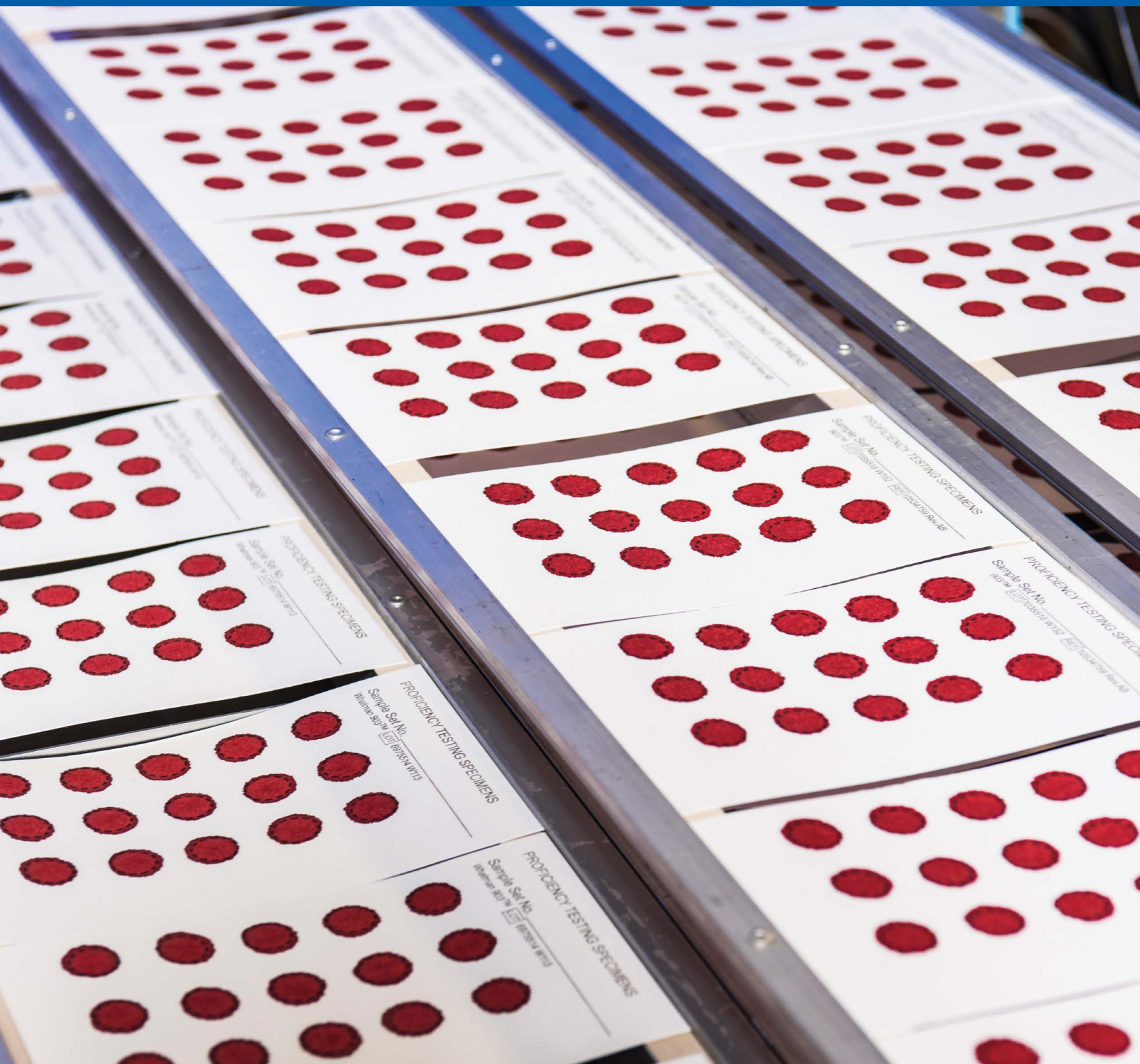
2020 ANNUAL SUMMARY REPORT

Newborn Screening Quality Assurance Program

Centers for Disease Control and Prevention
National Center for Environmental Health

Newborn Screening Quality Assurance Program
2020 Annual Summary Report, Volume 38

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.

Contents

Acronym Glossary ii

Introduction 1

New Activities 2

About NSQAP 3

- Countries Shown on World Map that Participated in NSQAP During 2020 4

Filter Paper 6

Proficiency Testing 7

- The Proficiency Testing Analytes 7
- Proficiency Testing Materials and Methods 8
- Proficiency Testing Data Handling 8
- Proficiency Testing Errors 8
- Proficiency Testing Cutoff Values 14

2020 Bias Plots 24

- Proficiency Testing Bias Plots 24

Appendix for Accessibility Descriptions 43

References 43

Acknowledgments 44

Acronym Glossary

Notation	Description
17OHP	17 α-hydroxyprogesterone
A2LA	American Association for Laboratory Accreditation
ALD	adrenoleukodystrophy
BIOT	biotinidase
BMSL	Biochemical Mass Spectrometry Laboratory
CAH	second-tier congenital adrenal hyperplasia
CDC	Centers for Disease Control and Prevention
CFDNA	cystic fibrosis DNA
CLSI	Clinical Laboratory Standards Institute
DBS	dried blood spot
EV	expected value
FDA	Food and Drug Administration
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
IEC	International Electrotechnical Commission
IRT	immunoreactive trypsinogen
ISO	International Organization for Standardization
LC	liquid chromatography
LSD	lysosomal storage disorder
MAP	Molecular Assessment Program
MQIP	Molecular Quality Improvement Program
MS/MS	tandem mass spectrometry
MSMS1	tandem MS 1
NSMBB	Newborn Screening and Molecular Biology Branch
NSQAP	Newborn Screening Quality Assurance Program
PT	proficiency testing
QC	quality control
RBC	red blood cells
RUSP	Recommended Uniform Screening Panel
SMA	Spinal Muscular Atrophy
SMN1	survival motor neuron 1
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 preventative health programs in the United States. Healthcare professionals collect dried blood spot (DBS) specimens from more than 98% of all US newborns shortly after birth. State and public health laboratories or associated laboratories screen these DBS specimens for certain genetic, metabolic, and endocrine disorders. The Centers for Disease Control and Prevention's (CDC) Newborn Screening Quality Assurance Program (NSQAP) helps newborn screening laboratories with these testing processes.

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

CDC's Newborn Screening and Molecular Biology Branch (NSMBB) has been granted International Organization for Standardization (ISO)/International Electrotechnical Commission (IEC) 17043 accreditation by the American Association for Laboratory Accreditation (A2LA). Accreditation was achieved after a thorough review of NSMBB's quality management system and ability to develop and administer specific PT protocols. The branch's NSQAP web-based PT programs are included in the A2LA Scope of Accreditation. The accreditation does not include testing for glucose- 6-phosphate dehydrogenase (G6PD) and NSQAP disease specific PT programs. Consult A2LA Certificate#4190.01 for a list of accredited NSMBB PT programs.

New Activities

- January – NSQAP launched the Participant Portal (https://nbs.dynamics365portals.us/) which allowed for direct entry of results by participants in the areas of:
  - PT – Participants entered results into both the new portal and legacy site for the following programs: amino acid PT, acylcarnitine PT, biotinidase (BIOT) PT, glucose-6-phosphate dehydrogenase (G6PD) PT, hormone + total galactose (HORM) PT, galactose-1-phosphate uridyltransferase (GALT) PT, immunoreactive trypsinogen (IRT) PT. Comparative analysis showed negligible differences between the modes of data entry.
    - Interactive Power BI reports for biochemical PT statistical reports were introduced. These reports allowed participants to view informational statistical data by specimen, by analyte, or by location of labs (US domestic or international).
    - Individual laboratory evaluations were enhanced. Specimens were evaluated as "Acceptable" or "Unacceptable". If the participant's reported clinical assessment differed from the NSQAP expected clinical assessment, the evaluation for the specimen was marked "Unacceptable". It was the responsibility of the laboratory to categorize unacceptable results according to their protocols.
    - Laboratory evaluations and reports were distributed directly to the NSQAP portal. Participants with access to the NSQAP portal viewed and/or downloaded reports and evaluations.
  - QC - Pilot testing of the NSQAP Participant Portal was introduced to a subset of domestic participants to validate its functionality for QC data entry of the following programs: 17 α-hydroxyprogesterone + total galactose (17OHP + TGAL) QC, lysosomal storage disorder (LSD) QC, tandem MS 1 (MSMS1) QC, thyroxine (T4) QC, thyroid stimulating hormone (TSH)QC, along with second-tier QC programs for congenital adrenal hyperplasia (CAH), maple syrup urine disease and phenylketonuria (MSUD-PKU), and methylmalonic/propionic acidemia and homocystinuria (MMA-tHCY).
- March - NSQAP and participating laboratories experienced unprecedented challenges due to the COVID-19 pandemic. CDC safety precautions were introduced to slow the spread of the disease and resulted in staffing and material production limitations, necessitating an adjustment to the routine material shipment schedule. Despite these circumstances, NSQAP provided two PT events and two QC events to all participants during the second half of 2020.
- July - A new PT program for Spinal Muscular Atrophy (SMA) was piloted. This program used DBS to determine the presence or absence of survival motor neuron 1 (SMN1) exon 7. The pilot program was a success and the SMA PT program will be available for all participants in 2021. For more information or to request participation in this program, email NSQAPDMT@cdc.gov.
- August through December – Official QC program data collection via the NSQAP Participant Portal was conducted for all participants. For this data set, statistical enhancements were developed to better access method peer group performance and will be available when the 2020 QC Summary Report for Set 2 is published.

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 US 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 US Recommended Uniform Screening Panel (RUSP) [1].

Although there was a slight decrease of participation for some programs in 2020 due to the COVID-19 pandemic, the NSQAP as a whole continued to grow. In 2020, 650 newborn screening laboratories in 88 countries (at least one laboratory per country) participated in the program (Figure 1). Of these laboratories, 484 participated in PT (Table 1) and 383 in QC (Table 2). The program distributed DBS materials for 75 analytes to participating laboratories (Tables 1 and 2).

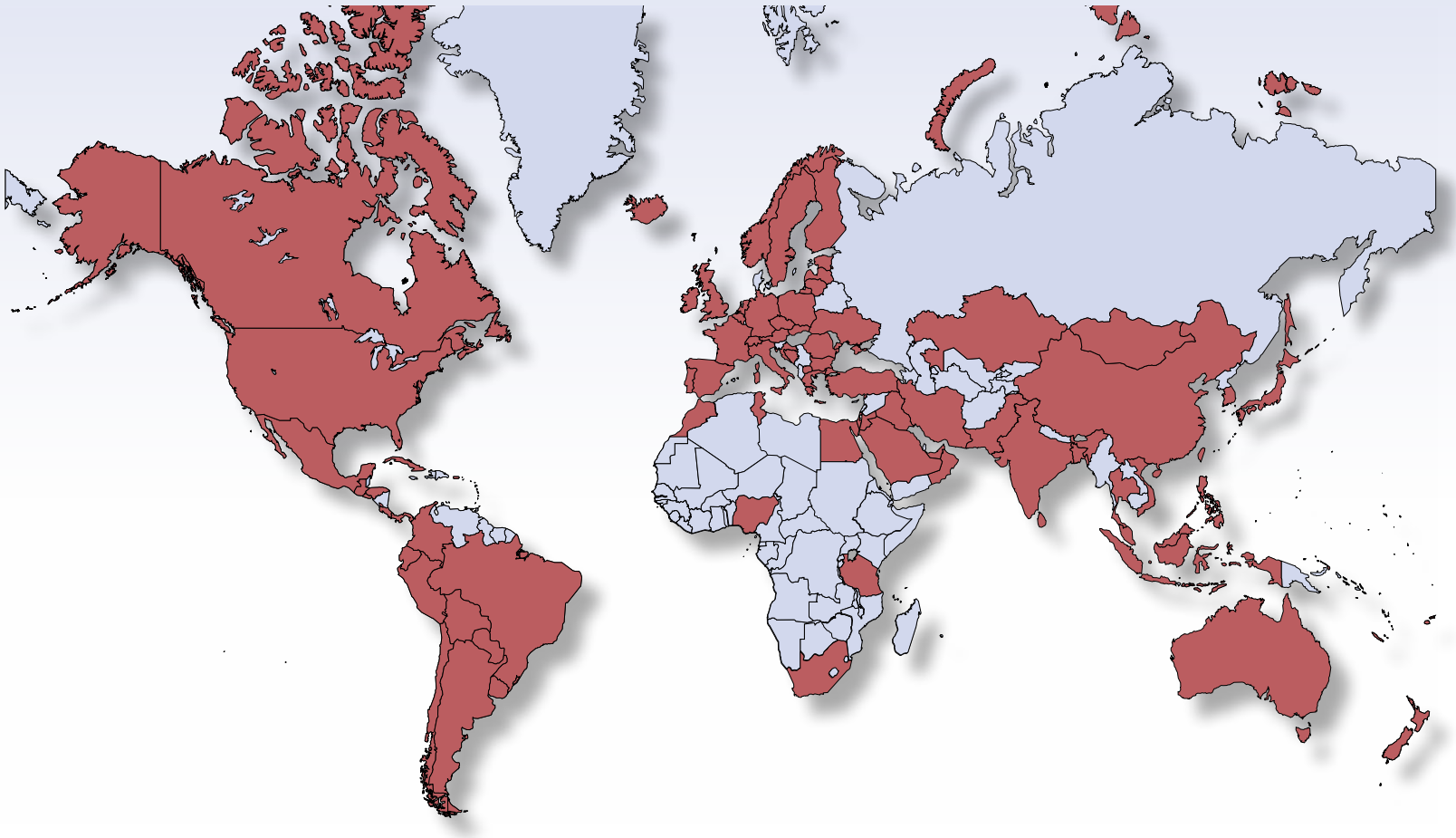
To offer more specialized services, NSQAP works with the Biochemical Mass Spectrometry Laboratory (BMSL) and the Molecular Quality Improvement Program (MQIP) in the NSMBB to produce and distribute DBS materials.

NSQAP provides quality assurance materials for T4, TSH, 17OHP, IRT, sickle cell and other hemoglobinopathies (Hb), anti-HIV-1 Antibodies (HIV), anti-Toxoplasma Antibodies (TOXO), and the second-tier congenital adrenal hyperplasia (CAH) programs.

BMSL offers newborn screening tandem mass spectrometry (MS/MS) quality assurance, education, and research opportunities. It also oversees the amino acids, acylcarnitines, adrenoleukodystrophy (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 cystic fibrosis DNA PT (CFDNA), T-cell receptor excision circle PT (TREC), and pilot SMA PT programs and provides molecular assay technical assistance to NSQAP participants. In addition, MQIP offers the Molecular Assessment Program (MAP) to US newborn screening laboratories. A MAP visit assesses components of molecular testing which includes guidance for laboratory-specific needs and assistance in 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. Eighty-eight countries participated in the Newborn Screening Quality Assurance Program.



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
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Macedonia
Malaysia
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New Zealand
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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 = 484)

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

Analyte	Total PT Participation in 2020
17OHP	282
T4	78
TSH	344
TGal	183
BIOT	213
GALT	145
IRT	237
G6PD	100
CFDNA	73
HGB	79
Anti-HIV-1	24
TOXO	17
TREC	72
Arg	273
Cit	300
Leu	333
Met	315
Phe	419
SUAC	169
Tyr	335
Val	300
C0(L)	318
C2(L)	222
C3	321
C3DC	117
C3DC+C4OH	140
C4	296
C4OH	107
C5	327
C5:1	290
C5DC	315
C5OH	282

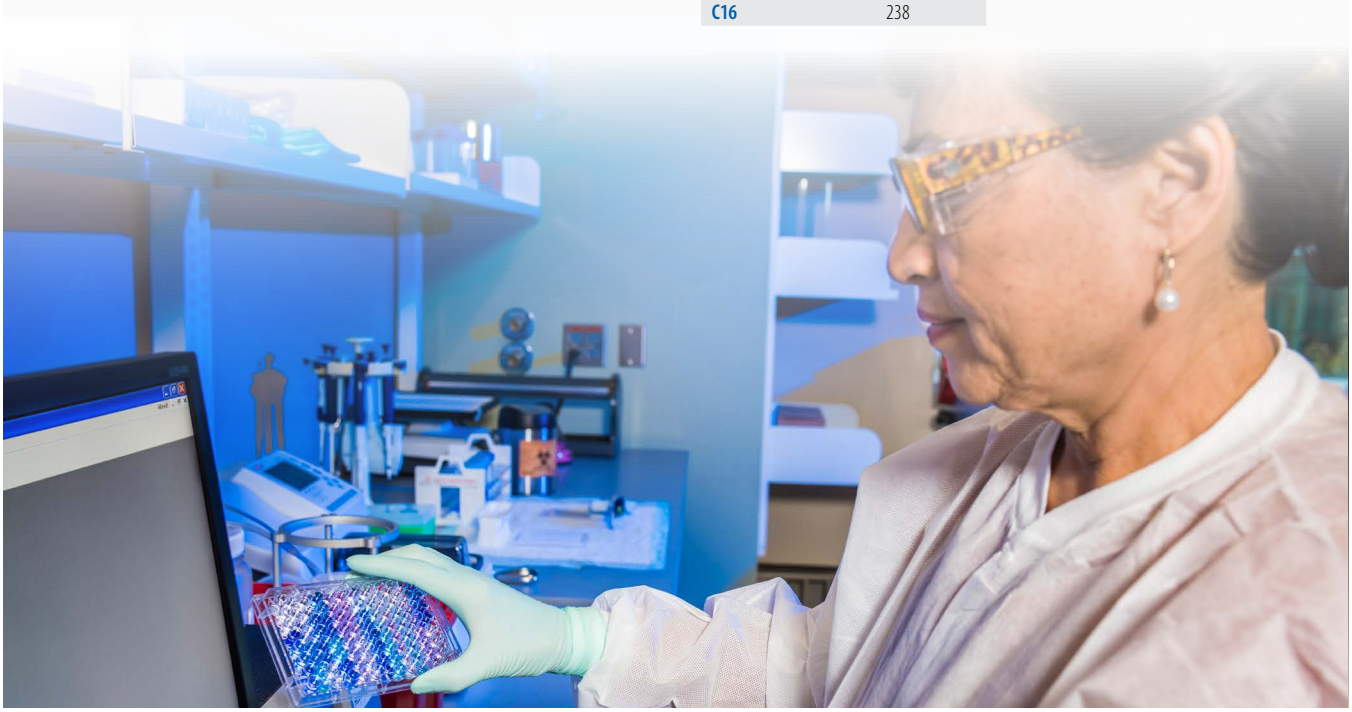
Analyte	Total PT Participation in 2020
C6	305
C8	332
C10	321
C10:1	285
C10:2	198
C14	303
C14:1	311
C16	311
C16OH	308
C18	290
C18:1	284
C18OH	252
17OHP2	29
4AD2	29
CORT2	29
11D2	21
21D2	22
GALC	11
GAA	23
IDUA	24
24-LPC	9
26-LPC	18

Table 2. Number of participants reporting quality control analytes, 2020 (N = 383)

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

Analyte	Total QC participation in 2020
17OHP	202
T4	53
TSH	280
TGal	129
GALT	73
IRT	165
Ala	196
Arg	209
Cit	231
Gly	171
Leu	246
Met	237
Orn	177
Phe	324
SUAC	122
Tyr	249
Val	231
C0	239
C2	232
C3	238
C3DC	82
C3DC+C4OH	123
C4	232
C4OH	73
C5	241
C5:1	205
C5DC	226
C5OH	211
C6	237
C8	244
C10	242
C12	229
C14	236
C14:1	214
C16	238

Analyte	Total QC participation in 2020
C16OH	234
C18	233
C18OH	196
17OHP2	29
4AD2	28
CORT2	28
11D2	22
21D2	22
GALC	20
GAA	40
IDUA	39
GLA	29
ABG	28
ASM	17
20-LPC	23
22-LPC	23
24-LPC	33
26-LPC	40
GUAC	11
CRE2	7
ALE2	21
ILE2	24
LEU2	24
PHE2	25
TYR2	24
VAL2	25
MMA2	31
EMA2	9
MCA2	22
tHCY2	30
MA2	2



Filter Paper

NSQAP evaluates absorption characteristics of all filter paper lots approved by the Food and Drug Administration (FDA) as a newborn screening collection device [2]. 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 T4 contained within a 3.2-mm disk with the serum absorption volume of the disks made from blood with washed, intact red blood cells (RBCs). The latest version of Clinical Laboratory Standards Institute (CLSI) Standard NBS01-A6, Blood Collection on Filter Paper for Newborn Screening Programs, describes the method.

