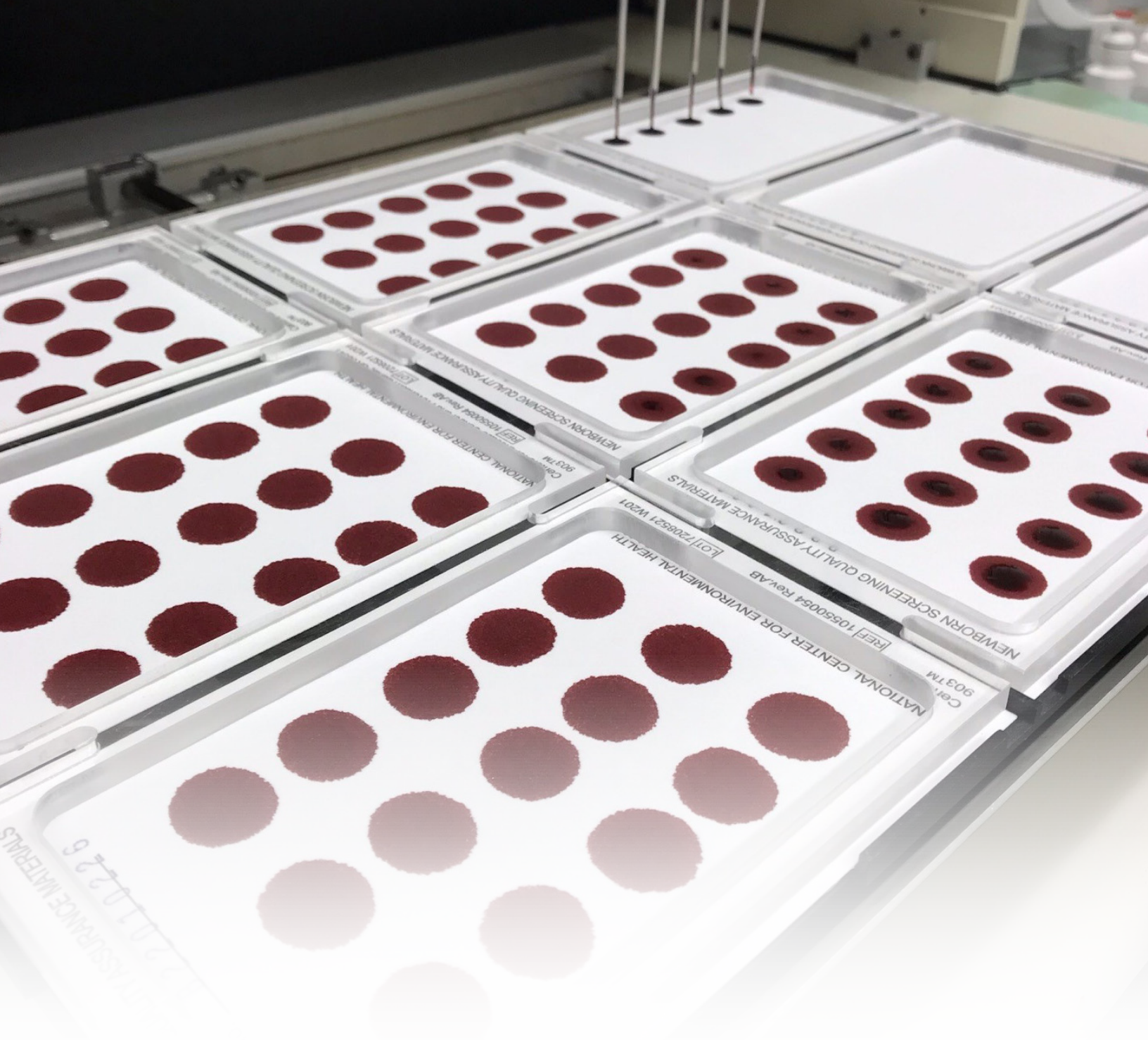


2022 ANNUAL SUMMARY REPORT

Newborn Screening Quality Assurance Program

Centers for Disease Control and Prevention
National Center for Environmental Health

Newborn Screening Quality Assurance Program

2022 Annual Summary Report, Volume 40

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

CDC Image

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

Contents

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
CRE	creatine
DBS	dried blood spot
DER	derivatized tandem mass spectrometry method
EBV	Epstein-Barr virus
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
GAMT	guanidinoacetate methyltransferase deficiency
GUAC	guanidinoacetic acid
Hb	sickle cell and other hemoglobinopathies
HIV	anti-human immunodeficiency virus-1 Antibody

Notation	Description
HORM	hormone + total galactose
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
NBS	Newborn Screening
NDER	non-derivatized tandem mass spectrometry method
NSQAP	Newborn Screening Quality Assurance Program
PE	PerkinElmer
PT	proficiency testing
QA	quality assurance
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 preventive 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 dried blood spot (DBS) specimens from more than 98% of all U.S. newborns shortly after birth. Newborn screening laboratories analyze the DBS for certain genetic, metabolic, and endocrine disorders. The Newborn Screening Quality Assurance Program (NSQAP) at the Centers for Disease Control and Prevention (CDC) helps 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. 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 (NSMBB) is accredited by the American Association for Laboratory Accreditation (A2LA) for the ISO/IEC 17043. Accreditation is renewed every four years after a thorough review of NSMBB's quality management system for the ability to develop and administer specific PT protocols. A2LA's Scope of Accreditation covers most biochemical PT analytes. The accreditation does not include testing for glucose-6-phosphate dehydrogenase (G6PD) and NSQAP's disease specific PT programs. Consult A2LA Certificate#4190.01 for a complete list of the accredited NSMBB PT programs.

William Harry Hannon—A Life Well Lived

Reprinted with permission from authors (Bradford L. Therrell, Robert F. Vogt, and Joanne V. Mei), with revisions.

Photo provided by family friend.

Dr. William Harry Hannon (Harry), Buford, Georgia found eternal peace on Friday, 6 May 2022, at Northeast Georgia Medical Center in Braselton, Georgia, USA.

Born 9 June 1941, in Covington, Georgia, USA, Hannon lived an outstanding life that included many significant and lasting contributions to the advancement in public health laboratory science. Hannon graduated from Tucker High School in 1959, received his BS in chemistry from Georgia State University in 1965, and his PhD in biochemistry from the University of Tennessee in 1972. He completed his formal education in 1974 with post- doctoral training at the Oak Ridge National Laboratories where he used novel methods that gave rise to the field of proteomics. His areas of expertise included immunochemistry, DBS technologies, newborn screening (NBS) for metabolic disorders, and laboratory quality assurance systems.

In 2009, Hannon retired from the CDC with 41 years of federal service, having spent more than 25 years as the chief of what is now known as the Newborn Screening and Molecular Biology Branch at CDC. In retirement, Hannon enjoyed spending time with his children and grandchildren. He continued his work in the field of public health, NBS, intiating, expanding, and improving NBS worldwide.

It would be difficult to overstate the impact of Hannon's work on public health newborn screening (NBS). He authored or co-authored more than 250 scientific publications and served on at least 30 national and international committees addressing various newborn laboratory issues. Hannon was careful not to overstep his knowledge or experience in answering requests for help and often included others with more relevant experiences as co-authors or co- committee members when addressing such requests. Examples of his inclusionary efforts include such items as

- guideline booklets prepared for the World Health Organization defining procedures useful in developing countries for implementing screening for phenylketonuria (1990) and congenital hypothyroidism (1991),
- 14 book chapters on topics such as laboratory methods for detecting congenital hypothyroidism (1993) and congenital hypothyroidism (2000), and
- an overview of the history and applications of dried-blood samples (2014).

Of particular importance were improvements in harmonizing and standardizing NBS methods. Chief among his accomplishments was his response to a request from Dr. Robert Guthrie in early 1979, to create a national NBS QC program at CDC. Under Hannon's direction, CDC's NSQAP became an integral part of the NBS systems in the United States and globally. By providing proficiency testing, training, reference materials, and consultative services, NSQAP serves as a center of expertise for all state NBS laboratories and approximately 670 NBS laboratories throughout the United States and 87 other countries. These activities have included working with commercial kit manufacturers and professional organizations with similar interests.

In 1981, in collaboration with the Texas Newborn Screening Laboratory, Hannon helped in founding the first U.S. National NBS Symposium (today, the Association of Public Health Laboratories APHL-sponsored Newborn Screening and Genetic Testing Symposium). Because he

was interested in international quality assurance (QA) issues in NBS, he attended the first international NBS QA meeting in Japan in 1987. The International Society for Neonatal Screening (ISNS) was organized at this meeting. Over the following years, Hannon would become an active ISNS member serving on the ISNS International QA Committee, the ISNS Council (1999–2002), as ISNS Vice-President (2002–2009), and as a member of the Editorial Committee of the journal Screening (the ISNS journal at the time). He received the *ISNS-Robert Guthrie Award* in 1999 in "Worldwide recognition of outstanding contributions to newborn screening" and was elected as an ISNS Honorary Member in 2009. Additionally, in 1987, the U.S. Health Resources and Services Administration organized a National NBS Review Team to review and improve U.S. NBS programs (34 reviews completed). He was also active as a proposal reviewer for the CDC Foundation's NBS Translational Research Initiative.

Hannon had an outstanding 41-year career at CDC that included receipt of more than 35 special recognition and service awards. He was awarded CDC's highest honor for scientific excellence, the Charles C. Shepard Science Award in 1992 and again in 2005. In 2006, he was awarded the CDC Sigma Xi's *Walter Dowdle Award* for "Achievements in Public Health Laboratory Science" in 2008, the APHL presented him with their Lifetime Achievement Award for "Leadership in the field of public health laboratory science and influencing public health policy on a national and global level." Additionally, the APHL created a global NBS award, *The Harry Hannon Laboratory Quality Improvement Award*, to be presented at each U.S. national NBS meeting. Harry was also involved with parent support activities serving as a board member of several such groups. In April 2009, he received the Jeffrey Modell Foundation's *Dream Makers Award* as a "Pioneer in Newborn Screening" for contributions to the early detection of severe combined immunodeficiency disorders (SCIDs) by NBS.

His committee work with the Clinical Laboratory Standards Institute (CLSI) was instrumental in setting CLSI standards and guidelines for national and international health laboratory practice. Hannon chaired the working groups on the first seven approved editions of the only "standard" specifically targeted at NBS, *NBS 01: Blood Collection on Filter Paper for Newborn Screening*. Hannon's vision for laboratory quality in NBS seeded the development of 13 CLSI standards and guidelines that have proven to be invaluable for NBS professionals worldwide. In 2008, CLSI awarded Harry its *Russell J. Eilers Award* (CLSI's highest award) for outstanding contributions in developing clinical laboratory standards. His contributions to NBS and public health will not soon be forgotten, and his accomplishments will stand for many years in testimony of a life well lived!

Harry was preceded in death by his parents James Henry and Jeanette Bentley Hannon of Covington, Georgia. He is survived by his daughter, Terri Fain; son, John Hannon; brother and sister-in-law, James H. (Jimmy) and Lynn Hannon, Jr.; sisters and brothers-in-law, Sandra and Gerald Yates, and Margaret and Mike Burgess; sister, Starr Strickland; grandchildren, Spencer Cape, Zachary Thomas, Shelby Opperman, Joseph Hannon, Austin Fain, and Katherine Fain; and three great-grandchildren. He was preceded in death by his beloved wife, Barbara Cheryl Hannon (Cherry).

Acknowledgments: The authors graciously acknowledge this opportunity to recognize the superb career of Dr. Hannon and our individual opportunities for participation in his accomplishments. Bradford L. Therrell was a trusted friend and colleague whose career in state government both paralleled and complemented that of Dr. Hannon. Robert F. Vogt and Joanne V Mei were long-time friends and colleagues at the CDC who supported and assisted his work.

Disclaimer: The views expressed here do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Source: Int. J. Neonatal Screen. 2022, 8(2), 37; https://doi.org/10.3390/ijns8020037

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].

NSQAP continues to grow each year. In 2022, 680 newborn screening laboratories in 86 countries participated in the program (Figure 1). Of these laboratories, 489 participated in PT (Table 1) and 363 in QC (Table 2). NSQAP distributed DBS materials for 78 newborn screening analytes to the participating laboratories (Tables 1 and 2).

The NSQAP Laboratory provides quality assurance materials for the thyroxine (T4), thyroid stimulating hormone (TSH), 17 α-hydroxyprogesterone (17OHP), immunoreactive trypsinogen (IRT), sickle cell and other hemoglobinopathies (Hb), anti-human immunodeficiency virus-1 antibody (HIV), anti-Toxoplasma antibody (TOXO), and the second-tier congenital adrenal hyperplasia (CAH) programs.

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

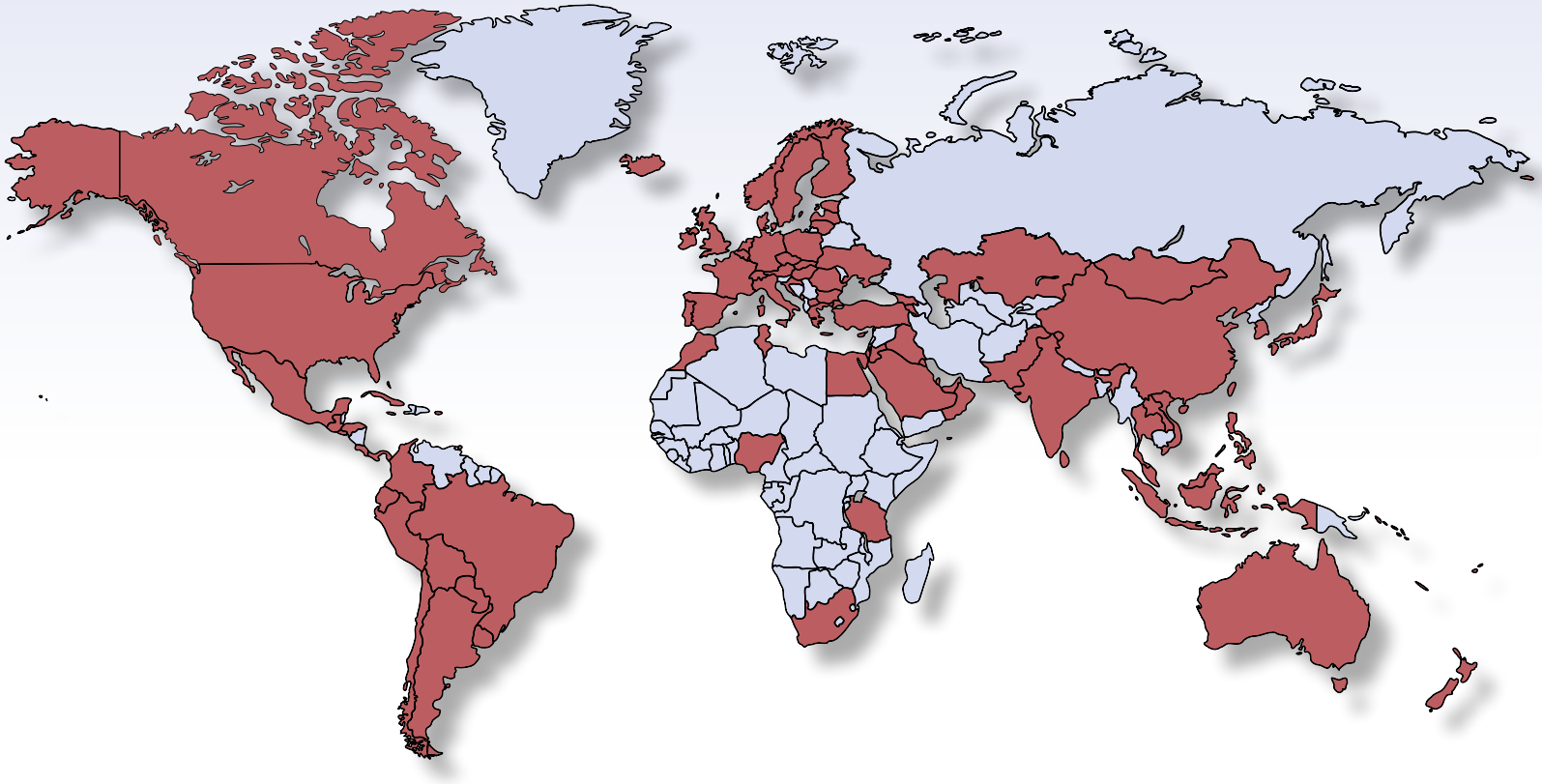
BMSL offers tandem mass spectrometry (MS/MS) quality assurance, education, and research opportunities for newborn screening. It also oversees the amino acids, acylcarnitines, X-linked adrenoleukodystrophy (ALD), biotinidase (BIOT), total galactose (TGAL), galactose-1-phosphate uridyltransferase (GALT), G6PD, lysosomal storage disorder (LSD), and filter paper evaluation programs. BMSL provides second-tier QC programs for maple syrup urine disease/phenylketonuria and homocystinuria. BMSL conducted a successful guanidinoacetate methyltransferase deficiency (GAMT) pilot event adding guanidinoacetic acid, creatine, and GAMT ratio to the amino acid PT program.

CDC Image

MQIP oversees the cystic fibrosis DNA (CFDNA), T-cell receptor excision circle (TREC), and spinal muscular atrophy (SMA) PT programs and provides molecular assay technical assistance to NSQAP 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. For more information, contact Christopher Greene at CGreene@cdc.gov.

