

Commutability Studies at NIST

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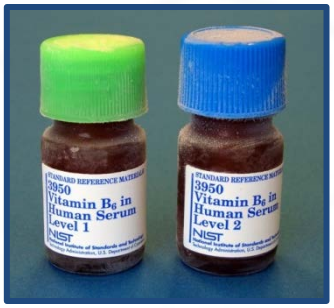
MATERIAL
MEASUREMENT
LABORATORY

NIST Clinical Reference Materials



- Approximately 50 clinical SRMs including pure substance, calibration solutions, and natural matrix materials (blood, serum, plasma, urine)
- Analytes include inorganic and organic species
- Currently few nucleic acid SRMs for clinical diagnostics
- Most serum or plasma materials now fresh-frozen, not lyophilized
- Greater use of CLSI C37-A protocols in material preparation

Mechanisms for Assessing Commutability

SRM 967

- Commutability studies performed in accordance with CLSI C53-A or EP14-A2
- Data from interlaboratory studies
- Inclusion of routine methods in value assignment

Potential obstacles or limitations to commutability studies:

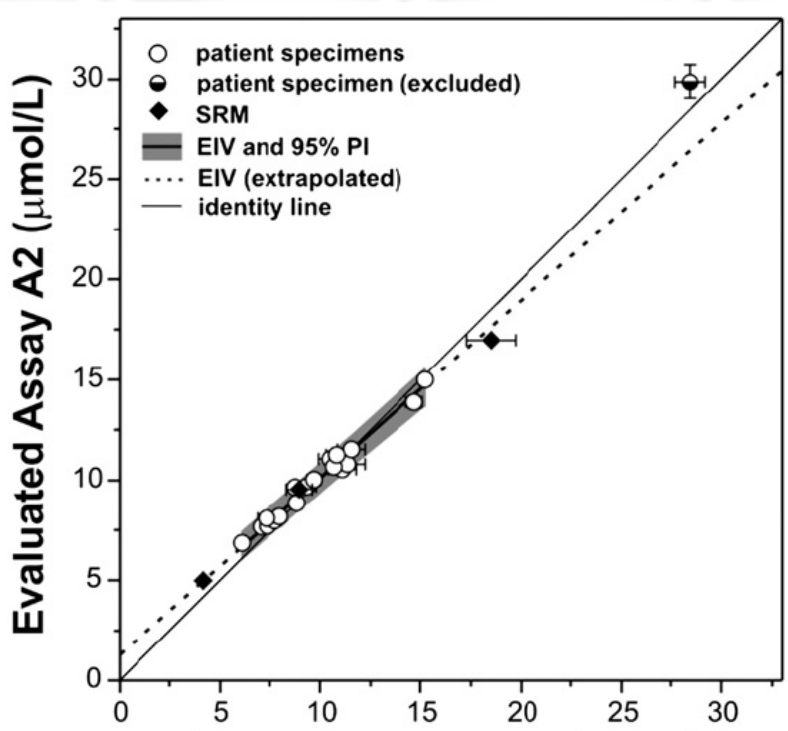
- Material sells out quickly
- Access to appropriate patient samples (and cost)
- Need partners to engage assay manufacturers
- End users unknown (manufacturers, clinical labs, research)

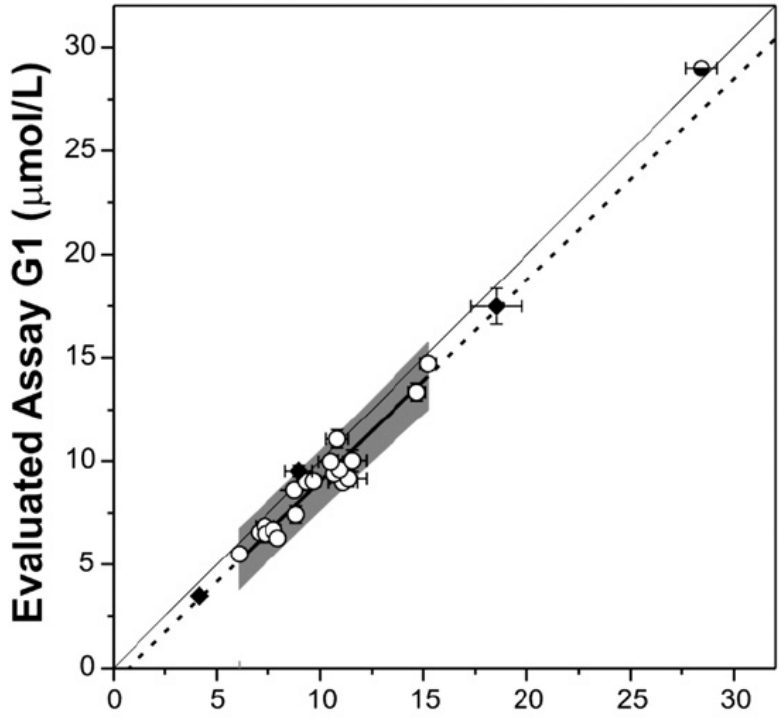
SRM 1955 Homocysteine and Folate in Human Serum