FDA-approved newborn screening filter paper manufacturers (Cytiva Life Sciences and PerkinElmer Health Sciences) provide NSQAP with statistically valid sample sets of unprinted filter paper from each production lot. Tables 3 and 4 show serum absorption volumes from the 10 most recent lots of these two filter paper sources. The published standardized acceptable serum absorption volume per 3.2-mm disk (mean value and 95% confidence interval) is 1.44 ± 0.20 µL, using blood with washed intact RBCs [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 and W181 to produce the QC and PT specimens distributed in 2020.

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 (1/8") Punch Average (StDev)	Absorption Time (sec) Average (StDev)	Spot Diameter (mm) Average (StDev)
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)
103649	March 2015	1.53 (0.10)	9.7 (3.1)	15.7 (0.7)

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

Filter Paper Lot No.	Date of Evaluation Month/Year	Serum Volume (µL) per 3.2 mm (1/8") Punch Average (StDev)	Absorption Time (sec) Average (StDev)	Spot Diameter (mm) Average (StDev)
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

NSQAP usually distributes PT panels three times per year, however due to limitations from the COVID-19 pandemic, two PT events were conducted during 2020. PT panels consisted of five blind-coded specimens. Specimen sets were packaged in a zip-closed, metalized plastic bag with desiccant. Instructions for analysis and reporting data were located online in the NSQAP portal at https://nbs.dynamics365portals.us/. 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)
- tiglylcarnitine (5:1)
- 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-galactosidase (GLA)
- 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)
- T-cell receptor excision circle (TREC)
- thyroid-stimulating hormone (TSH)
- thyroxine (T4)
- total galactose (TGAL)

Proficiency Testing Materials and Methods

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

Purified analytes were used for PT enrichments. Enrichments made with commercially available or custom-synthesized analytes were 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 were enriched with measured amounts of T4 and TSH after reconstituting washed RBCs with purchased T4-depleted charcoal-stripped serum.

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

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).

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

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

C0(L) and C2(L) deficient 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, carriers, or unaffected individuals without hematocrit adjustment.

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.

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

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.

Anti-Toxoplasma Antibody (TOXO) PT DBS 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 new NSQAP Data reporting portal https://nbs.dynamics365portals.us/. 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

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

A consensus of 80% of US laboratories, as long as 10 or more US laboratories report results, must be reached for a specimen to be evaluated. If there were less than 10 US laboratories reporting results for any one specimen, all submitted results are evaluated. NSQAP occasionally challenged cutoff levels by enriching samples in the cutoff range and are closely reviewed by the NSQAP PT committee. Not-evaluated specimens were considered educational.

Tables 5–8 show the unacceptable assessments reported in 2020 by domestic and international laboratories by disorder/analyte. The rates for unacceptable misclassifications were based on the total number of specimens tested. Not-evaluated specimens were not included in the error calculations.

The CFDNA PT program provides evaluations based on allele identification and clinical assessment. Allele detection was dependent on the method used. Table 9 summarizes the CFDNA variant challenges distributed in 2020. Table 10 shows the challenges distributed in 2020 for sickle cell disease and other hemoglobinopathies. Participants were evaluated on reported hemoglobin phenotypes and the ability to provide correct clinical assessments.

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

Analyte/ Disorders	Specimens assayed (N)	Unacceptable Assessments (%)
anti-HIV-1 Antibodies	65	0.0%
anti-Toxoplama Antibodies	20	0.0%
Congenital Adrenal Hyperplasia	405	1.7%
Biotinidase Deficiency	405	2.5%
G6PD Deficiency	25	0.0%
GALT Deficiency	420	1.0%
Immunoreactive Trypsinogen	420	1.2%
Congenital Hypothyroidism	415	0.0%
Galactosemia	200	1.0%
Lysosomal Storage Disorder Krabbe	105	0.0%
Lysosomal Storage Disorder Pompe	215	0.5%
Lysosomal Storage Disorder Mucopolysaccharidosis Type 1	220	0.0%
T-Cell Receptor Excision Circle	287	0.7%
Second-tier Congenital Adrenal Hyperplasia	77	6.5%
ALD 24:0 Lysophosphatidylcholine	65	1.5%
ALD 26:0 Lysophosphatidylcholine	160	0.0%
Sickle Cell and Other Hemoglobinopathies Phenotype Errors	435	0.5%
Sickle Cell and Other Hemoglobinopathies Clinical Assessment Errors	435	0.5%
Cystic Fibrosis DNA Variant Allelle Errors	337	0.3%
Cystic Fibrosis DNA Variant Clinical Assessment Errors	337	0.0%

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

Analyte/ Disorders	Specimens Assayed (N)	Unacceptable Assessments (%)
anti-HIV-1 Antibodies	100	1.0%
anti-*Toxoplama* Antibodies	55	7.3%
Congenital Adrenal Hyperplasia	1780	0.7%
Biotinidase Deficiency	1315	2.4%
G6PD Deficiency	670	1.6%
GALT Deficiency	850	1.3%
Immunoreactive Trypsinogen	1495	1.9%
Congenital Hypothyroidism	2190	0.8%
Galactosemia	1215	1.6%
T-Cell Receptor Excision Circle	194	2.1%
Second-tier Congenital Adrenal Hyperplasia	186	7.5%
ALD 24:0 Lysophosphatidylcholine	70	4.3
ALD 26:0 Lysophosphatidylcholine	95	5.3
Sickle Cell and Other Hemoglobinopathies Phenotype Errors	345	3.2%
Sickle Cell and Other Hemoglobinopathies Clinical Assessment Errors	345	2.4%
Cystic Fibrosis DNA Variant Allelle Errors	190	0.0%
Cystic Fibrosis DNA Variant Clinical Assessment Errors	190	0.0%

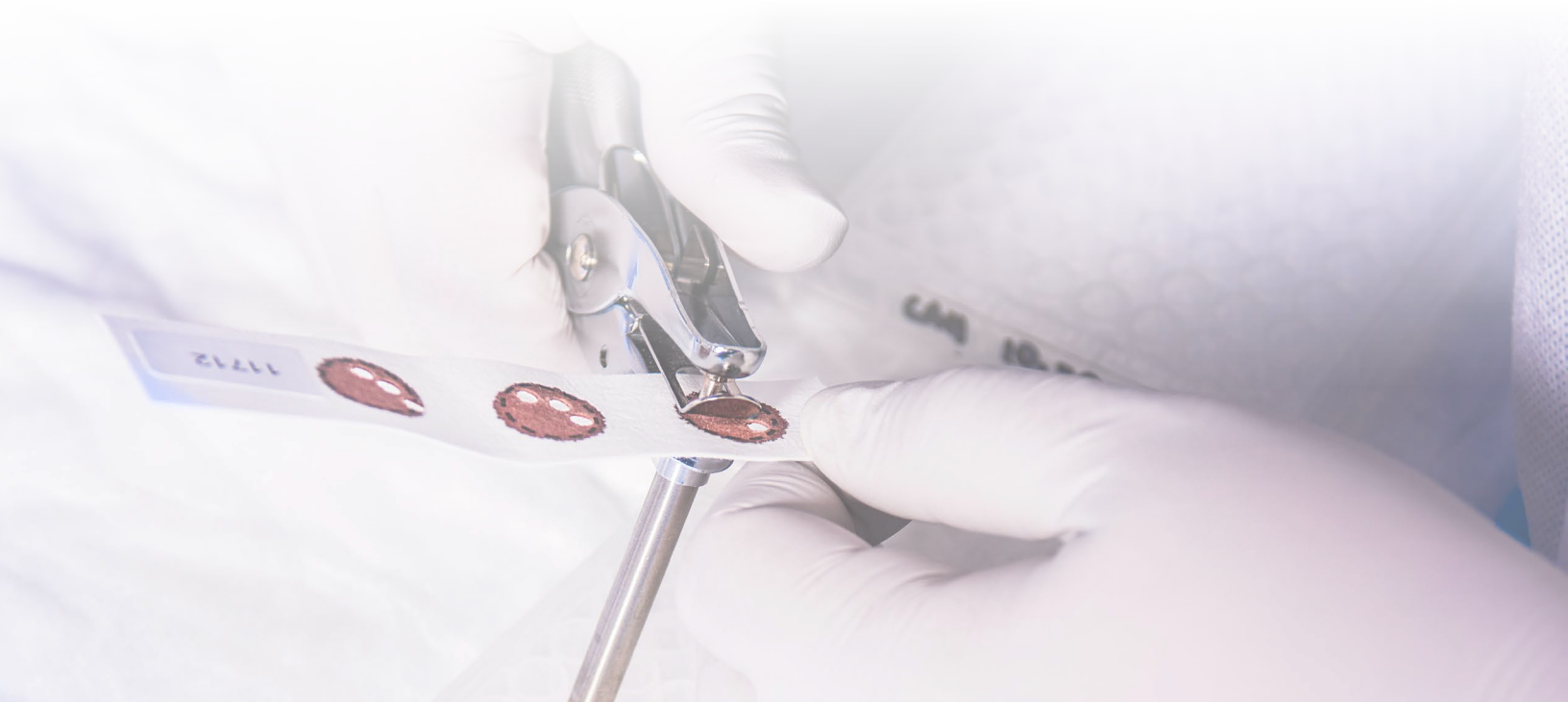


Table 7. Summary of amino acid and acylcarnitine proficiency test errors by domestic laboratories

Analyte	Specimens Assayed (N)	Unacceptable Assessments (%)
Arginine Screen	345	0.6%
Citrulline Screen	435	1.8%
Leucine Screen	435	2.8%
Methionine Screen	425	0.5%
Phenylalanine Screen	510	0.8%
Succinylacetone Screen	365	0.0%
Tyrosine Screen	455	1.8%
Valine Screen	305	1.6%
C0(L) Screen	455	0.7%
C2(L) Screen	225	5.3%
C3 Screen	455	0.4%
C3DC Screen	120	0.8%
C3DC+C4OH Screen	240	0.0%
C4 Screen	400	0.8%
C4OH Screen	110	0.0%
C5 Screen	455	0.0%
C5:1 Screen	445	2.0%
C5DC Screen	445	0.4%
C5OH Screen	445	1.1%
C6 Screen	415	0.7%
C8 Screen	455	0.2%
C10 Screen	415	0.0%
C10:1 Screen	385	0.3%
C10:2 Screen	265	3.0%
C14 Screen	405	0.7%
C14:1 Screen	455	0.4%
C16 Screen	425	0.0%
C16OH Screen	455	0.0%
C18 Screen	370	3.5%
C18:1 Screen	395	1.8%
C18OH Screen	350	0.9%

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

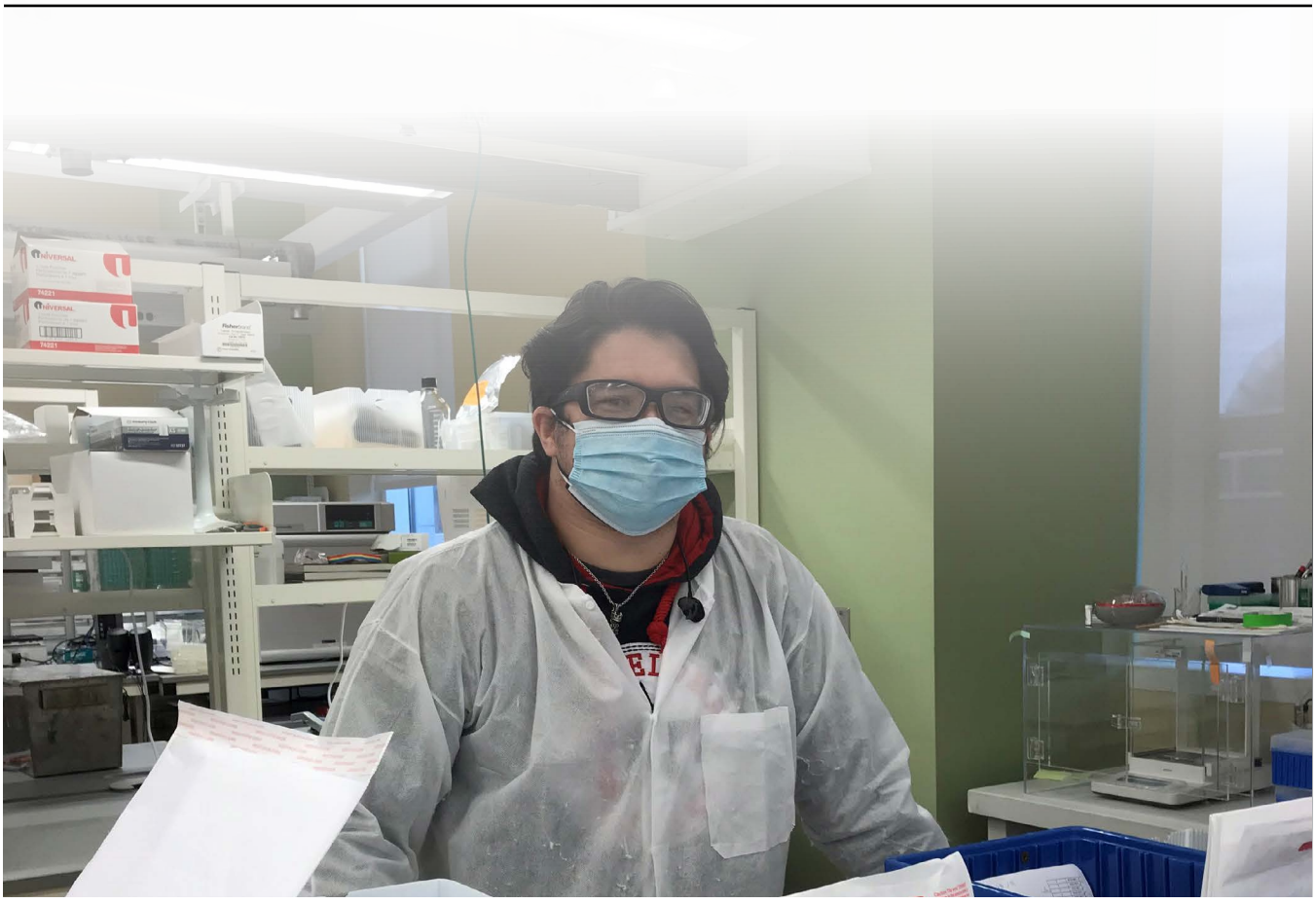
Analyte	Specimens Assayed (N)	Unacceptable Assessments (%)
Arginine Screen	1740	1.2%
Citrulline Screen	990	0.4%
Leucine Screen	2180	1.4%
Methionine Screen	2040	2.5%
Phenylalanine Screen	2680	1.7%
Succinylacetone Screen	985	0.4%
Tyrosine Screen	2135	0.6%
Valine Screen	2010	1.5%
C0(L) Screen	2065	2.6%
C2(L) Screen	1435	3.2%
C3 Screen	2070	1.6%
C3DC Screen	770	1.9%
C3DC+C4OH Screen	740	0.7%
C4 Screen	1900	0.3%
C4OH Screen	680	2.6%
C5 Screen	2125	0.9%
C5:1 Screen	1830	1.3%
C5DC Screen	2050	1.3%
C5OH Screen	1810	6.8%
C6 Screen	1955	1.4%
C8 Screen	2155	0.9%
C10 Screen	2090	0.8%
C10:1 Screen	1830	1.6%
C10:2 Screen	1220	2.5%
C14 Screen	1940	0.8%
C14:1 Screen	2005	0.9%
C16 Screen	1995	0.4%
C16OH Screen	1990	0.8%
C18 Screen	1875	2.5%
C18:1 Screen	1825	0.9%
C18OH Screen	1590	0.8%

Table 9. Cystic Fibrosis DNA variant (CTFR gene) challenges distributed in 2020

Variant (Legacy Name)	Variant (HGVS Nomenclature)	Variants Sent
F508del	(c.1521_1523delCTT)	5
1717-1G>A	(c.1585-1G>A)	1
2105-2117del13insAGAAA	(c.1973_1985del13insAGAAA)	1
2183AA>G	(c.2051_2052delAAinsG)	1
3849+10kb C>T	(c.3717+12191C>T)	1
D1152H	(c.3454G>C)	1
N1303K	(c.3909C>G)	1
R347P	(c.1040G>C)	1
Y1092X	(c.3276C>A or c.3276C>G)	1
Wild type	Wild type	7

Table 10. Hemoglobinopathies accepted presumptive phenotype distributed in 2020

Quarter	Specimen 1	Specimen 2	Specimen 3	Specimen 4	Specimen 5
Quarter 1	FAC	FA	FS	FAS	FAS
Quarter 4	FAS	FAC	FA	FAS	FAC



Proficiency Testing Cutoff Values

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

Tables 11–14 summarize the reported cutoff values for domestic and international laboratories. The tables show summary statistics for each analyte. Tables 15–17 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)	40	34.7	33.0	30.0	20.0	70.0
IRT (ng/mL blood)	40	61.2	60.0	65.0	39.7	100.0
T4 (µg/dL serum)	18	6.0	6.0	5.0	5.0	8.0
TGal (mg/dL blood)	17	10.7	10.0	10.0	6.0	15.0
TSH (µIU/mL serum)	41	30.5	25.5	20.0	10.0	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)	175	21.4	18.3	35.0	5.2	60.0
IRT (ng/mL blood)	137	64.2	63.0	60.0	20.0	90.8
T4 (µg/dL serum)	31	7.2	6.0	6.0	1.9	22.0
TGal (mg/dL blood)	110	16.5	10.0	10.0	1.5	30.0
TSH (µIU/mL serum)	213	21.9	20.0	20.0	4.5	44.4
Phe (µmol/L blood)	58	157.7	136.7	121.2	103.0	303.0