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

NSQAP Participants (N=680 labs)



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
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Peru
Philippines
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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 (PT) analytes. (N = 489)

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

Analyte	Total PT Participation in 2022	Analyte	Total PT Participation in 2022
17OHP	285	C4OH	86
T4	68	C5	317
TSH	342	C5:1	280
TGal	177	C5DC	300
BIOT	219	C5OH	271
GALT	148	C6	294
IRT	237	C8	323
G6PD	95	C10	311
CFDNA	71	C10:1	270
HGB	80	C10:2	193
Anti-HIV-1	17	C14	293
SMA	79	C14:1	299
TOXO	11	C16	301
TREC	101	C16OH	301
ARG	268	C18	285
CIT	296	C18:1	272
LEU	321	C18OH	249
MET	309	17OHP2	27
PHE	399	4AD2	26
SUAC	185	CORT2	26
TYR	327	11D2	18
VAL	291	21D2	16
C0(L)	310	GALC	13
C2(L)	239	GAA	29
C3	310	IDUA	29
C3DC	95	24-LPC	26
C3DC+C4OH	149	26-LPC	53
C4	291		

Table 2. Number of participants reporting quality control (QC) analytes (N = 363)

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

Analyte	Total QC participation in 2022	Analyte	Total QC participation in 2022
17OHP	202	C16	216
T4	56	C16OH	216
TSH	271	C18	210
TGAL	128	C18OH	181
GALT	82	17OHP2	32
IRT	169	4AD2	30
ALA	189	CORT2	31
ARG	197	11D2	24
CIT	211	21D2	25
GLY	157	GALC	25
LEU	222	GAA	51
MET	216	IDUA	55
ORN	160	GLA	37
PHE	286	ABG	33
SUAC	126	ASM	24
TYR	226	C20-LPC	30
VAL	211	C22-LPC	31
C0	226	C24-LPC	41
C2	214	C26-LPC	56
C3	222	GUAC	13
C3DC	71	ALE2	20
C3DC+C4OH	124	CRE2	9
C4	210	CRN2	6
C4OH	66	ILE2	21
C5	223	LEU2	23
C5:1	197	PHE2	23
C5DC	209	TYR2	20
C5OH	190	VAL2	24
C6	211	MMA2	33
C8	229	EMA2	12
C10	226	MCA2	23
C12	204	MA2	1
C14	216	tHCY2	34
C14:1	206		

Filter Paper

NSQAP evaluates absorption characteristics of all filter paper lots approved by the U.S. Food and Drug Administration (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 and are not required for lot release by the manufacturer.

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 3.2 mm 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.

Revvity (previously PerkinElmer) 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 red blood cells (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-sheet variances were within acceptable limits). CDC used 903™ filter paper lots W181, W191, and W201 to produce PT specimens distributed in 2022.

Table 3. Revvity 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)
115541	Aug 2022	1.40 (0.07)	13.9 (2.2)	15.8 (0.6)
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)

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)
W221	Nov 2022	1.40 (0.10)	10.8 (2.3)	16.0 (0.8)
W211	Jan 2022	1.48 (0.12)	18.3 (2.8)	16.0 (0.6)
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)

Proficiency Testing

In 2023, NSQAP conducted three PT events. 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.

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 (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 (SMA)
- 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 were 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 Epstein-Barr virus (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 fewer 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 specimens in the cutoff range. Specimens 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 2022 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 2022.

Table 10 shows the challenges distributed in 2022 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	110	1.8%
26:0 Lysophosphatidylcholine	421	0.5%
anti-*Toxoplama* antibodies	15	0.0%
Biotinidase deficiency	605	0.8%
Congenital adrenal hyperplasia	615	0.0%
Congenital hypothyroidism	605	0.0%
Cystic Fibrosis DNA variant clinical assessment errors	495	0.0%
G6PD deficiency	30	0.0%
GALT deficiency	610	0.3%
Total galactose screen	290	0.0%
Human immunodeficiency virus	85	0.0%
Immunoreactive trypsinogen	625	0.3%
Lysosomal storage disorder Krabbe	185	0.0%
Lysosomal storage disorder Pompe	415	0.0%
Lysosomal storage disorder Mucopolysaccharidosis type 1	415	1.9%
T-cell receptor excision circle	625	1.3%
Second-tier congenital adrenal hyperplasia	101	6.9%
Sickle cell and other hemoglobinopathies phenotype errors	625	1.0%
Sickle cell and other hemoglobinopathies clinical assessment errors	625	2.1%
Spinal muscular atrophy	450	1.3%

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	210	6.2%
26:0 Lysophosphatidylcholine	260	2.75
anti-*Toxoplama* antibodies	115	6.1%
Biotinidase deficiency	2380	16.8%
Congenital adrenal hyperplasia	3185	3.8%
Congenital hypothyroidism	3910	1.8%
Cystic fibrosis DNA variant clinical assessment errors	500	2.6%
G6PD deficiency	1260	4.0%
GALT deficiency	1460	2.1%
Total galactose screen	2155	5.8%
Immunoreactive trypsinogen	2550	4.9%
Human immunodeficiency virus	135	0.0%
T-cell receptor excision circle	760	8.0%
Second-tier congenital adrenal hyperplasia	271	9.6%
Sickle cell and other hemoglobinopathies phenotype errors	490	5.5%
Sickle cell and other hemoglobinopathies clinical assessment errors	490	5.1%
Spinal muscular atrophy	665	11.1%

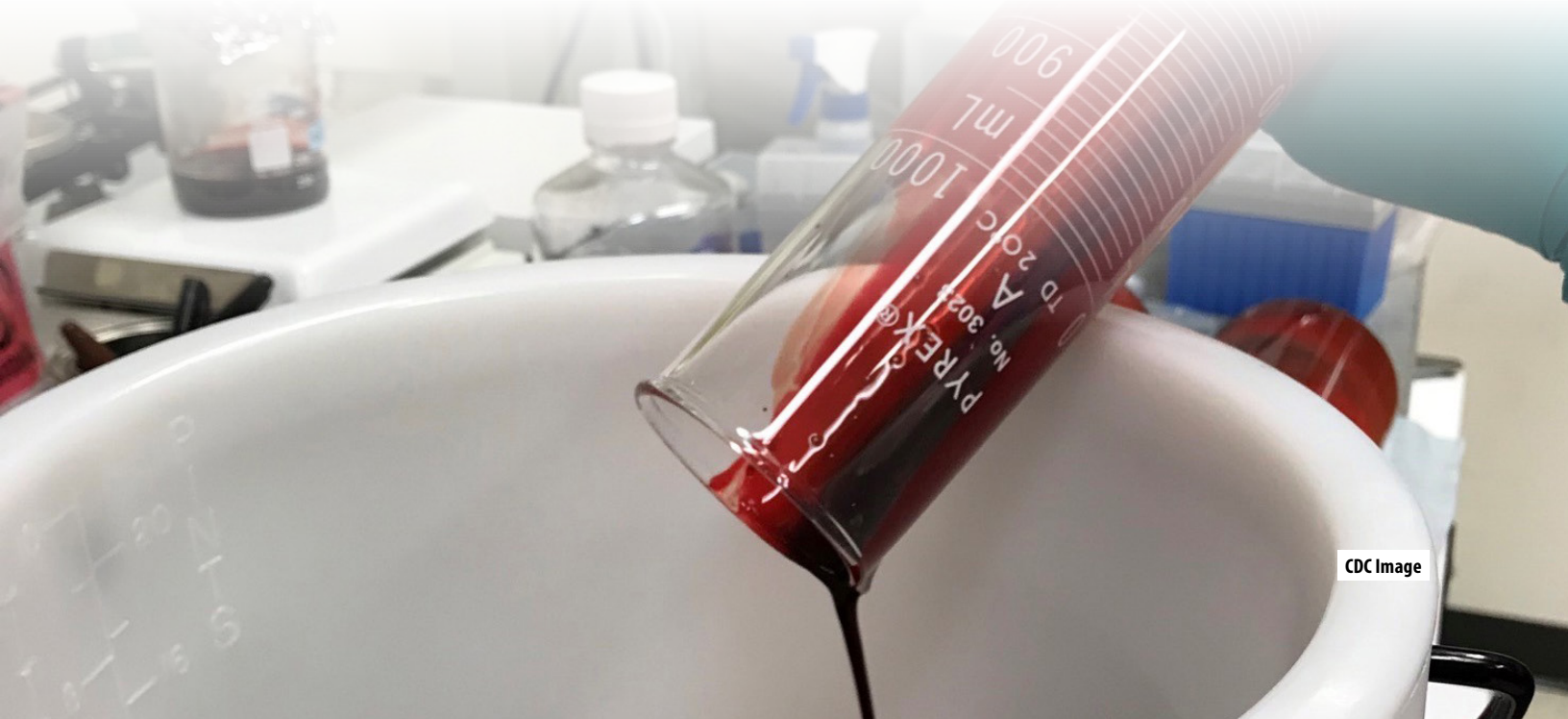


Table 7. Summary of amino acid and acylcarnitine proficiency testing errors by domestic laboratories

Analyte Screen	Specimens Assayed (N)	Unacceptable Assessments (%)
Arginine	540	1.5%
Citrulline	635	1.1%
Leucine	635	0.5%
Methionine	625	0.2%
Phenylalanine	735	0.0%
Succinylacetone	605	0.2%
Tyrosine	700	1.1%
Valine	435	0.0%
C0(L)	655	0.5%
C2(L)	290	0.0%
C3	660	0.2%
C3DC	145	0.0%
C3DC+C4OH	420	0.0%
C4	620	0.0%
C4OH	120	0.0%
C5	660	0.0%
C5:1	640	0.9%
C5DC	635	0.0%
C5OH	635	1.6%
C6	575	0.0%
C8	660	0.0%
C10	585	0.0%
C10:1	535	0.0%
C10:2	370	0.0%
C14	575	0.7%
C14:1	660	0.3%
C16	640	0.2%
C16OH	660	0.2%
C18	535	0.0%
C18:1	570	1.1%
C18OH	510	0.6%

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

Analyte Screen	Specimens Assayed (N)	Unacceptable Assessments (%)
Arginine	2880	3.8%
Citrulline	3175	17.5%
Leucine	3520	4.4%
Methionine	3370	4.5%
Phenylalanine	4445	6.0%
Succinylacetone	1795	6.7%
Tyrosine	3505	2.7%
Valine	3310	3.3%
C0(L)	3360	13.2%
C2(L)	2725	19.4%
C3	3355	5.4%
C3DC	1005	5.5%
C3DC+C4OH	1440	6.6%
C4	3140	3.7%
C4OH	925	15.1%
C5	3450	3.3%
C5:1	3000	5.3%
C5DC	3250	6.5%
C5OH	2870	31.4%
C6	3200	4.4%
C8	3530	3.0%
C10	3430	2.6%
C10:1	2975	2.2%
C10:2	2110	2.4%
C14	3220	5.0%
C14:1	3230	3.1%
C16	3245	5.5%
C16OH	3240	2.5%
C18	3145	3.7%
C18:1	2975	3.7%
C18OH	2685	3.0%

Table 9. 2022 Cystic Fibrosis DNA variant (CTFR gene) PT challenges distributed

Variant (Legacy Name)	Variant (HGVS Nomenclature)	Variants Sent
F508del	p.Phe508del	8
2055del9>A	p.Ser641ArgfsX5	1
2183AA>G	p.Lys684SerfsX38	1
3905insT	p.Leu1258PhefsX7	1
935delA	p.Asn268IlefsX17	1
G542X	p.Gly542X	1
G551D	p.Gly551Asp	1
Q890X	p.Gln890X	1
R75X	p.Arg75X	1
W1282X	p.Trp1282X	1
Y1092X	p.Tyr1092X	1

Table 10. 2022 Hemoglobinopathies accepted presumptive phenotype PT challenges distributed

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


CDC Image

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 either outside normal limits (presumptive positive) or 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)	40	34.7	33.0	30.0	20.0	75.0
IRT (ng/mL blood)	38	60.7	58.0	71.0	42.7	100.0
T4 (µg/dL serum)	17	6.3	6.0	5.0	5.0	8.0
TGal (mg/dL blood)	19	11.6	10.0	10.0	6.0	20.0
TSH (µIU/mL serum)	35	28.4	25	20.0	18.0	60.0

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

Analyte	N	Mean	Median	Mode	Minimum	Maximum
17OHP (ng/mL serum)	209	23.1	19.8	20.0	6.0	80.0
IRT (ng/mL blood)	163	65.5	65.0	70.0	25.0	150.0
T4 (µg/dL serum)	37	6.6	6.0	6.0	3.0	15.6
TGal (mg/dL blood)	136	12.2	10.0	10.0	2.7	30.0
TSH (µIU/mL serum)	256	21.4	20.0	20.0	7.0	49.8
Phe (µmol/L blood)	42	151.3	130.2	121.2	103.0	242.2

Table 13. Summary of Cutoff Values for Domestic Laboratories (µmol/L blood) (Analytes N<3 not shown)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine	35	73.9	63.0	63.0	27.0	120.0
Citrulline	41	52.4	50.0	49.0	31.0	75.0
Leucine	42	290.7	274.0	230.0	145.0	425.0
Methionine	41	73.3	74.0	100.0	35.0	130.0
Phenylalanine	48	140.7	140.0	130.0	74.0	182.0
Succinylacetone	40	2.5	2.0	1.0	0.4	6.1
Tyrosine	46	389.9	367.5	350.0	91.0	680.0
Valine	28	285.2	277.5	300.0	180.0	530.0

Table 13. Continued

Analyte	N	Mean	Median	Mode	Minimum	Maximum
C0(L)	42	7.22	7.00	6.40	5.00	10.00
C2(L)	18	6.85	7.00	5.00	2.00	9.50
C3	44	6.17	6.27	5.00	3.10	9.69
C3DC	9	0.20	0.20	0.20	0.10	0.43
C3DC+ C4OH	28	0.57	0.48	0.48	0.25	3.03
C4	41	1.28	1.30	1.20	0.49	1.90
C4OH	7	0.64	0.75	0.75	0.20	0.80
C5	44	0.71	0.68	0.60	0.34	1.20
C5:1	43	0.18	0.10	0.10	0.03	0.50
C5DC	43	0.37	0.38	0.38	0.05	0.80
C5OH	43	0.93	0.91	0.80	0.36	1.70
C6	37	0.38	0.26	0.95	0.15	0.95
C8	44	0.42	0.44	0.45	0.15	0.70
C10	39	0.45	0.41	0.40	0.22	0.70
C10:1	35	0.27	0.25	0.20	0.12	0.45
C10:2	26	0.14	0.10	0.10	0.04	0.38
C14	38	0.73	0.70	0.70	0.27	1.20
C14:1	44	0.63	0.62	0.60	0.17	0.90
C16	42	8.28	8.00	12.00	2.14	12.00
C16OH	44	0.12	0.10	0.10	0.07	0.25
C18	34	2.47	2.30	3.50	1.31	3.50
C18:1	38	3.61	3.00	3.00	2.00	7.00
C18OH	34	0.09	0.10	0.10	0.04	0.18
24:0-LPC - 1st tier	8	0.81	0.79	n/a	0.40	1.60
24:0-LPC - 2nd tier	n/a	n/a	n/a	n/a	n/a	n/a
26:0-LPC - 1st tier	31	0.43	0.45	0.53	0.13	0.80
26:0-LPC - 2nd tier	13	0.19	0.16	0.15	0.13	0.31

Table 14. Summary of MS/MS Cutoff Values for International Laboratories (µmol/L blood) (Analytes N<3 not shown)

Analyte	N	Mean	Median	Mode	Minimum	Maximum
Arginine	188	55.6	52.3	70.0	9.3	160.0
Citrulline	203	49.0	45.5	55.0	20.0	92.0
Leucine	227	305.3	297.0	300.0	15.9	601.7
Methionine	218	53.2	48.8	75.0	23.0	100.0
Phenylalanine	246	130.2	120.0	120.0	13.1	266.6
Succinylacetone	112	2.3	1.8	2.0	0.4	8.0
Tyrosine	223	298.5	290.0	350.0	91.0	600.0
Valine	213	270.7	270.0	300.0	129.6	465.0
C0(L)	216	13.5	8.1	8.0	4.0	99.7
C2(L)	167	16.58	7.00	7.00	0.00	96.00
C3	217	5.45	5.20	5.00	0.81	11.00
C3DC	57	0.25	0.25	0.25	0.04	0.70
C3DC+ C4OH	99	0.47	0.45	0.45	0.01	2.53
C4	202	0.93	0.92	1.30	0.16	2.50
C4OH	54	0.56	0.54	0.50	0.05	1.00
C5	223	0.67	0.60	1.00	0.06	2.00
C5:1	197	0.13	0.10	0.25	0.01	0.66
C5DC	209	0.34	0.30	0.35	0.04	1.06
C5OH	186	0.72	0.69	1.00	0.18	1.60
C6	204	0.26	0.20	0.20	0.04	1.30
C8	225	0.33	0.30	0.30	0.05	0.80
C10	214	0.36	0.34	0.45	0.07	0.91
C10:1	191	0.22	0.20	0.30	0.05	0.70
C10:2	139	0.12	0.10	0.15	0.01	1.00
C14	205	0.61	0.55	0.75	0.08	1.30
C14:1	209	0.46	0.40	0.40	0.04	2.50
C16	205	6.93	7.00	7.50	0.97	12.00
C16OH	213	0.11	0.10	0.10	0.02	0.75
C18	199	2.12	2.07	2.30	0.56	4.00
C18:1	190	3.13	3.01	3.50	1.10	5.80
C18OH	174	0.08	0.06	0.10	0.01	0.50
24:0-LPC - 1st tier	14	1.05	0.845	0.8	0.09	4.44
24:0-LPC - 2nd tier	n/a	n/a	n/a	n/a	n/a	n/a
26:0-LPC - 1st tier	16	0.6	0.5	0.5	0.14	1.97
26:0-LPC - 2nd tier	n/a	n/a	n/a	n/a	n/a	n/a

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

17 OHP ng/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**40**	**34.7**	**33.0**	**30.0**	**20.0**	**75.0**
AutoDELFIA® Neonatal 17OHP PerkinElmer	11	35.3	33.0	33.0	25.0	60.0
GSP® 17OHP Neonatal PerkinElmer	28	34.9	31.0	30.0	20.0	75.0

TSH µIU/mL serum

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**35**	**28.4**	**25**	**20.0**	**18.0**	**60.0**
AutoDELFIA® Neonatal hTSH PerkinElmer	6	31.8	32.8	n/a	20.0	58.0
GSP® hTSH Neonatal PerkinElmer	29	27.2	25.0	20.0	18.0	60.0

