Supplemental Data

S1. Supplemental Table 1. Examples of reference materials prepared using the original CLSI C37-A guideline

Material	Analyte(s)	Organization	Published reference (if available)	Notes from commutability assessment
NIST 967 and 967a, Creatinine in frozen human serum	creatinine	NIST	1. Dodder NG, Tai SS, Sniegoski LT, Zhang NF, Welch MJ. Certification of creatinine in a human serum reference material by GC-MS and LC-MS. *Clin Chem* 2007;53:1694–9. 2. Myers G, Miller G, Coresh J, Fleming J, Greenberg N, Greene T, Hostetter T, Levey A, Panteghini M, Welch M, Eckfeldt J. Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clin Chem.*2006; 52 (1): 5-18 *3.* National Kidney Disease Education Program. Commutability study results: NIST SRM 967 and CAP LN24: spring/summer 2006. **https://www.niddk.nih.gov/health-information/communication-programs/nkdep/laboratory-evaluation/glomerular-filtration-rate/creatinine-standardization/commutability-study** (accessed August 2019).* 4. SRM 967a Certificate of Analysis. https://www-s.nist.gov/srmors/certificates/967A.pdf	Commutability study was performed for 15 clinical laboratory measuring systems from 7 IVD manufacturers. The NIST 967 material was found to be commutable among all of the measuring systems. * For SRM 967a, no separate commutability studies were conducted.
NIST 971 and 971a, Hormones in Frozen Human Serum	cortisol, progesterone, testosterone, total thyroxine (T4) total 3,3',5-triiodothyronine (T3)	NIST	SRM 971 Certificate of Analysis. https://www-s.nist.gov/srmors/certificates/971.pdf SRM 971a Certificate of Analysis. https://www-s.nist.gov/srmors/certificates/971a.pdf	Commutability evaluation is not available.
NIST 972a, Vitamin D Metabolites in Frozen Human Serum	25-hydroxyvitamin D2, 25-hydroxyvitamin D3, 3-epi-25-hydroxyvitamin D3, 24R,25-dihydroxyvitamin D3	NIST	1.Sempos C, Vesper H, Phinney K, Thienpont L, Coates P and the Vitamin D Standardization Program (VDSP). Vitamin D status as an international issue: National surveys and the problem of standardization. *Scand J Clin Lab Invest*. 2012; 72 (sup243): 32-40. 2.Phinney K, Tai S, Bedner M, Camara J, et al. Development of an Improved Standard Reference Material for Vitamin D Metabolites in Human Serum. *Anal Chem.* 2017; 89(9):4907-4913. 3. Phinney K, Sempos C, Vesper H, Botelho J, Tai S, Camara J, Wise S, Myers G, Durazo-Arvizu R, Tian L, Eckfeldt J, Hoofnagle A, Miller G, Bachmann L, et al. Baseline Assessment of 25-Hydroxyvitamin D Reference Material and Proficiency Testing/External Quality Assurance Material Commutability: A Vitamin D Standardization Program Study. *J AOAC Int.* 2017; 100(5):1288-1293.* 4. SRM 972a Certificate of Analysis. https://www-s.nist.gov/srmors/certificates/972A.pdf	Results from 9 laboratories performing 3 LC-MS/MS and 6 immunoassays (IA) were published. Two JCTLM -recognized RMPs (NIST and University of Ghent) were used to assign target values to materials. All four levels of NIST 972a were found commutable with all IAs and one of the LC-MS/MS methods. Only some of the levels were commutable with the other two LC-MS/MS methods. Overall good commutability for IA and LC-MS/MS methods was observed. *