Table 13. Summary of amino acid and acylcarnitine cutoff values for domestic laboratories (µmol/L blood)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine Screen	33	74.3	70.0	50.0	35.0	120.0
Citrulline Screen	43	58.2	55.0	60.0	34.0	200.0
Leucine Screen	43	287.9	275.0	250.0	145.0	400.0
Methionine Screen	42	73.6	75.0	100.0	40.0	100.0
Phenylalanine Screen	50	141.7	150.0	130.0	75.0	188.0
Succinylacetone Screen	37	2.3	1.9	1.0	0.8	5.4
Tyrosine Screen	45	414.1	360.0	300.0	92.0	850.0
Valine Screen	30	291.5	291.0	250.0	180.0	530.0
C0(L) Screen	44	8.21	7.00	6.00	5.00	24.00
C2(L) Screen	23	6.54	7.00	9.00	0.00	10.00
C3 Screen	45	5.72	6.00	6.30	3.10	8.00
C3DC Screen	10	0.24	0.22	0.22	0.10	0.45
C3DC+C4OH Screen	24	0.55	0.41	0.38	0.25	3.03
C4 Screen	39	1.26	1.27	1.70	0.49	1.90
C4OH Screen	9	0.63	0.70	0.70	0.20	0.80
C5 Screen	45	0.70	0.62	0.60	0.34	1.20
C5:1 Screen	44	0.19	0.13	0.10	0.02	0.50
C5DC Screen	44	0.38	0.43	0.50	0.05	0.80
C5OH Screen	44	0.85	0.84	0.80	0.32	1.50
C6 Screen	41	0.38	0.26	0.24	0.14	0.95
C8 Screen	45	0.44	0.43	0.60	0.12	0.73
C10 Screen	41	0.44	0.40	0.40	0.20	0.70
C10:1 Screen	38	0.27	0.25	0.25	0.12	0.45
C10:2 Screen	26	0.14	0.10	0.10	0.02	0.38
C14 Screen	40	0.72	0.70	0.70	0.27	1.20
C14:1 Screen	45	0.60	0.60	0.60	0.17	0.80
C16 Screen	42	7.80	7.85	10.00	2.14	10.36
C16OH Screen	45	0.12	0.10	0.10	0.06	0.25
C18 Screen	35	2.33	2.20	3.50	0.70	3.50
C18:1 Screen	39	3.59	3.00	3.00	2.00	7.00
C18OH Screen	34	0.09	0.10	0.10	0.03	0.18

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

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine Screen	166	57.6	57.7	70.0	10.0	150.0
Citrulline Screen	181	49.8	49.1	55.0	20.0	100.0
Leucine Screen	205	308.4	294.0	300.0	112.0	686.7
Methionine Screen	193	55.0	50.0	75.0	20.0	140.0
Phenylalanine Screen	199	130.2	120.0	150.0	48.0	300.0
Succinylacetone Screen	90	2.2	1.7	2.0	0.3	8.0
Tyrosine Screen	200	296.3	290.0	350.0	79.9	600.0
Valine Screen	191	270.2	271.4	300.0	142.0	470.0
C0(L) Screen	185	8.37	8.00	8.00	1.70	24.70
C2(L) Screen	110	7.03	7.00	7.00	0.00	21.20
C3 Screen	197	5.31	5.20	5.65	1.30	11.02
C3DC Screen	69	0.27	0.25	0.25	0.04	1.40
C3DC+C4OH Screen	72	0.49	0.45	0.45	0.15	2.53
C4 Screen	183	0.95	0.97	1.30	0.16	2.50
C4OH Screen	61	0.60	0.61	0.65	0.05	1.20
C5 Screen	201	0.67	0.60	0.70	0.10	2.00
C5:1 Screen	176	0.15	0.11	0.25	0.01	0.90
C5DC Screen	195	0.34	0.30	0.35	0.03	1.00
C5OH Screen	172	0.71	0.74	0.80	0.15	1.50
C6 Screen	184	0.27	0.20	0.40	0.04	1.30
C8 Screen	206	0.34	0.30	0.45	0.05	1.30
C10 Screen	193	0.36	0.35	0.45	0.07	1.10
C10:1 Screen	172	0.25	0.21	0.30	0.06	1.00
C10:2 Screen	123	0.15	0.10	0.15	0.01	2.00
C14 Screen	182	0.60	0.56	0.75	0.08	1.30
C14:1 Screen	191	0.46	0.40	0.60	0.04	2.50
C16 Screen	187	6.92	7.00	7.50	0.57	14.00
C16OH Screen	189	0.11	0.10	0.10	0.02	0.75
C18 Screen	179	2.10	2.00	2.30	0.10	9.00
C18:1 Screen	176	3.09	3.00	3.50	0.15	7.00
C18OH Screen	153	0.08	0.07	0.10	0.01	0.50

Table 15. Summary of cutoff values by analyte and method for domestic laboratories — hormones, galactose, and immunoreactive trypsinogen, (methods N<3 not shown)

17 α-Hydroxyprogesterone ng/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**40**	**34.7**	**33.0**	**30.0**	**20.0**	**70.0**
AutoDELFIA® Neonatal 17OHP PerkinElmer	13	37.3	33.0	33.0	25.0	70.0
GSP® TGal Neonatal PerkinElmer	26	33.5	31.0	30.0	20.0	55.0

Immunoreactive Trypsinogen ng/mL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**40**	**61.2**	**60.0**	**65.0**	**39.7**	**100.0**
AutoDELFIA® Neonatal IRT PerkinElmer	19	67.4	65.0	65.0	51.0	100.0
GSP® TGal Neonatal PerkinElmer	21	55.5	55.0	55.0	39.7	70.0

Thyroxine µg/dL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**18**	**6.0**	**6.0**	**5.0**	**5.0**	**8.0**
AutoDELFIA® Neonatal T4 PerkinElmer	4	6.0	6.3	n/a	5.0	6.6
GSP® TGal Neonatal PerkinElmer	13	6.0	5.5	5.0	5.0	8.0

Thyroid-Stimulating Hormone µIU/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**41**	**30.5**	**25.5**	**20.0**	**10.0**	**58.0**
AutoDELFIA® Neonatal hTSH PerkinElmer	15	39.4	36.0	20.0	20.0	58.0
GSP® TGal Neonatal PerkinElmer	25	25.6	25.0	20.0	10.0	54.0

Total Galactose mg/dL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**17**	**10.7**	**10.0**	**10.0**	**6.0**	**15.0**
50hr Reagent Kit Spotcheck® TGal Astoria-Pacific	3	12.0	11.0	n/a	10.0	15.0
GSP® TGal Neonatal PerkinElmer	10	11.2	11.0	10.0	7.3	14.0

Table 16. 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 METHODS	**33**	**74.3**	**70.0**	**50.0**	**35.0**	**120.0**
Derivatized - MS/MS non-kit	6	64.7	65.0	n/a	35.0	100.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	76.5	80.0	50.0	48.0	120.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	6	80.8	92.5	50.0	50.0	105.0

Citrulline

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**58.2**	**55.0**	**60.0**	**34.0**	**200.0**
Derivatized - MS/MS non-kit	9	57.2	55.0	55.0	34.0	75.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	21	58.0	60.0	60.0	40.0	75.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	49.0	50.0	50.0	45.0	56.0
Non-derivatized - MS/MS non-kit	4	84.8	52.0	n/a	35.0	200.0

Leucine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**43**	**287.9**	**275.0**	**250.0**	**145.0**	**400.0**
Derivatized - MS/MS non-kit	9	280.7	289.0	220.0	220.0	400.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	21	298.4	275.0	250.0	225.0	400.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	275.7	250.0	n/a	145.0	378.0
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	**42**	**73.6**	**75.0**	**100.0**	**40.0**	**100.0**
Derivatized - MS/MS non-kit	9	65.8	67.0	70.0	44.0	83.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	21	82.0	85.0	100.0	50.0	100.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	67.7	74.0	45.0	45.0	90.0
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**	**141.7**	**150.0**	**130.0**	**75.0**	**188.0**
Derivatized - MS/MS non-kit	11	137.5	150.0	150.0	75.0	182.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	21	148.1	160.0	165.0	120.0	180.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	138.1	150.0	n/a	100.0	160.0
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	4	127.5	130.0	130.0	100.0	150.0
Non-derivatized - MS/MS non-kit	6	124.2	125.5	150.0	74.0	150.0

Succinylacetone

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**37**	**2.3**	**1.9**	**1.0**	**0.8**	**5.4**
Derivatized - MS/MS non-kit	8	3.1	2.4	2.0	1.9	5.4
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	2.4	1.8	4.5	0.8	4.5
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	1.5	1.0	1.0	0.9	2.8

Tyrosine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**45**	**414.1**	**360.0**	**300.0**	**92.0**	**850.0**
Derivatized - MS/MS non-kit	10	317.2	327.5	300.0	92.0	500.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	19	536.9	450.0	850.0	300.0	850.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	359.6	350.0	350.0	243.0	500.0
Non-derivatized - MS/MS non-kit	4	297.5	290.0	290.0	250.0	360.0

Valine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**30**	**291.5**	**291.0**	**250.0**	**180.0**	**530.0**
Derivatized - MS/MS non-kit	7	275.0	240.0	240.0	180.0	420.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	11	332.0	325.0	300.0	250.0	530.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	6	250.3	241.0	180.0	180.0	360.0
Non-derivatized - MS/MS non-kit	3	238.7	250.0	n/a	210.0	256.0

Table 17. 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	**44**	**8.21**	**7.00**	**6.00**	**5.00**	**24.00**
Derivatized - MS/MS non-kit	11	10.82	9.20	10.00	5.60	24.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	6.64	6.00	6.00	5.00	10.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	6.74	6.65	6.00	6.00	7.50
Non-derivatized - MS/MS non-kit	4	9.38	7.50	n/a	6.50	16.00

C2(L)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**23**	**6.54**	**7.00**	**9.00**	**0.00**	**10.00**
Derivatized - MS/MS non-kit	6	6.72	7.16	n/a	2.00	10.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	8	6.90	7.00	7.00	4.00	9.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	3	7.17	9.00	9.00	3.50	9.00
Non-derivatized - MS/MS non-kit	4	4.83	5.85	n/a	0.00	7.60

C3

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**5.72**	**6.00**	**6.30**	**3.10**	**8.00**
Derivatized - MS/MS non-kit	11	5.10	4.81	n/a	3.30	7.70
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	5.97	6.05	6.30	4.80	8.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	6.14	6.25	n/a	4.00	7.55
Non-derivatized - MS/MS non-kit	4	5.63	6.25	n/a	3.10	6.92

C3DC

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**10**	**0.24**	**0.22**	**0.22**	**0.10**	**0.45**
Derivatized - MS/MS non-kit	8	0.24	0.22	0.22	0.10	0.45

C3DC + C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**24**	**0.55**	**0.41**	**0.38**	**0.25**	**3.03**
Non-derivatized - MS/MS NeoBase™ PerkinElmer	16	0.39	0.38	0.38	0.25	0.60
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	5	0.47	0.50	0.50	0.41	0.52
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	**39**	**1.26**	**1.27**	**1.70**	**0.49**	**1.90**
Derivatized - MS/MS non-kit	8	1.24	1.33	0.80	0.79	1.90
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	1.35	1.30	1.70	1.00	1.70
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	1.30	1.31	1.30	0.90	1.70
Non-derivatized - MS/MS non-kit	4	1.00	1.15	1.20	0.49	1.20

C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**9**	**0.63**	**0.70**	**0.70**	**0.20**	**0.80**
Derivatized - MS/MS non-kit	7	0.63	0.70	0.80	0.20	0.80

C5

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.70**	**0.62**	**0.60**	**0.34**	**1.20**
Derivatized - MS/MS non-kit	11	0.74	0.66	0.70	0.34	1.20
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	0.73	0.68	1.00	0.45	1.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	0.68	0.60	0.58	0.54	1.00
Non-derivatized - MS/MS non-kit	4	0.55	0.55	n/a	0.40	0.68

C5:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**0.19**	**0.13**	**0.10**	**0.02**	**0.50**
Derivatized - MS/MS non-kit	11	0.22	0.15	0.08	0.07	0.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	0.22	0.15	0.10	0.03	0.50
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	0.15	0.10	0.10	0.02	0.50
Non-derivatized - MS/MS PerkinElmer NeoBase Kit	4	0.09	0.07	n/a	0.04	0.19
Non-derivatized - MS/MS non-kit	4	0.23	0.19	0.10	0.03	0.50

C5DC

Method	N	Mean	Median	Mode	Min	Max
All Methods	**44**	**0.38**	**0.43**	**0.50**	**0.05**	**0.80**
Derivatized - MS/MS non-kit	11	0.18	0.15	0.13	0.10	0.30
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	0.50	0.50	0.50	0.30	0.80
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	0.38	0.45	0.24	0.24	0.51
Non-derivatized - MS/MS non-kit	4	0.35	0.38	n/a	0.05	0.60

C5OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**0.85**	**0.84**	**0.80**	**0.32**	**1.50**
Derivatized - MS/MS non-kit	11	0.82	0.80	0.80	0.32	1.36
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	0.80	0.80	0.85	0.60	1.05
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	1.06	0.92	1.50	0.70	1.50
Non-derivatized - MS/MS non-kit	4	0.93	0.99	n/a	0.52	1.20

C6

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**41**	**0.38**	**0.26**	**0.24**	**0.14**	**0.95**
Derivatized - MS/MS non-kit	10	0.35	0.31	n/a	0.14	0.63
Non-derivatized - MS/MS NeoBase™ PerkinElmer	18	0.45	0.25	0.95	0.16	0.95
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	0.36	0.26	0.24	0.16	0.95
Non-derivatized - MS/MS non-kit	4	0.21	0.20	0.15	0.15	0.30

C8

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.44**	**0.43**	**0.60**	**0.12**	**0.73**
Derivatized - MS/MS non-kit	11	0.42	0.49	0.50	0.12	0.73
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	0.48	0.44	0.60	0.32	0.70
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	0.46	0.46	0.60	0.29	0.60
Non-derivatized - MS/MS non-kit	4	0.33	0.30	0.30	0.23	0.50

C10

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**41**	**0.44**	**0.40**	**0.40**	**0.20**	**0.70**
Derivatized - MS/MS non-kit	10	0.40	0.43	0.50	0.24	0.55
Non-derivatized - MS/MS NeoBase™ PerkinElmer	18	0.49	0.47	0.65	0.30	0.70
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	0.46	0.45	0.55	0.25	0.65
Non-derivatized - MS/MS non-kit	4	0.29	0.28	n/a	0.20	0.40

C10:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**38**	**0.27**	**0.25**	**0.25**	**0.12**	**0.45**
Derivatized - MS/MS non-kit	9	0.28	0.25	0.25	0.17	0.37
Non-derivatized - MS/MS NeoBase™ PerkinElmer	16	0.30	0.25	0.45	0.15	0.45
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	0.23	0.16	0.13	0.12	0.45
Non-derivatized - MS/MS non-kit	4	0.23	0.19	n/a	0.15	0.40

C10:2

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**26**	**0.14**	**0.10**	**0.10**	**0.02**	**0.38**
Derivatized - MS/MS non-kit	7	0.21	0.20	0.10	0.10	0.38
Non-derivatized - MS/MS NeoBase™ PerkinElmer	9	0.10	0.10	0.10	0.04	0.15
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	6	0.12	0.10	0.10	0.02	0.21
Non-derivatized - MS/MS non-kit	3	0.07	0.06	n/a	0.04	0.12

C14

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**40**	**0.72**	**0.70**	**0.70**	**0.27**	**1.20**
Derivatized - MS/MS non-kit	10	0.66	0.70	0.70	0.32	0.96
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	0.82	0.70	0.70	0.46	1.20
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	0.72	0.60	0.60	0.57	1.20
Non-derivatized - MS/MS non-kit	4	0.54	0.55	n/a	0.27	0.80

C14:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.60**	**0.60**	**0.60**	**0.17**	**0.80**
Derivatized - MS/MS non-kit	11	0.54	0.60	0.60	0.24	0.75
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	0.68	0.68	0.80	0.50	0.80
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	0.61	0.60	0.60	0.50	0.80
Non-derivatized - MS/MS non-kit	4	0.45	0.51	n/a	0.17	0.60

C16

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**7.80**	**7.85**	**10.00**	**2.14**	**10.36**
Derivatized - MS/MS non-kit	10	7.41	7.40	n/a	5.19	10.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	18	8.29	8.00	10.00	5.00	10.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	8.33	8.91	6.00	6.00	10.36
Non-derivatized - MS/MS non-kit	4	6.04	6.65	n/a	2.14	8.70

C16OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**45**	**0.12**	**0.10**	**0.10**	**0.06**	**0.25**
Derivatized - MS/MS non-kit	11	0.13	0.11	0.10	0.10	0.25
Non-derivatized - MS/MS NeoBase™ PerkinElmer	20	0.10	0.10	0.10	0.07	0.16
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	8	0.11	0.10	0.10	0.06	0.16
Non-derivatized - MS/MS non-kit	4	0.17	0.16	n/a	0.11	0.25

C18

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**35**	**2.33**	**2.20**	**3.50**	**0.70**	**3.50**
Derivatized - MS/MS non-kit	6	1.79	1.75	n/a	1.31	2.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	2.58	2.46	3.50	1.55	3.50
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	6	2.66	2.43	2.30	2.20	3.50
Non-derivatized - MS/MS non-kit	4	1.79	2.00	2.00	0.70	2.47

C18:1

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**39**	**3.59**	**3.00**	**3.00**	**2.00**	**7.00**
Derivatized - MS/MS non-kit	9	2.80	3.00	3.00	2.00	3.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	17	4.34	3.50	7.00	2.00	7.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	7	3.41	2.70	2.70	2.50	7.00
Non-derivatized - MS/MS non-kit	4	3.03	3.07	n/a	2.00	4.00

C18OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**34**	**0.09**	**0.10**	**0.10**	**0.03**	**0.18**
Derivatized - MS/MS non-kit	6	0.09	0.09	0.10	0.03	0.18
Non-derivatized - MS/MS NeoBase™ PerkinElmer	16	0.09	0.10	0.10	0.03	0.16
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	6	0.08	0.09	0.04	0.04	0.13
Non-derivatized - MS/MS non-kit	4	0.09	0.11	n/a	0.04	0.12

2020 Bias Plots

Proficiency Testing Bias Plots

Figures 2–37 are illustrated for PT analytes reported using the NSQAP Participant Portal. Bias plots for each analyte were selected to compare PT results by different methods The CDC expected value (EV) 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 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 these analytes separately. The 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 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. Ideally, 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.