T4 µg/dL serum

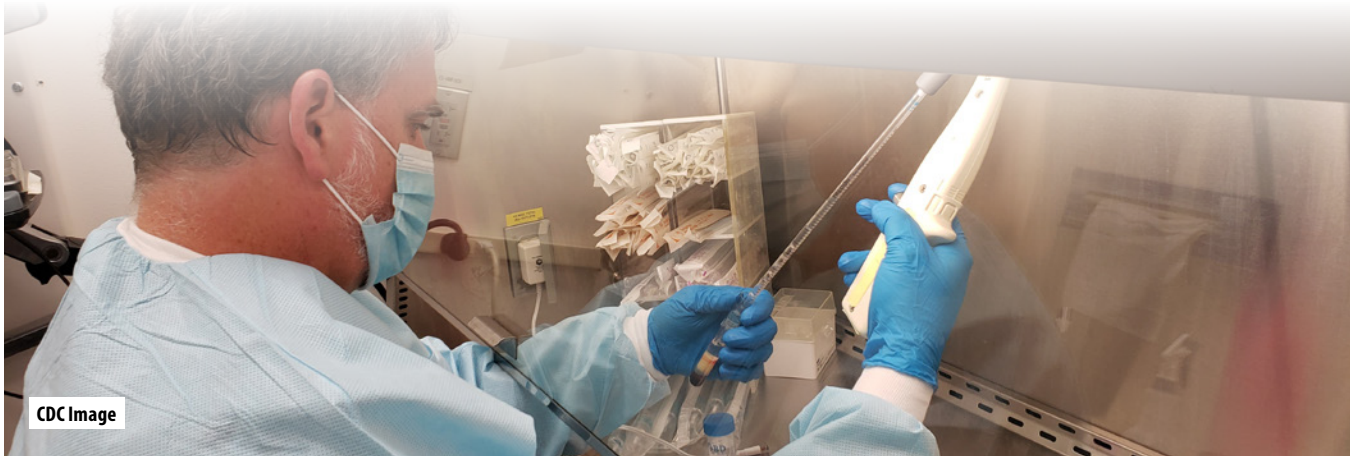
Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**17**	**6.3**	**6.0**	**5.0**	**5.0**	**8.0**
GSP® T4 Neonatal PerkinElmer	15	6.3	6.0	5.0	5.0	8.0

TGal mg/dL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**19**	**11.6**	**10.0**	**10.0**	**6.0**	**20.0**
50hr Reagent Kit Spotcheck® TGal Astoria-Pacific	3	12.0	11.0	n/a	10.0	15.0
GSP® TGal Neonatal PerkinElmer	12	11.0	10.0	10.0	6.0	18.0

IRT ng/mL blood

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**38**	**60.7**	**58.0**	**71.0**	**42.7**	**100.0**
AutoDELFIA® Neonatal IRT PerkinElmer	13	67.5	71.0	71.0	51.0	90.0
GSP® IRT Neonatal PerkinElmer, ng/mL blood	25	57.1	55.0	55.0	42.7	100.0



CDC Image

Table 16. Summary of cutoff values by analyte and method for domestic laboratories—lysosomal storage disorders (methods N<3 not shown)

Galactoceramidase (GALC)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**11**	**0.51**	**0.49**	**n/a**	**0.14**	**0.83**
LC-MS/MS non-kit	3	0.34	0.43	n/a	0.14	0.44
NeoLSD™ MSMS Kit PerkinElmer	5	0.61	0.64	n/a	0.30	0.83

Acid α-glucosidase (GAA)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**25**	**3.35**	**2.00**	**1.88**	**0.61**	**10.00**
Digital Microfluidic Fluorescence	6	8.40	8.85	n/a	6.60	10.00
Flow Injection Analysis (FIA)-MS/MS multiplexed enzyme reaction	6	1.83	1.96	n/a	1.10	2.10
LC-MS/MS non-kit	4	1.37	1.50	n/a	0.61	1.88
NeoLSD™ MSMS Kit PerkinElmer	9	1.89	1.98	n/a	1.46	2.50

α-L-iduronidase (IDUA)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**26**	**2.33**	**1.73**	**1.80**	**0.49**	**6.00**
Digital Microfluidic Fluorescence	6	4.94	4.95	n/a	3.94	6.00
Flow Injection Analysis (FIA)-MS/MS multiplexed enzyme reaction	6	1.27	1.30	n/a	0.65	1.80
LC-MS/MS non-kit	4	2.73	2.24	n/a	1.65	4.79
NeoLSD™ MSMS Kit PerkinElmer	9	1.19	1.19	n/a	0.49	2.25

Table 17. Summary of cutoff values by analyte and method for domestic laboratories — amino acids (µmol/L blood) (Methods N<3 not shown)

Arginine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**35**	**73.9**	**63.0**	**63.0**	**27.0**	**120.0**
Derivatized - MS/MS non-kit	5	46.4	50.0	50.0	27.0	60.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	8	94.8	100.0	100.0	48.0	120.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	19	74.6	63.0	63.0	50.0	120.0

Citrulline

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**41**	**52.4**	**50.0**	**49.0**	**31.0**	**75.0**
Derivatized - MS/MS non-kit	6	53.2	55.0	55.0	34.0	70.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	59.2	60.0	60.0	40.0	75.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	50.3	49.0	49.0	40.0	75.0
Non-derivatized - MS/MS non-kit	3	49.7	49.0	n/a	45.0	55.0

Table 17. Continued

Leucine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS*	**42**	**290.7**	**274.0**	**230.0**	**145.0**	**425.0**
Derivatized - MS/MS non-kit	6	285.7	278.0	n/a	250.0	345.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	313.7	320.5	270.0	225.0	400.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	289.9	270.0	230.0	145.0	425.0
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	**41**	**73.3**	**74.0**	**100.0**	**35.0**	**130.0**
Derivatized - MS/MS non-kit	6	56.3	57.9	n/a	35.0	70.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	75.1	80.0	80.0	50.0	100.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	81.7	85.0	100.0	45.0	130.0
Non-derivatized - MS/MS non-kit	3	53.3	60.0	60.0	40.0	60.0

Phenylalanine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**48**	**140.7**	**140.0**	**130.0**	**74.0**	**182.0**
Derivatized - MS/MS non-kit	7	150.7	150.0	n/a	130.0	182.0
LC-MS/MS non-kit	3	115.1	120.0	n/a	104.3	121.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	141.5	130.0	130.0	120.0	180.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	146.9	150.0	175.0	100.0	175.0
Non-derivatized - MS/MS non-kit	5	116.8	130.0	130.0	74.0	150.0

Succinylacetone

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**40**	**2.5**	**2.0**	**1.0**	**0.4**	**6.1**
Derivatized - MS/MS non-kit	6	2.9	2.6	2.0	2.0	5.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	1.6	1.6	1.0	1.0	3.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	2.6	1.3	6.1	0.4	6.1
Non-derivatized - MS/MS non-kit	3	3.2	2.5	n/a	1.8	5.4

Tyrosine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**46**	**389.9**	**367.5**	**350.0**	**91.0**	**680.0**
Derivatized - MS/MS non-kit	7	360.6	414.0	414.0	99.0	500.0
LC-MS/MS non-kit	3	244.2	204.2	n/a	128.5	400.0
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	375.1	363.0	300.0	300.0	480.0
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	20	468.4	434.5	680.0	243.0	680.0
Non-derivatized - MS/MS non-kit	5	242.2	290.0	n/a	91.0	360.0

Table 17. Continued

Valine

Method	N	Mean	Median	Mode	Min	Max
ALL MS/MS METHODS	**28**	**285.2**	**277.5**	**300.0**	**180.0**	**530.0**
Derivatized - MS/MS non-kit	4	281.3	240.0	240.0	225.0	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	11	273.4	280.0	180.0	180.0	360.0
Non-derivatized - MS/MS non-kit	3	220.0	210.0	n/a	200.0	250.0

24:0-lysophosphatidylcholine 1st Tier

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**8**	**0.81**	**0.79**	**n/a**	**0.40**	**1.60**
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	5	1.02	0.90	n/a	0.78	1.60

24:0-lysophosphatidylcholine 2nd Tier

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**n/a**	**n/a**	**n/a**	**n/a**	**n/a**	**n/a**

26:0-lysophosphatidylcholine 1st Tier

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**31**	**0.43**	**0.45**	**0.53**	**0.13**	**0.80**
Flow Injection Analysis (FIA) - MS/MS non-derivitized non-kit	5	0.51	0.50	0.50	0.36	0.80
LC-MS/MS negative ion mode	8	0.19	0.19	0.18	0.13	0.28
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	18	0.51	0.53	0.53	0.40	0.70

26:0-lysophosphatidylcholine 2nd Tier

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**13**	**0.19**	**0.16**	**0.15**	**0.13**	**0.31**
LC-MS/MS negative ion mode	9	0.17	0.15	0.15	0.13	0.30
LC-MS/MS positive ion mode	4	0.24	0.23	n/a	0.20	0.31

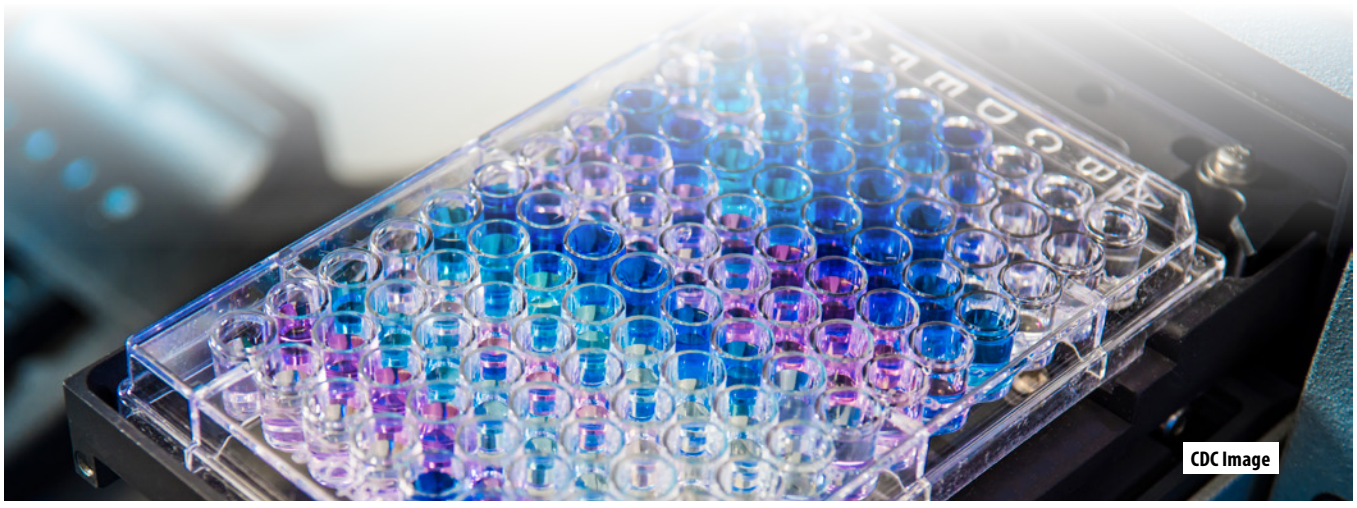


Table 18. Summary of cutoff values by analyte and method for domestic laboratories — acylcarnitines (µmol/L blood) (Methods N<3 not shown)

C0(L)

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**7.22**	**7.00**	**6.40**	**5.00**	**10.00**
Derivatized - MS/MS non-kit	8	8.00	8.25	10.00	5.00	10.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	7.42	7.00	7.00	5.74	10.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	6.84	6.40	6.40	5.30	9.00
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	**18**	**6.85**	**7.00**	**5.00**	**2.00**	**9.50**
Derivatized - MS/MS non-kit	4	6.20	6.66	n/a	2.00	9.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	5	7.36	8.00	n/a	4.00	9.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	6	7.17	7.50	5.00	5.00	9.00
Non-derivatized - MS/MS non-kit	3	6.23	6.70	n/a	5.00	7.00

C3

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**6.17**	**6.27**	**5.00**	**3.10**	**9.69**
Derivatized - MS/MS non-kit	10	5.14	4.88	n/a	3.10	7.70
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	5.60	5.40	5.00	4.00	8.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	6.83	6.85	7.90	4.00	9.69
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	**9**	**0.20**	**0.20**	**0.20**	**0.10**	**0.43**
Derivatized - MS/MS non-kit	9	0.20	0.20	0.20	0.10	0.43

C3DC + C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**28**	**0.57**	**0.48**	**0.48**	**0.25**	**3.03**
Non-derivatized - MS/MS NeoBase™ PerkinElmer	7	0.39	0.40	n/a	0.25	0.60
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	18	0.49	0.48	0.48	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	**41**	**1.28**	**1.30**	**1.20**	**0.49**	**1.90**
Derivatized - MS/MS non-kit	9	1.19	1.20	1.20	0.49	1.90
Non-derivatized - MS/MS NeoBase™ PerkinElmer	9	1.22	1.20	1.10	1.00	1.40
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	20	1.35	1.31	1.70	0.60	1.80
Non-derivatized - MS/MS non-kit	3	1.27	1.20	n/a	1.10	1.50

Table 18. Continued

C4OH

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**7**	**0.64**	**0.75**	**0.75**	**0.20**	**0.80**
Derivatized - MS/MS non-kit	7	0.64	0.75	0.75	0.20	0.80

C5

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**0.71**	**0.68**	**0.60**	**0.34**	**1.20**
Derivatized - MS/MS non-kit	10	0.69	0.64	n/a	0.34	1.20
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	0.63	0.60	0.60	0.45	1.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	0.76	0.75	0.95	0.43	0.95
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	**43**	**0.18**	**0.10**	**0.10**	**0.03**	**0.50**
Derivatized - MS/MS non-kit	10	0.19	0.13	n/a	0.05	0.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	9	0.13	0.10	0.10	0.03	0.20
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	0.22	0.10	0.50	0.04	0.50
Non-derivatized - MS/MS non-kit	3	0.11	0.10	n/a	0.04	0.19

C5DC

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**43**	**0.37**	**0.38**	**0.38**	**0.05**	**0.80**
Derivatized - MS/MS non-kit	10	0.17	0.17	0.13	0.05	0.30
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	0.52	0.50	0.50	0.30	0.80
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	20	0.37	0.38	0.38	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	**43**	**0.93**	**0.91**	**0.80**	**0.36**	**1.70**
Derivatized - MS/MS non-kit	10	0.78	0.76	n/a	0.36	1.25
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	0.82	0.80	0.80	0.60	1.05
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	20	1.05	0.98	1.15	0.60	1.70
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	**37**	**0.38**	**0.26**	**0.95**	**0.15**	**0.95**
Derivatized - MS/MS non-kit	8	0.34	0.31	n/a	0.24	0.59
Non-derivatized - MS/MS NeoBase™ PerkinElmer	8	0.25	0.22	0.20	0.16	0.50
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	18	0.48	0.26	0.95	0.16	0.95
Non-derivatized - MS/MS non-kit	3	0.20	0.15	0.15	0.15	0.30

Table 18. Continued

C8

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**44**	**0.42**	**0.44**	**0.45**	**0.15**	**0.70**
Derivatized - MS/MS non-kit	10	0.39	0.42	0.50	0.15	0.50
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	0.46	0.42	0.40	0.32	0.70
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	0.43	0.45	0.45	0.24	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	**39**	**0.45**	**0.41**	**0.40**	**0.22**	**0.70**
Derivatized - MS/MS non-kit	9	0.38	0.40	0.30	0.22	0.55
Non-derivatized - MS/MS NeoBase™ PerkinElmer	9	0.41	0.40	0.30	0.30	0.70
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	18	0.51	0.53	0.65	0.25	0.65
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	**35**	**0.27**	**0.25**	**0.20**	**0.12**	**0.45**
Derivatized - MS/MS non-kit	8	0.26	0.25	0.25	0.17	0.37
Non-derivatized - MS/MS NeoBase™ PerkinElmer	8	0.23	0.23	0.20	0.15	0.30
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	16	0.30	0.27	0.45	0.12	0.45
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	7	0.20	0.15	n/a	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	10	0.12	0.10	0.10	0.05	0.20

C14

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**38**	**0.73**	**0.70**	**0.70**	**0.27**	**1.20**
Derivatized - MS/MS non-kit	9	0.60	0.70	0.70	0.27	0.80
Non-derivatized - MS/MS NeoBase™ PerkinElmer	9	0.67	0.70	0.70	0.46	0.79
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	17	0.85	0.75	1.20	0.55	1.20
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	**44**	**0.63**	**0.62**	**0.60**	**0.17**	**0.90**
Derivatized - MS/MS non-kit	9	0.50	0.60	0.60	0.17	0.70
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	0.63	0.63	0.60	0.50	0.80
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	0.69	0.65	0.90	0.47	0.90
Non-derivatized - MS/MS non-kit	3	0.54	0.56	n/a	0.45	0.60

Table 18. Continued

C16

Method	N	Mean	Median	Mode	Min	Max
ALL METHODS	**42**	**8.28**	**8.00**	**12.00**	**2.14**	**12.00**
Derivatized - MS/MS non-kit	10	6.95	7.00	7.00	2.14	10.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	7.73	7.95	8.00	5.00	9.50
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	19	9.40	9.50	12.00	3.50	12.00
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	**44**	**0.12**	**0.10**	**0.10**	**0.07**	**0.25**
Derivatized - MS/MS non-kit	10	0.14	0.12	0.10	0.10	0.25
Non-derivatized - MS/MS NeoBase™ PerkinElmer	10	0.10	0.09	0.08	0.07	0.15
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	21	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	**34**	**2.47**	**2.30**	**3.50**	**1.31**	**3.50**
Derivatized - MS/MS non-kit	6	2.11	2.03	n/a	1.31	3.00
Non-derivatized - MS/MS NeoBase™ PerkinElmer	9	2.20	2.20	2.50	1.55	3.00
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	16	2.82	2.77	3.50	2.00	3.50
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	**38**	**3.61**	**3.00**	**3.00**	**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	9	3.24	3.00	3.00	2.00	4.50
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	17	4.30	3.00	7.00	2.50	7.00
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	**34**	**0.09**	**0.10**	**0.10**	**0.04**	**0.18**
Derivatized - MS/MS non-kit	6	0.11	0.10	0.10	0.07	0.18
Non-derivatized - MS/MS NeoBase™ PerkinElmer	8	0.09	0.09	0.05	0.05	0.16
Non-derivatized - MS/MS NeoBase™2 PerkinElmer	17	0.08	0.10	0.10	0.04	0.13
Non-derivatized - MS/MS non-kit	3	0.09	0.10	n/a	0.04	0.12

2022 Bias Plots

Proficiency Testing Bias Plots

Figures 2–37 were created for PT analytes reported during 2022. 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 can 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 expected value (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 show 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 might vary between methods. Because some of the pools in a routine PT survey represent a unique donor specimen, differences in endogenous concentrations 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.

