µmol/L blood

Quarter 1

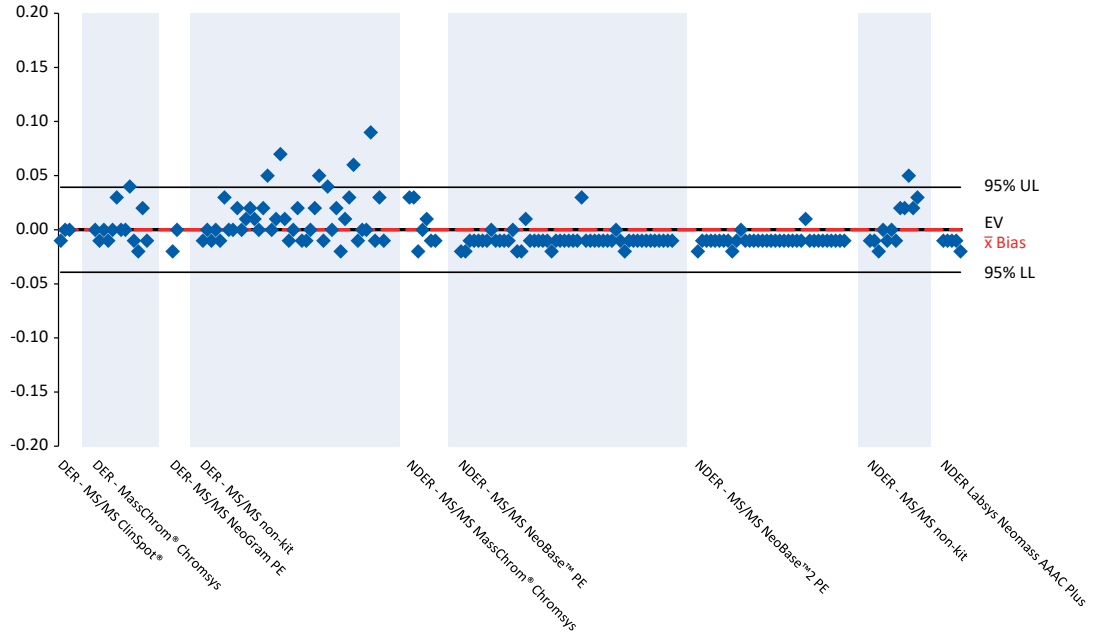
Specimen: 20211006001

Enriched: 0.00

CDC Assayed: 0.03

Participant Mean: 0.02

Participant Bias: 0.00



The C10:2 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 0.00. This plot shows little to no bias with respect to the expected value for most methods

Figure 31. Bias Plot of Myristoylcarnitine (C14) Values by Method Quarter 1, Specimen 20211006004 Expected Value (EV) = 1.47 µmol/L blood