SRM 1955

- Three level material, with two levels prepared through either dilution or spiking
- SRM issued in 2005 with certified and reference values for homocysteine, 5mTHF, and folic acid
- Commutability study performed for homocysteine using modification of CLSI EP14-A2 guidelines, collaboration with CDC
- Participating laboratories included 14 immunoassays and/or enzymatic assays
- Only 20 single donor patient samples used
- Reference assay was NIST LC-MS/MS method

Homocysteine in SRM 1955





- Statistical analysis using error-in-variables approach, based on Deming regression
- Weighted least-squares regression analysis incorporating uncertainty in x- and y-axis
- One patient sample excluded because of potentially spurious results
- Statement of commutability limited by range and number of patient samples

SRM 972a Vitamin D Metabolites in Human Serum

- Renewal material to replace SRM 972
- Four levels with varying concentrations of vitamin D metabolites
- Endogenous concentrations of all metabolites, except Level 4

- Commutability study performed as part of Vitamin D Standardization Program (VDSP)
- Additional materials from CAP and DEQAS also evaluated
- Reference method was ID LC-MS/MS (NIST and Ghent)
- Reference labs determined 25(OH)D_2, 25(OH)D_3, and 3-epi-25(OH)D_3
- Fifty single donor patient samples spanning range of concentrations

SRM 972a Vitamin D Metabolites in Human Serum

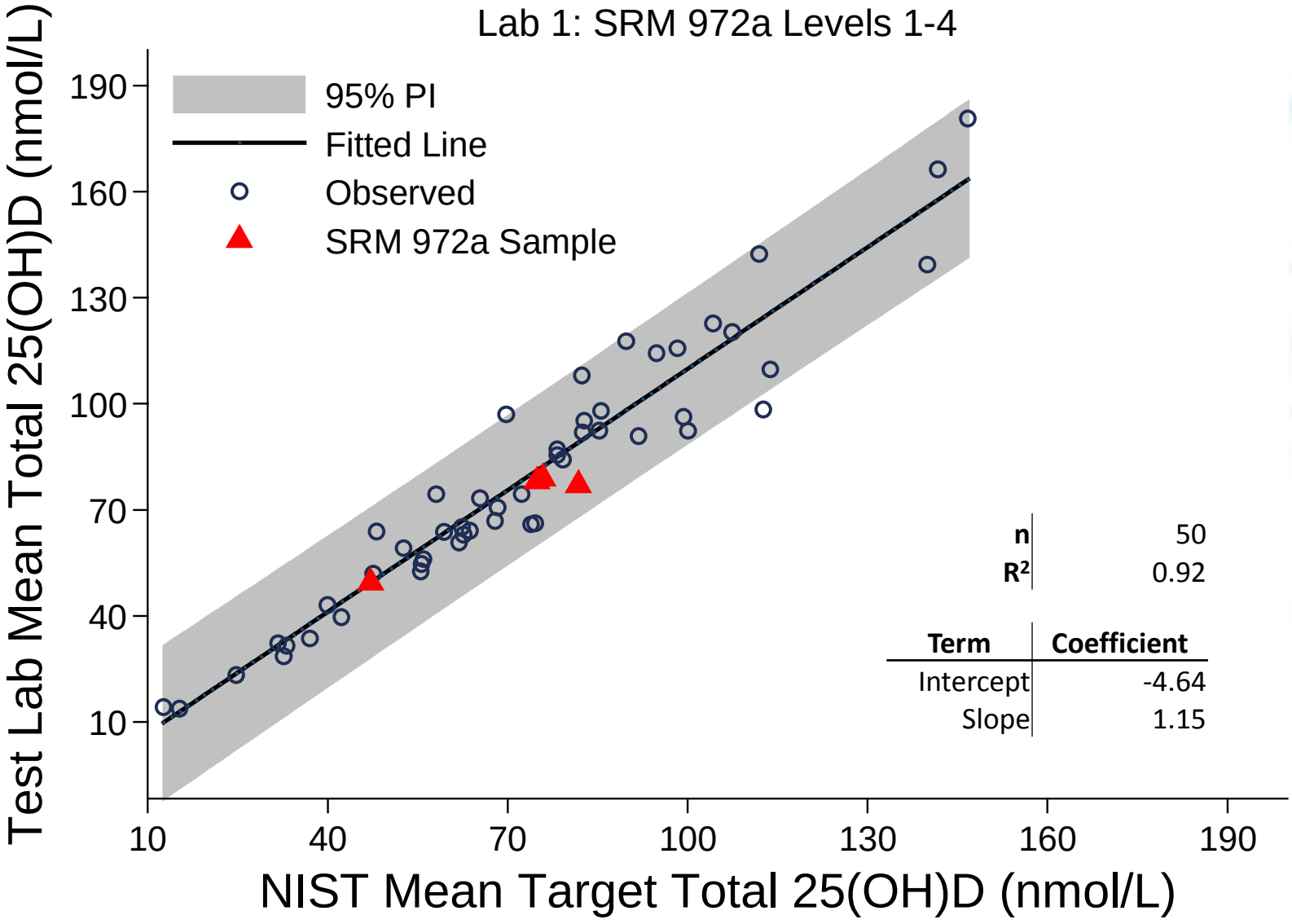
- Participating Labs:
  - 20 Total: 4 LC-MS/MS and 16 Immunoassay
    - 2 dropout
    - 5 – Open reporting
    - 4 – Anonymous reporting
    - 2 – Results not to be used
    - 7 – TBA