17OHP

Specimen: 20221001005

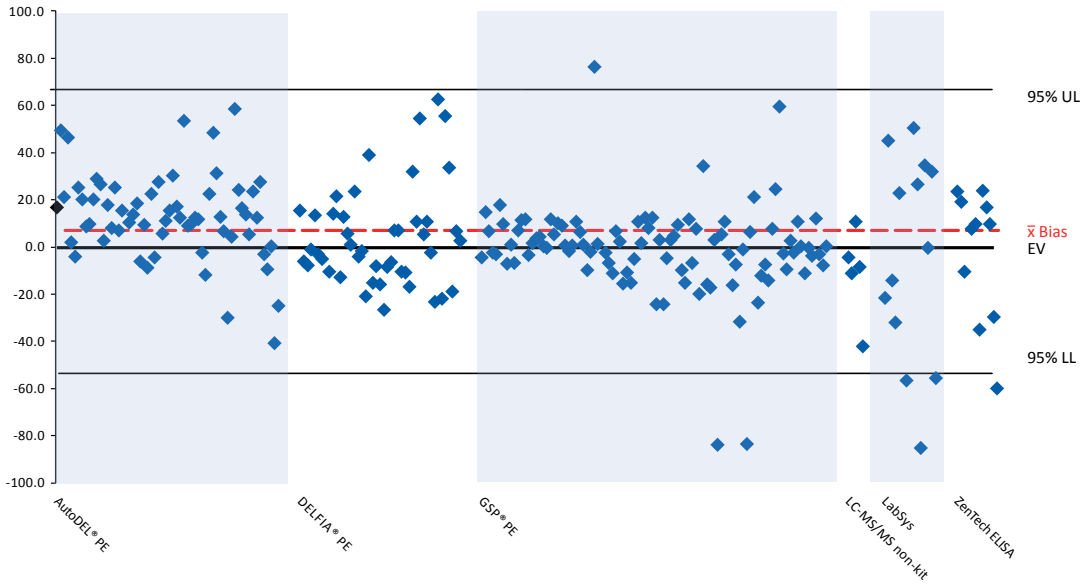
Enriched: 85.0

CDC Characterized Value: 79.9

Participant Mean: 92.4

Participant Bias: 6.8

Figure 2.
Bias Plot of 17 α-Hydroxyprogesterone (17OHP) Values by Method
Quarter 1, Specimen 20221001005
Expected Value (EV) = 85.6 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 6.8 ng/mL serum. The data on this plot shows an even scatter among all participants.

T4

Specimen: 20221001003

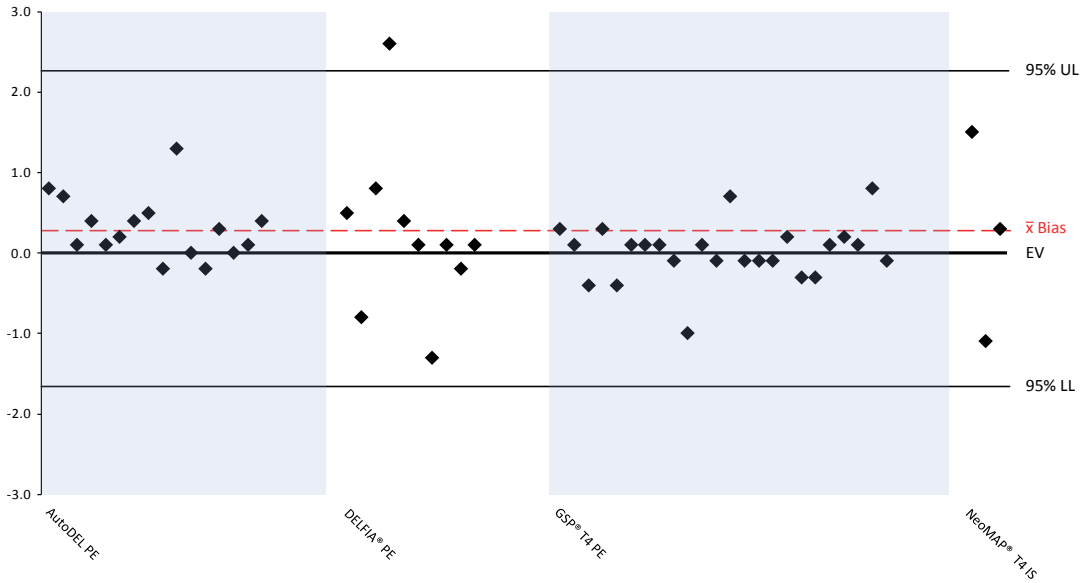
Enriched: 1.5

CDC Characterized Value: 1.4

Participant Mean: 1.8

Participant Bias: 0.3

Figure 3.
Bias Plot of Thyroxine (T4) Values by Method
Quarter 1, Specimen 20221001003
Expected Value (EV) = 1.5 µg/dL serum



The T4 bias plot shows units of measure on the y-axis ranging from 3.0 µg/dL serum to -3.0 µg/dL serum. The bias for this plot is 0.3. The data on this plot show an even scatter with some outliers.

Figure 4.
Bias Plot of Thyroid-Stimulating Hormone (TSH) Values by Method
Quarter 1 , Specimen 20221001003
Expected Value (EV) = 80.1 µIU/mL serum

TSH

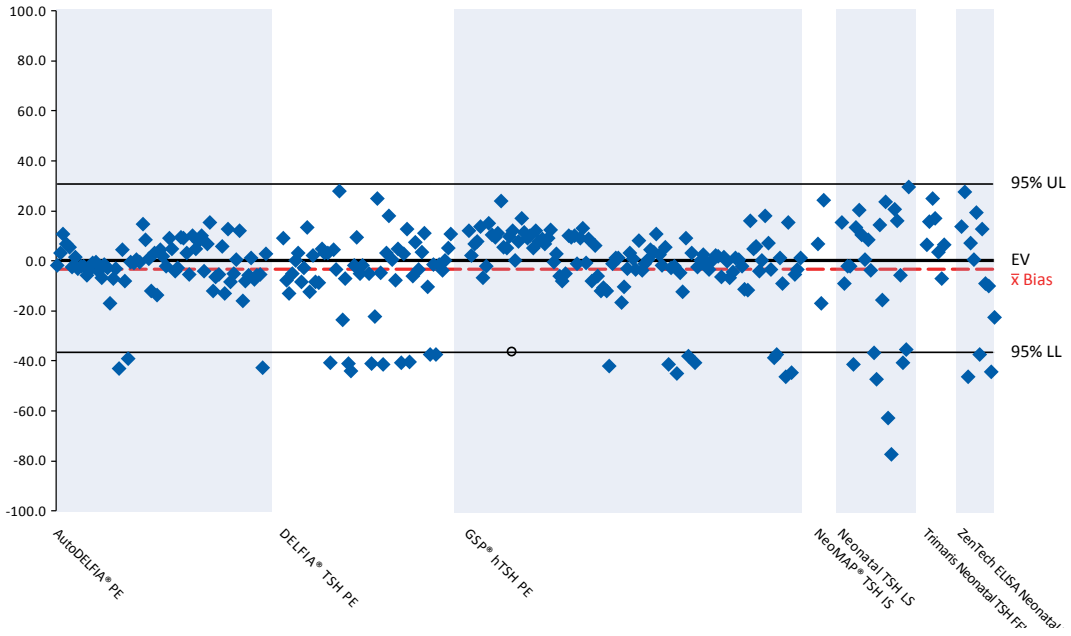
Specimen: 20221001003

Enriched: 80.0

CDC Characterized Value: 94.2

Participant Mean: 77.3

Participant Bias: -2.8



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 -2.8. The data show an even bias scatter across methods.

Figure 5.
Bias Plot of Total Galactose (TGAL) Values by Method
Quarter 4, Specimen 20224001005
Expected Value (EV) = 25.0 mg/dL blood

TGAL

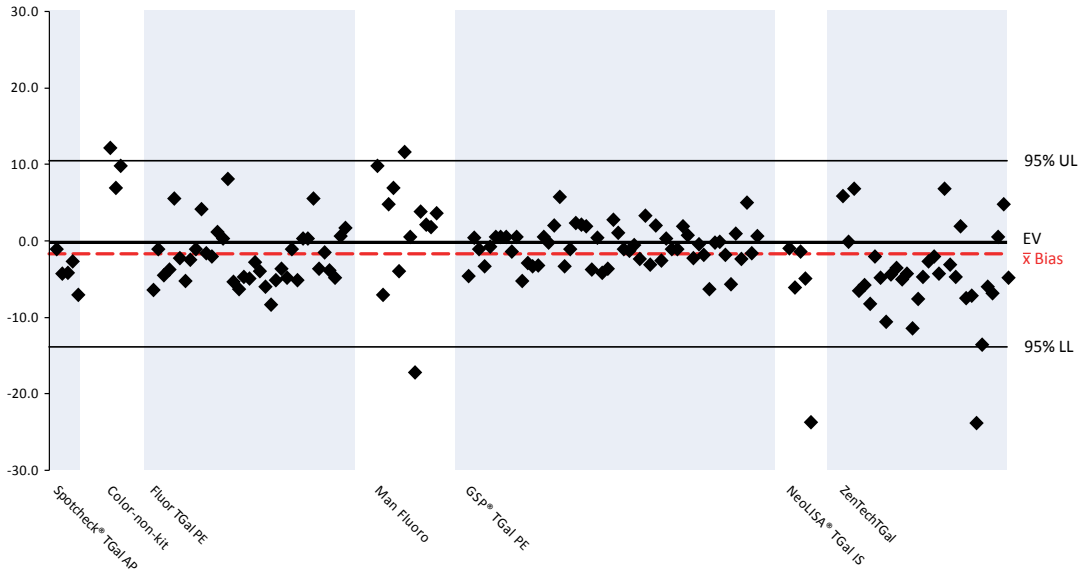
Specimen: 20224001005

Enriched: 25.0

CDC Characterized Value: 20.7

Participant Mean: 23.5

Participant Bias: -1.5



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 -1.5. One method demonstrates slightly lower bias than others.

Figure 6.
Bias Plot of Immunoreactive Trypsinogen (IRT) Values by Method
Quarter 4, Specimen 20224008001
Assayed Value (AV) = 142.9 ng/mL blood

IRT

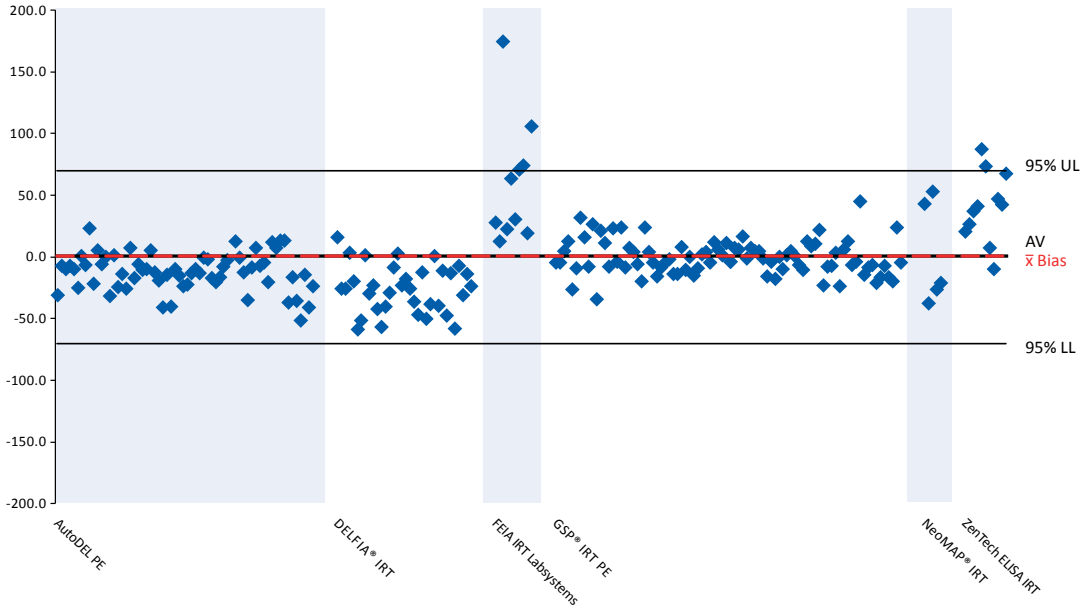
Specimen: 20224008001

Enriched: 250.0

CDC Characterized Value: 142.9

Participant Mean: 142.6

Participant Bias: -0.3



The IRT bias plot shows units of measure on the y-axis ranging from 200.0 ng/mL blood to -200.0 ng/mL blood. The bias for this plot is -0.3. A few methods show a moderately lower bias than others while one method shows a high bias.

Figure 7.
Bias Plot of Arginine (ARG) Values by Method
Quarter 3, Specimen 20223005001
Expected Value (EV) = 215.7 µmol/L blood

ARG

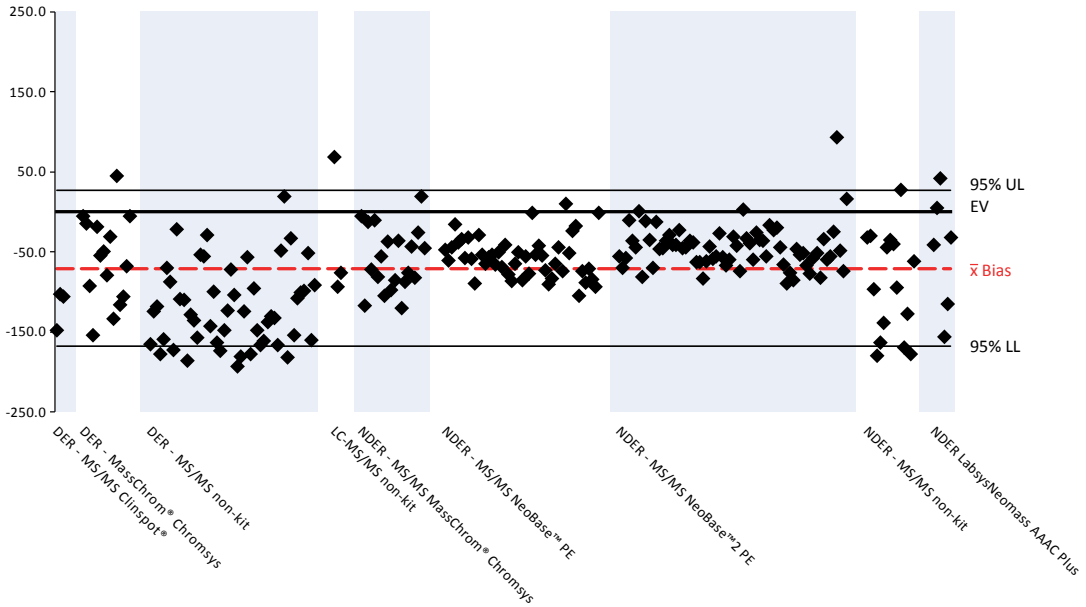
Specimen: 20223005001

Enriched: 180.0

CDC Characterized Value: 192.5

Participant Mean: 145.1

Participant Bias: -70.6



The ARG bias plot shows units of measure on the y-axis ranging from 250.0 µmol/L blood to -250.0 µmol/L blood. The bias for this plot is -70.6. This plot shows all methods demonstrated a low bias.

Figure 8.
Bias Plot of Citrulline (CIT) Values by Method
Quarter 1, Specimen 20221005001
Expected Value (EV) = 223.5 µmol/L blood

CIT

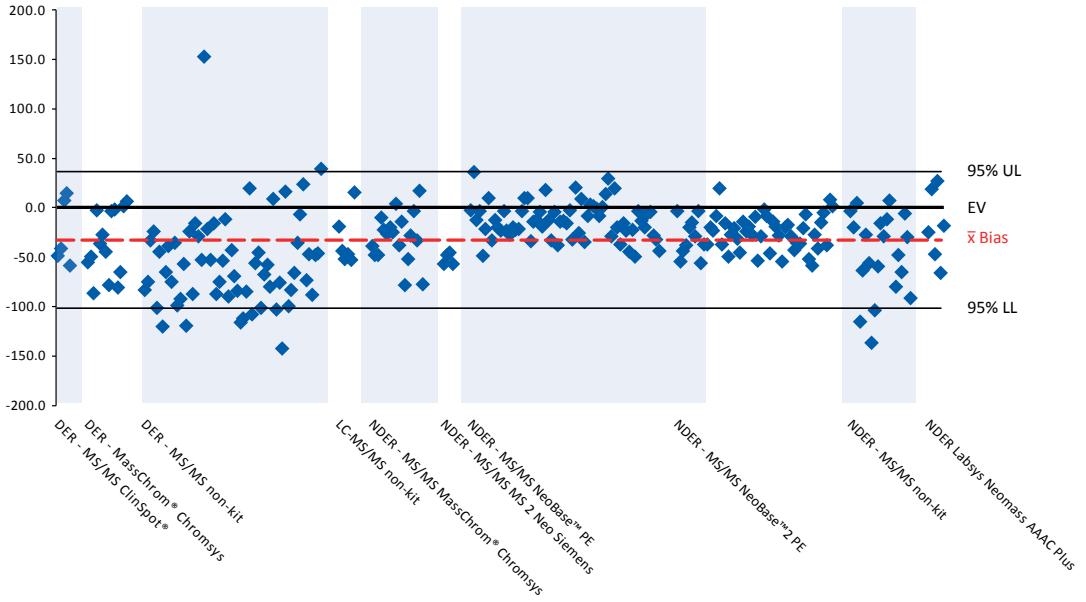
Specimen: 20221005001

Enriched: 180.0

CDC Characterized Value: 211.5

Participant Mean: 190.8

Participant Bias: -32.7



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 -32.7. This plot shows a moderately negative bias across methods.