Figure 2. Reproducibility of Results: Bias Plot of 17 α-Hydroxyprogesterone (17OHP) Values by Method Quarter 1 , Specimen 20201001004 Expected Value (EV) = 86.0 mg/mL serum

Quarter 1

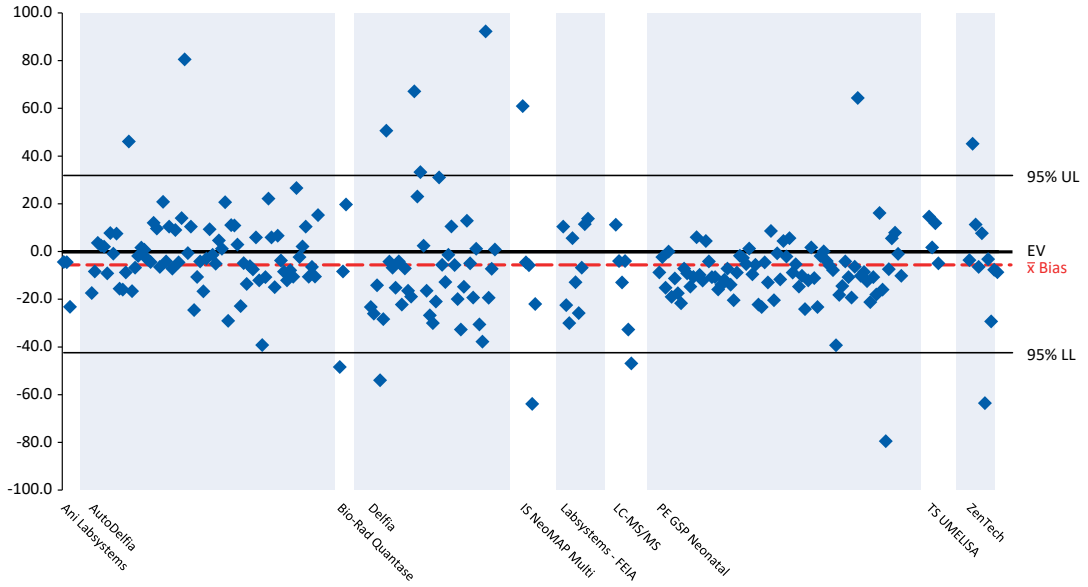
Specimen: 20201001004

Enriched: 85.0

CDC Assayed: 78.2

Participant Mean: 79.6

Participant Bias: -6.4



The 17OHP bias plot shows units of measure on the y-axis ranging from 100 mg/mL serum to -100 ng/mL serum. The bias for this plot is -6.4 ng/mL serum. The data shows an even scatter among most participants with some results outside the 95% upper and lower bias confidence intervals.

Figure 3. Reproducibility of Results: Bias Plot of Thyroxine (T4) Values by Method Quarter 1, Specimen 20201001003 Expected Value (EV) = 13.1 µg/dL serum

Quarter 1

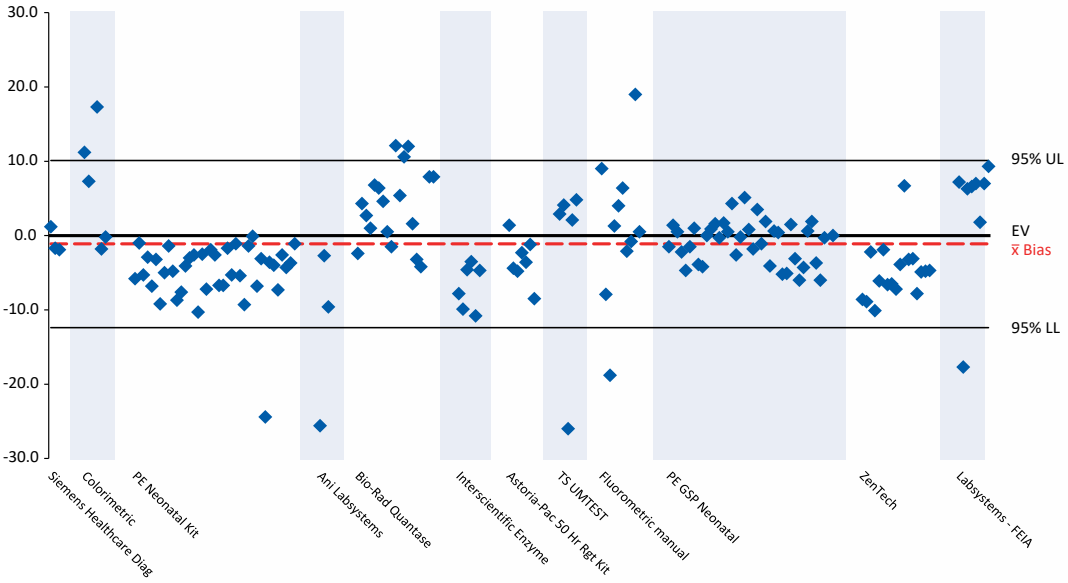
Specimen: 20201001003

Enriched: 10.0

CDC Assayed: 14.2

Participant Mean: 12.9

Participant Bias : -0.2



The T4 bias plot shows units of measure on the y-axis ranging from 30 µg/dL serum to -30 µg/dL serum. The bias for this plot is -0.2. The data shows a good agreement among participants with only a few points above the 95% upper limit.

Quarter 1

Specimen: 20201001003

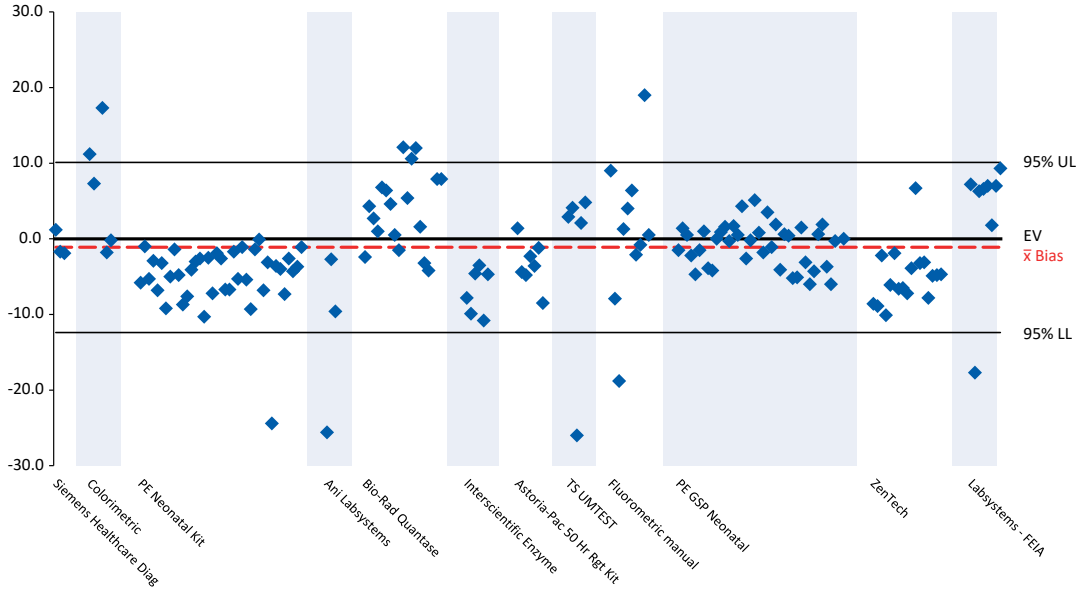
Enriched: 25.0

CDC Assayed: 21.7

Participant Mean: 24.9

Participant Bias: -1.1

Figure 4. Reproducibility of Results: Bias Plot of Total Galactose (TGal) Values by Method Quarter 1, Specimen 20201001002 Expected Value (EV) = 26.0 mg/dL blood



The TGal bias plot shows units of measure on the y-axis ranging from 30 µg/dL serum to -30 mg/dL blood. The bias for this plot is -1.1. The data on this plot shows variable bias across methods .

Quarter 1

Specimen: 20201001005

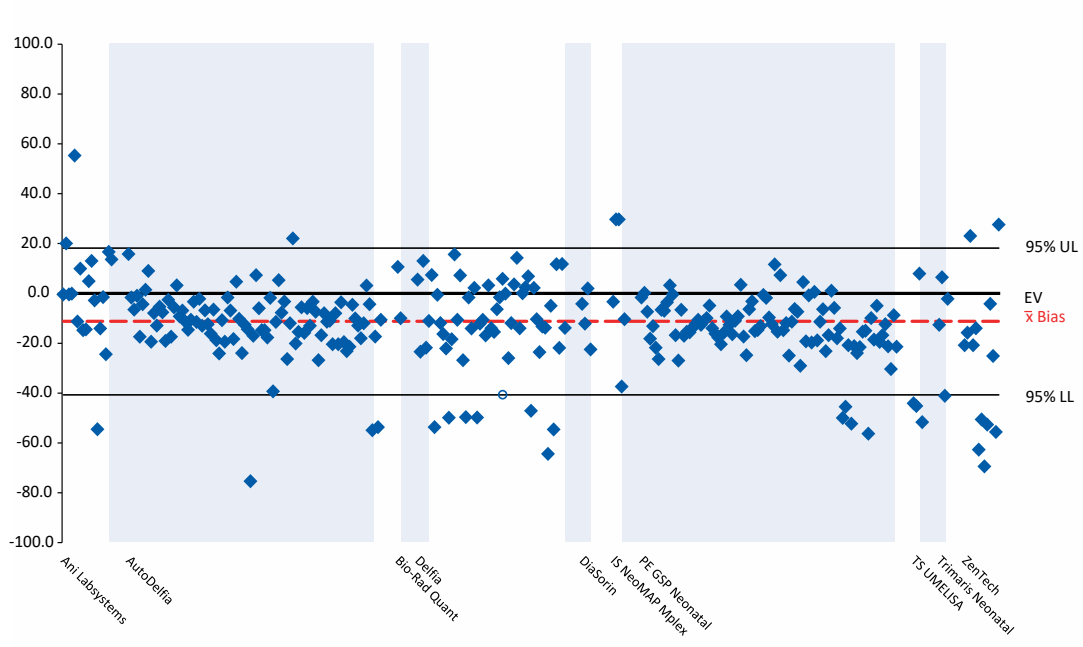
Enriched: 85.0

CDC Assayed: 79.4

Participant Mean: 74.2

Participant Bias: -11.2

Figure 5. Reproducibility of Results: Bias Plot of Thyroid-Stimulating Hormone (TSH) Values by Method Quarter 1 , Specimen 20201001005 Expected Value (EV) = 85.4 µIU/mL serum



The TSH bias plot shows units of measure on the y-axis ranging from 100 µg/dL serum to -100 mg/dL blood. The bias for this plot is -11.2. The data on this plot show an even bias scatter across methods .

Figure 6. Reproducibility of Results: Bias Plot of Immunoreactive Trypsinogen (IRT) Values by Method Quarter 1, Specimen 20201008002 Assayed Value (AV) = 168.2 ng/mL blood

Quarter 1

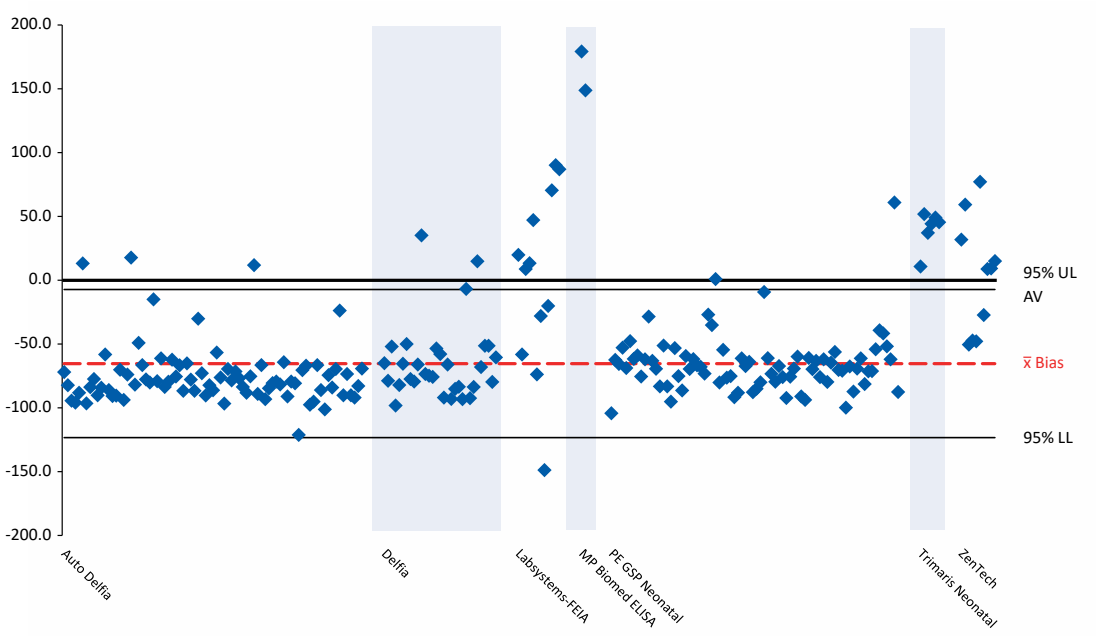
Specimen: 20201008002

Enriched: 250.0

CDC Assayed: 168.2

Participant Mean: 102.9

Participant Bias: -65.3



The IRT bias plot shows units of measure on the y-axis ranging from 200 µg/dL serum to -200 mg/dL blood. The bias for this plot is -65.3. This negative bias was attributed to methods with a higher participation rate.

Figure 7. Reproducibility of Results: Bias Plot of Arginine (Arg) Values by Method Quarter 1, Specimen 20201005005 Expected Value (EV) = 11.4 µmol/L blood

Quarter 1

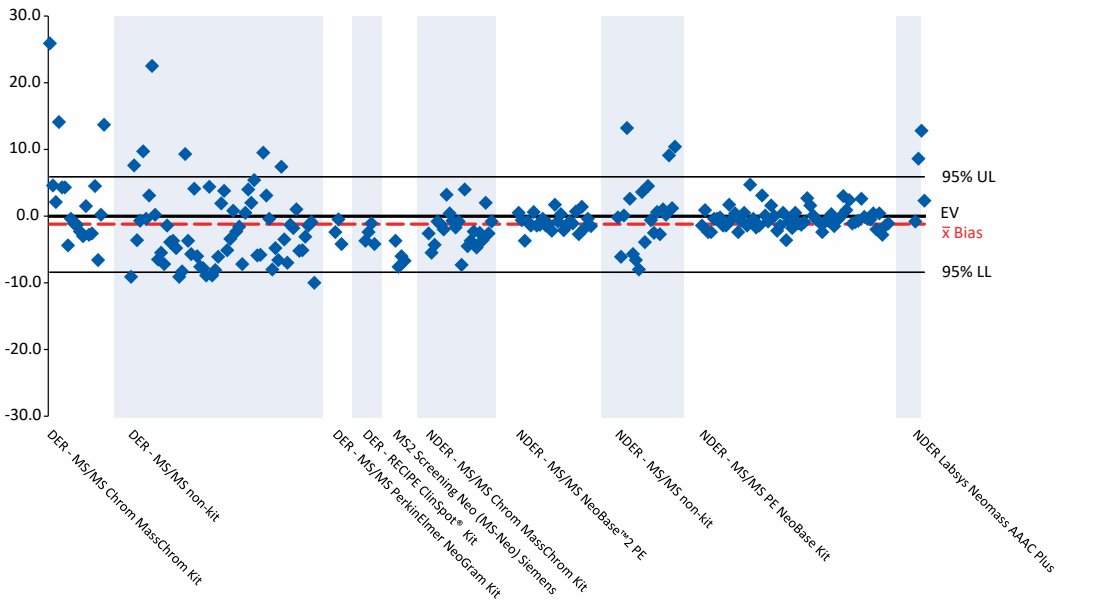
Specimen: 20201005005

Enriched: 0.0

CDC Assayed: 11.9

Participant Mean: 10.2

Participant Bias: -1.2



The Arg bias plot shows units of measure on the y-axis ranging from 30 µmol/L blood to -30 µmol/L blood. The bias for this plot is -1.2. This plot shows a tight scatter around the expected value across methods.

Figure 8. Reproducibility of Results: Bias Plot of Citrulline (Cit) Values by Method Quarter 4, Specimen 20204005005 Expected Value (EV) = 179.6 µmol/L blood

Quarter 4

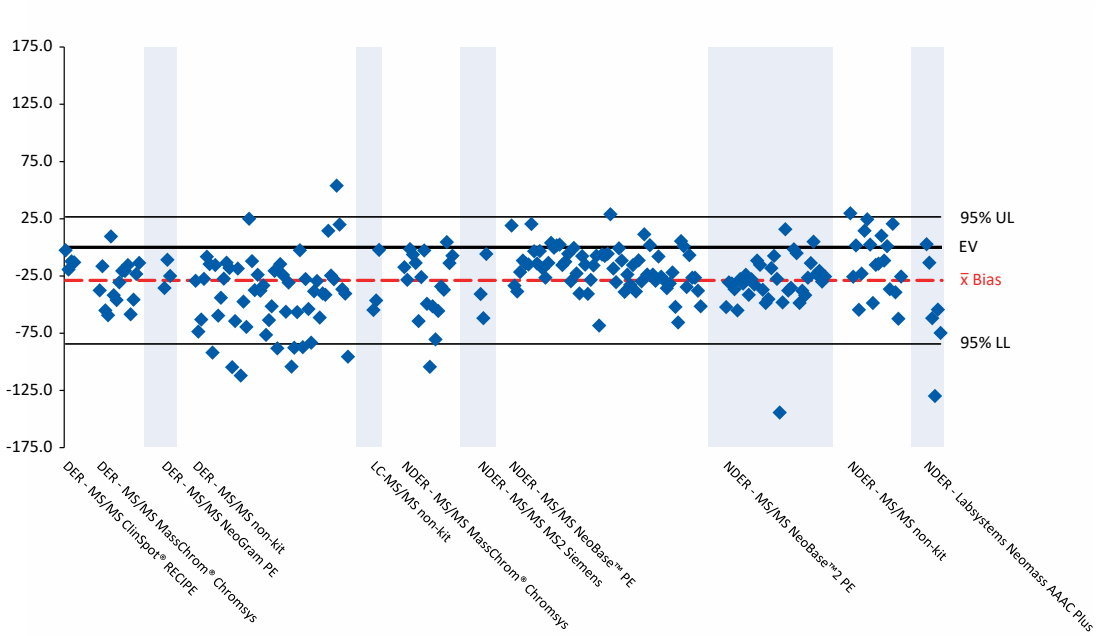
Specimen: 20201005005

Enriched: 150.0

CDC Assayed: 166.2

Participant Mean: 150.7

Participant Bias: -28.9



The Cit bias plot shows units of measure on the y-axis ranging from 175 µmol/L blood to -175 µmol/L blood. The bias for this plot is -28.9. This plot shows a moderately negative bias across methods.