Material	Analyte(s)	Organization	Published reference (if available)	Notes from commutability assessment
NIST 2973, Vitamin D Metabolites in Frozen Human Serum (High Level)	25-hydroxyvitamin D2, 25-hydroxyvitamin D3, 3-epi-25-hydroxyvitamin D3, 24R,25-dihydroxyvitamin D3	NIST	1.Tai S, Nelson M, Bedner M, Lang B, Phinney K, Sander L, Yen J, Betz J, Sempos C, Wise S. Development of Standard Reference Material (SRM) 2973 Vitamin D Metabolites in Frozen Human Serum (High Level). *J AOAC Int.* 2017; 100 (5): 1294-1303. 2. SRM 2973 Certificate of Analysis. https://www-s.nist.gov/srmors/certificates/2973.pdf *	Commutability study results are provided in the SRM 2973 Certificate of Analysis. It was found that SRM 2773 is commutable for majority of IA and LC-based methods used in the study.*
NIST 1951c, Lipids in Frozen Human Serum	TC, TG, HDL-C, LDL-C	NIST	SRM 1951c Certificate of Analysis. https://www-s.nist.gov/srmors/certificates/1951C.pdf	The certificate is referencing the commutability study provided in the original CLSI C37A. No separate commutability studies were conducted.
NIST 2378, Fatty Acids in Frozen Human Serum	myristic acid, palmitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid, alpha-linoleic acid, gamma-linoleic acid, arachidonic acid, EPA, DPA, DHA	NIST	1.Benner BA Jr, Schantz MM, Powers CD, Schleicher RL, Camara JE, Sharpless KE, Yen JH, Sniegoski LT. Standard Reference Material (SRM) 2378 fatty acids in frozen human serum. Certification of a clinical SRM based on endogenous supplementation of polyunsaturated fatty acids. *Anal Bioanal Chem*. 2018; 410(9): 2321-2329. 2. SRM 2378 Certificate of Analysis. https://www-s.nist.gov/srmors/certificates/2378.pdf	Commutability evaluation is not available.
NMIJ CRM 6401-b, cortisol in human serum (4 concentration levels)	cortisol	National Metrology Institute of Japan (NMIJ) (prepared by Reference Materials Institute for Clinical Chemistry Standards (Kanagawa, Japan)	NMIJ CRM 6401-b Certificate of Analysis. https://unit.aist.go.jp/nmij/english/refmate/crm/certificate_sds/42/6401b_en.pdf	Commutability evaluation is not available
NMIJ CRM 6402-a, aldosterone in human serum	aldosterone		Nishikawa T, Omura M, Kawaguchi M, Takatsu A, Satoh F, Ito S, Kurihara I, Itoh H, Yanase T, Shibata H, Oki Y, Naruse M, Sakurai K, Sasamoto H, Kuwa K. Calibration and evaluation of routine methods by serum certified reference material for aldosterone measurement in blood. *Endocrine J.(Japan Endocrine Society).* 2016;Sept:1-16	Commutability evaluation is not available
LNE CRM BIO 101a	glucose, creatinine, total cholesterol, total glycerides, HDL-C, LDL-C	French Labarotorie d'National (LNE)	https://www.lne.fr/en/metrology-measurement/certified-reference-materials-clinically-relevant-biomarkers (accessed August 2019)	LNE website states these CRMs are commutable for all major routine methods.
JCCRM 611-1, Certified Reference Material for Measurements of Glycated Albumin in Human Serum	glycated albumin	Reference Material Institute for Clinical Chemistry Standards (ReCCS)	www.reccs.or.jp/en/files/item_certif.000010.004.pdf (accessed August 2019)	Commutability evaluation is not available.

Material	Analyte(s)	Organization	Published reference (if available)	Notes from commutability assessment
JCCRM 211-3, Certified Reference Material for Measurement of Total Cholesterol in Human Serum	total cholesterol	Reference Material Institute for Clinical Chemistry Standards ReCCS	www.reccs.or.jp/pdf/JCCRM211.pdf (accessed August 2019)	Commutability evaluation is not available.
HRM-2011A, Sodium, chloride, copper, selenium and phosphorous in frozen human serum	Na, Cl, Cu, Se, P	Health Science Authority, Singapore		Commutability evaluation is not available.
HRM-3002A, Creatinine, glucose, total cholesterol, total glycerides, urea and uric acid in frozen human serum	glucose, creatinine, total cholesterol, total glycerides, urea, uric acid	Health Science Authority, Singapore		Commutability evaluation is not available
HRM-3002B, Creatinine, glucose, total cholesterol, total glycerides, HDL-cholesterol, LDL-cholesterol, urea and uric acid in frozen human serum	creatinine, glucose, total cholesterol, total glycerides, HDL-cholesterol, LDL-cholesterol, urea, uric acid	Health Science Authority, Singapore		Commutability evaluation is not available.

S2.

Supplemental Table 2. Examples of studies that used materials prepared using the original C37-A guideline.