Figure 9.
Bias Plot of Leucine (LEU) Values by Method
Quarter 3, Specimen 20223005004
Expected Value (EV) = 661.8 µmol/L blood

LEU

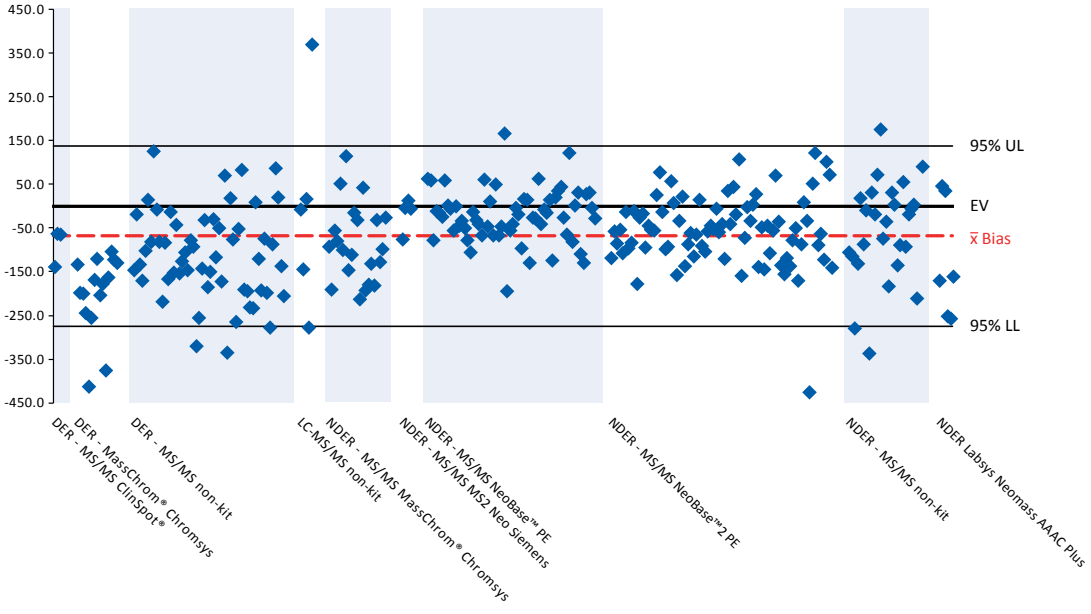
Specimen: 20223005004

Enriched: 475.0

CDC Characterized Value: 597.2

Participant Mean: 593.6

Participant Bias: -68.2



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 -68.2 This plot shows an even scatter across methods.

Figure 10.
Bias Plot of Methionine (MET) Values by Method
Quarter 4, Specimen 20224005002
Expected Value (EV) = 175.4 µmol/L blood

MET

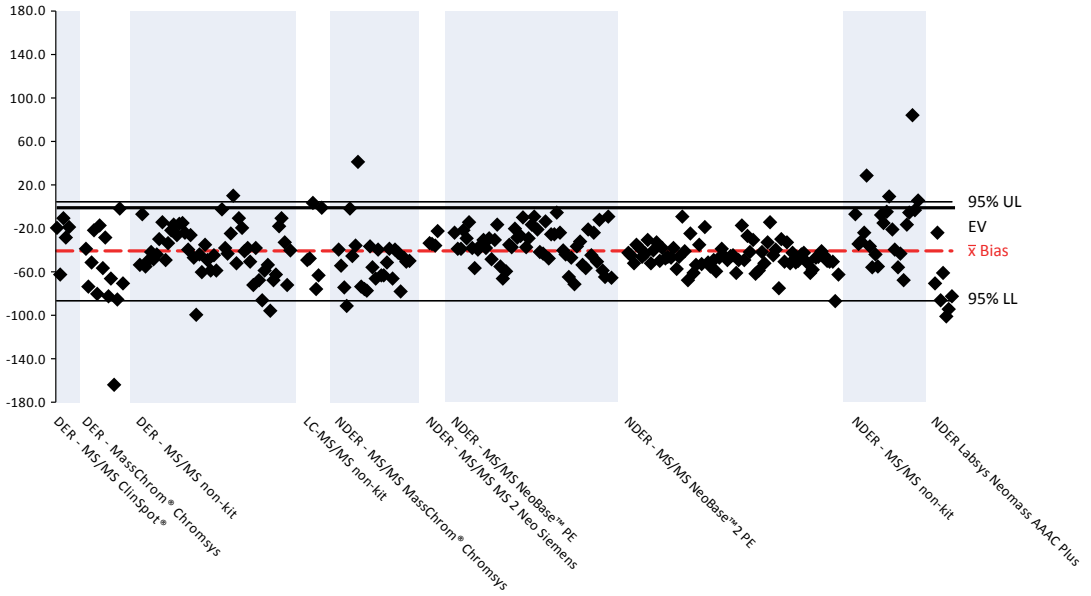
Specimen: 20224005002

Enriched: 150.0

CDC Characterized Value: 140.7

Participant Mean: 134.8

Participant Bias: -40.6



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 -40.6. This plot shows a moderately negative bias across methods.

Figure 11.
Bias Plot of Phenylalanine (PHE) Values by Method
Quarter 4, Specimen 20224005005
Expected Value (EV) = 313.0 µmol/L blood

PHE

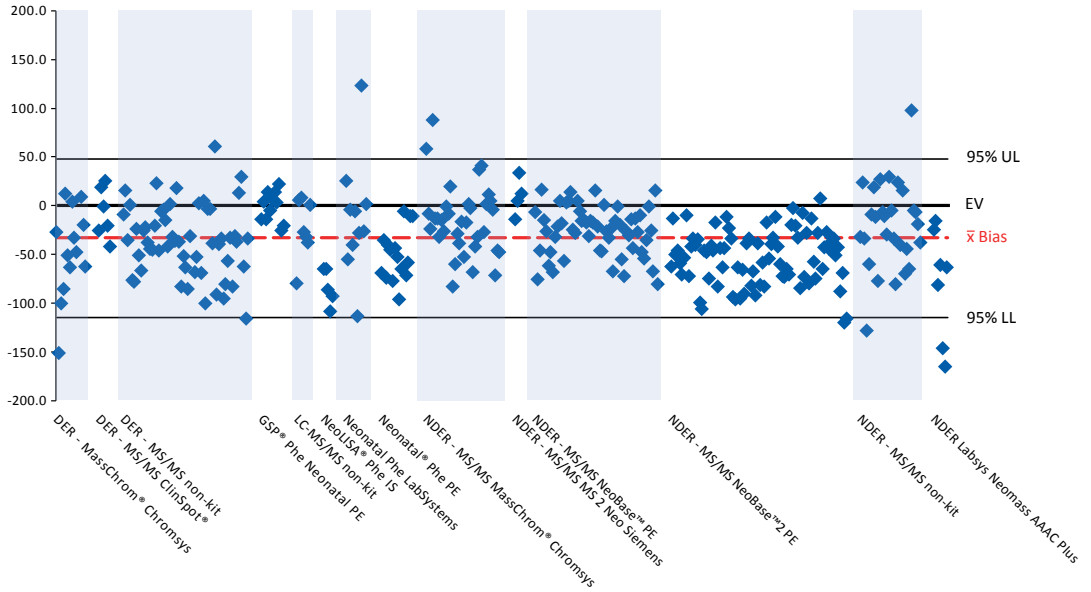
Specimen: 20224005005

Enriched: 250.0

CDC Characterized Value: 284.5

Participant Mean: 279.4

Participant Bias: -33.6



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 -33.6. This plot shows an even scatter across across the expected value for most methods.

SUAC

Specimen: 20224005001

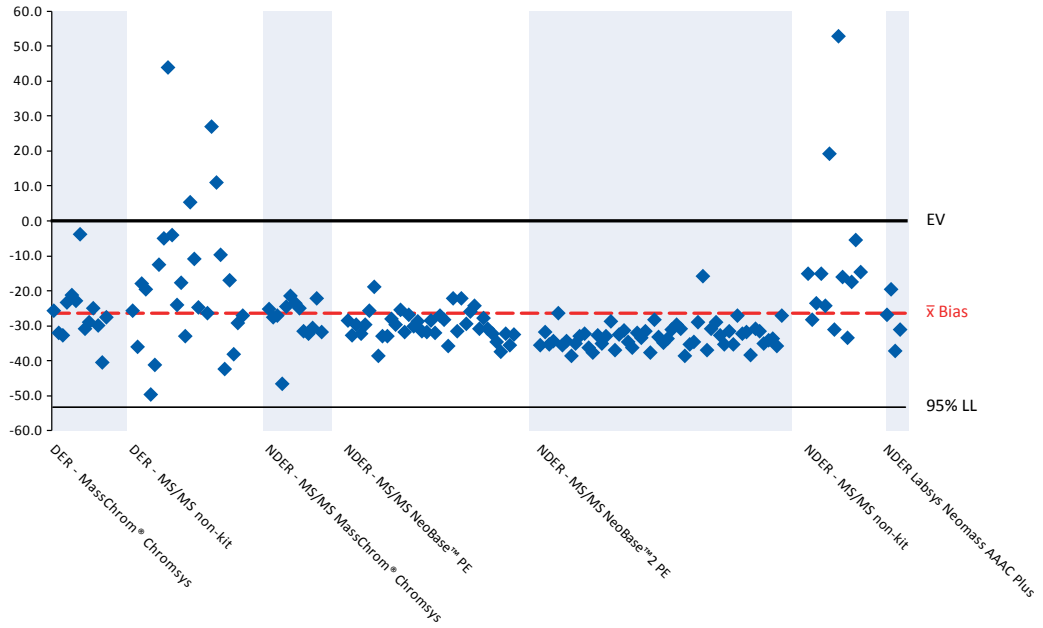
Enriched: 50.0

CDC Characterized Value: 31.5

Participant Mean: 23.4

Participant Bias: -26.6

Figure 12.
Bias Plot of Succinylacetone (SUAC) Values by Method
Quarter 4, Specimen 20224005001
Expected Value (EV) = 50.2 µmol/L blood



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 -26.6. This plot shows a strongly negative bias across methods, which is historical for this analyte.

TYR

Specimen: 20221005005

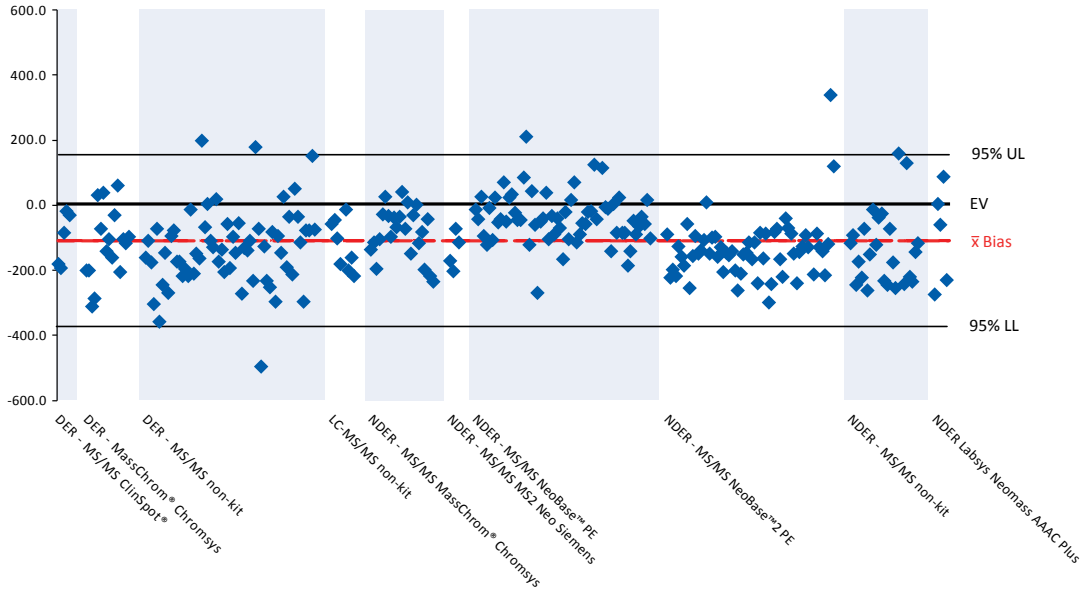
Enriched: 750.0

CDC Characterized Value: 752.4

Participant Mean: 689.5

Participant Bias: -108.4

Figure 13.
Bias Plot of Tyrosine (TYR) Values by Method
Quarter 1, Specimen 20221005005
Expected Value (EV) = 797.9 µmol/L blood



The TYR bias plot shows units of measure on the y-axis ranging from 600.0 µmol/L blood to -600.0 µmol/L blood. The bias for this plot is -108.4. This plot shows a slightly negative bias across methods.

VAL

Specimen: 20223005004

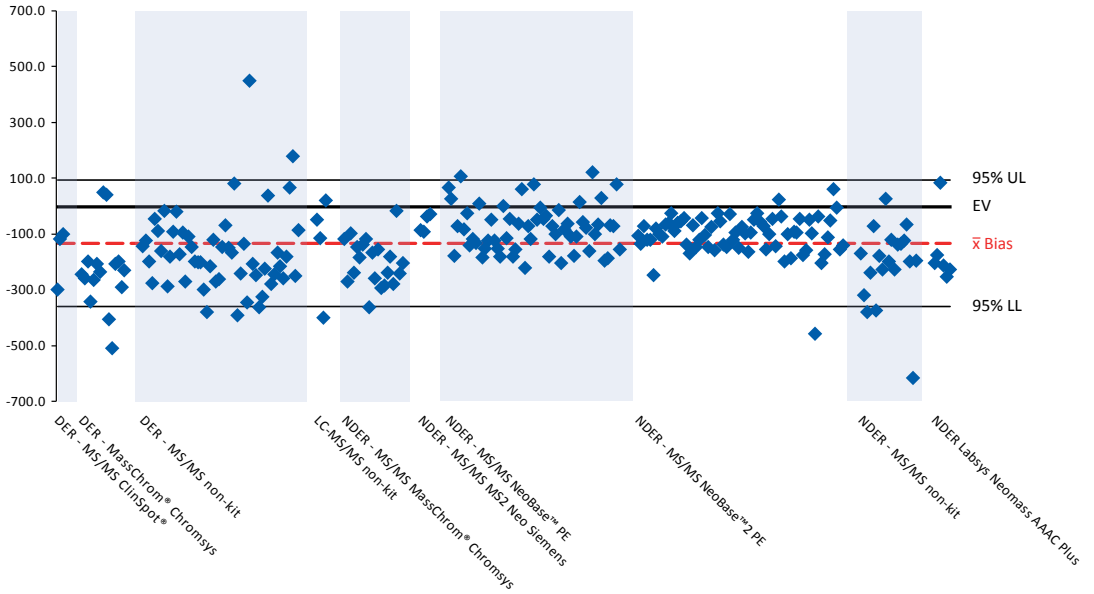
Enriched: 470.0

CDC Characterized Value: 592.4

Participant Mean: 545.0

Participant Bias: -132.3

Figure 14.
Bias Plot of Valine (VAL) Values by Method
Quarter 3, Specimen 20223005004
Expected Value (EV) = 677.3 µmol/L blood



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 -132.3 This plot shows a moderately negative bias across methods.

C0(L)

Specimen: 20221006003

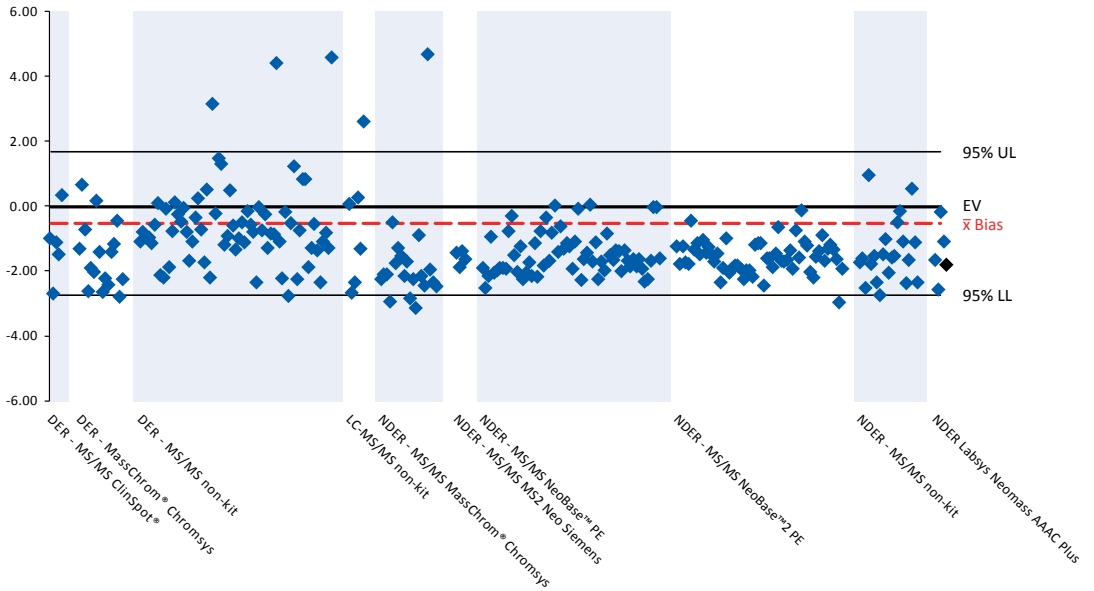
Enriched: 0.00

CDC Characterized Value: 5.44

Participant Mean: 4.08

Participant Bias: -0.56

Figure 15.
Bias Plot of Low Free Carnitine (C0(L)) Values by Method
Quarter 1, Specimen 20221006003
Expected Value (EV) = 5.35 µmol/L blood



The C0(L) bias plot shows units of measure on the y-axis ranging from 6.00 µmol/L blood to -6.00 µmol/L blood. The bias for this plot is -0.56. This plot shows a slightly negative bias across methods.