Quarter 1

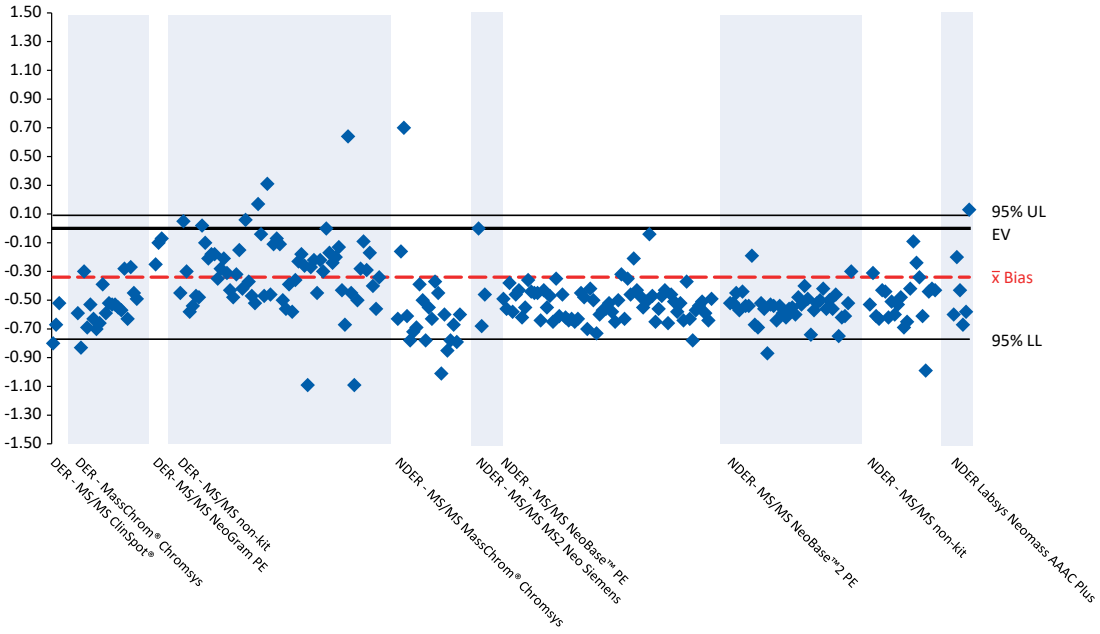
Specimen: 20211006004

Enriched: 1.40

CDC Assayed: 1.18

Participant Mean: 1.13

Participant Bias: -0.34



The C14 bias plot shows units of measure on the y-axis ranging from 1.50 µmol/L blood to -1.50 µmol/L blood. The bias for this plot is -0.34. This plot shows a moderately negative bias across methods.

Figure 32. Reproducibility of Results: Bias Plot of Tetradecenoylcarnitine (C14:1) Values by Method Quarter 1, Specimen 20211006004 Expected Value (EV) = 1.55 µmol/L blood

Quarter 1

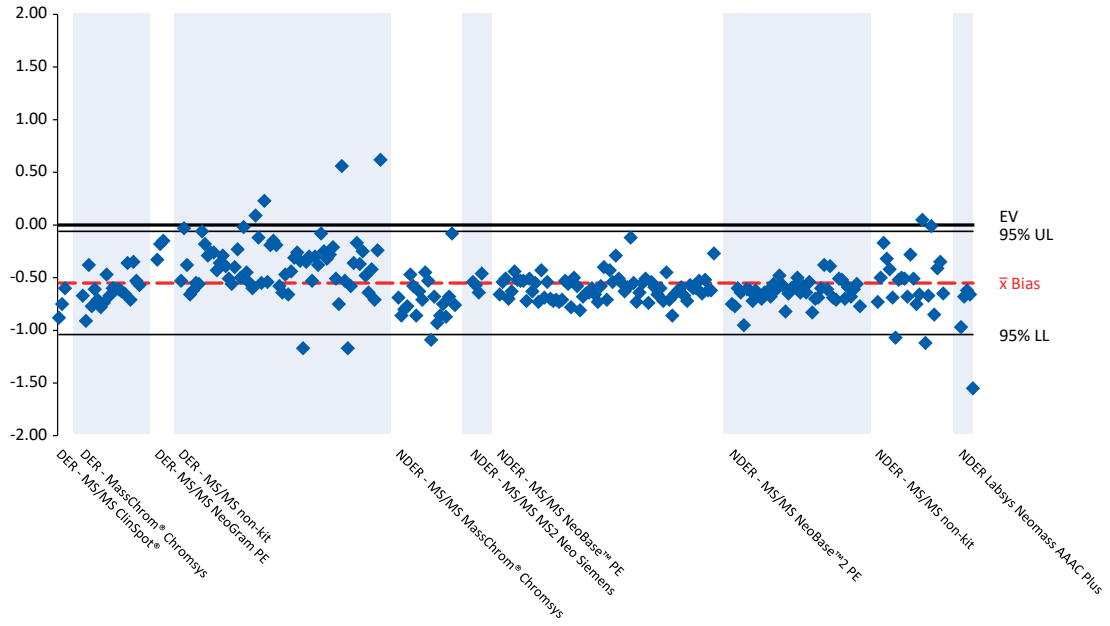
Specimen: 20211006004

Enriched: 1.50

CDC Assayed: 1.21

Participant Mean: 1.00

Participant Bias: -0.55



The C14:1 bias plot shows units of measure on the y-axis ranging from 2.00 µmol/L blood to -2,00 µmol/L blood. The bias for this plot is -0.55. This plot shows a moderately negative bias across methods.

Figure 33. Bias Plot of Palmitoylcarnitine (C16) Values by Method Quarter 1, Specimen 20211006001 Expected Value (EV) = 0.99 µmol/L blood