Figure 9. Reproducibility of Results: Bias Plot of Leucine (Leu) Values by Method Quarter 1, Specimen 20201005003 Expected Value (EV) = 620.2 µmol/L blood

Quarter 1

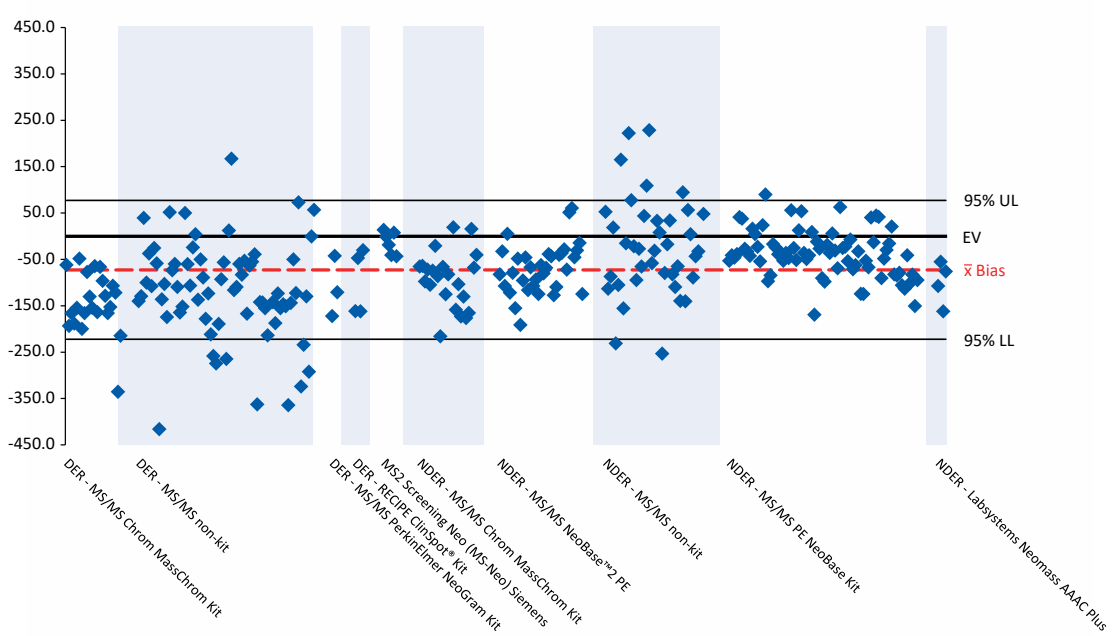
Specimen: 20201005003

Enriched: 470.0

CDC Assayed: 563.9

Participant Mean: 547.6

Participant Bias: -72.6



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 -72.6. This plot shows a moderately negative bias across methods.

Figure 10. Reproducibility of Results: Bias Plot of Methionine (Met) Values by Method Quarter 1, Specimen 20201005004 Expected Value (EV) = 169.6 µmol/L blood

Quarter 1

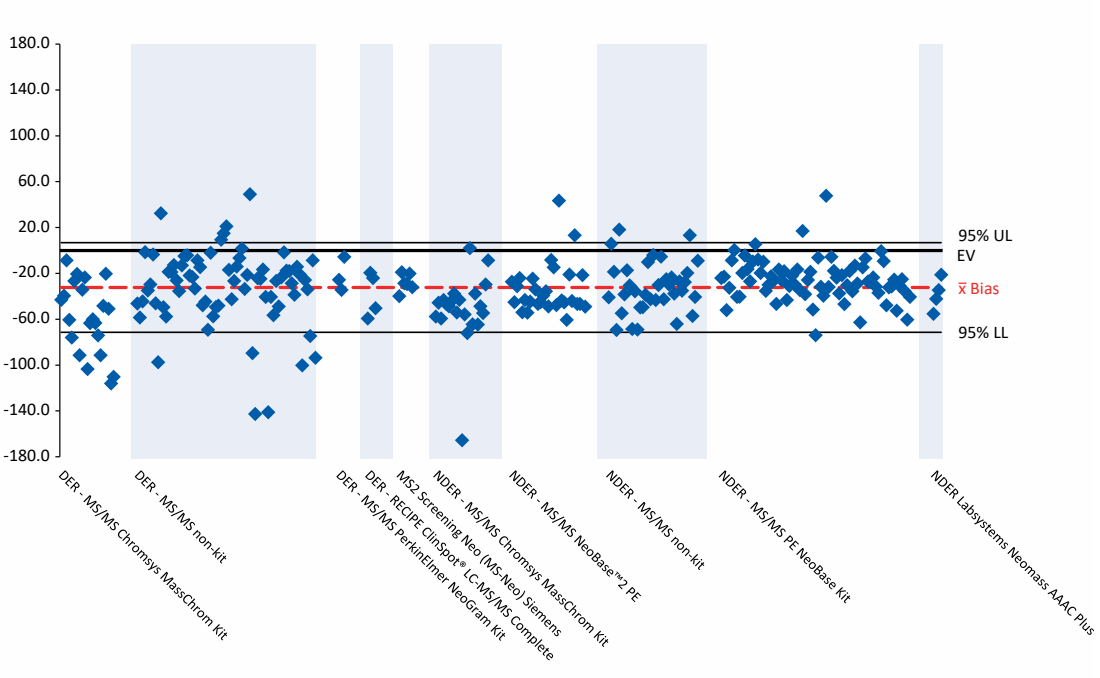
Specimen: 20201005004

Enriched: 150.0

CDC Assayed: 139.7

Participant Mean: 137.3

Participant Bias: -32.3



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 -32.3. This plot shows a moderately negative bias across methods.s

Figure 11. Reproducibility of Results: Bias Plot of Phenylalanine (Phe) Values by Method Quarter 1, Specimen 20201005001 Expected Value (EV) = 308.0 µmol/L blood

Quarter 1

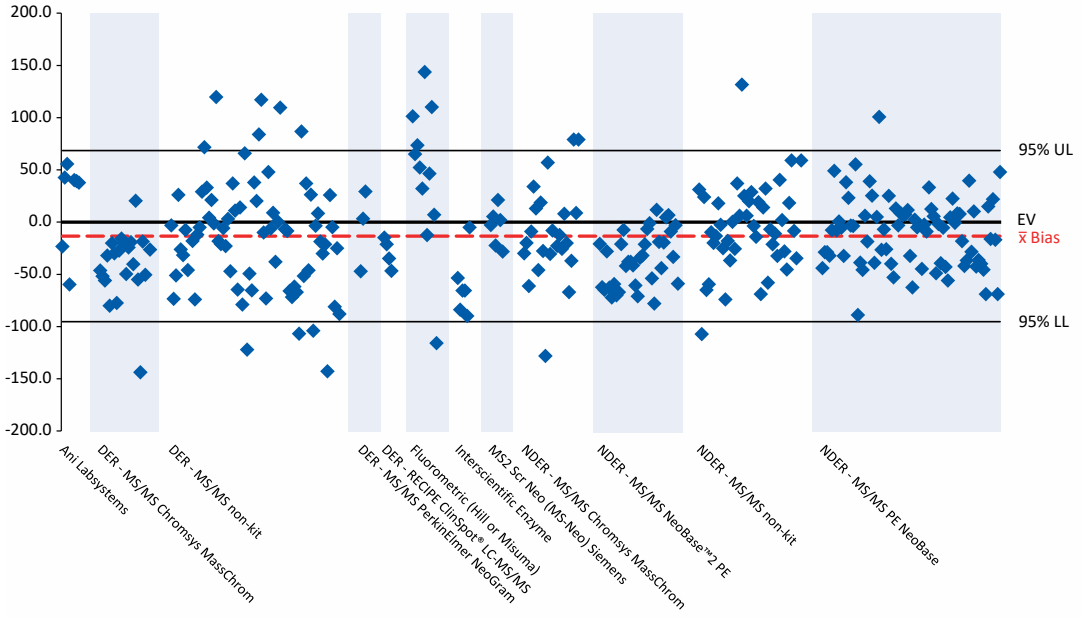
Specimen: 20201005001

Enriched: 250.0

CDC Assayed: 298.0

Participant Mean: 294.5

Participant Bias: 13.5



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 -13.5. This plot shows an even scatter across acorss the expected value for most methods.

Figure 12. Reproducibility of Results: Bias Plot of Succinylacetone (SUAC) Values by Method Quarter 1, Specimen 20201005005 Expected Value (EV) = 35.3 µmol/L blood

Quarter 1

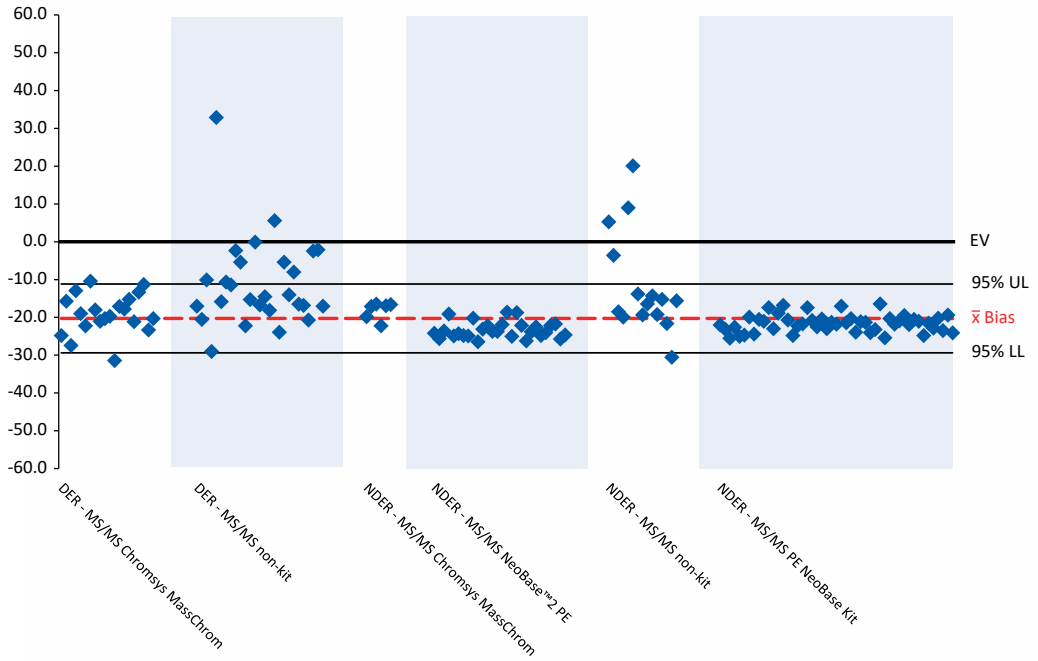
Specimen: 20201005005

Enriched: 35.0

CDC Assayed: 21.0

Participant Mean: 15.0

Participant Bias: -20.3



The SUAC bias plot shows units of measure on the y-axis ranging from 60.0 µmol/L blood to -60.0 µmol/L blood. The bias for this plot is -20.3. This plot shows a strongly negative bias across methods, which is historical for this analyte.

Figure 13. Reproducibility of Results: Bias Plot of Tyrosine (Tyr) Values by Method Quarter 1, Specimen 20201005005 Expected Value (EV) = 784.0 µmol/L blood

Quarter 1

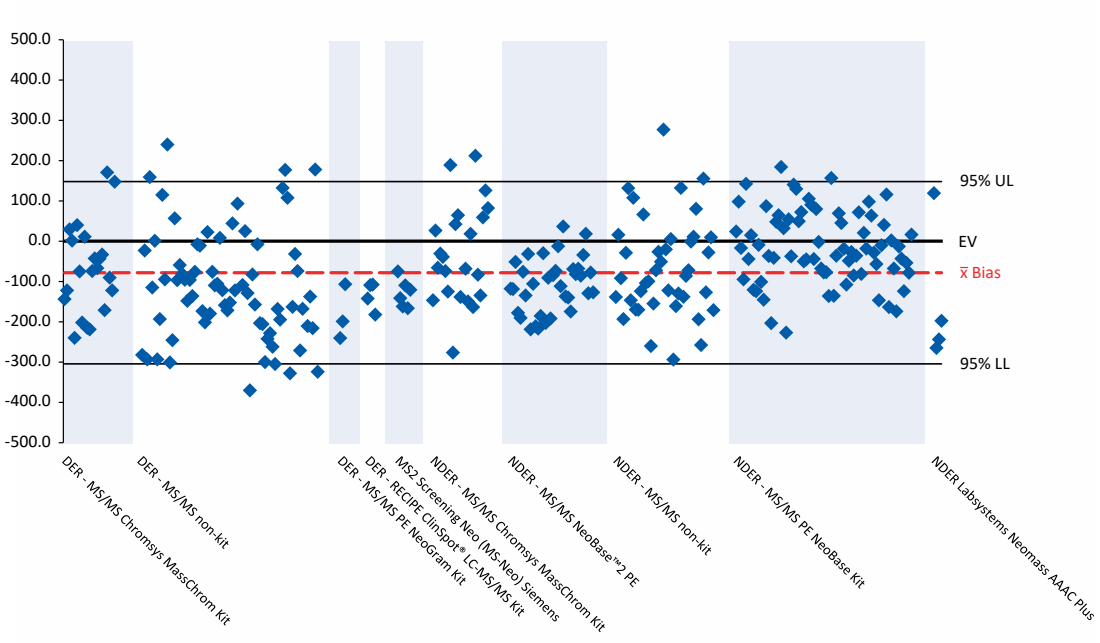
Specimen: 20201005005

Enriched: 700.0

CDC Assayed: 723.9

Participant Mean: 705.6

Participant Bias: -78.4



The Tyr bias plot shows units of measure on the y-axis ranging from 500.0 µmol/L blood to -500.0 µmol/L blood. The bias for this plot is -78.4. This plot shows a slightly negative bias across methods.

Figure 14. Reproducibility of Results: Bias Plot of Valine (Val) Values by Method Quarter 1, Specimen 20201005003 Expected Value (EV) = 599.4 µmol/L blood

Quarter 1

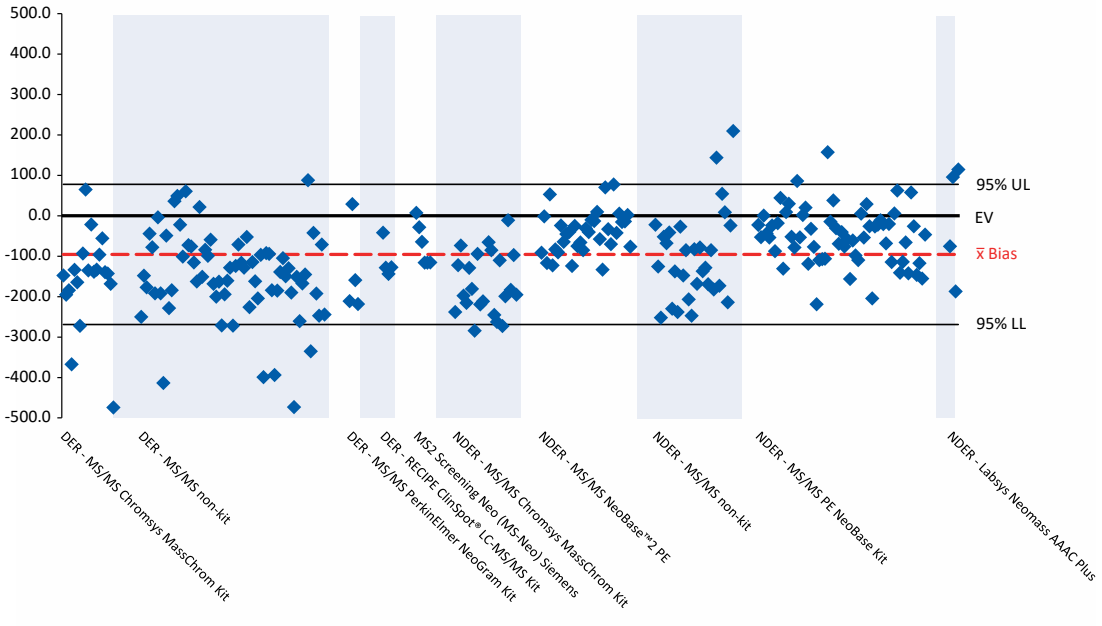
Specimen: 20201005003

Enriched: 450.0

CDC Assayed: 493.7

Participant Mean: 503.8

Participant Bias: -95.6



The Val bias plot shows units of measure on the y-axis ranging from 500.0 µmol/L blood to -500.0 µmol/L blood. The bias for this plot is -95.6. This plot shows a moderately negative bias across methods.

Figure 15. Reproducibility of Results: Bias Plot of Low Free Carnitine (C0(L)) Values by Method Quarter 1, Specimen 20201006001 Expected Value (EV) = 7.13 µmol/L blood

Quarter 1

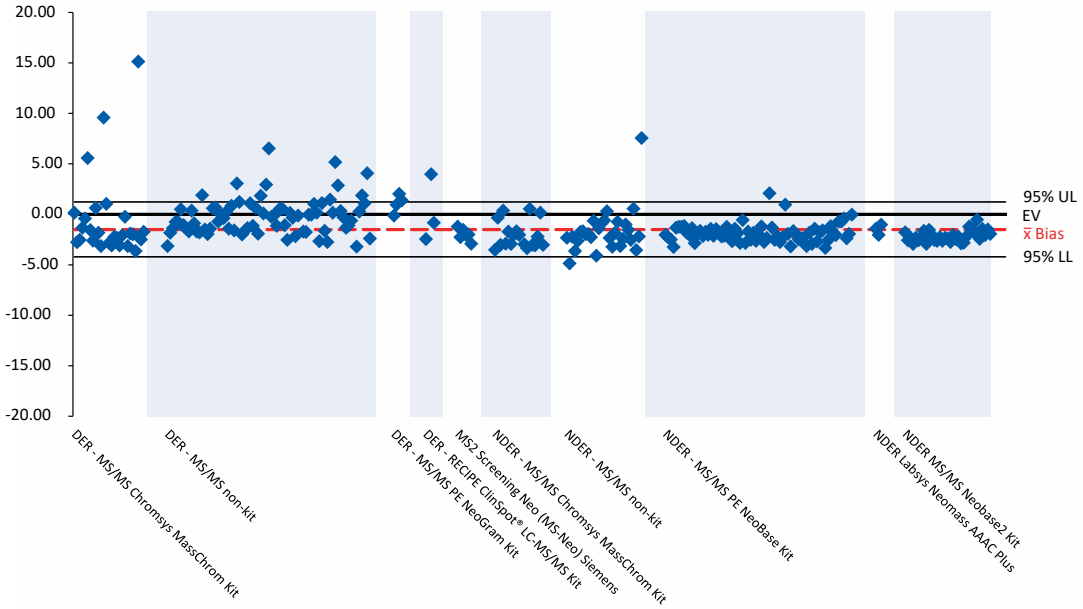
Specimen: 20201006001

Enriched: 0.00

CDC Assayed: 7.30

Participant Mean: 5.63

Participant Bias: -1.50



The C0(L) 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 -1.50. This plot shows a slightly negative bias across methods.

Figure 16. Reproducibility of Results: Bias Plot of Low Acetylcarnitine (C2(L)) Values by Method Quarter 1, Specimen 20201006001 Expected Value (EV) = 6.84 µmol/L blood

Quarter 1

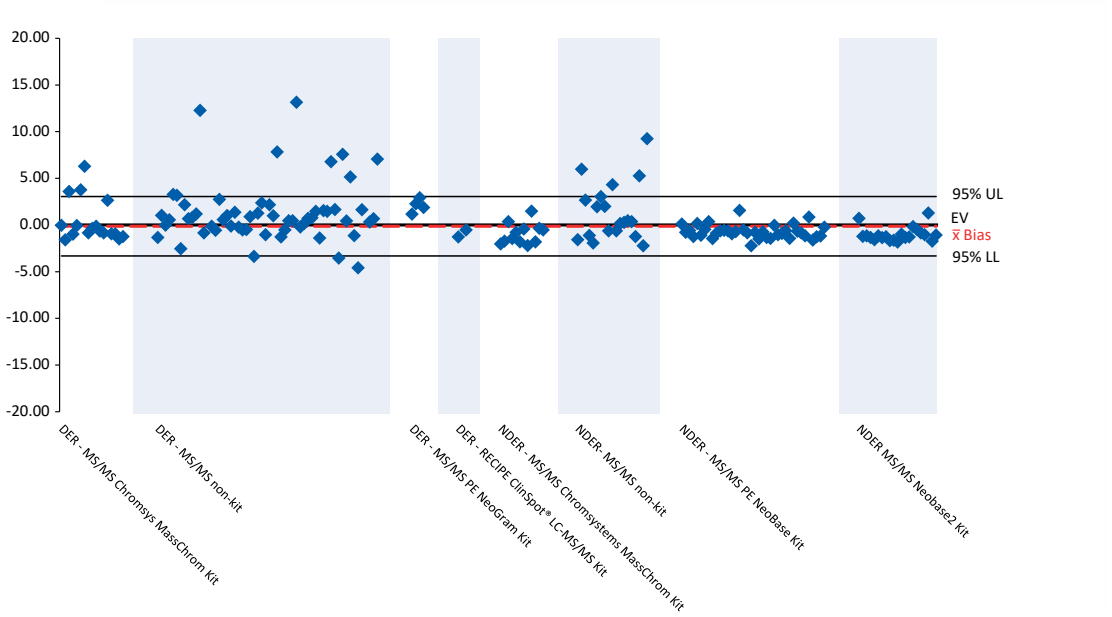
Specimen: 20201006001

Enriched: 0.00

CDC Assayed: 6.83

Participant Mean: 6.70

Participant Bias: -0.14



The C2(L) 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 -0.14. This plot shows a tight scatter across methods.