C2 (L)

Specimen: 20221006003

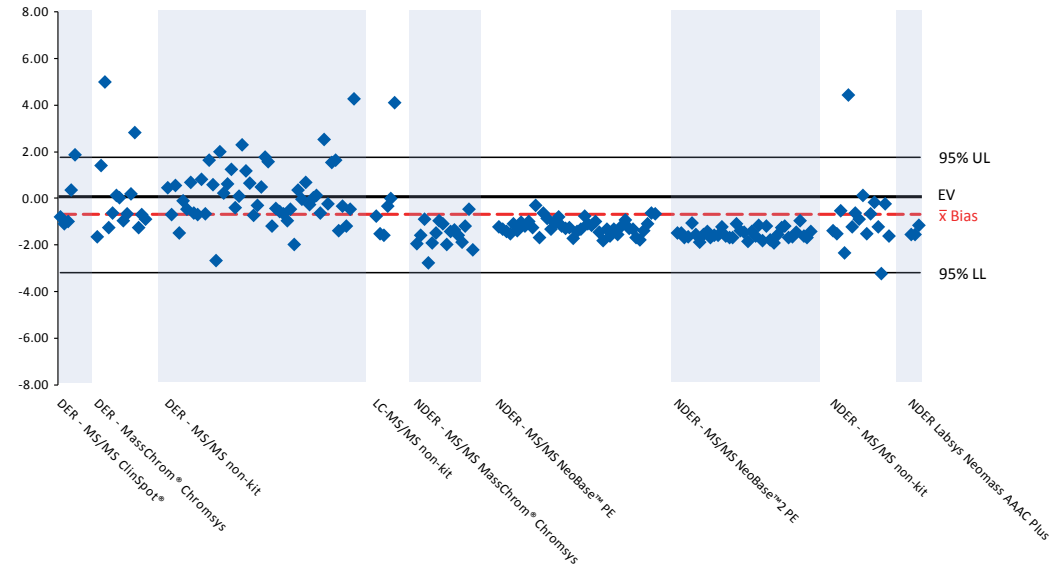
Enriched: 0.00

CDC Characterized Value: 5.54

Participant Mean: 3.85

Participant Bias: -0.74

Figure 16.
Bias Plot of Low Acetylcarnitine (C2(L)) Values by Method
Quarter 1, Specimen 20221006003
Expected Value (EV) = 4.59 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 -0.74. This plot shows three methods with a slightly more negative bias than the others.

C3

Specimen: 20223006004

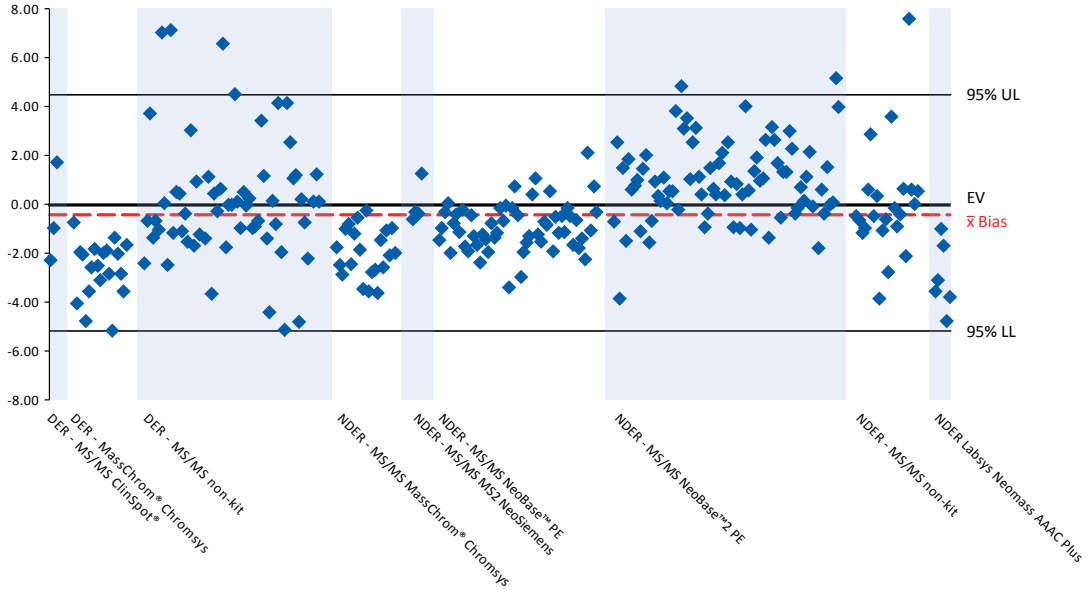
Enriched: 12.00

CDC Characterized Value: 13.69

Participant Mean: 12.79

Participant Bias: -0.37

Figure 17.
Bias Plot of Propionylcarnitine (C3) Values by Method
Quarter 3, Specimen 20223006004
Expected Value (EV) = 13.07 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 -0.37. This plot shows an even scatter across methods.

Figure 18.
Bias Plot of Malonylcarnitine (C3DC) Values by Method
Quarter 4, Specimen 20224006001
Expected Value (EV) = 13.02 µmol/L blood

C3DC

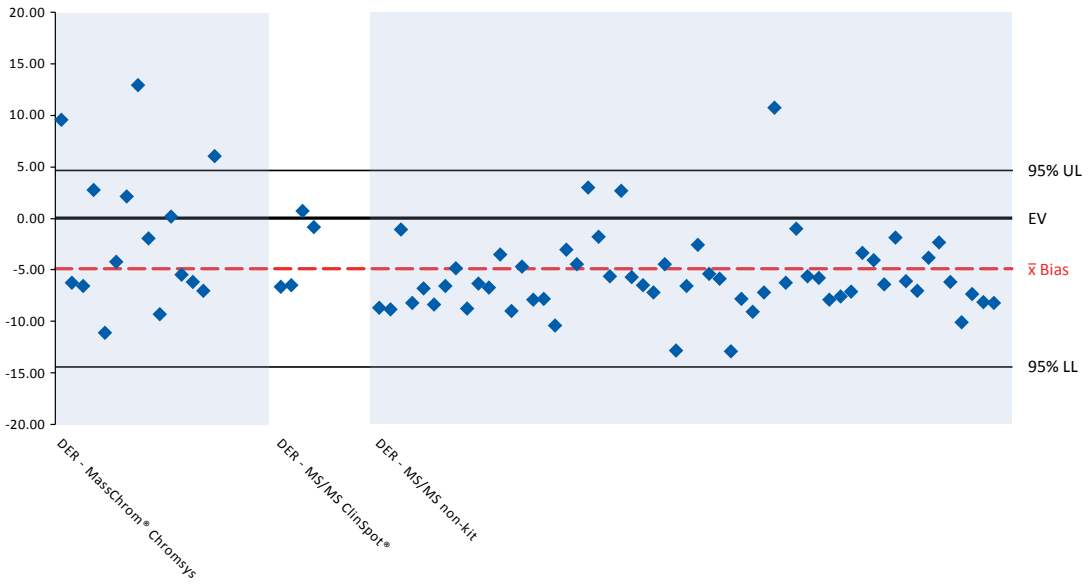
Specimen: 20224006001

Enriched: 13.00

CDC Characterized Value: 11.17

Participant Mean: 8.12

Participant Bias: -4.90



The C3DC bias plot shows units of measure on the y-axis ranging from 20.0 µmol/L blood to -30.0 µmol/L blood. The bias for this plot is -4.90. This plot shows a slightly negative bias across methods.

Figure 19.
Bias Plot of C3DC+C4OH Non-derivatized Values by Method
Quarter 1, Specimen 20221006005
Expected Value (EV) = 4.03 µmol/L blood

C3DC+C4OH

Specimen: 20221006005

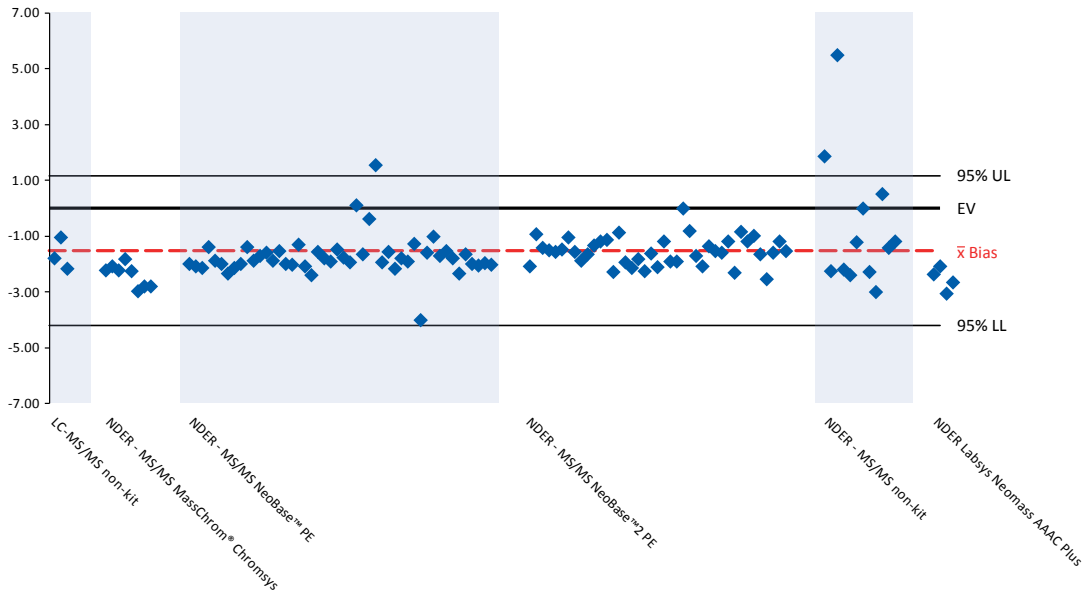
Enriched C3DC: 0.00

Enriched C4OH: 4.00

CDC Characterized Value: 1.74

Participant Mean: 2.52

Participant Bias: -1.51



The C3DC+C4OH bias plot shows units of measure on the y-axis ranging from 7.00 µmol/L blood to -7.00 µmol/L blood. The bias for this plot is -1.51. This plot shows a negative bias across methods as historically observed.

C4

Specimen: 20221006005

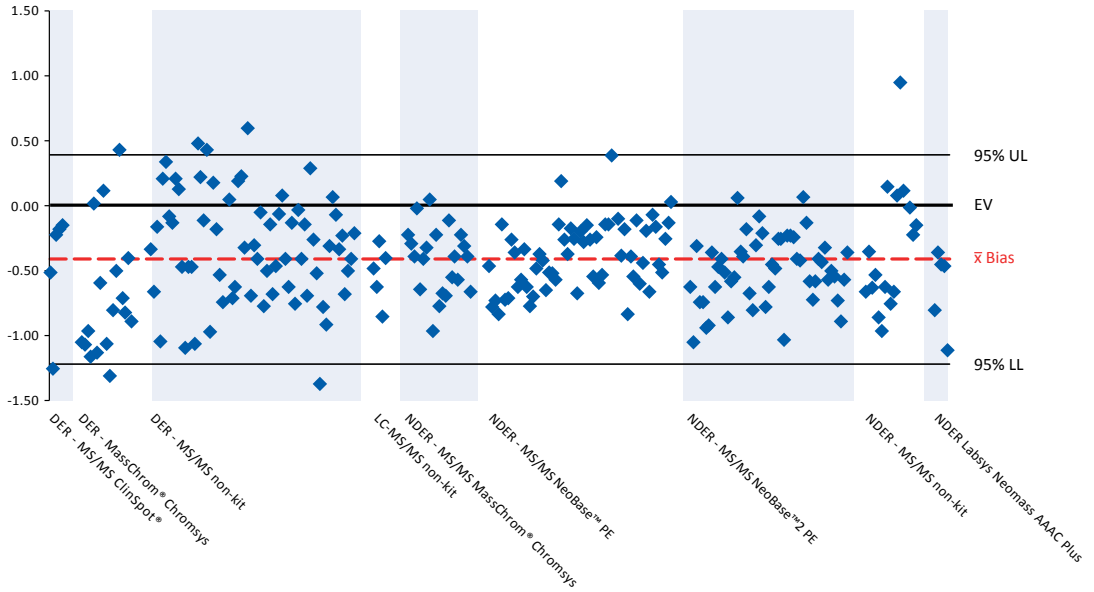
Enriched: 3.00

CDC Characterized Value: 2.81

Participant Mean: 2.66

Participant Bias: -0.41

Figure 20.
Bias Plot of Butyrylcarnitine (C4) Values by Method
Quarter 1, Specimen 20221006005
Expected Value (EV) = 3.07 µmol/L blood



The C4 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 -0.41. This plot shows a moderately negative bias across methods.

C4OH

Specimen: 20221006005

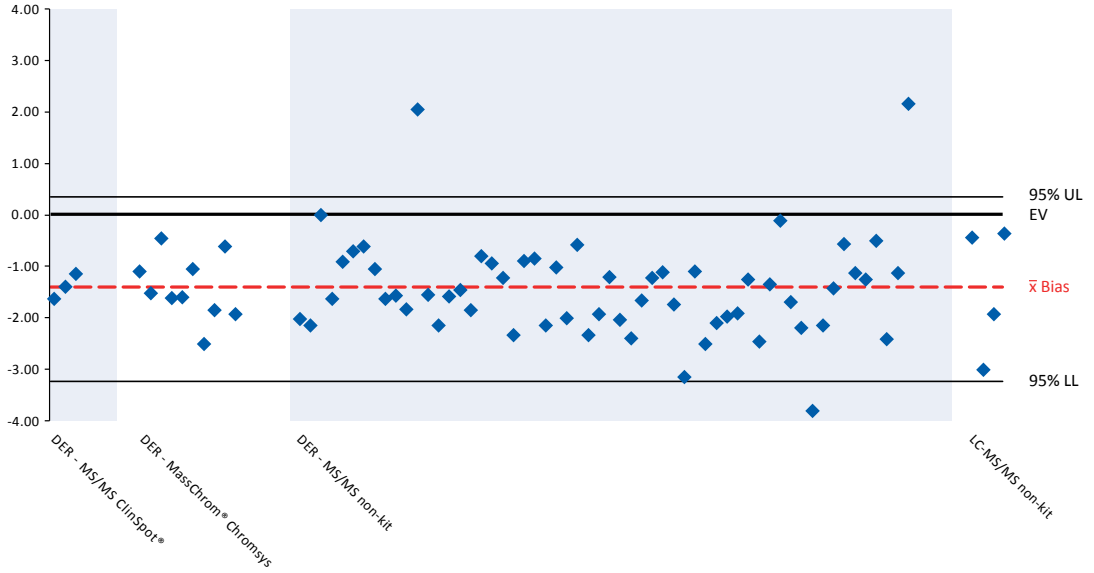
Enriched: 4.00

CDC Characterized Value: 3.34

Participant Mean: 2.61

Participant Bias: -1.43

Figure 21.
Bias Plot of Hydroxybutyrylcarnitine (C4OH) Values by Method
Quarter 1, Specimen 20221006005
Expected Value (EV) = 4.04 µmol/L blood



The C4OH bias plot shows units of measure on the y-axis ranging from 4.00 µmol/L blood to -4.00 µmol/L blood. The bias for this plot is -1.43. This plot shows a moderately negative bias across methods.

C5

Specimen: 20221006005

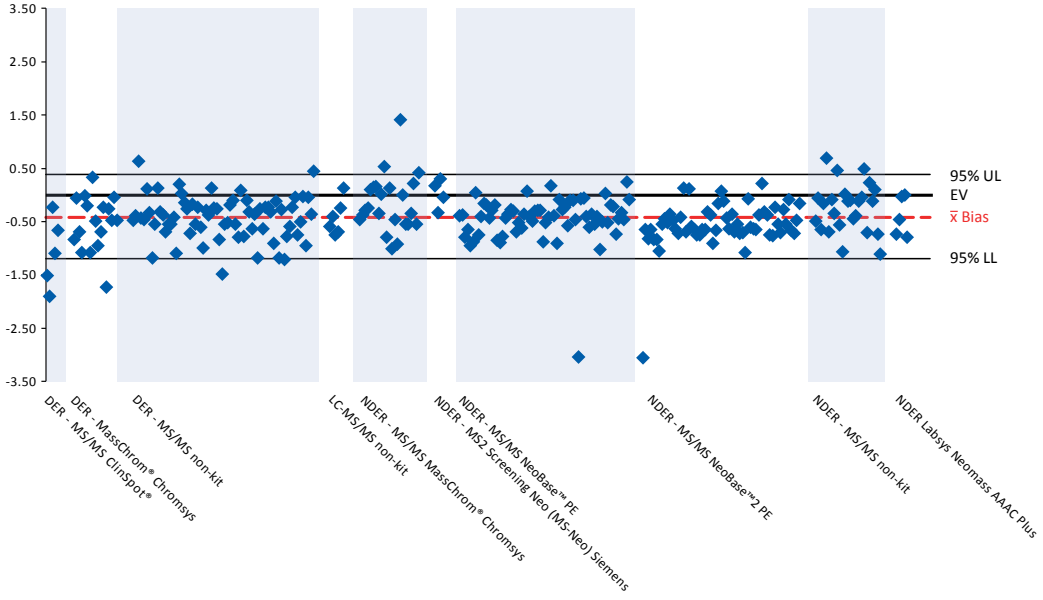
Enriched: 3.00

CDC Characterized Value: 3.25

Participant Mean: 2.64

Participant Bias: -0.41

Figure 22.
Bias Plot of Isovalerylcarnitine (C5) Values by Method
Quarter 1, Specimen 20221006005
Expected Value (EV) = 3.05 µmol/L blood



The C5 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 -0.41. This plot shows a slight negative bias across methods.