Quarter 1

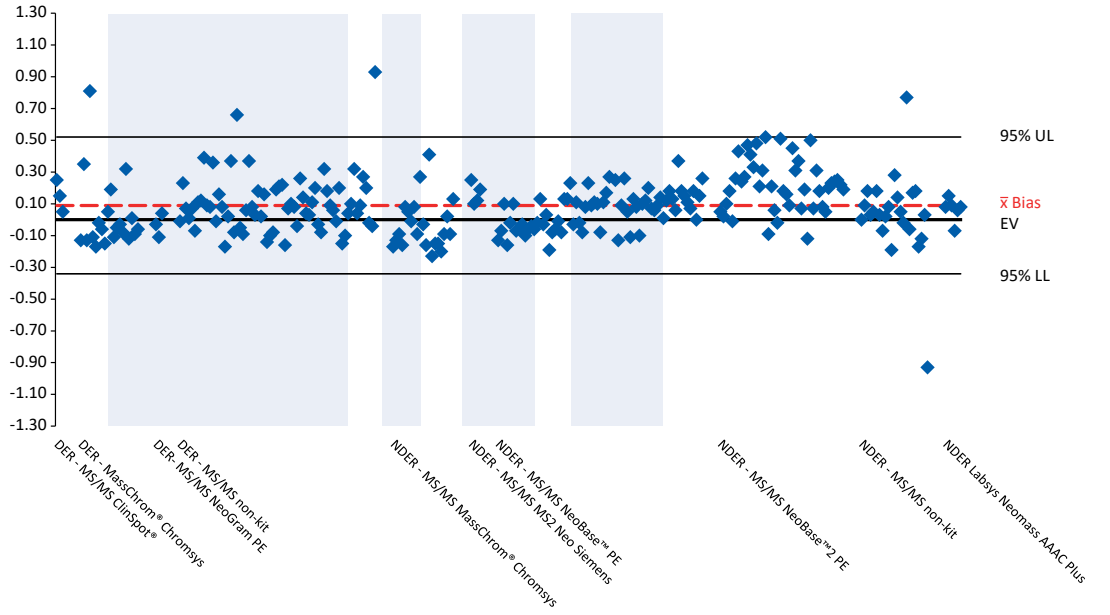
Specimen: 20211006001

Enriched: 0.00

CDC Assayed: 1.04

Participant Mean: 1.08

Participant Bias: 0.09



The C16 bias plot shows units of measure on the y-axis ranging from 1.30 µmol/L blood to -1.30 µmol/L blood. The bias for this plot is -0.09. This plot shows a moderately negative bias across methods.

Figure 34.
Bias Plot of Hydroxypalmitoylcarnitine (C16OH) Values by Method
Quarter 1, Specimen 20211006004
Expected Value (EV) = 1.02 µmol/L blood

Quarter 1

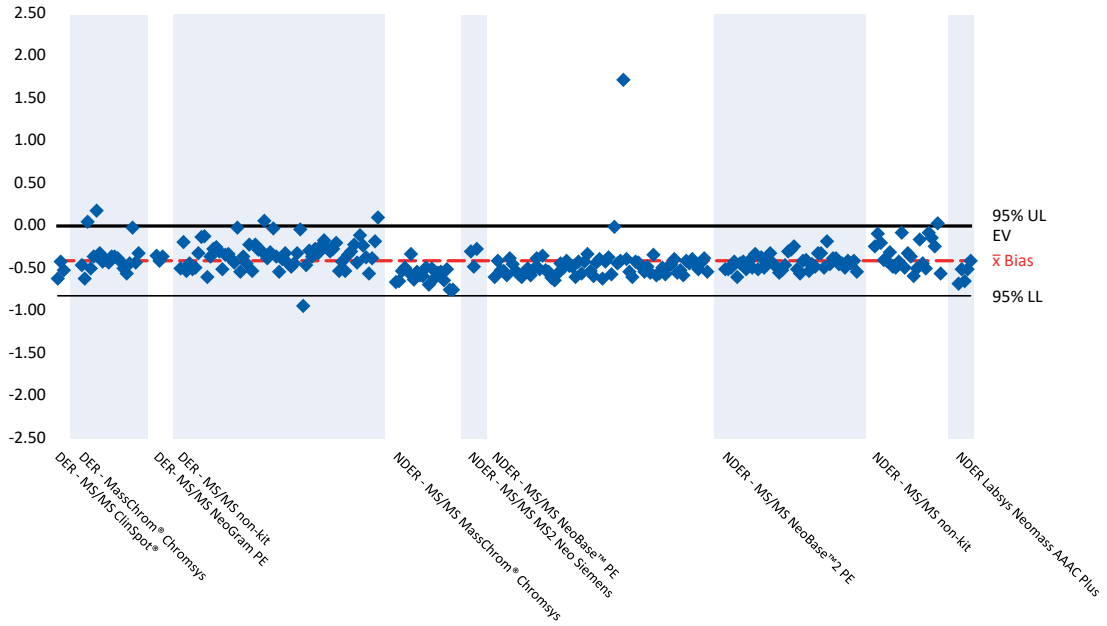
Specimen: 20211006004

Enriched: 1.00

CDC Assayed: 0.79

Participant Mean: 0.61

Participant Bias: -0.41



The C16OH bias plot shows units of measure on the y-axis ranging from 2.50 µmol/L blood to -2.50 µmol/L blood. The bias for this plot is -0.41. This plot shows a negative bias and tight scatter across methods.