Figure 17. Reproducibility of Results: Bias Plot of Propionylcarnitine (C3) Values by Method Quarter 1, Specimen 20201006003 Expected Value (EV) = 10.89 µmol/L blood

Quarter 1

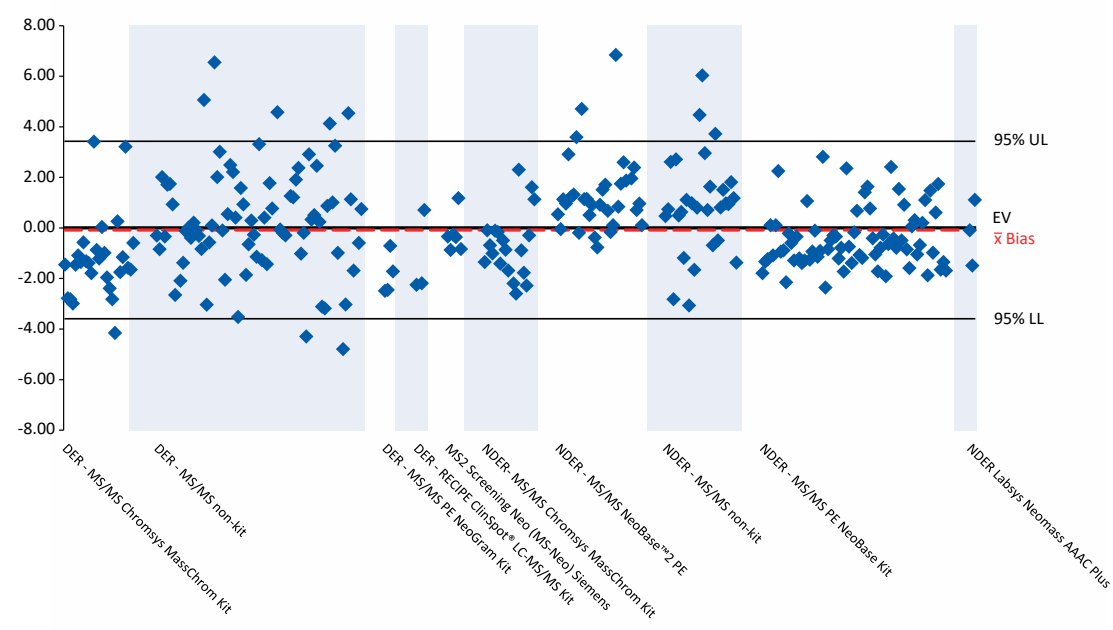
Specimen: 20201006003

Enriched: 10.00

CDC Assayed: 11.00

Participant Mean: 10.81

Participant Bias: -0.08



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 -0.08. This plot shows an even scatter across methods.

Figure 18. Reproducibility of Results: Bias Plot of Malonylcarnitine (C3DC) Values by Method Quarter 1, Specimen 20201006004 Expected Value (EV) = 11.02 µmol/L blood

Quarter 1

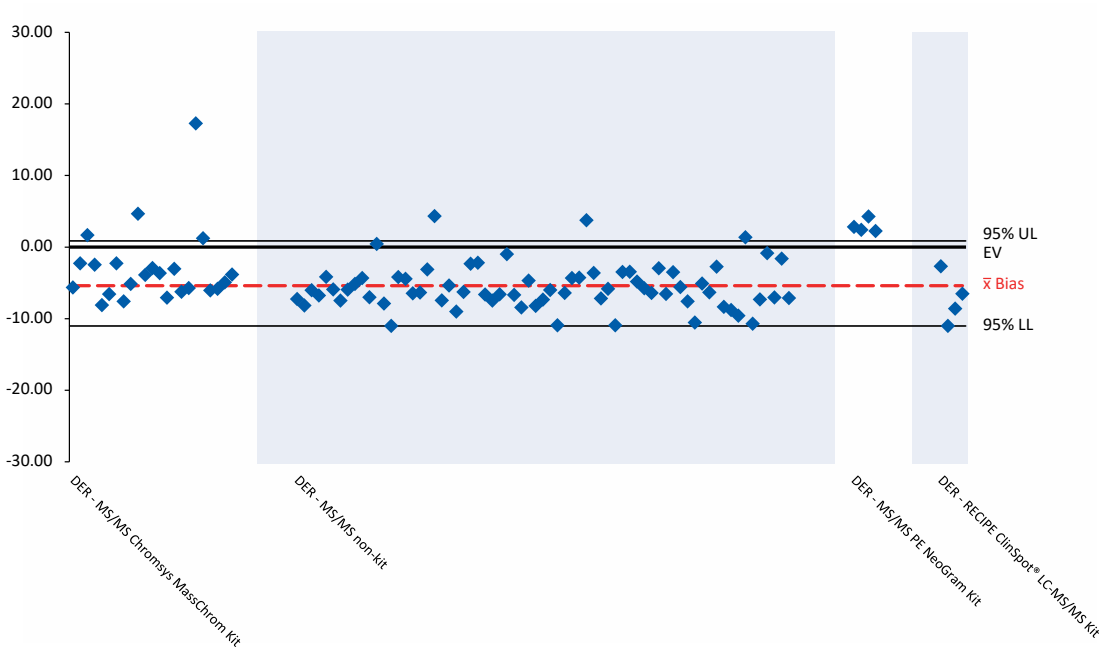
Specimen: 20201006004

Enriched: 11.00

CDC Assayed: 8.60

Participant Mean: 5.62

Participant Bias: -5.4



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.

Figure 19. Reproducibility of Results: Bias Plot of C3DC+C4OH Non-derivatized Values by Method Quarter 1, Specimen 20201006004 Expected Value (EV) = 11.03 µmol/L blood

Quarter 1

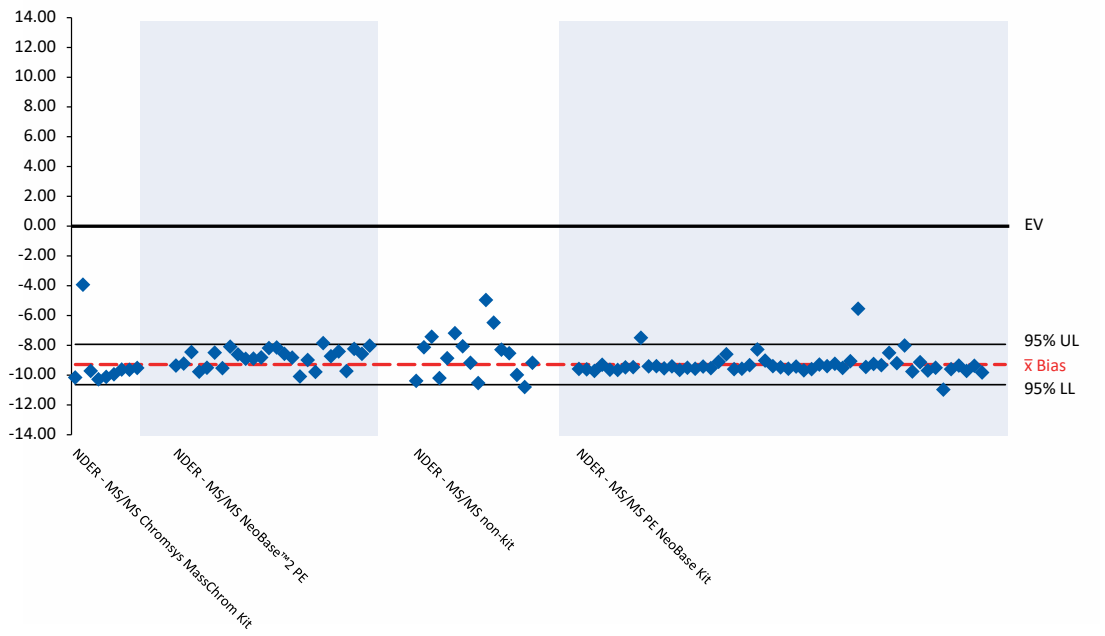
Specimen: 20201006004

Enriched: 11.00

CDC Assayed: 0.78

Participant Mean: 1.74

Participant Bias: -9.29



The C3DC+C4OH bias plot shows units of measure on the y-axis ranging from 14.00 µmol/L blood to -14.00 µmol/L blood. The bias for this plot is -9.29. 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 4, Specimen 20204006005 Expected Value (EV) = 2.63 µmol/L blood

Quarter 1

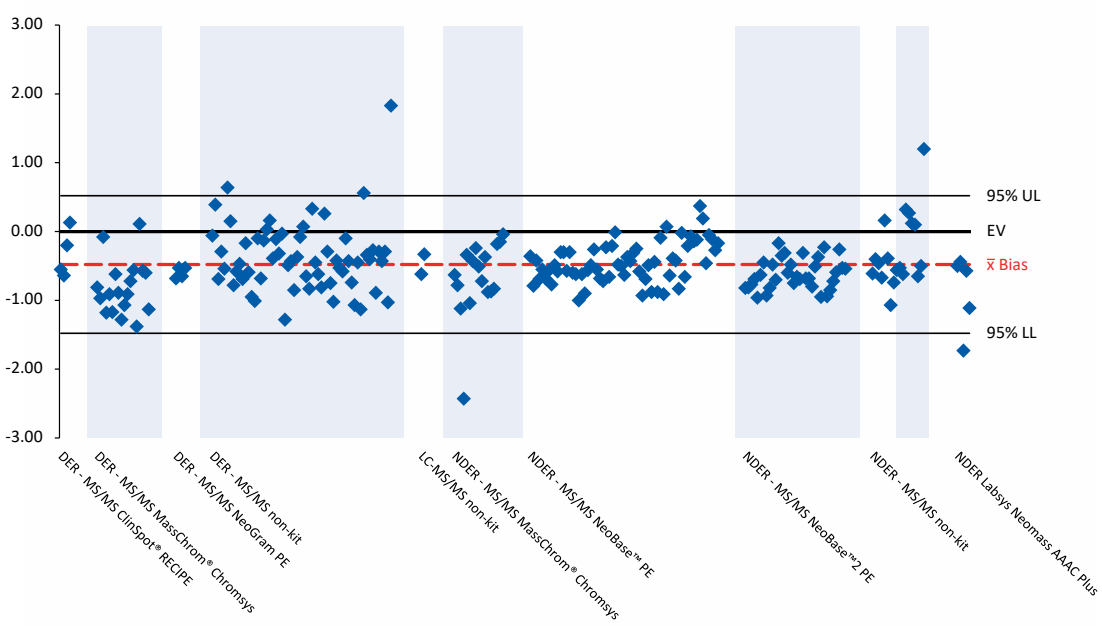
Specimen: 20204006005

Enriched: 2.50

CDC Assayed: 2.18

Participant Mean: 2.15

Participant Bias: -0.48



The C4 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 -0.48. This plot shows a moderately negative bias across methods.

Figure 21. Reproducibility of Results: Bias Plot of Hydroxybutyrylcarnitine (C4OH) Values by Method Quarter 4, Specimen 20204006005 Expected Value (EV) = 4.06 µmol/L blood

Quarter 4

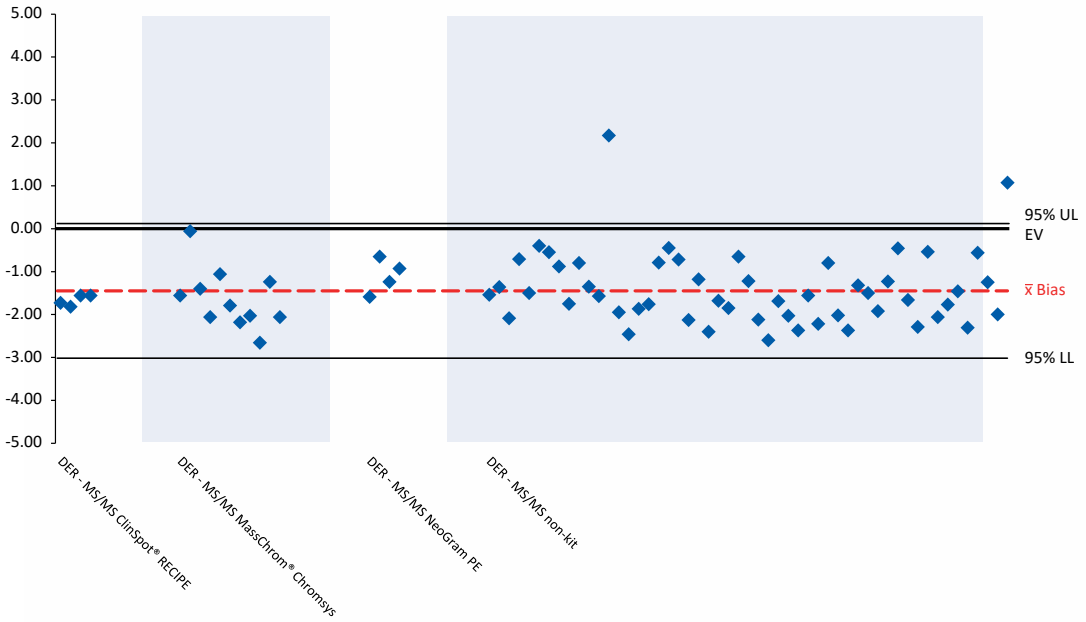
Specimen: 20204006005

Enriched: 4.00

CDC Assayed: 2.86

Participant Mean: 2.61

Participant Bias: -1.45



The C4OH 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 -1.45. This plot shows a moderately negative bias across methods.

Quarter 1

Specimen: 20204006005

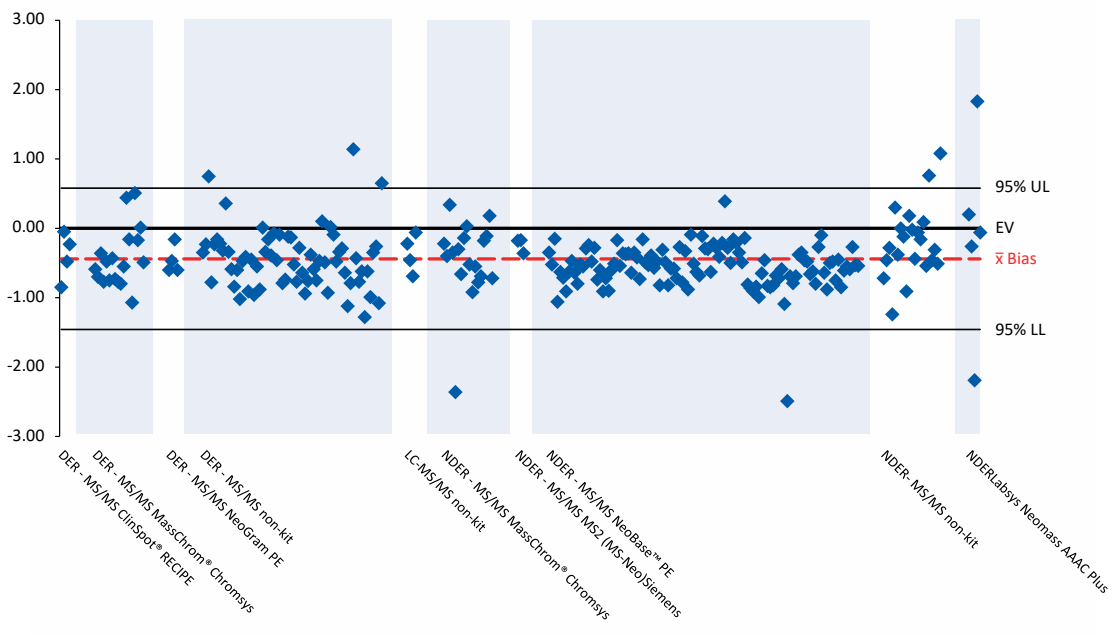
Enriched: 2.50

CDC Assayed: 2.34

Participant Mean: 2.15

Participant Bias: -0.44

Figure 22. Reproducibility of Results: Bias Plot of Isovalerylcarnitine (C5) Values by Method Quarter 4, Specimen 20204006005 Expected Value (EV) = 2.59 µmol/L blood



The C5 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 -0.44.. This plot shows a moderately negative bias across methods.

Quarter 4

Specimen: 20204006004

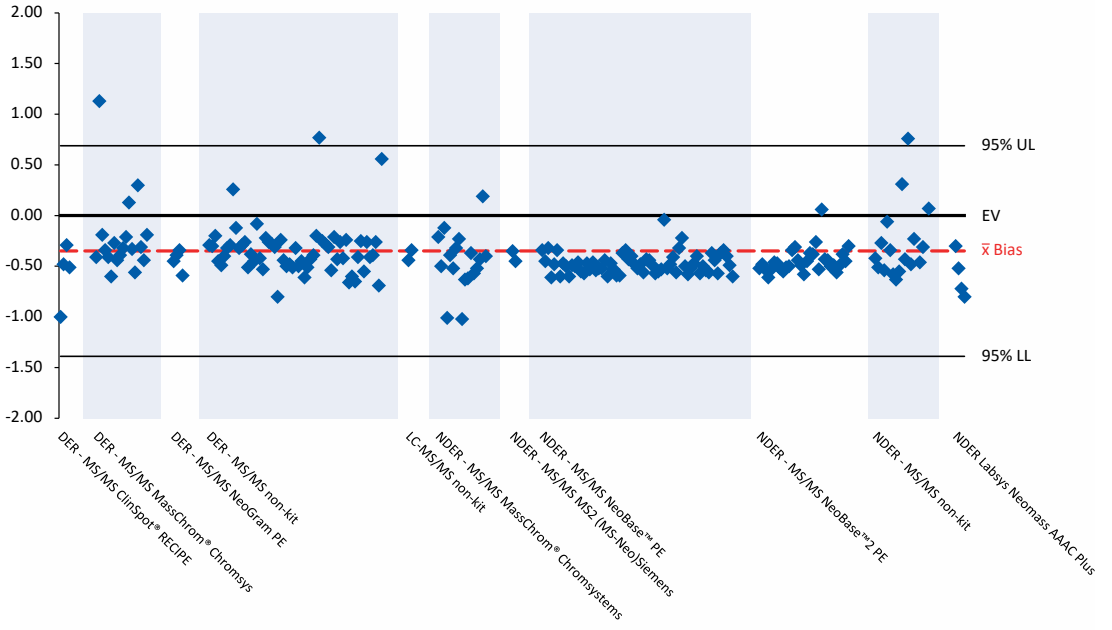
Enriched: 1.00

CDC Assayed: 0.74

Participant Mean: 0.67

Participant Bias: -0.35

Figure 23. Reproducibility of Results: Bias Plot of Tiglylcarnitine (C5:1) Values by Method Quarter 4, Specimen 20204006004 Expected Value (EV) = 1.02 µmol/L blood



The C5:1 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 -0.35. This plot shows a moderately negative bias across methods.