C5:1

Specimen: 20221006004

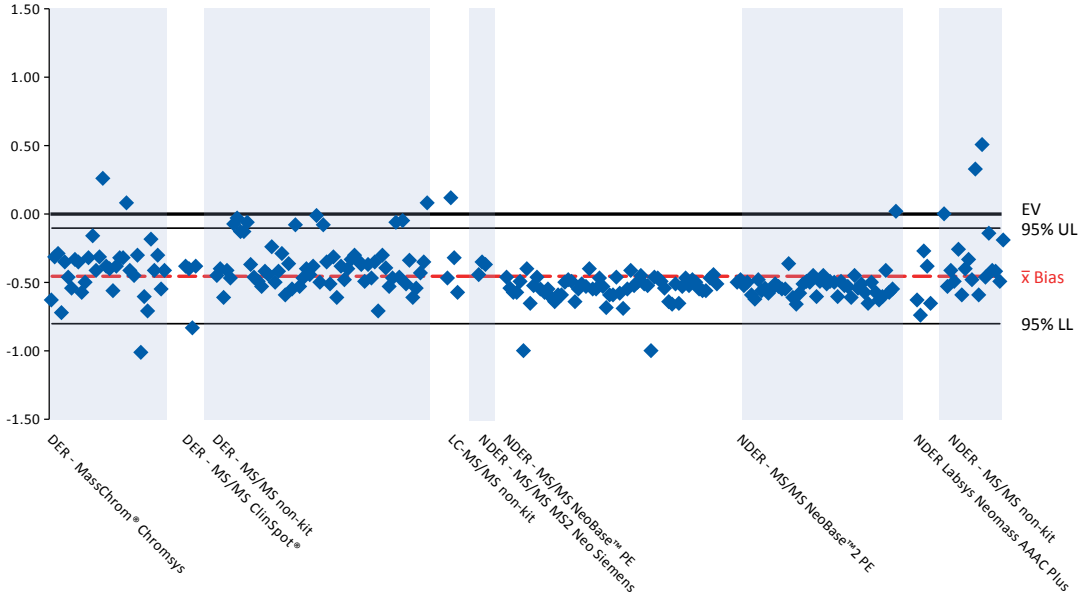
Enriched: 1.00

CDC Characterized Value: 0.69

Participant Mean: 0.56

Participant Bias: -0.45

Figure 23.
Bias Plot of Tiglylcarnitine (C5:1) Values by Method
Quarter 1, Specimen 20221006004
Expected Value (EV) = 1.01 µmol/L blood



The C5:1 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 -0.45. This plot shows a slightly negative bias across all methods.

C5DC

Specimen: 20223006001

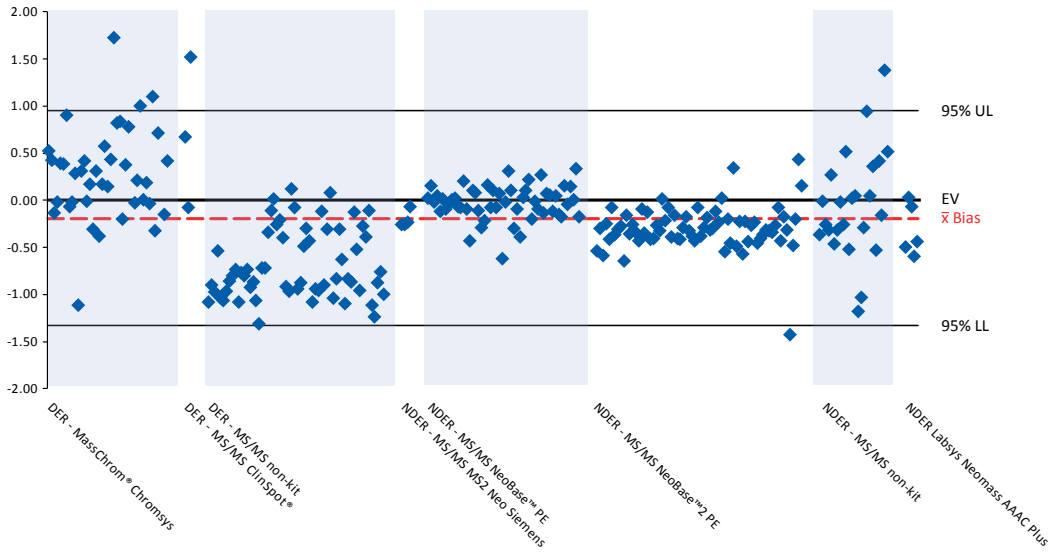
Enriched: 1.50

CDC Characterized Value: 1.55

Participant Mean: 1.33

Participant Bias: -0.19

Figure 24.
Bias Plot of Glutarylcarnitine (C5DC) Values by Method
Quarter 3, Specimen 20223006001
Expected Value (EV) = 1.52 µmol/L blood



The C5OH 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 -0.19. Two methods show moderate positive bias while the rest show slight negative bias.

C5OH

Specimen: 20224006004

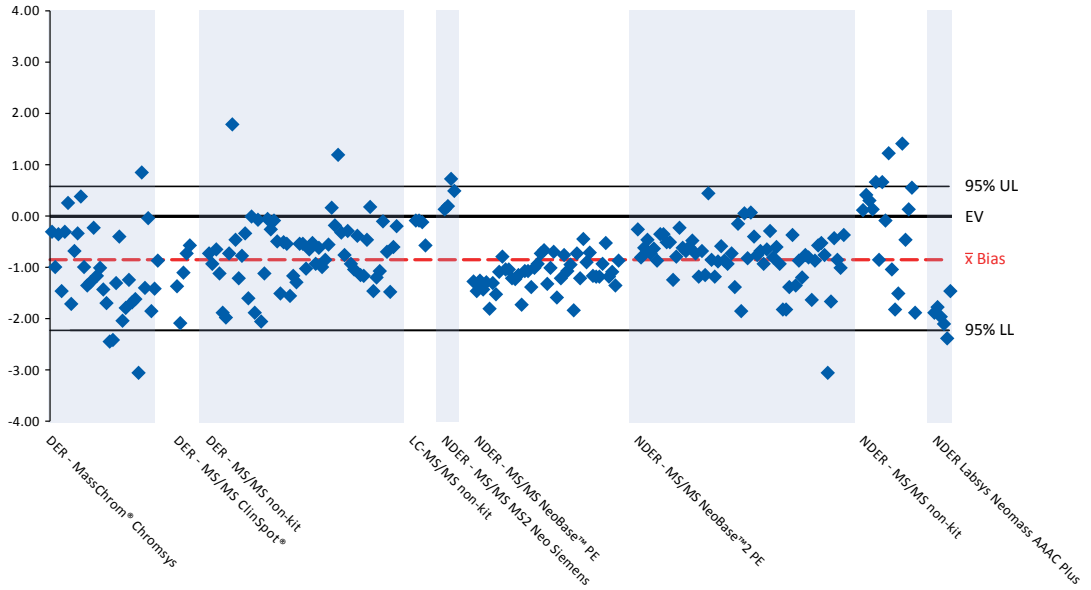
Enriched: 2.00

CDC Characterized Value: 3.26

Participant Mean: 2.55

Participant Bias: -0.84

Figure 25.
Bias Plot of Hydroxyisovalerylcarnitine (C5OH) Values by Method
Quarter 4, Specimen 20224006004
Expected Value (EV) = 3.39 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 -0.84. This plot shows a moderately negative bias across methods.

Figure 26.
Bias Plot of Hexanoylcarnitine (C6) Values by Method
Quarter 3, Specimen 20223006003
Expected Value (EV) = 1.41 µmol/L blood

C6

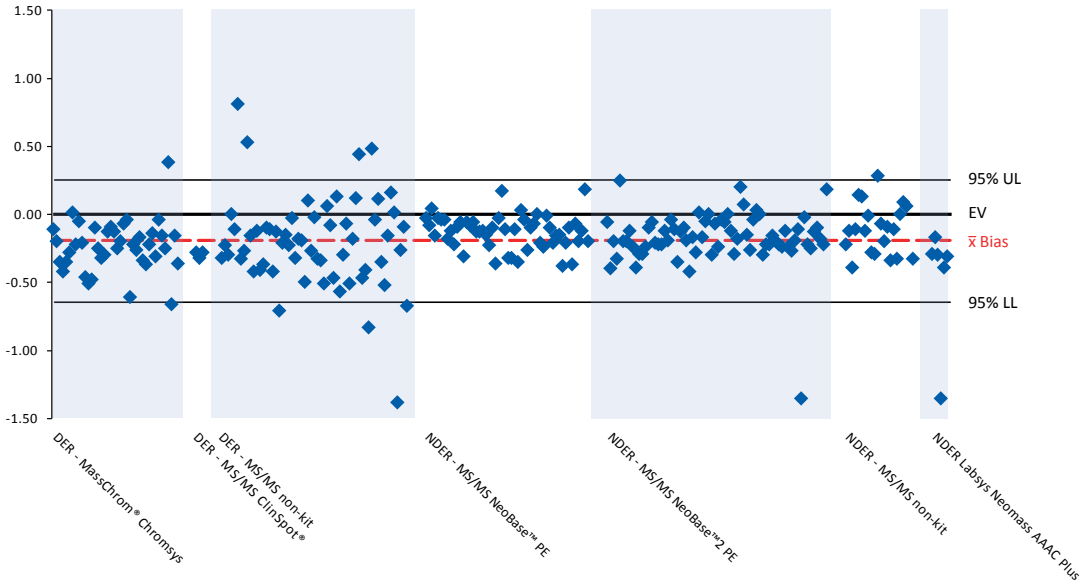
Specimen: 20223006003

Enriched: 1.40

CDC Characterized Value: 1.31

Participant Mean: 1.22

Participant Bias: -0.19



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 -0.19. This plot shows a moderately negative bias across all methods.

Figure 27.
Bias Plot of Octanoylcarnitine (C8) Values by Method
Quarter 3, Specimen 20223006003
Expected Value (EV) = 1.61 µmol/L blood

C8

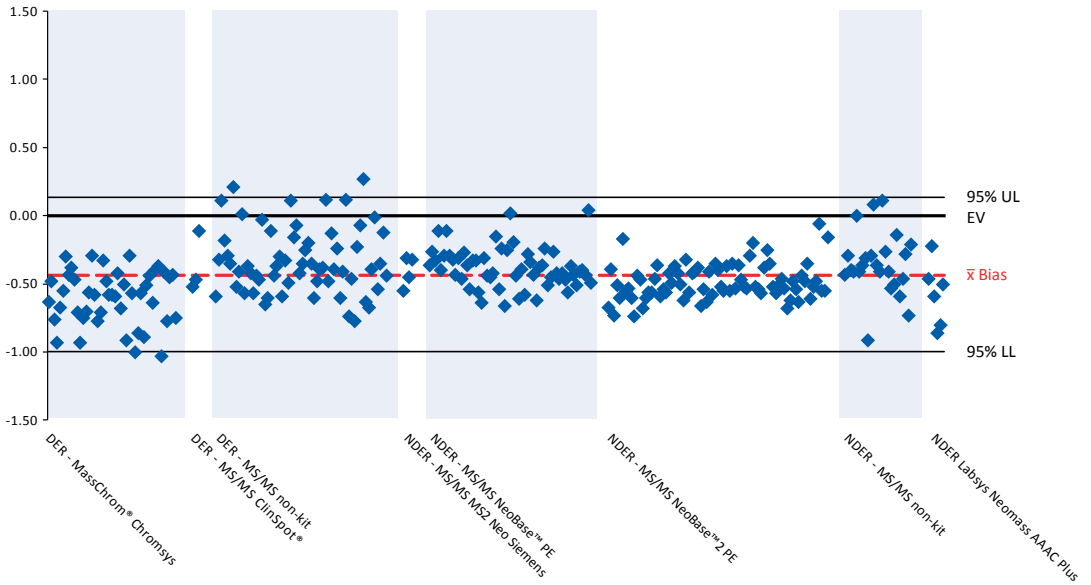
Specimen: 20223006003

Enriched: 1.60

CDC Characterized Value: 1.32

Participant Mean: 1.18

Participant Bias: -0.43



The C8 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 -0.43. This plot shows a negative bias across all methods.

Figure 28.
Bias Plot of Decanoylcarnitine (C10) Values by Method
Quarter 3, Specimen 20223006003
Expected Value (EV) = 1.22 µmol/L blood

C10

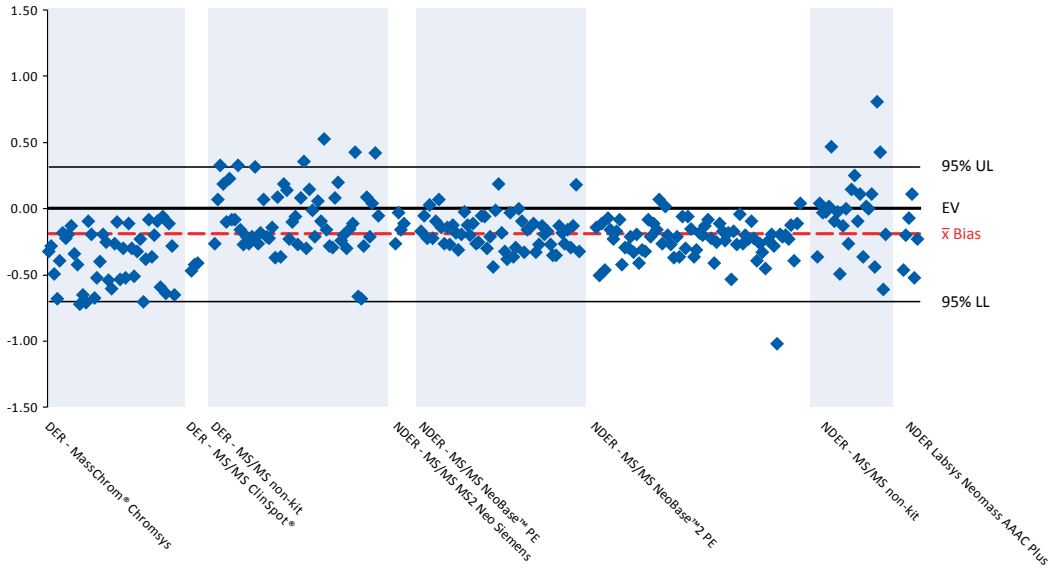
Specimen: 20223006003

Enriched: 1.20

CDC Characterized Value: 1.24

Participant Mean: 1.03

Participant Bias: -0.19



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 -0.19. This plot shows a slightly negative bias across all methods.

Figure 29.
Bias Plot of Decenoylcarnitine (C10:1) Values by Method
Quarter 3, Specimen 20223006003
Expected Value (EV) = 1.01 µmol/L blood

C10:1

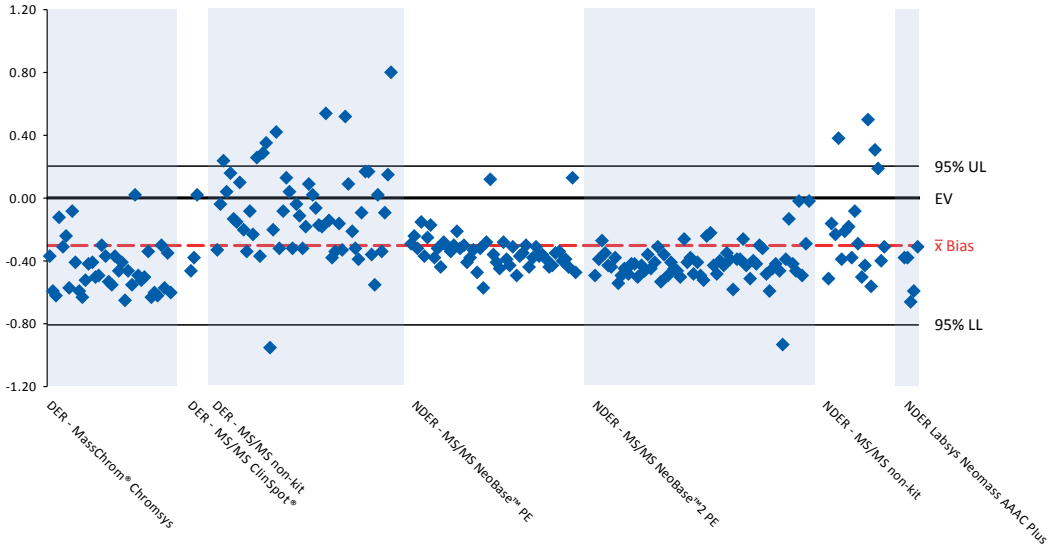
Specimen: 20223006003

Enriched: 1.00

CDC Characterized Value: 0.94

Participant Mean: 0.71

Participant Bias: -0.30



The C10:1 bias plot shows units of measure on the y-axis ranging from 1.20 µmol/L blood to -1.20 µmol/L blood. The bias for this plot is -0.30. This plot shows the derivitized MassChrom kit as having a slightly more negative bias than other reported methods

C10:2

Specimen: 20221006005

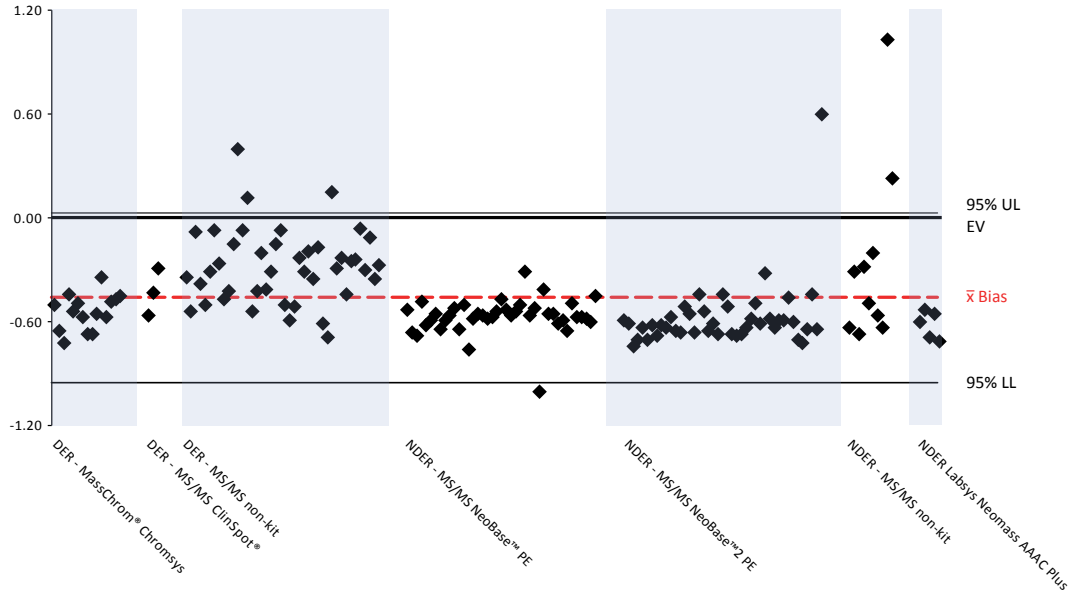
Enriched: 1.00

CDC Characterized Value: 0.87

Participant Mean: 0.54

Participant Bias: -0.46

Figure 30.
Bias Plot of Decadienoylcarnitine (C10:2) Values by Method
Quarter 1, Specimen 20221006005
Expected Value (EV) = 1.00 µmol/L blood



The C10:2 bias plot shows units of measure on the y-axis ranging from 1.20 µmol/L blood to -1.20 µmol/L blood. The bias for this plot is -0.46. This plot shows a moderately negative bias for all methods.