Analyte(s)	Published Reference	Notes from commutability assessment
Studies that used pooled serum only		
HDL-cholesterol	Baadenhuijsen H, Steigstra H, Cobbaert C, Kuypers A, Weykamp C, Jansen R. Commutability Assessment of Potential Reference Materials Using a Multicenter Split-Patient-Sample Between-Field-Methods (Twin-Study) Design: Study within the Framework of the Dutch Project "Calibration 2000" *Clin Chem. 2002;* 48(9): 1520-1525.	Materials prepared based on C37A guideline demonstrated commutability among 43 laboratory pairs using 8 different commercial methods.
Total cholesterol HDL-cholesterol LDL-cholesterol triglycerides apo A-1 apo B	Cobbaert C, Weykamp C, Baadenhuijsen H, Kuypers A, Lindemans J, Jansen R. Selection, Preparation, and Characterization of Commutable Frozen Human Serum Pools as Potential Secondary Reference Materials for Lipid and Apolipoprotein Measurements: Study within the Framework of the Dutch Project "Calibration 2000" *Clin Chem.* 2002; 48(9): 1526-1538.	Materials prepared based on C37A guideline demonstrated commutability among 43 laboratory pairs using 6 different commercial methods for total cholesterol. HDL- and LDL-cholesterol, and triglycerides; and 3 commercial methods for Apo A1 and B.
cortisol IgE	Palmer-Toy DE, Wang E, Winter, et al. Comparison of pooled fresh frozen serum to proficiency testing material in College of American Pathologists surveys: cortisol and immunoglobulin E. *Arch Pathol Lab Med*. 2005.129:305–309.	Materials prepared based on the C37A guideline were assumed to be commutable.
cortisol ferritin thyroxin free thyroxine thyroid-stimulating hormone	Steele BW, Wang E, Palmer-Toy DE, Killeen A, Elin RJ, Klee G. Total long-term within-laboratory precision of cortisol, ferritin, thyroxine, free thyroxine, and thyroid-stimulating hormone assays based on a College of American Pathologists Fresh Frozen Serum Study: do available methods meet medical needs for precision? *Arch Pathol Lab Med.* 2005;129:318–322	Materials prepared based on the C37A guideline were assumed to be commutable.
ferritin folate vitamin B12	Bock JL, Endres DB, Elin RJ, Wang E, Rosenzweig B, Klee G. Comparison of fresh frozen serum to traditional proficiency testing material in a College of American Pathologists survey for ferritin, folate, and vitamin B12. *Arch Pathol Lab Med.* 2005; 129:323–327.	Materials prepared based on the C37A guideline were assumed to be commutable
chorionic gonadotropin–related components	Knight GJ, Palomaki G, Klee G, Schreiber W, Cole L. A comparison of human chorionic gonadotropin–related components in fresh frozen serum with the proficiency testing material used by the College of American Pathologists. *Arch Pathol Lab Med.* 2005;129:328–330.	Materials prepared based on the C37A guideline were assumed to be commutable
creatinine	Miller G, Myers G, Ashwood E. et al. Creatinine measurement: state of the art in accuracy and interlaboratory harmonization. *Arch Pathol Lab Med.* 2005; 129:297–304.	Materials prepared based on the C37A guideline were assumed to be commutable
alpha fetoprotein, carcinoembryonic antigen, human chorionic gonadotropin prostate-specific antigen	Schreiber WE, Endres DB, McDowell GA. et al. Comparison of fresh frozen serum to proficiency testing material in College of American Pathologists surveys: alpha fetoprotein, carcinoembryonic antigen, human chorionic gonadotropin, and prostatespecific antigen. *Arch Pathol Lab Med*; 2005; 129:331–337.	Materials prepared based on the C37A guideline were assumed to be commutable
LDL-cholesterol HDL-cholesterol	Delatour V, Liu Q, Vesper H. Commutability Assessment of External Quality Assessment Materials with the Difference in Bias Approach: Are Acceptance Criteria Based on Medical Commutability Assessment of External Quality Assessment Materials with the Difference in Bias Approach: Are Acceptance Criteria Based on Medical Requirements too Strict? *Clin Chem;* 2016; 62(12): 1670–1673.	Thirty one medical laboratories participated in the commutability study of five C-37 serum pools. The results showed that 78-100% of LDL-C pairwise comparisons and 47%-81% of HDL-C pairwise comparisons demonstrated commutability.
LDL-cholesterol HDL-cholesterol	Korzun WJ, Nilsson G, Bachmann LM, Myers GL,Sakurabayashi I, Nakajima K, Nakamura M, Shamburek RD, Remaley AT, Miller WG. Difference in bias approach for commutability assessment: application to frozen pools of human serum measured by 8 direct	Based on random error criteria, all four frozen pools were commutable for HDL-C methods and one frozen pool was commutable for