- All samples run in duplicate on 3 different days

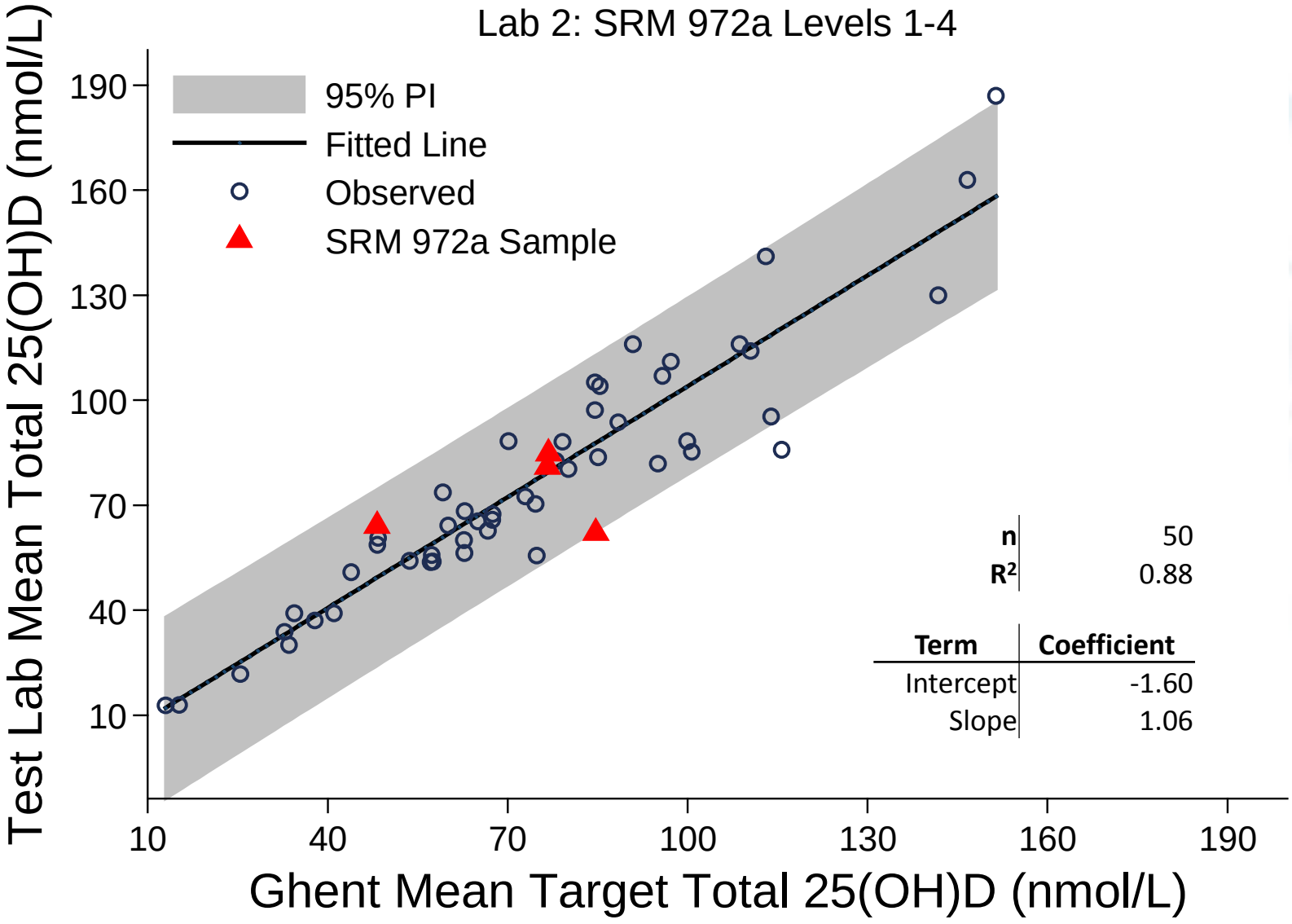
- Total 25(OH)D = 25(OH)D_2 + 25(OH)D_3*