C14

Specimen: 20223006005

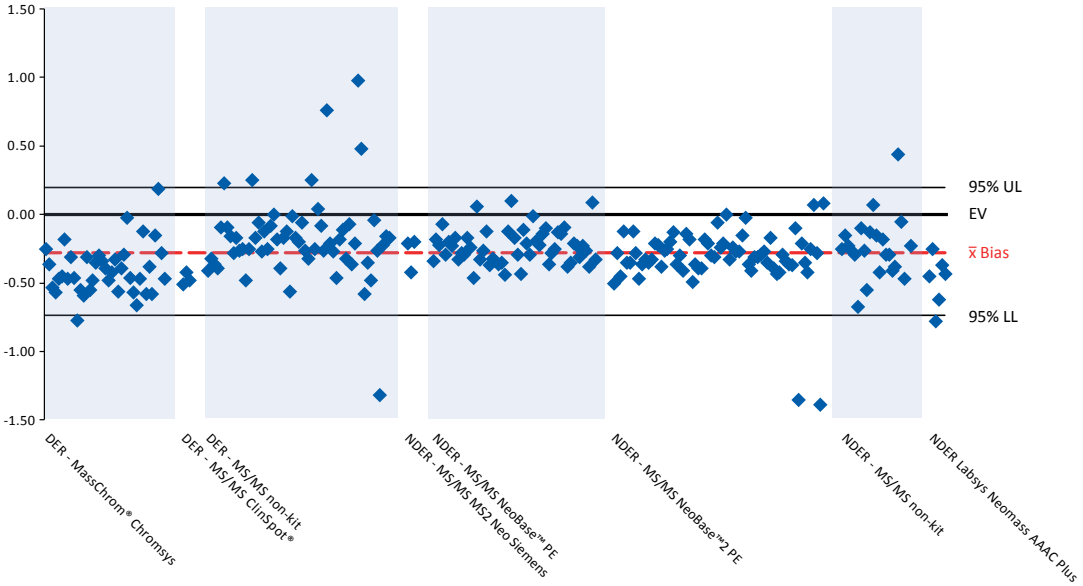
Enriched: 1.40

CDC Characterized Value: 1.30

Participant Mean: 1.19

Participant Bias: -0.27

Figure 31.
Bias Plot of Myristoylcarnitine (C14) Values by Method
Quarter 3, Specimen 20223006005
Expected Value (EV) = 1.46 µmol/L blood



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 -0.27. This plot shows a moderately negative bias across methods.

C14:1

Specimen: 20221006001

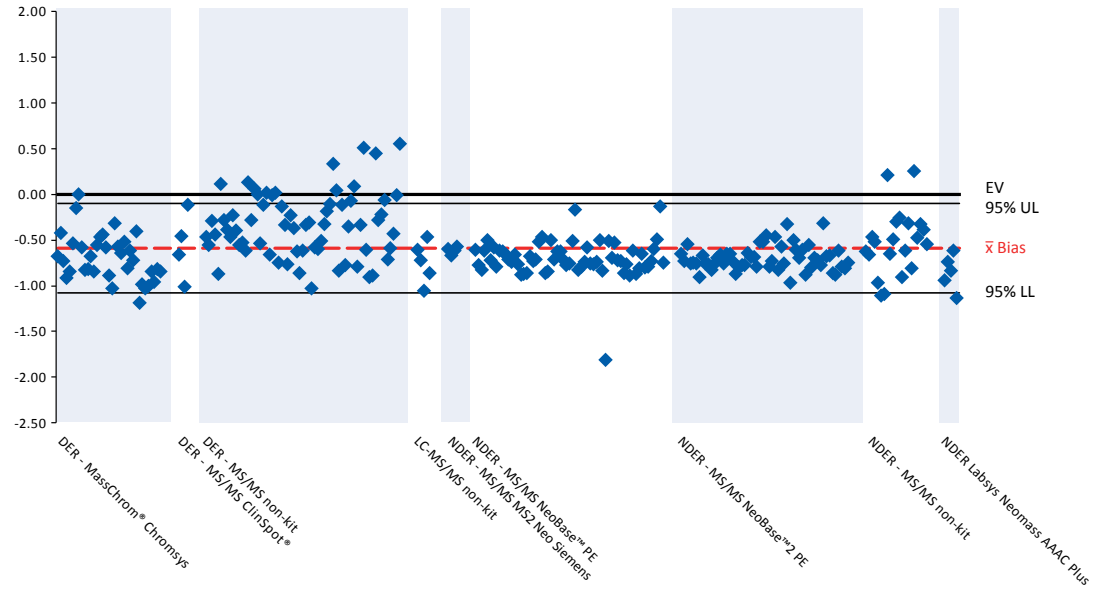
Enriched: 1.80

CDC Characterized Value: 1.40

Participant Mean: 1.23

Participant Bias: -0.59

Figure 32.
Bias Plot of Tetradecenoylcarnitine (C14:1) Values by Method
Quarter 1, Specimen 20221006001
Expected Value (EV) = 1.82 µmol/L blood



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 -0.59. This plot shows a moderately negative bias across methods.

C16

Specimen: 20221006005

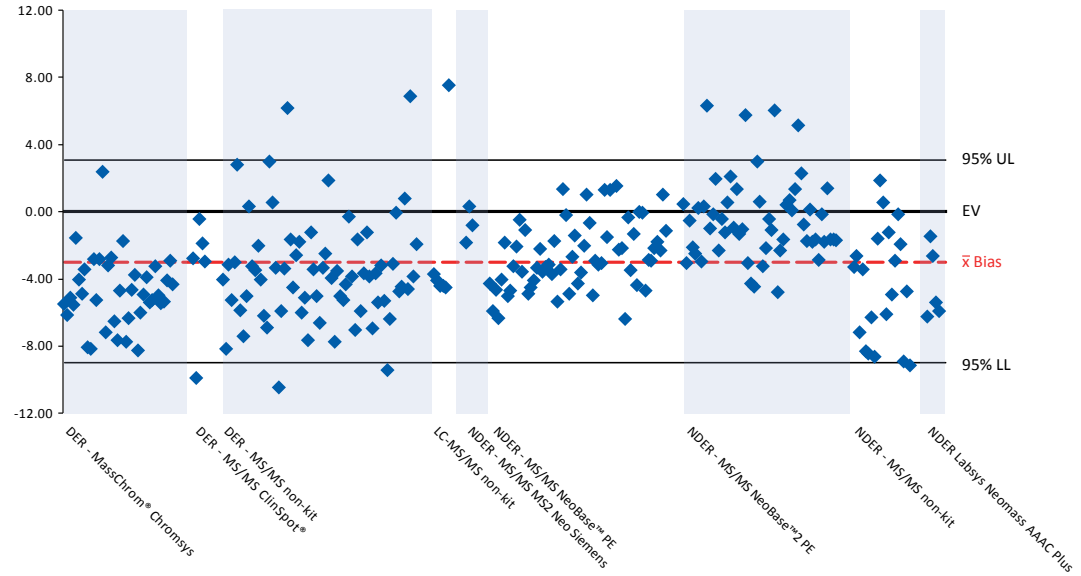
Enriched: 20.00

CDC Characterized Value: 18.74

Participant Mean: 17.48

Participant Bias: -2.94

Figure 33.
Bias Plot of Palmitoylcarnitine (C16) Values by Method
Quarter 1, Specimen 20221006005
Expected Value (EV) = 20.42 µmol/L blood



The C16 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 -2.94. This plot shows a moderately negative bias across methods.

C16OH

Specimen: 20223006005

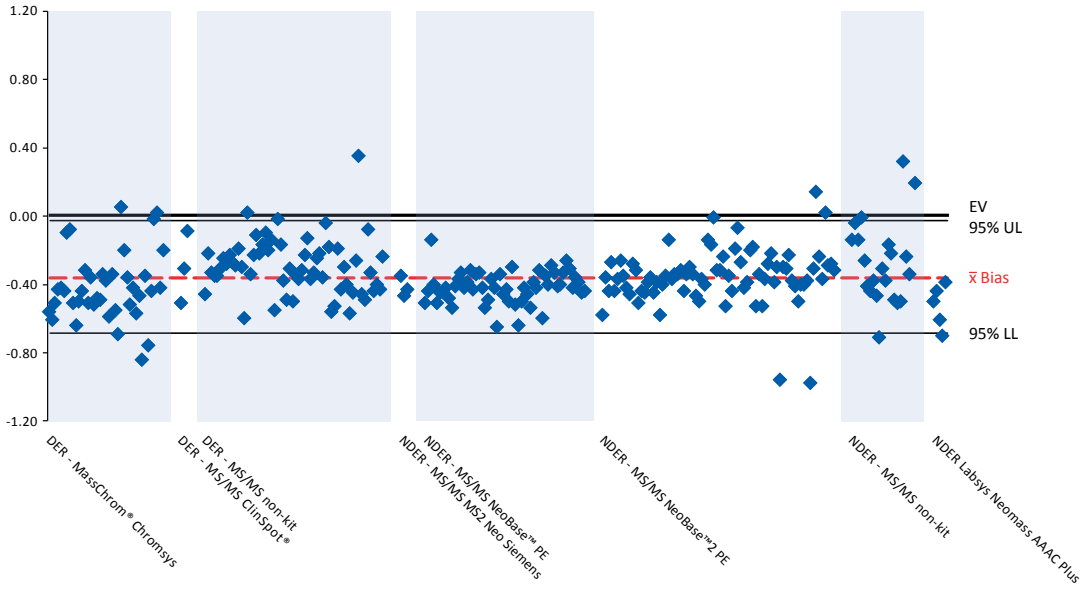
Enriched: 1.00

CDC Characterized Value: 0.90

Participant Mean: 0.65

Participant Bias: -0.36

Figure 34.
Bias Plot of Hydroxypalmitoylcarnitine (C16OH) Values by Method
Quarter 3, Specimen 20223006005
Expected Value (EV) = 1.01 µmol/L bloodd



The C16OH bias plot shows units of measure on the y-axis ranging from 1.20 µmol/L blood to -1.20 µmol/L blood. The bias for this plot is -0.36. This plot shows a negative bias and tight scatter across methods.

C18

Specimen: 20221006005

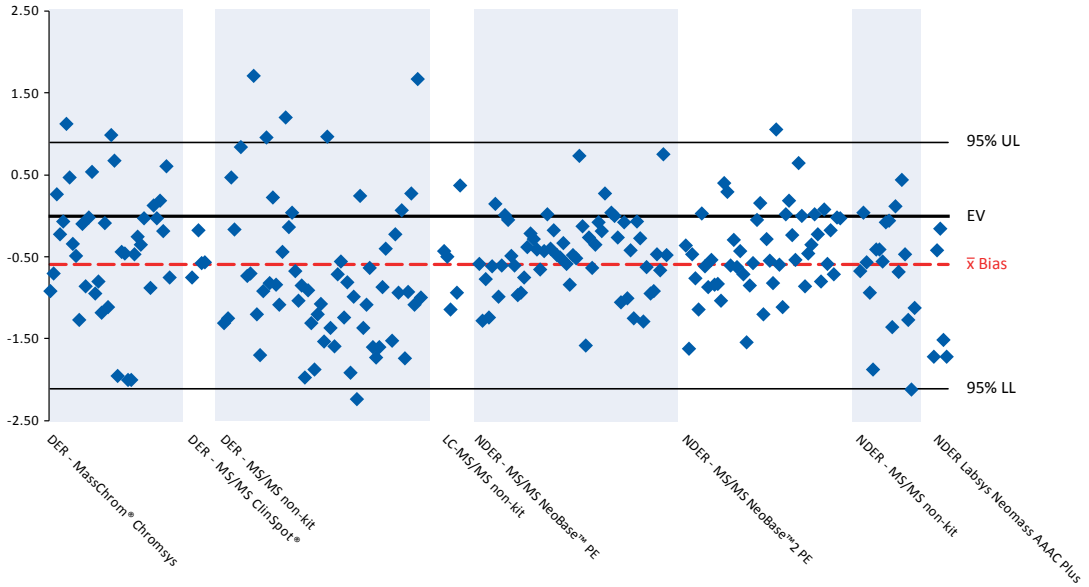
Enriched: 5.00

CDC Characterized Value: 5.02

Participant Mean: 4.73

Participant Bias: -0.61

Figure 35.
Bias Plot of Stearoylcarnitine (C18) Values by Method
Quarter 1, Specimen 20221006005
Expected Value (EV) = 5.34 µmol/L blood



The C18 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 -0.61 This plot shows even scatter across methods.

C18:1

Specimen: 20221006005

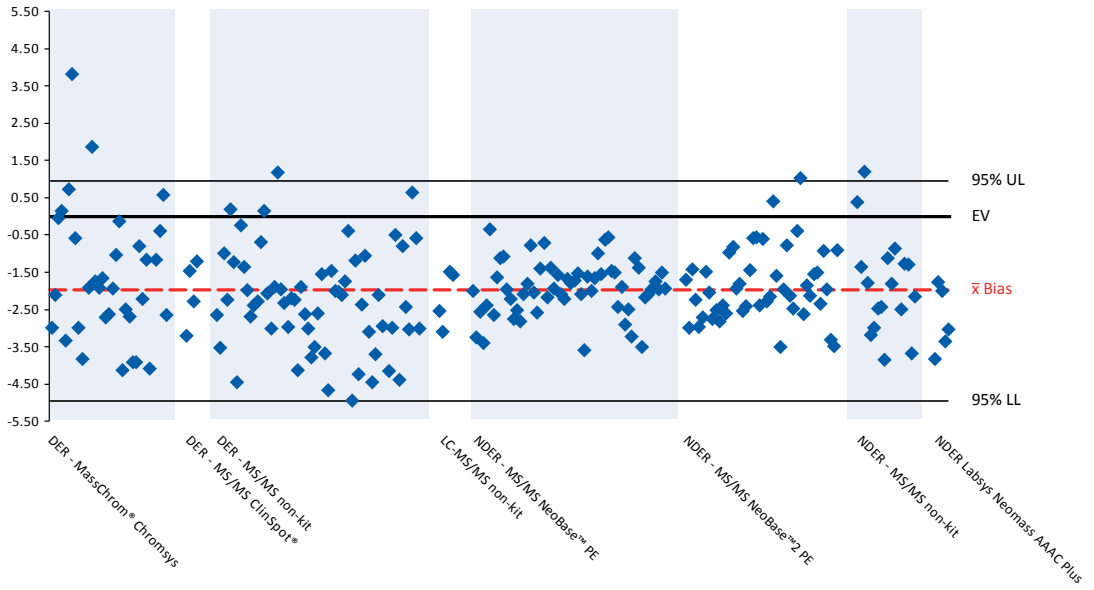
Enriched: 8.00

CDC Characterized Value: 7.20

Participant Mean: 6.59

Participant Bias: -1.99

Figure 36.
Bias Plot of Oleoylcarnitine (C18:1) Values by Method
Quarter 1, Specimen 20221006005
Expected Value (EV) = 8.58 µmol/L blood



The C18:1 bias plot shows units of measure on the y-axis ranging from 5.50 µmol/L blood to -5.50 µmol/L blood. The bias for this plot is -1.99. This plot shows low bias across all methods.

C18OH

Specimen: 20223006005

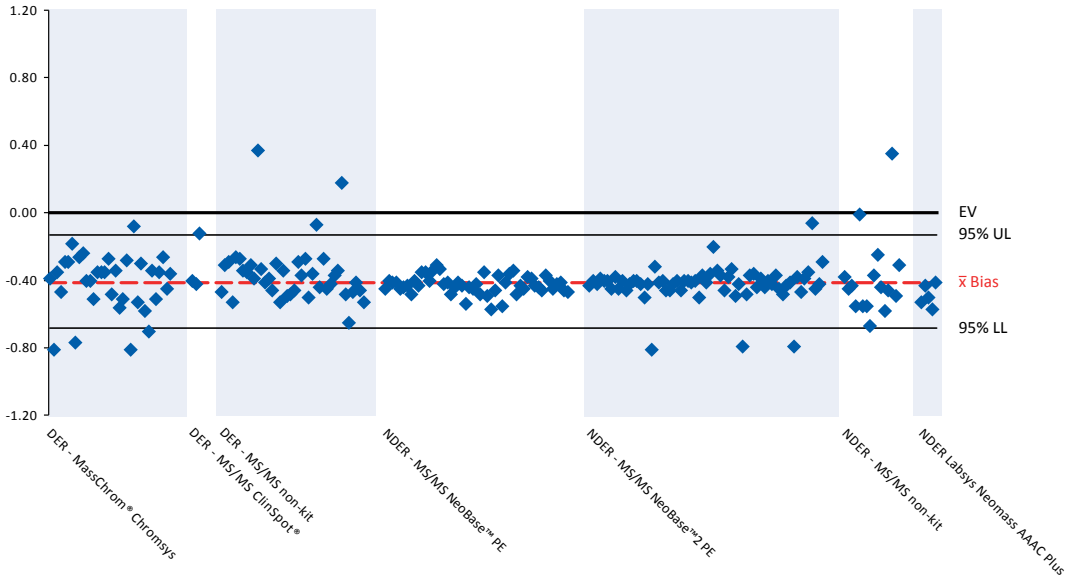
Enriched: 0.80

CDC Characterized Value: 0.43

Participant Mean: 0.40

Participant Bias: -0.41

Figure 37.
Bias Plot of Hydroxystearoylcarnitine (C18OH) Values by Method
Quarter 3, Specimen 20223006005
Expected Value (EV) = 0.81 µmol/L blood



The C18OH bias plot shows units of measure on the y-axis ranging from 1.20 µmol/L blood to -1.20 µmol/L blood. The bias for this plot is -0.41. 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] Watson MS, Lloyd-Puryear MA, Mann MY, Rinaldo P, Howell RR, eds. Newborn screening: towards a uniform screening panel and system. Genet Med 2006;8(5) Suppl: 12S–252S. https://www.acmg.net/PDFLibrary/NBS-Uniform-Screening-Panel.pdf.

[2] Clinical and Laboratory Standards Institute. Dried blood spot specimen collection for newborn screening. 7th ed. CLSI Standard NBS01. Malvern, PA: Clinical and Laboratory Standards Institute; 2021.

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