Analyte(s)	Published Reference	Notes from commutability assessment
	methods for HDL and LDL cholesterol. *Clin Chem.* 2015;61:1107–13.	LDL-C. Fewer combinations were commutable when medical requirement criteria were used.
LDL-cholesterol HDL-cholesterol	Miller WG, Myers GL, Sakurabayashi I, Bachmann LM, Caudill SP, Dziekonski A, Edwards S, Kimberly MM, Korzun WJ, Leary ET, Nakajima K, Nakamura M, Nilsson G, Shamburek RD, Vetrovec GW, Warnick GR, Remaley AT. Seven direct methods for measuring HDL and LDL cholesterol compared with ultracentrifugation reference measurement procedures. *Clin Chem.* 2010; 56:977– 86.	Commutability of pooled serum was reported in *Clin Chem.* 2015;61:1107–13.
25-hydroxyvitamin D	1.Sempos C, Vesper H, Phinney K, Thienpont L, Coates P and the Vitamin D Standardization Program (VDSP). Vitamin D status as an international issue: National surveys and the problem of standardization. *Scand J Clin Lab Invest.* 2012; 72 (sup243): 32-40. 2.Phinney K, Sempos C, Vesper H, Botelho J, Tai S, Camara J, Wise S, Myers G, Durazo-Arvizu R, Tian L, Eckfeldt J, Hoofnagle A, Miller G, Bachmann L, et al. Baseline Assessment of 25-Hydroxyvitamin D Reference Material and Proficiency Testing/External Quality Assurance Material Commutability: A Vitamin D Standardization Program Study. *J AOAC Int*. 2017; 100(5):1288-1293.*	Results from 9 laboratories performing 3 LC-MS/MS and 6 immunoassays (IA) were published. Two JCTLM -recognized RMPs (NIST and University of Ghent) were used to assign target values to materials. All four levels of NIST 972a were found commutable with all IAs and one of the LC-MS/MS methods. Only some of the levels were commutable with the other two LC-MS/MS methods. Overall good commutability for IA and LC-MS/MS methods was observed. *
thyroid-stimulating hormone thyroxine triiodothyronine free thyroxine free triiodothyronine	Steele BW. Wang W, Klee G. Analytical bias of thyroid function tests: analysis of a College of American Pathologists fresh frozen serum pool by 3900 clinical laboratories. *Arch Pathol Lab Med*. 2005;129:310–317	Materials prepared based on the C37A guideline were assumed to be commutable
overview of CAP fresh frozen serum (FFS)	Klee G. and Killeen A. College of American Pathologists 2003 Fresh Frozen Serum Proficiency Testing Studies. *Arch Pathol Lab Med*. 2005; 129:292-293	Materials prepared based on the C37A guideline were assumed to be commutable.

Analyte(s)	Published Reference	Notes from commutability assessment
sodium chloride calcium magnesium phosphorus potassium urea creatinine glucose albumin total protein alkaline phosphatase amylase alanine aminotransferase aspartate aminotransferase	1. Cobbaert C, Weykamp C, Franck F, de Jonge R, Kuypers A, Steigstra H, Klein Gunnewiek J, van Loon D, Jansen R. Systematic monitoring of standardization and harmonization status with commutable EQA-samples—Five year experience from the Netherlands. *Clinica Chimica Acta*. 2012; 414:234–240 2.Baadenhuijsen H, Weykamp C, Kuypers A, Franck P, Jansen R and Cobbaert C. Commuteerbaarheid van het huidige monstermateriaal in de SKML-rondzendingen van de algemene klinische chemie. *Ned Tijdschr Klin Chem Labgeneesk.* 2008; 33: 154-157 (in danish).*	Materials prepared based on C37A guideline demonstrated commutability for six clinical laboratory measuring systems.*
creatinine	1.Delanghe J, Cobbaert C, Galteau MM, Harmoinen A, Jansen R, Kruse R, Laitinen P, Thienpont L, Wuyts B, Weykamp C, Panteghini M. Trueness verification of actual creatinine assays in the European market demonstrates a disappointing variability that needs substantial improvement. An international study in the framework of the EC4 creatinine standardization working group. Clin Chem Lab Med. 2008;46(9):1319–1325 2.Baadenhuijsen H, Weykamp C, Kuypers A, Franck P, Jansen R and Cobbaert C. Commuteerbaarheid van het huidige monstermateriaal in de SKML-rondzendingen van de algemene klinische chemie. Ned Tijdschr Klin Chem Labgeneesk. 2008; 33: 154-157 (in danish).*	Materials prepared based on C37A guideline demonstrated commutability for six clinical laboratory measuring systems.*