* Does not include concentration of 3-epimers

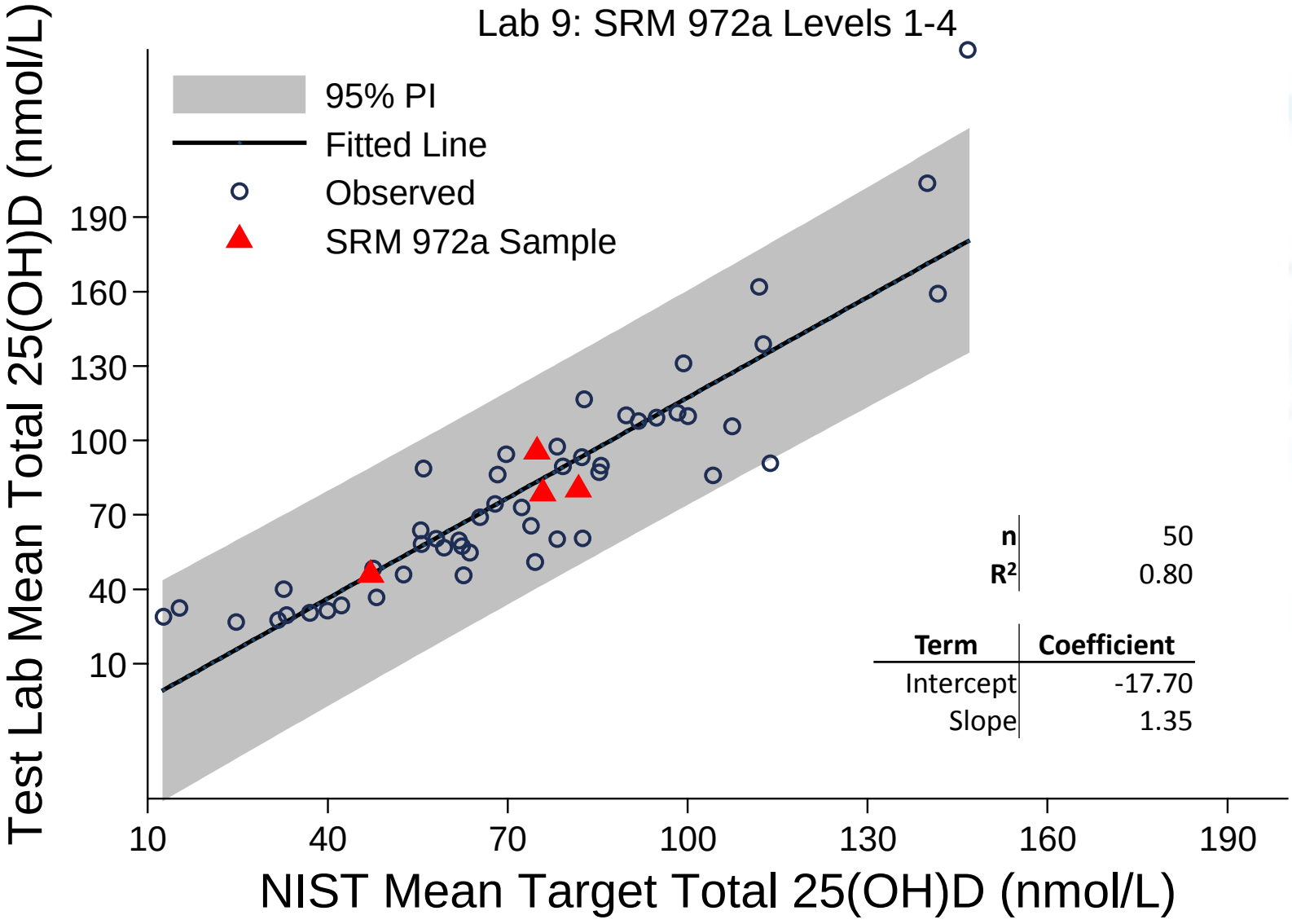
VDSP Commutability Study: Immunoassay



VDSP Commutability Study: Immunoassay

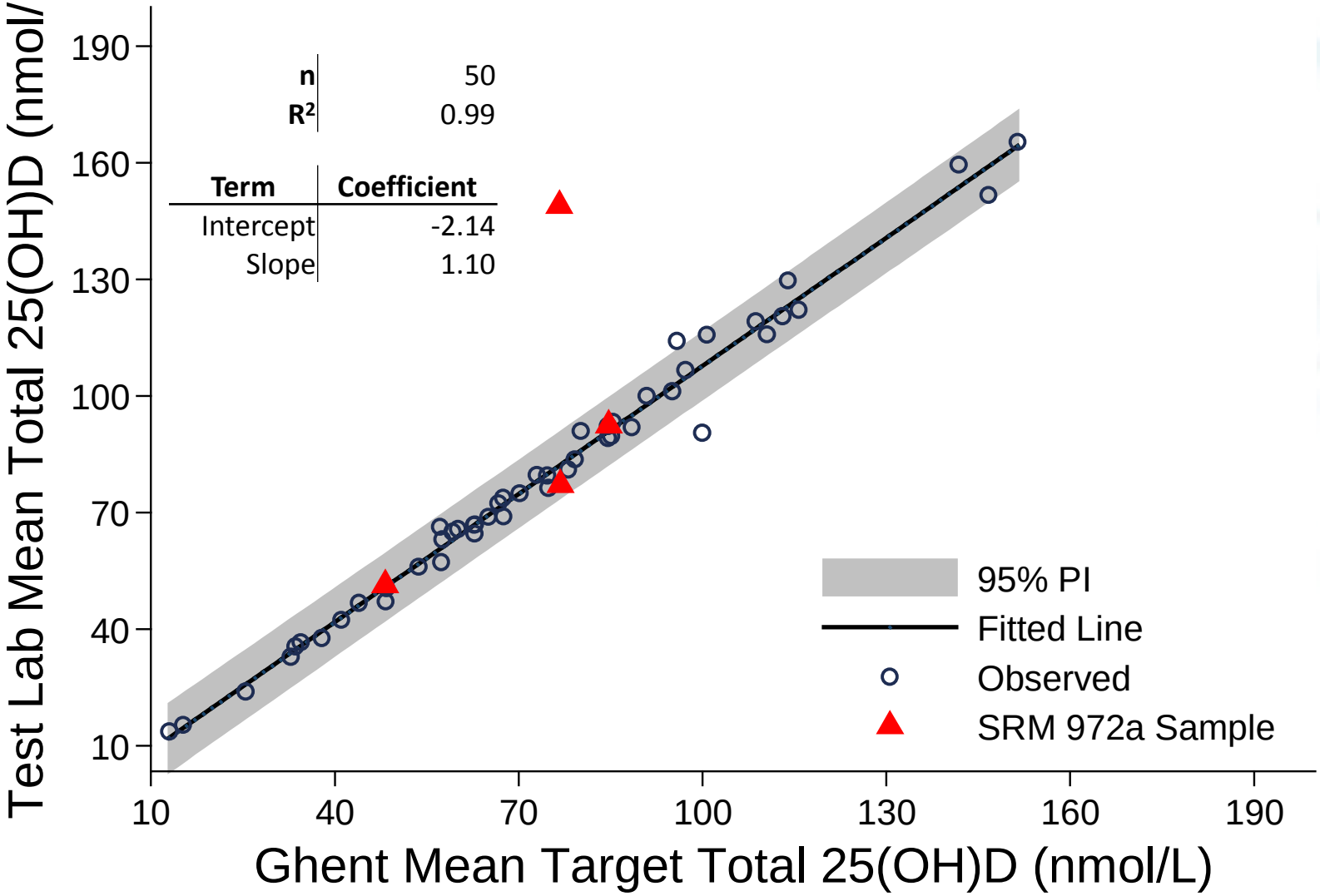