Figure 35.
Bias Plot of Stearoylcarnitine (C18) Values by Method
Quarter 1, Specimen 20211006004
Expected Value (EV) = 1.79 µmol/L blood

Quarter 1

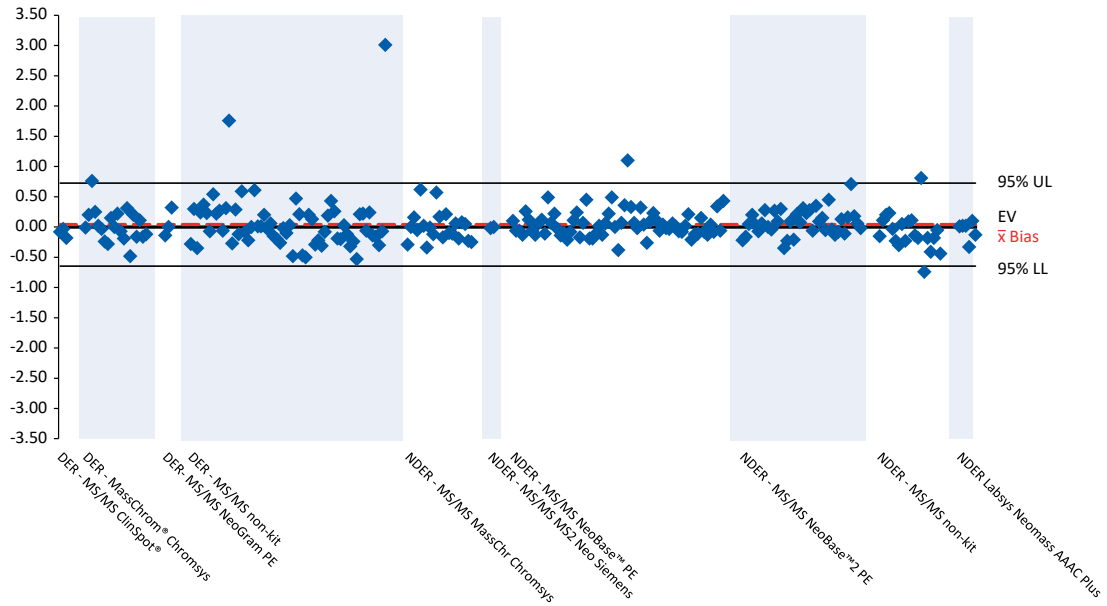
Specimen: 20211006004

Enriched: 0.00

CDC Assayed: 1.80

Participant Mean: 1.83

Participant Bias: 0.04



The C18 bias plot shows units of measure on the y-axis ranging from 3.50 µmol/L blood to -3.50 µmol/L blood. The bias for this plot is 0.04. This plot shows an even scatter across methods