Analyte(s)	Published Reference	Notes from commutability assessment
alkaline phosphatase alanine aminotransferase aspartate aminotransferase lactate dehydrogenase γ-glutamyltransferase creatine kinase	1 .Baadenhuijsen H, Kuypers A, Weykamp C, Cobbaert C, Jansen R. External quality assessment in The Netherlands: time to introduce commutable survey specimens. Lessons from the Dutch ''Calibration 2000'' project. Clin Chem Lab Med 2005;43:304–7. 2.Baadenhuijsen H, Weykamp C, Kuypers A, Franck P, Jansen R and Cobbaert C. Commuteerbaarheid van het huidige monstermateriaal in de SKML-rondzendingen van de algemene klinische chemie. Ned Tijdschr Klin Chem Labgeneesk. 2008; 33: 154-157 (in danish)	Material prepared based on C37A guideline demonstrated commutability for an unspecified number of measuring systems based on wet chemistry in the Netherlands EQA program.
bilirubin chloride glucose iron magnesium phosphate potassium sodium urea uric acid	Miller WG, Myers GL, Ashwood ER, Killeen AK, Wang E, Ehlers GW, Hassemer D, Lo SF, Seccombe D, Siekmann L, Thienpont LM, Toth A. State of the art in trueness and inter-laboratory harmonization for 10 analytes in general clinical chemistry. *Arch Pathol Lab Med.* 2008;132:838-846	Material prepared based on the C37A guideline was assumed to be commutable.
albumin total protein	Lo SF, Miller WG, Doumas BT. Laboratory performance in albumin and total protein measurement using a commutable specimen. *Arch Pathol Lab Med.* 2013;137:912-20.	Material prepared based on the C37A guideline was assumed to be commutable.
Studies that used both pooled serum and individual units		
insulin	Miller WG, Thienpont LM, Van Uytfanghe K, Clark PM, Lindstedt P, Nilsson G, Steffes MW. Toward standardization of insulin immunoassays. *Clin Chem.* 2009; 55:1011-1018.	The relationship for results among 10 measuring systems were equivalent using either individual units or pooled serum.
Studies that used individual serum units only		
thyroid-stimulating hormone	Thienpont LM, Van Uytfanghe K, Beastall G, Faix JD, Ieiri T, Miller WG, Nelson JC, Ronin C, Ross HA, Thijssen JH, Toussaint B. Report of the IFCC Working Group for Standardization of Thyroid Function Tests; Part 1: Thyroid-Stimulating Hormone. *Clin Chem.* 2010;56:902-11.	Single donor units were used.
free thyroxine free triiodothyronine	Thienpont LM, Van Uytfanghe K, Beastall G, Faix JD, Ieiri T, Miller WG, Nelson JC, Ronin C, Ross HA, Thijssen JH, Toussaint B. Report of the IFCC Working Group for Standardization of Thyroid Function Tests; Part 2: Free Thyroxine and Free Triiodothyronine. *Clin Chem.* 2010;56:912-20.	Single donor units were used.
total thyroxine and total triiodothyronine	Thienpont LM, Van Uytfanghe K, Beastall G, Faix JD, Ieiri T, Miller WG, Nelson JC, Ronin C, Ross HA, Thijssen JH, Toussaint B. Report of the IFCC Working Group for Standardization of Thyroid Function Tests; Part 3: Total Thyroxine and Total Triiodothyronine. *Clin Chem.* 2010;56:921-29.	Single donor units were used.

Analyte(s)	Published Reference	Notes from commutability assessment
creatinine glucose phosphate uric acid total cholesterol HDL-cholesterol LDL-cholesterol triglycerides	Stepman H.C.M., Tiikkainen U., Stöckl D., Vesper H.W., Edwards S., Laitinen H.,Pelanti J. and Thienpont L.M. Measurements for 8 common analytes in native sera identify inadequate standardization among 6 routine laboratory assays. *Clin Chem.* 2014; 60 (6): 855–863	Single donor units were used.
thyroid-stimulating hormone	Thienpont LM, Van Uytfanghe K, De Grande, Reynders D, Das B,5 Faix JD, MacKenzie F, Decallonne B, Hishinuma A, Lapauw B, Taelman P, Van Crombrugge P, Van den Bruel A, Velkeniers B, Williams P on behalf of the IFCC Committee for Standardization of Thyroid Function Tests (C-STFT). Harmonization of Serum Thyroid-Stimulating Hormone Measurements Paves the Way for the Adoption of a More Uniform Reference Interval. *Clin Chem.* 2017;63:1248-60.	Single donor units were used.

S3.

Supplemental Table 3. Examples of Standardization and External Quality Assurance Programs that use materials prepared using the original C37-A guideline