VDSP Commutability Study: Immunoassay



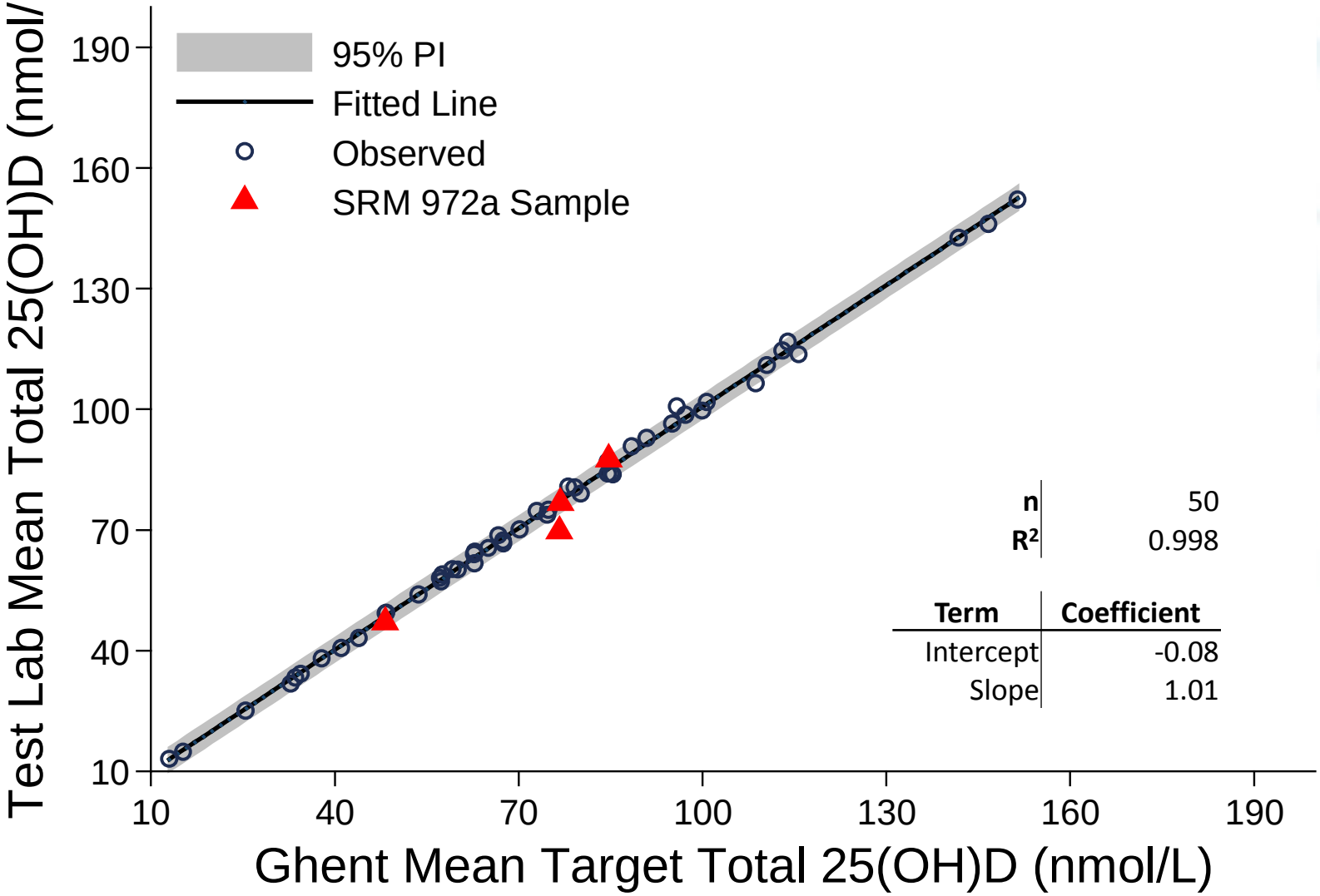
VDSP Commutability Study: LC-MS/MS

Lab 10: SRM 972a Levels 1-4

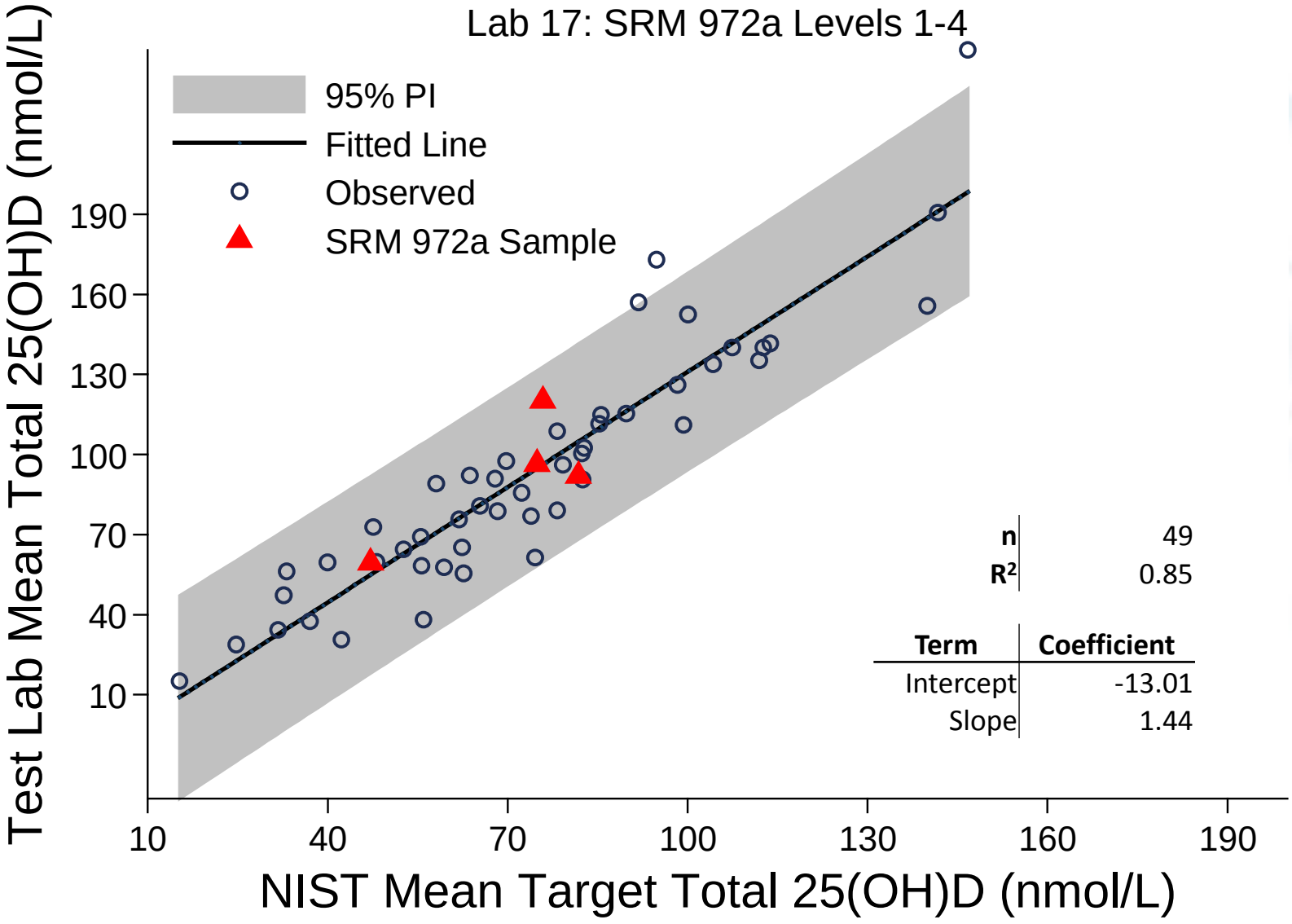


VDSP Commutability Study: LC-MS/MS

Lab 16: SRM 972a Levels 1-4



VDSP Commutability Study: Immunoassay



Conclusions from Commutability Study

SRM 972a

- SRM 972a appears commutable with most assays
- Remaining questions about response to certain metabolites ($25OHD_2$ and 3-epimers)
- Performance of some immunoassays makes nearly any material appear commutable

- Need to require participants to be identified in any future studies
- Set minimum performance criteria for participating assays