Quarter 3

Specimen: 20213006002

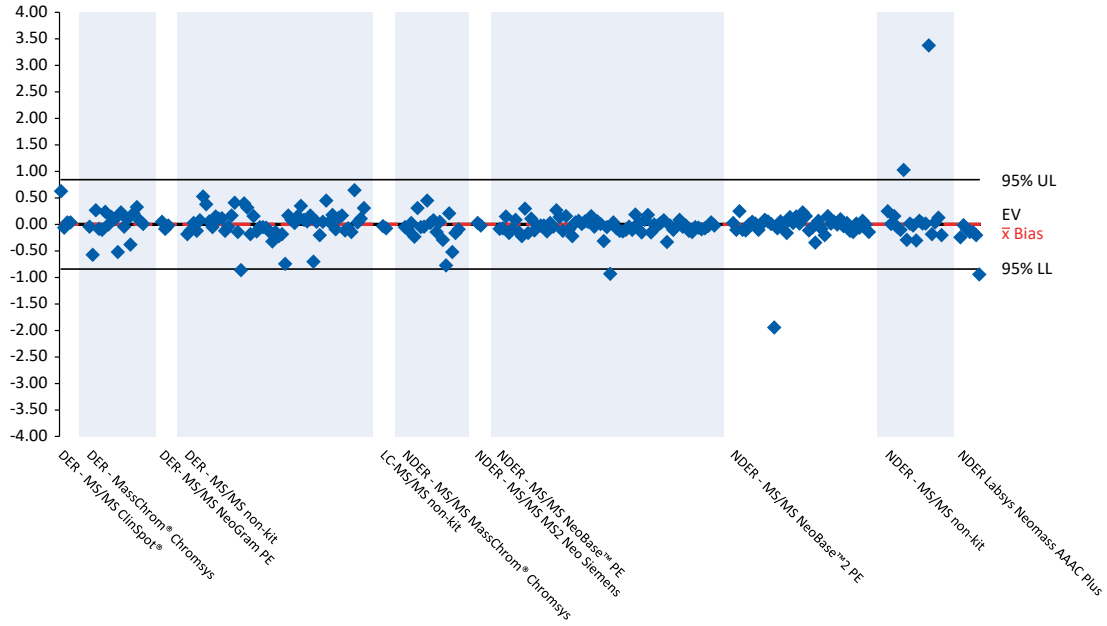
Enriched: 0.00

CDC Assayed: 0.87

Participant Mean: 0.94

Participant Bias: 0.00

Figure 36.
Bias Plot of Oleoylcarnitine (C18:1) Values by Method
Quarter 3, Specimen 20213006002
Expected Value (EV) = 0.94 µmol/L blood



The C18:1 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 0.00. This plot shows a tight scatter across methods.

Quarter 1

Specimen: 20211006004

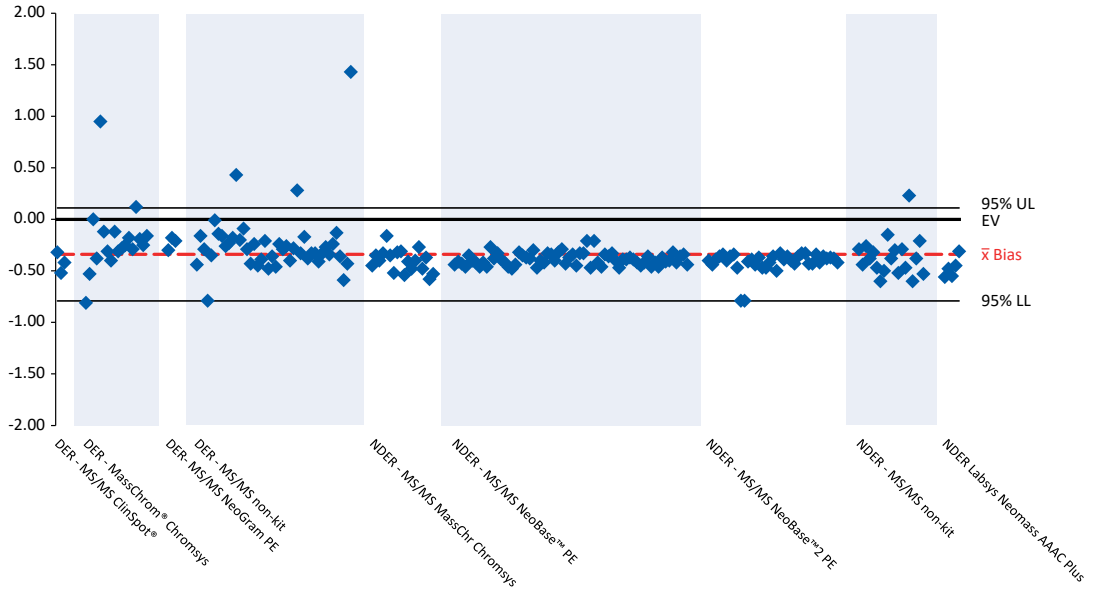
Enriched: 0.80

CDC Assayed: 0.45

Participant Mean: 0.47

Participant Bias: -0.34

Figure 37.
Bias Plot of Hydroxystearoylcarnitine (C18OH) Values by Method
Quarter 1, Specimen 20211006004
Expected Value (EV) = 0.81 µmol/L blood



The C18OH bias plot shows units of measure on the y-axis ranging from 2.00 µmol/L blood to -2.00 µmol/L blood. The bias for this plot is -0.34,. The plot shows a slightly negative bias across methods.

Appendix for Accessibility Descriptions

Figures 2–37, Bias Plots: Bias plots have been created to show a wide range of PT challenge specimens. Bias plots compare two measurements of the same variable. The bias is calculated by subtracting the participant mean value from the CDC expected value. The bias is represented by a broken line. The EV 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 method-related differences in analyte recoveries, we grouped 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 showed representative bias plots for all 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] CLSI. Dried Blood Spot Specimen Collection for Newborn Screening. 7th ed. CLSI Standard NBS01. Clinical and Laboratory Standards Institute; 2021.

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