Survey/Organization	Analytes	Published Reference	Notes from commutability assessment
Commutable Frozen Serum (CFS)/ The College of American Pathologists (CAP)	albumin bilirubin chloride cortisol creatinine glucose iron magnesium phosphorus potassium total protein sodium total thyroxine (T4) urea nitrogen (BUN) uric acid	1. Klee G. and Killeen A. College of American Pathologists 2003 Fresh Frozen Serum Proficiency Testing Studies. *Arch Pathol Lab Med.* 2005; 129:292-293	Materials prepared based on the C37A guideline were assumed to be commutable.
Accuracy-Based Vitamin D Survey (ABVD Survey)/ The College of American Pathologists (CAP)	25-OH vitamin D (D2 and D3)	1.Phinney K, Sempos C, Vesper H, Botelho J, Tai S, Camara J, Wise S, Myers G, Durazo-Arvizu R, Tian L, Eckfeldt J, Hoofnagle A, Miller G, Bachmann L, et al. Baseline Assessment of 25-Hydroxyvitamin D Reference Material and Proficiency Testing/External Quality Assurance Material Commutability: A Vitamin D Standardization Program Study. *J AOAC Int.* 2017; 100(5):1288-1293.* 2.www.cap.org	Materials were commutable based on the studies found in literature*
Harmonized thyroid - ABTH / The College of American Pathologists	triiodothyronine, free, triiodothyronine, total thyroxine, free thyroxine, total thyroid-stimulating hormone (TSH)	The College of American Pathologists, www.cap.org (accessed December 26, 2017)	Materials prepared based on the C37A guideline were assumed to be commutable.
Accuracy Based Lipids (ABL)/ The College of American Pathologists (CAP)	total cholesterol triglycerides HDL-cholesterol LDL-cholesterol	The College of American Pathologists, www.cap.org (accessed December 26, 2017)	Materials are commutable based on the studies found in literature.
Accuracy based testosterone and estradiol/ The College of American Pathologists (CAP)	Testosterone estradiol	The College of American Pathologists, www.cap.org (accessed December 26, 2017)	Materials prepared based on the C37A guideline were assumed to be commutable.
Cholesterol Reference Method Laboratory Network (CRMLN)/ Centers for Disease Control and Prevention (CDC)	total glycerides total cholesterol HDL-cholesterol LDL-cholesterol	1.Warnick GR, Kimberly M, Waymack P, Leary E, Myers G. Standardization of measurements for cholesterol, triglycerides, and major lipoproteins. *Lab Med.* 2008;39(8):481-490 2. Kimberly M, Myers G. Little R. Clinical Laboratory Reference Networks. 2004; *Accred Qual Assur.* 9:18–23 3. Centers for Disease Control and Prevention. Cholesterol Reference Method Laboratory Networkwww.cdc.gov/labstandards/crmln (accessed December 26, 2017)	Commutability was verified internally and based on studies found in literature.

Survey/Organization	Analytes	Published Reference	Notes from commutability assessment
CDC Lipids Standardization Program (LSP)/ Centers for Disease Control and Prevention (CDC)	total glycerides total cholesterol HDL-cholesterol LDL-cholesterol	1.Warnick GR, Kimberly M, Waymack P, Leary E, Myers G. Standardization of measurements for cholesterol, triglycerides, and major lipoproteins. *Lab Med.* 2008;39(8):481-490 2. Centers for Disease Control and Prevention. Lipids Standardization Program. www.cdc.gov/labstandards/lsp (accessed December 26, 2017)	Commutability was verified internally and based on studies found in literature
Accuracy-based EQA program for lipids as part of Calibration 2.000 EQA-scheme of the Foundation for Quality Assessment of Medical Laboratory Diagnostics (SKML)	HDL-cholesterol LDL-cholesterol triglycerides apo A-1 apo B Lp(a)	Cobbaert C, Weykamp C, Baadenhuijsen H, Kuypers A, Lindemans J, Jansen R. Selection, Preparation, and Characterization of Commutable Frozen Human Serum Pools as Potential Secondary Reference Materials for Lipid and Apolipoprotein Measurements: Study within the Framework of the Dutch Project "Calibration 2000" *Clin Chem*. 2002; 48(9): 1526-1538	Materials prepared based on C37A guideline were commutable for all analytes and can be used as secondary reference materials.
Calibration 2.000 EQA-scheme of the Foundation for Quality Assessment of Medical Laboratory Diagnostics (SKML)	17 general chemistry analytes: sodium chloride calcium magnesium phosphorus potassium urea creatinine glucose albumin total protein alkaline phosphatase amylase alanine aminotransferase aspartate aminotransferase Cholesterol HDL-cholesterol	Jansen RTP, Cobbaert CM, Weykamp C, Thelen M. The quest for equivalence of test results: the pilgrimage of the Dutch Calibration 2.000 program for metrological traceability. *Clin Chem Lab Med*. 2018; 56: 1673-1684.	Commutable native spy material prepared according to C37A is included in one challenge per year to verify commutability of other samples.
Hormone Standardization Program (HoST)/ Centers for Disease Control and Prevention (CDC)	estradiol testosterone	1. Vesper H, Botelho J. Standardization of testosterone measurements in humans. J *Steroid Biochem Mol Biol.* 2010; 121:513–519 2. Botelho J, Ribera A, Cooper H, Vesper H. Evaluation of an Isotope Dilution HPLC Tandem Mass Spectrometry Candidate Reference Measurement Procedure for Total 17-β Estradiol in Human Serum. *Anal. Chem.*, 2016, 88 (22), pp 11123–11129 3. Centers for Disease Control and Prevention. Laboratory Quality Assurance and Standardization Programs: Hormone Standardization Program, www.cdc.gov/labstandards/hs (accessed December 26, 2017)	Single donor units were used.
Accuracy-based Monitoring Program (AMP)/	estradiol testosterone	Centers for Disease Control and Prevention. Laboratory Quality Assurance and Standardization	Commutability was verified internally and based on studies found in literature.