Figure 24. Reproducibility of Results: Bias Plot of Glutarylcarnitine (C5DC) Values by Method Quarter 4, Specimen 20204006003 Expected Value (EV) = 2.05 µmol/L blood

Quarter 4

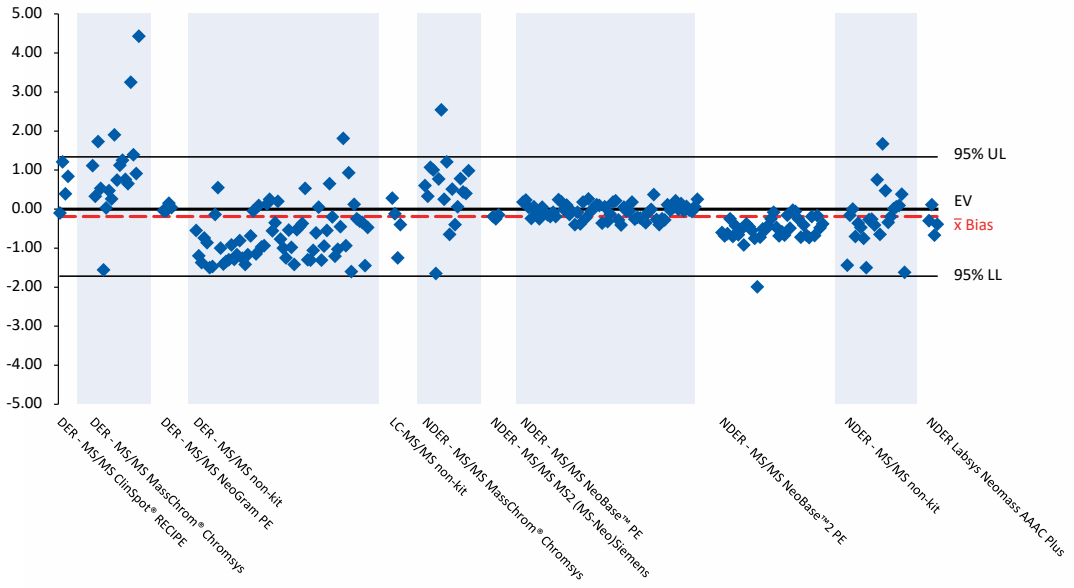
Specimen: 20204006003

Enriched: 2.00

CDC Assayed: 2.05

Participant Mean: 1.86

Participant Bias: -0.19



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 -0.19. This plot shows even scatter for most methods, two methods show a positive bias and one shows a negative bias

Figure 25. Reproducibility of Results: Bias Plot of Hydroxyisovalerylcarnitine (C5OH) Values by Method Quarter 1, Specimen 20201006005 Expected Value (EV) = 2.56 µmol/L blood

Quarter 1

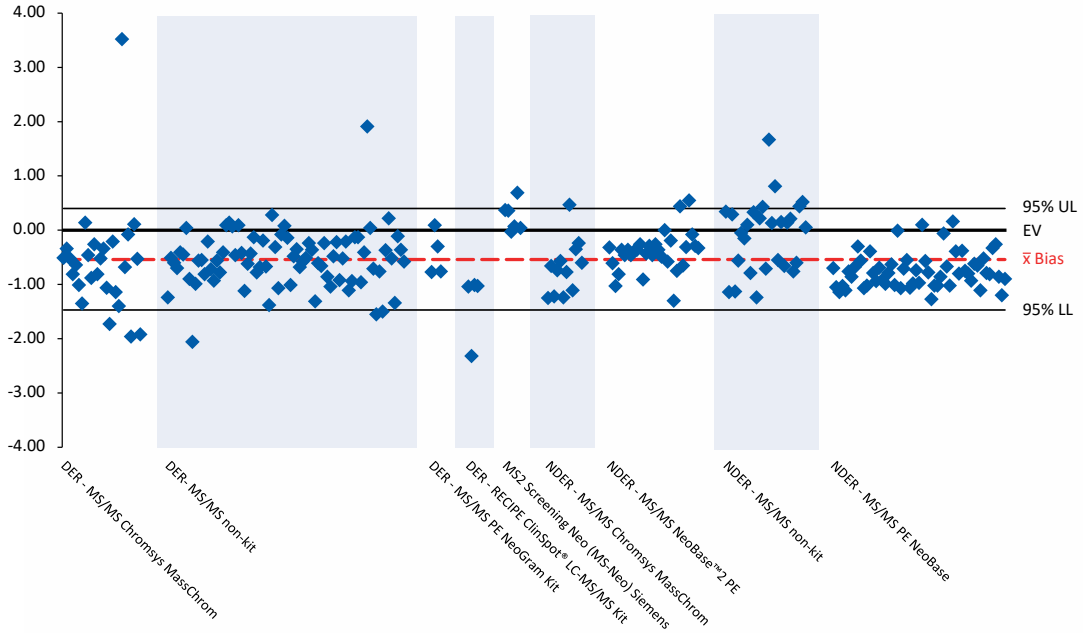
Specimen: 20201006005

Enriched: 2.00

CDC Assayed: 2.35

Participant Mean: 2.02

Participant Bias: -0.54



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 -0.54. 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 20201006002 Expected Value (EV) = 1.37 µmol/L blood

Quarter 1

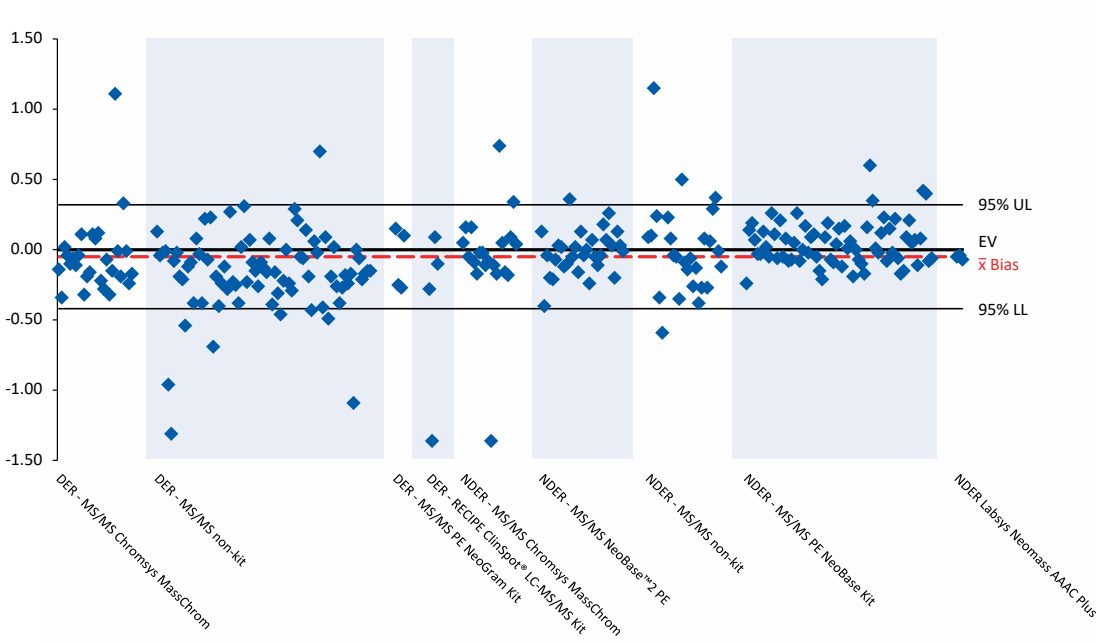
Specimen: 20201006002

Enriched: 1.30

CDC Assayed: 1.37

Participant Mean: 1.32

Participant Bias: -0.05



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 -0.05. This plot shows an even scatter across all methods

Figure 27. Reproducibility of Results: Bias Plot of Octanoylcarnitine (C8) Values by Method Quarter 1, Specimen 20201006002 Expected Value (EV) = 2.01 µmol/L blood

Quarter 1

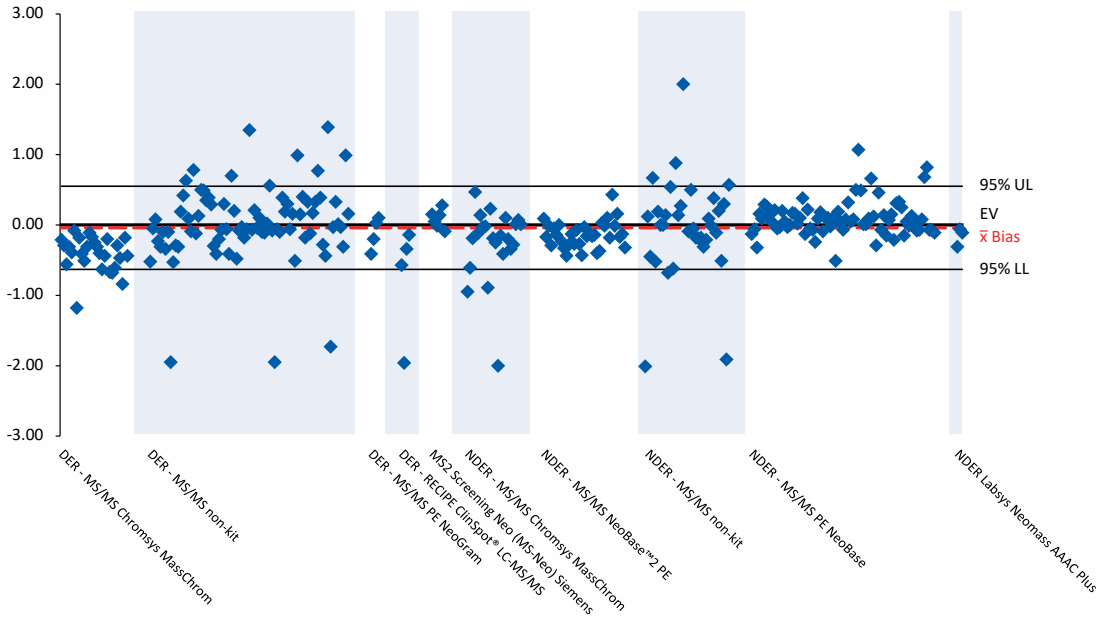
Specimen: 20201006002

Enriched: 1.80

CDC Assayed: 2.15

Participant Mean: 1.97

Participant Bias: -0.04



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 -0.04. This plot shows a even scatter across all methods.

Figure 28. Reproducibility of Results: Bias Plot of Decanoylcarnitine (C10) Values by Method Quarter 1, Specimen 20201006002 Expected Value (EV) = 1.36 µmol/L blood

Quarter 1

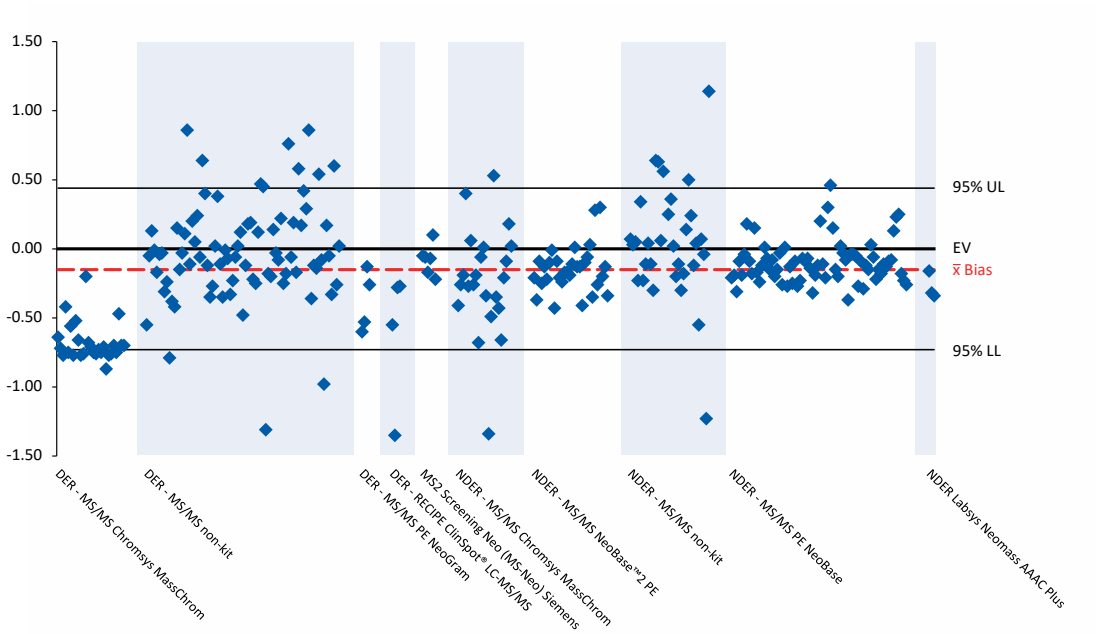
Specimen: 20201006002

Enriched: 1.10

CDC Assayed: 1.41

Participant Mean: 1.21

Participant Bias: -.0.15



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 -0.15. This plot shows the derivitized MassChrom kit as having a slightly more negative bias than other reported methods

Figure 29. Reproducibility of Results: Bias Plot of Decenoylcarnitine (C10:1) Values by Method Quarter 1, Specimen 20201006002 Expected Value (EV) = 1.08 µmol/L blood

Quarter 1

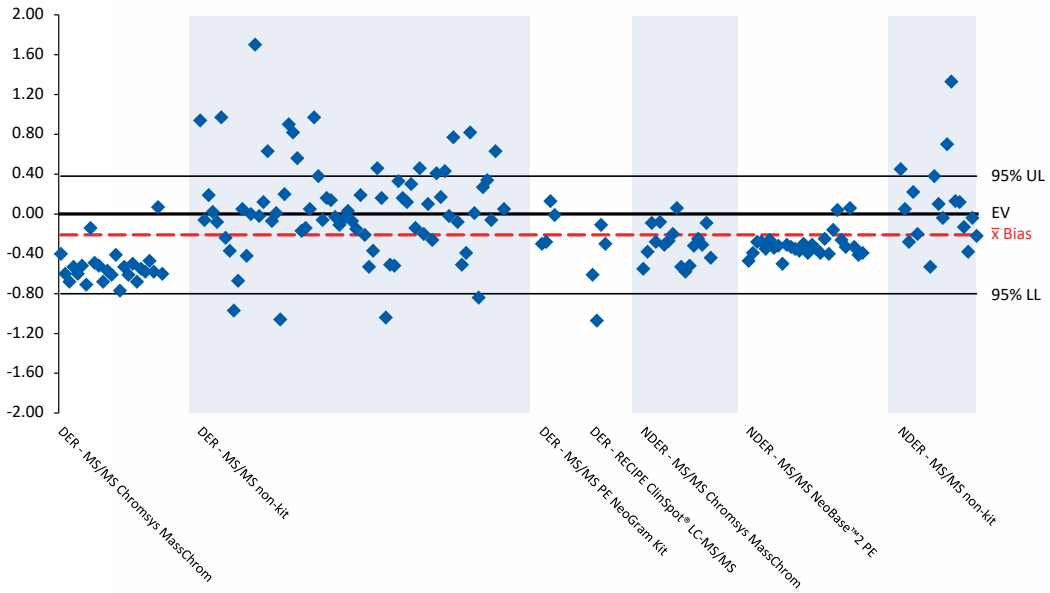
Specimen: 20201006002

Enriched: 0.90

CDC Assayed: 1.14

Participant Mean: 0.87

Participant Bias: -0.21



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 -0.21. 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 4, Specimen 20204006005 Expected Value (EV) = 0.51 µmol/L blood

Quarter 4

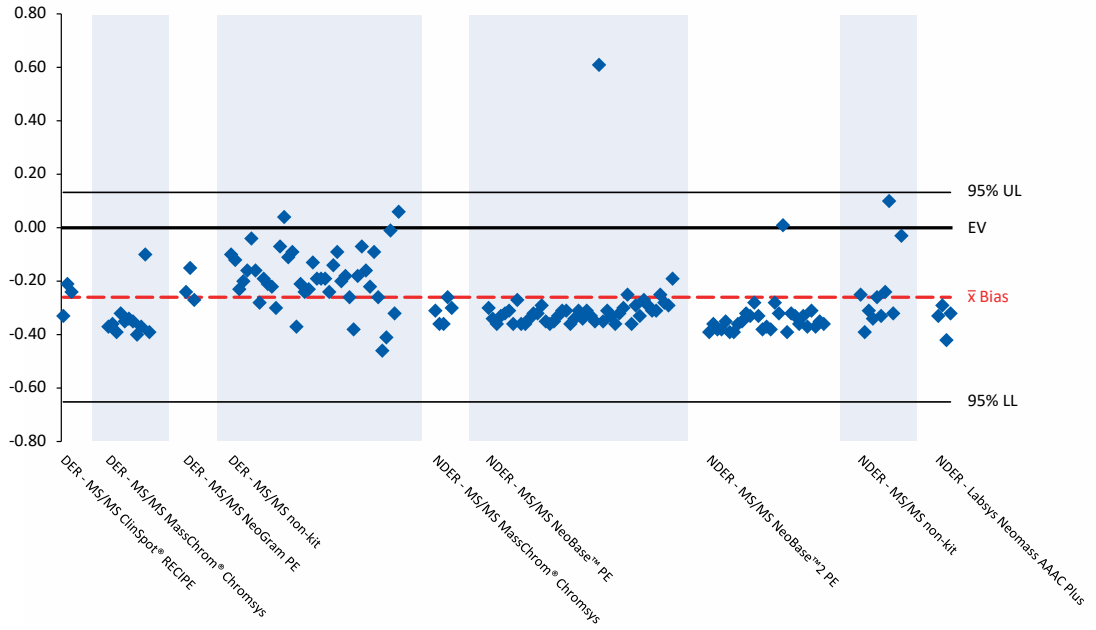
Specimen: 20204006005

Enriched: 0.50

CDC Assayed: 0.34

Participant Mean: 0.25

Participant Bias: -0.26



The C10:2 bias plot shows units of measure on the y-axis ranging from 0.80 µmol/L blood to -0.80 µmol/L blood. The bias for this plot is -0.26. This plot shows a moderately negative bias across methods.