SRM 3667 Creatinine in Frozen Human Urine

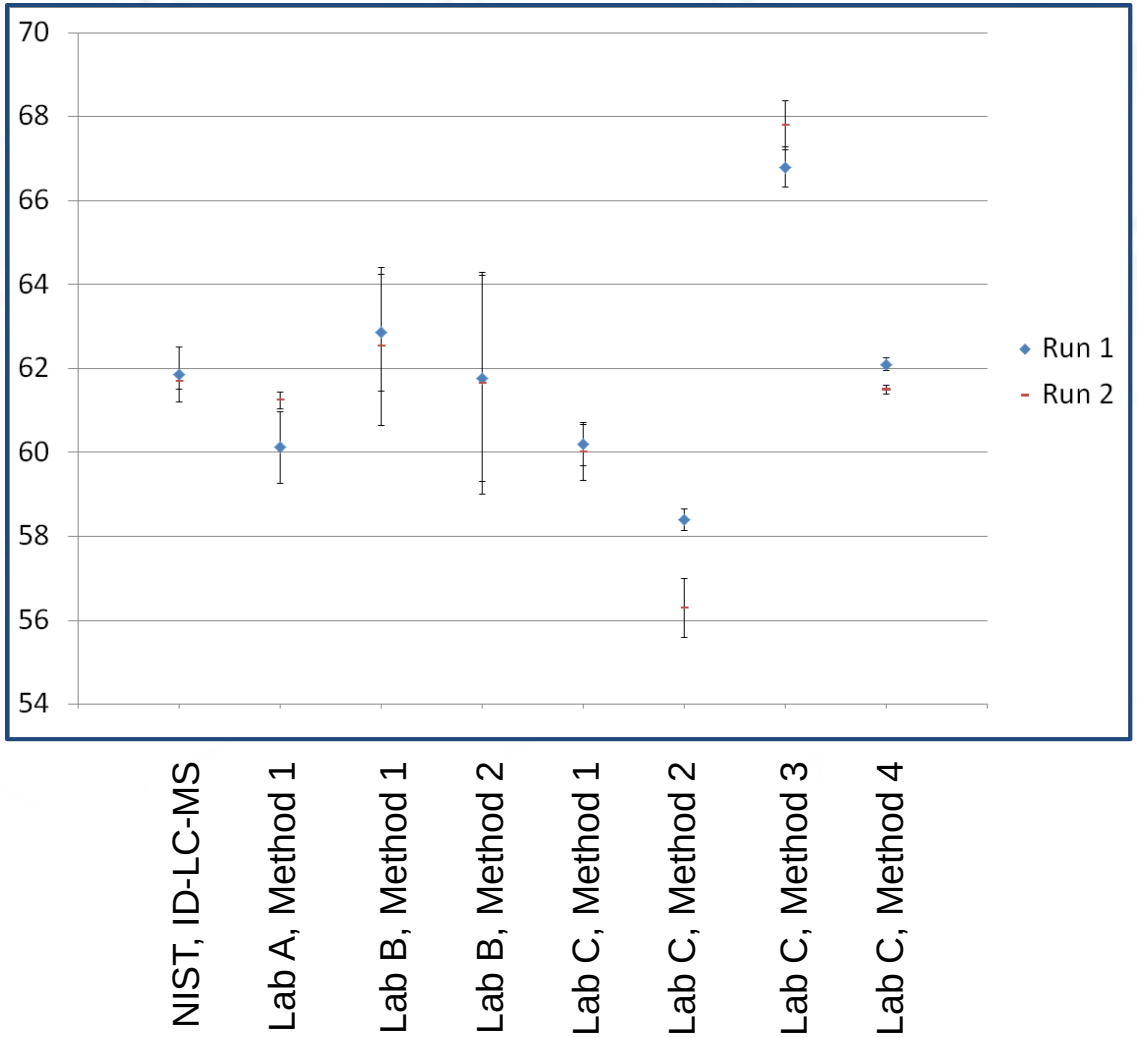
SRM 3667

- Single level material with endogenous creatinine concentration
- Value assignment at NIST by ID LC-MS using variation of method for serum
- No previous materials for creatinine in urine

- Small comparison organized through NKDEP to compare results from routine methods to those obtained by NIST
- Samples sent to three participants, both enzymatic and Jaffe methods

Mass fraction (µg/g)	Mass concentration[a] (mg/dL)
631 ± 13	61.8 ± 1.3

SRM 3667 Study Results



Use of Data from Interlaboratory Studies – SRM 968e

Analyte	NIST LC-UV 1	NIST LC-UV 2	Study median
Total retinol	0.346 (0.016)	0.326 (0.008)	0.351
γ/β-Tocopherol	2.03 (0.10)	1.84 (0.03)	1.72
α-Tocopherol	6.96 (0.34)	5.84 (0.10)	6.75
Total lutein	0.069 (0.004)	0.059 (0.003)	0.072
Total lycopene	0.173 (0.004)	0.294 (0.008)	0.236
Total β-carotene	0.114 (0.004)	0.093 (0.004)	0.090
Total zeaxanthin	0.029 (0.003)	0.029 (0.001)	0.037

Data for Level 1 of SRM 968e from NIST methods and from participants in the NIST Micronutrients Measurement QA Program (MMQAP). All results in μg/mL.

SRMs with Multiple Purposes

SRM 1950 Metabolites in Human Plasma

Should commutability be assessed, and by whom?

Acknowledgments

- National Institutes of Health (NIH)
  - Office of Dietary Supplements (ODS)
  - National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
- Centers for Disease Control and Prevention (CDC)
- Ghent University
- National Kidney Disease Education Program (NKDEP)
- Vitamin D Standardization Program (VDSP)
- NIST Chemical Sciences Division