Survey/Organization	Analytes	Published Reference	Notes from commutability assessment
Centers for Disease Control and Prevention (CDC)		Programs: Hormone Standardization Program, www.cdc.gov/labstandards/hs (accessed December 26, 2017)	
Vitamin D Standardization Certification Program (VDSCP)/ Centers for Disease Control and Prevention (CDC)	total 25-(OH) vitamin D	Centers for Disease Control and Prevention. Vitamin D Standardization-Certification Program, www.cdc.gov/labstandards/vdscp.html (accessed December 26, 2017)	Single donor units were used.
Vitamin D Standardization Program (VDSP) VDSP Commutability Study	total 25(OH)D 3-epi-25(OH)D3	Phinney K, Sempos C, Vesper H, Botelho J, Tai S, Camara J, Wise S, Myers G, Durazo-Arvizu R, Tian L, Eckfeldt J, Hoofnagle A, Miller G, Bachmann L, et al. Baseline Assessment of 25-Hydroxyvitamin D Reference Material and Proficiency Testing/External Quality Assurance Material Commutability: A Vitamin D Standardization Program Study. *J AOAC Int.* 2017; 100(5):1288-1293.	Materials are commutable based on the studies found in literature.
Vitamin D Standardization Program (VDSP) VDSP Commutability 2 Study/ National Institutes of Health (NIH), National Institute of Standards and Technology (NIST), College of American Pathologists (CAP) and Vitamin D External Quality Assessment Scheme (DEQAS)	total 25(OH)D 3-epi-25(OH)D3 24,25(OH)2D3	Camara J, Hoofnagle A, Carter G, Sempos C. Take Two: Gearing Up for the next vitamin D commutability study. *Clin Lab News*. 2015; February: 8-10	Materials are commutable based on the studies found in literature.
Vitamin D External Quality Assessment Scheme (DEQAS)	total 25(OH)D 3-epi-25(OH)D3 1,25(OH)2D	1.Vitamin D External Quality Assessment Scheme, www.deqas.org (accessed December 26, 2017) 2. Phinney K, Sempos C, Vesper H, Botelho J, Tai S, Camara J, Wise S, Myers G, Durazo-Arvizu R, Tian L, Eckfeldt J, Hoofnagle A, Miller G, Bachmann L, et al. Baseline Assessment of 25-Hydroxyvitamin D Reference Material and Proficiency Testing/External Quality Assurance Material Commutability: A Vitamin D Standardization Program Study. *J AOAC Int.* 2017; 100(5):1288-1293.*	Materials are commutable based on the studies found in literature.*
NIST/NIH Vitamin D Metabolites Quality Assurance Program (VitDQAP)	total 25(OH)D 3-epi-25(OH)D3	Bender M, Lippa KA, Tai, S.S.-C. An Assessment of 25-Hydroxyvitamin D Measurements in Comparability Studies Conducted by the Vitamin D Metabolites Quality Assurance Program. *Clin Chem Acta*. 2013; 426:6-11.	Materials are commutable based on the studies found in literature.

*****reference that describes commutability study

S4. Validation of Commutability using aliquots of each donor unit to the pool

The original CLSI C37-A guideline (3) included results from experiments conducted to validate the suitability of the C37-A protocol by preparing two serum pools and assessing their commutability among a group of measurement procedures for total cholesterol. Those results from 1999 are included in this supplement with updates to the protocol description and clarification of limitations of this approach for commutability assessment.

S4.1 Principle of commutability assessment using individual donors to a pool.

Commutability of a pool can be evaluated by measuring the measurand in the pool and in a frozen aliquot of each individual donor unit to the pool using each measurement procedure for which the pool is intended to be used as a reference material. Aliquots of each original individual donor serum unit are retained and stored at -70 °C or lower. The individual donor aliquots and vials of the pool are thawed, mixed and measured for the measurand(s) of interest. A suitable replication design should be determined based on the precision characteristics of the measurement procedures involved and the criterion for acceptable commutability. Reference 4 in the main report provides recommendations for establishing a criterion for acceptable commutability. The measurements of individual aliquots and pools should be made within a run to minimize imprecision influences.

The measurand value in the pooled serum is predictable as the mathematical average of the results for the individual donors when weighted by the volume of each donor unit used to prepare the pool. This predictable relationship assumes there is no significant pooling effect such as forming aggregates that bind the measurand, no loss of measurand or measurand binding molecules in the filtration step, and no altered concentration ratios between measurand binding molecules in individual donors and in the serum pool. A conclusion that the pool is non-commutable when assessed as described here may be caused by alterations in the matrix, measurand or binding molecules during the pooling process and/or the freeze/thaw cycle. When the assumptions are not valid, a commutability assessment must be performed based on the equivalence of the relationship between the pool result and the individual samples results for all combinations of measurement procedures for which the pool is intended to be used as a reference material as described in other commutability assessment protocols (main report references 4,5,6).