Figure 31. Reproducibility of Results: Bias Plot of Myristoylcarnitine (C14) Values by Method Quarter 4, Specimen 20204006001 Expected Value (EV) = 1.71 µmol/L blood

Quarter 4

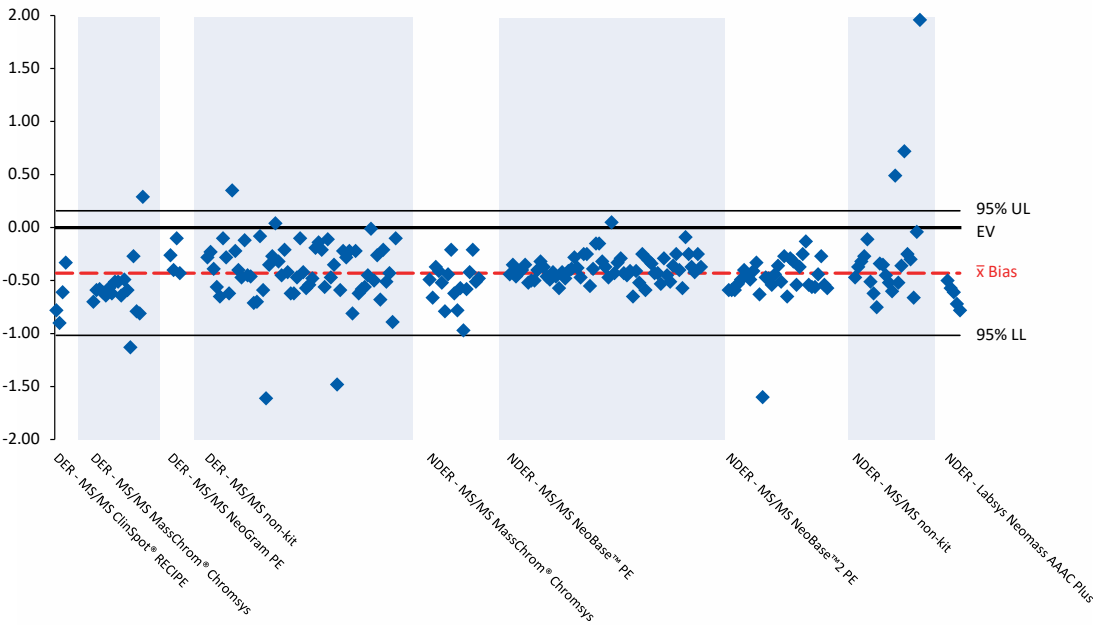
Specimen: 20204006001

Enriched: 1.60

CDC Assayed: 1.71

Participant Mean: 1.28

Participant Bias: -0.43



The C14 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 -0.43. This plot shows a moderately negative bias across methods

Figure 32. Reproducibility of Results: Bias Plot of Tetradecenoylcarnitine (C14:1) Values by Method Quarter 4, Specimen 20204006001 Expected Value (EV) = 1.88 µmol/L blood

Quarter 4

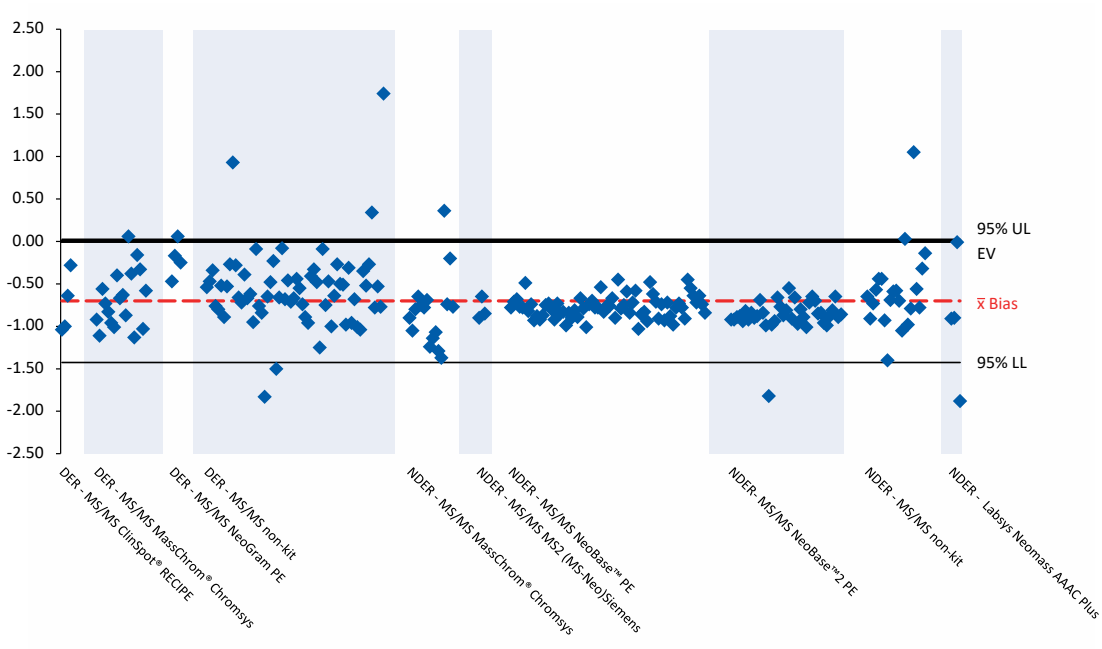
Specimen: 20204006001

Enriched: 1.80

CDC Assayed: 1.42

Participant Mean: 1.18

Participant Bias: -0.70



The C14:1 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 -0.70. This plot shows a moderately negative bias across methods

Figure 33. Reproducibility of Results: Bias Plot of Palmitoylcarnitine (C16) Values by Method Quarter 4, Specimen 20204006002 Expected Value (EV) = 20.58 µmol/L blood

Quarter 4

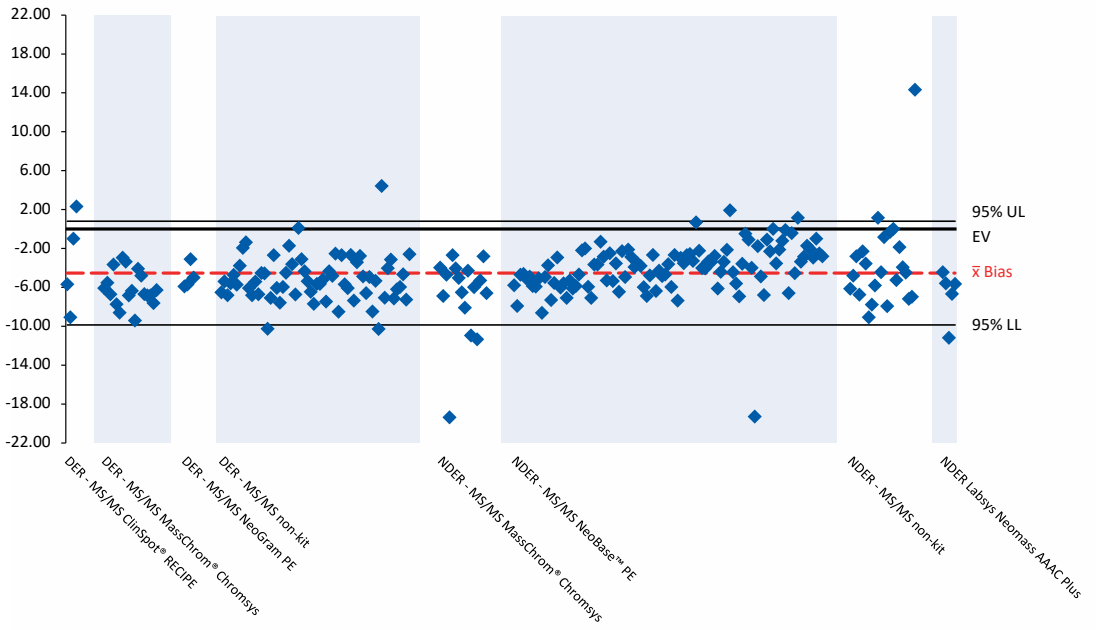
Specimen: 20204006002

Enriched: 20.00

CDC Assayed: 17.47

Participant Mean: 16.05

Participant Bias: -4.53



The C16 bias plot shows units of measure on the y-axis ranging from 22.00 µmol/L blood to -22.00 µmol/L blood. The bias for this plot is -4.53. This plot shows a moderately negative bias across methods.

Figure 34. Reproducibility of Results: Bias Plot of Hydroxypalmitoylcarnitine (C16OH) Values by Method Quarter 4, Specimen 20204006002 Expected Value (EV) = 0.02 µmol/L blood

Quarter 4

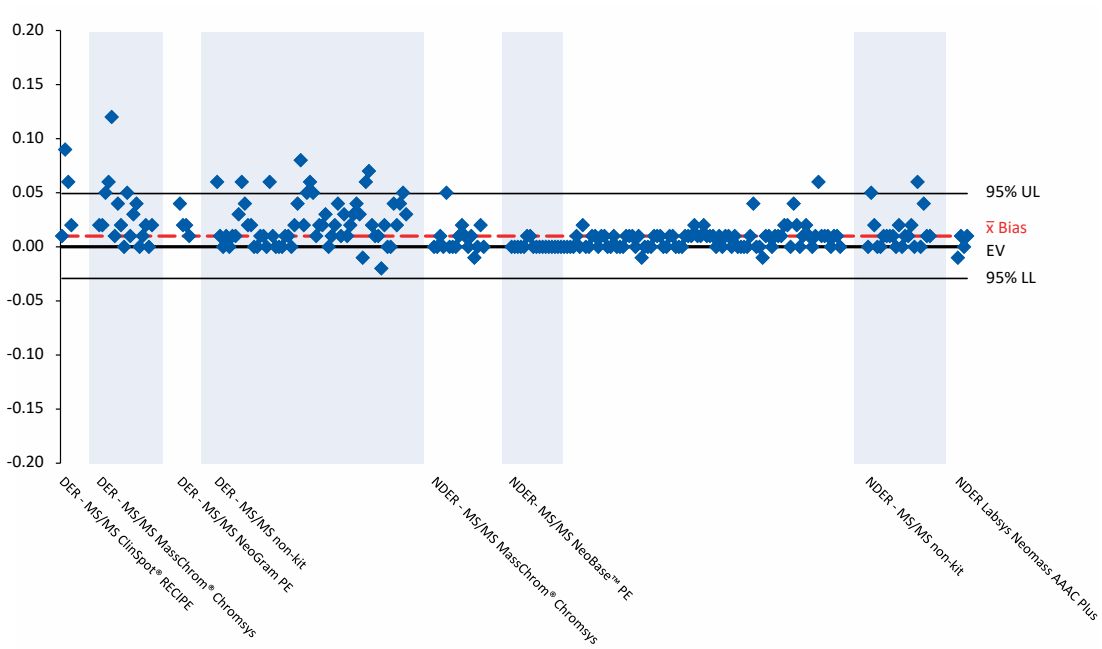
Specimen: 20204006002

Enriched: 0.0

CDC Assayed: 0.06

Participant Mean: 0.03

Participant Bias: 0.01



The C16OH 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 0.01. This plot shows a tight scatter among all methods around the bias.

Figure 35. Reproducibility of Results: Bias Plot of Stearoylcarnitine (C18) Values by Method Quarter 4, Specimen 20204006002 Expected Value (EV) = 5.47 µmol/L blood

Quarter 4

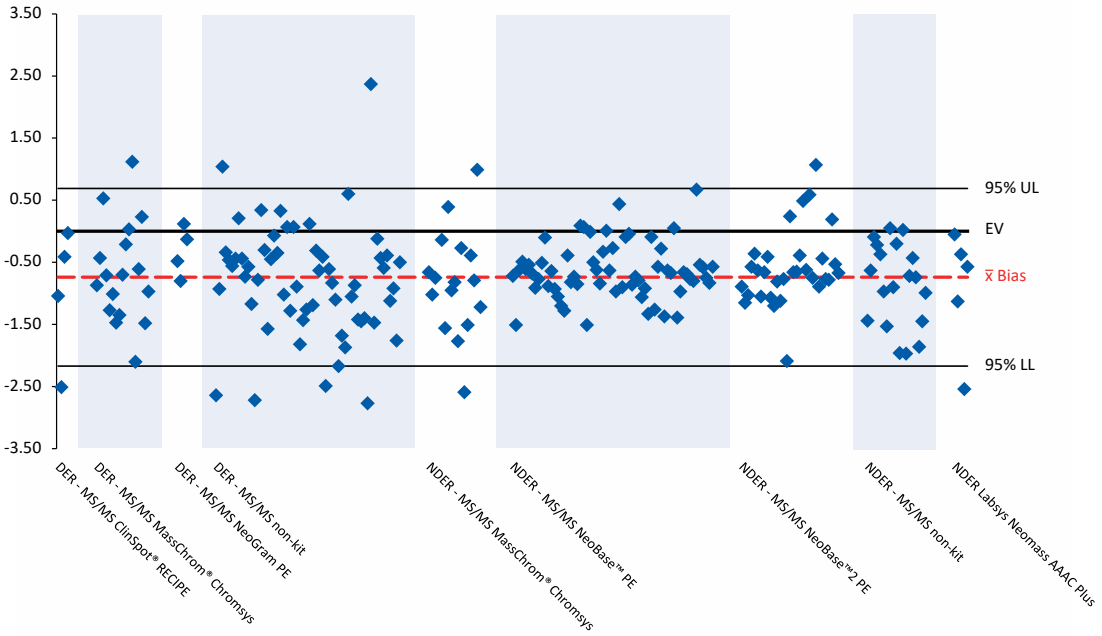
Specimen: 20204006002

Enriched: 5.00

CDC Assayed: 5.21

Participant Mean: 4.73

Participant Bias: -0.74



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 -0.74. This plot shows a moderately negative bias across methods.

Figure 36. Reproducibility of Results: Bias Plot of Oleoylcarnitine (C18:1) Values by Method Quarter 4, Specimen 20204006002 Expected Value (EV) = 11.52 µmol/L blood

Quarter 4

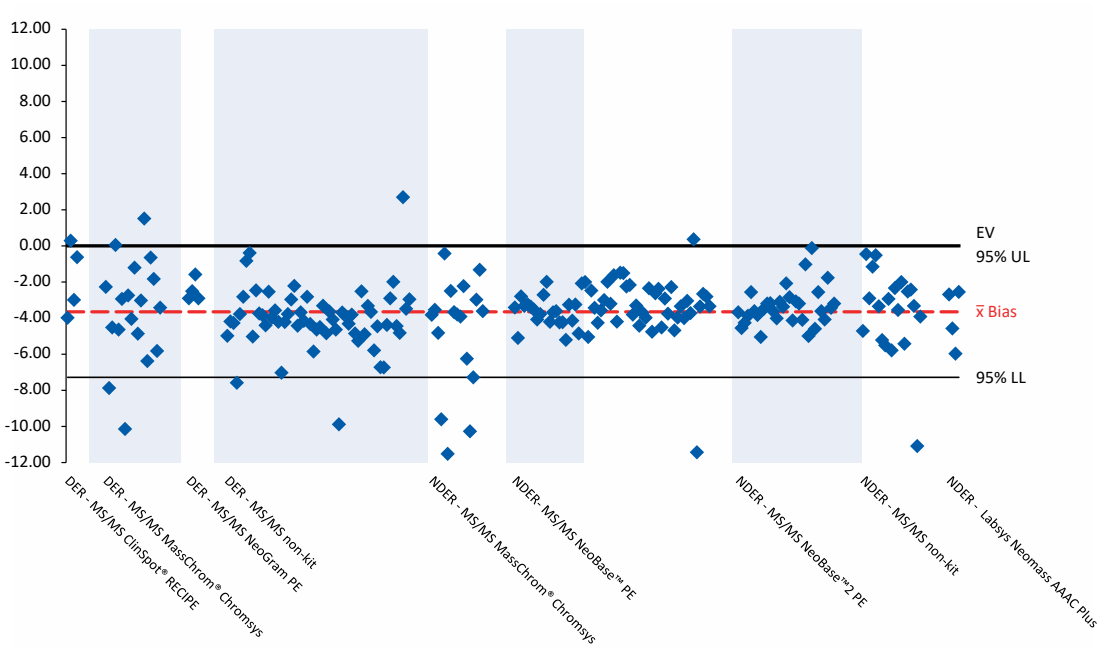
Specimen: 20204006002

Enriched: 10.00

CDC Assayed: 9.32

Participant Mean: 7.87

Participant Bias: -3.65



The C18:1 bias plot shows units of measure on the y-axis ranging from 12.00 µmol/L blood to -12.00 µmol/L blood. The bias for this plot is -3.65. This plot shows a moderately negative bias across methods.

Figure 37. Reproducibility of Results: Bias Plot of Hydroxystearoylcarnitine (C18OH) Values by Method Quarter 1, Specimen 20201006002 Expected Value (EV) = 0.01 µmol/L blood

Quarter 1

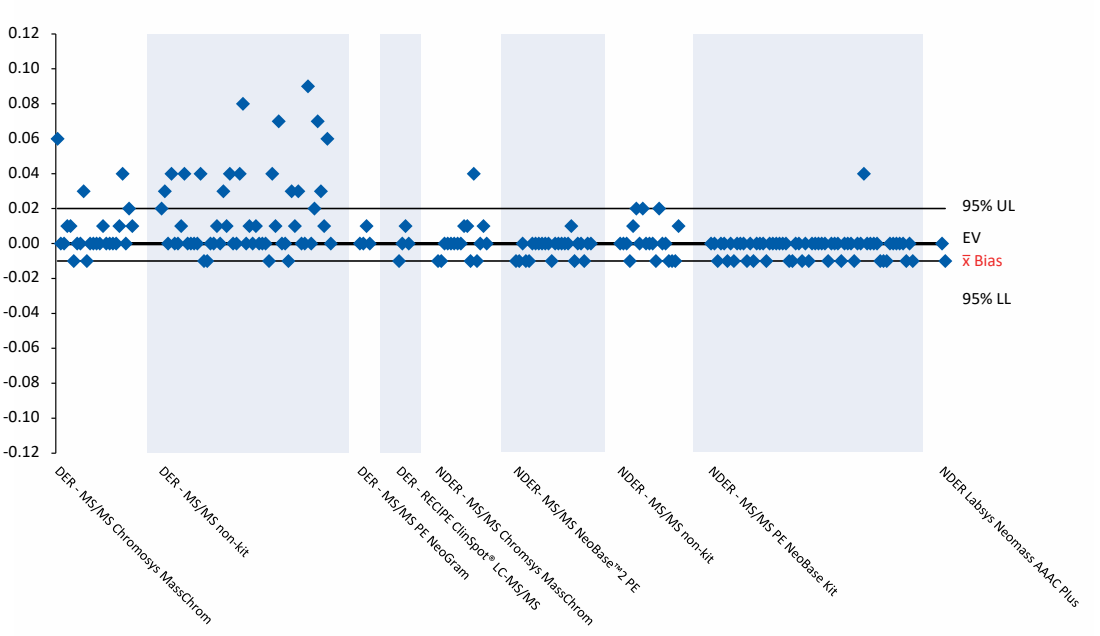
Specimen: 20201006002

Enriched: 0.00

CDC Assayed: 0.01

Participant Mean: 0.01

Participant Bias: 0.00



The C18OH bias plot shows units of measure on the y-axis ranging from 0.12 µmol/L blood to -0.12 µmol/L blood. The bias for this plot is 0.00. The deriviatized MS/MS non-kit method shows a slightly higher bias than other methods

Appendix for Accessibility Descriptions

Figures 2–37, 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. 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 any 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 those analytes distributed in PT challenges that required a quantitative measurement to determine the presumptive clinical assessments.

References

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

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

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