S4.2. Validation Study Materials for the Cholesterol Pools in C37-A

Two pools of off-the-clot human serum were prepared, packaged in 1 mL aliquots, each in a labeled 3 mL glass vial, and frozen at -70 ºC. Sixty 1 mL aliquots, each in a uniquely labeled 3 mL glass vial traceable to the original donor unit, were collected from each of the 87 individual donor units (44 for Pool 1 and 43 for Pool 2).

S4.3. Donor Selection Criteria

Donors were identified based on previous history of lipid values and their willingness to provide a minimum 8 hour fasting unit of whole blood. Donors with expected cholesterol concentrations of less than 5.18 mmol/L (200 mg/dL)) and triglyceride concentrations of less than 2.26 mmol/L (200 mg/dL) had blood collected during the morning hours of two consecutive days for preparation of pool 1 with low lipid concentrations. A week later, donors with expected cholesterol concentrations of 6.73 to 9.06 mmol/L (260 to 350 mg/dL) and triglycerides concentrations <3.39 mmol/L (300 mg/dL) had blood collected during the morning hours of two consecutive days to prepare pool 2 with high lipid concentrations.

S4.4. Blood Collection and Processing

Sixty 1.0 mL frozen aliquots were prepared from each serum unit collected for each pool preparation. The aliquots from each individual unit were labeled and frozen at -70 °C. The residual material of the individual units was used for the pool preparation. Forty-four individual serum units were included in pool 1, 37 of which had 120 mL, 5 had 90 mL, and 2 had 60 mL for a total pool volume of 5,010 mL. Similarly, 43 individual serum units were used for the pool 2 with 29, 10, and 4 units providing 120, 90, and 150 mL each, for a total pool volume of 4,980 mL. Both pool preparations were completed within 42 hours of the initial whole blood collection. Each pool was incubated for 18 hours at 4 °C with constant mixing with a magnetic stirrer at low speed to ensure homogeneity of the final pool and allow any nonspecific aggregation or further clotting process to occur. Filtration using an 0.22 µm hydrophilic Durapore filter (Millipore)[1], vial filling and other steps were performed as described in the guideline.

The number of donors used to prepare each pool considered the sample size needed to estimate bias, with sufficient statistical power, between the weighted mean of individual donor cholesterol results and the result for the pool. A statistical design was developed that permitted detection of bias differences in excess of 2 % between the pool and the mean of individual patient donor sera. Assuming that medical laboratory measurement procedures for cholesterol should perform with a CV of at least 3 % (based on National Cholesterol Education Program performance guidelines), it was determined that 40 donors were required to detect a 2 % bias between the pool and donors with 90 % confidence. This number of donors was also sufficient to minimize the potential contribution of an interfering substance in one or a few individual donors. For example, if a single donor sample had a cholesterol bias of 30 % due to interferences, a 0.75 % bias is expected in a pool comprised of 40 donors.

S4.5. Results of the Commutability Assessment

Twenty-six instrument/reagent systems representing 13 manufacturers and one reagent vendor participated in the commutability validation study. Each participating manufacturer was provided with vials from the two pools and each of the donor units comprising each pool shipped on dry ice. Nineteen measuring systems assayed all samples for cholesterol in a single analytical run with appropriate replication for the desired statistical power. The pools were tested 15 times, the donor units in duplicate, and two levels of controls in singlet at the beginning and end of the run. The remaining seven measuring systems made two or more analytical runs with a replication design suitable to identify a bias >2 % between the pool value predicted by the individual donors and the measured value of each pool. At the time this validation of the C37-A protocol was performed (1999), the results were coded so that the identities of measuring system manufacturers were unknown.

The results from 26 measuring systems evaluated in this study showed that none had a consistent bias between the weighted mean of donor sample results and the serum pool results for cholesterol. The pool result was the mean of all measurements of cholesterol in a pool by a single measuring system. The individual donor's mean result was the weighted mean of the donor sample measurements by the same measuring system. Weights were computed from the serum volume fractions for each donor used to create each pool. For measuring systems with multiple runs, an additional weighting factor was computed from the controls in each run to minimize run effects. These weighted means are the "expected" values for the pools in the absence of matrix-related bias. All biases, with the exception of one measuring system for Pool 2 with bias 2.2 %, were less than the 2 % criterion used to determine a statistical difference between the result for a pool and the weighted mean for a population of patient sera used to prepare the pool. In fact, all biases with the exception of one different measuring system for Pool 1 and one different measuring system for Pool 2, were less than 1.5 %. The results in this study were sufficient to conclude that the serum pools prepared according to this guideline were commutable with the individual donor samples for the 26 measuring systems evaluated.

[1]Certain commercial equipment or materials are identified in this paper to specify adequately the experimental procedure. Such identification does not imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that the materials or equipment identified are necessarily the best available for the purpose.

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