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Revision 1

Dietary Supplement Laboratory Quality Assurance Program: Exercise N Final Report

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National Institute of Standards and Technology
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Wilbur L. Ross, Jr., Secretary

National Institute of Standards and Technology
Walter Copan, NIST Director and Under Secretary of Commerce for Standards and Technology

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ABSTRACT

The NIST Dietary Supplement Laboratory Quality Assurance Program (DSQAP) was established in collaboration with the National Institutes of Health (NIH) Office of Dietary Supplements (ODS) in 2007 to enable members of the dietary supplement community to improve the accuracy of measurements for demonstration of compliance with various regulations, including the dietary supplement current good manufacturing practices (cGMPs). Exercise N of this program offered the opportunity for laboratories to assess their in-house measurements of nutritional elements (chromium), contaminants (arsenic, cadmium, and lead), water-soluble vitamins (folic acid), fat-soluble vitamins (vitamin D_2 and vitamin D_3), fatty acids, and botanical marker compounds (ginsenosides) in foods and/or botanical dietary supplement ingredients and finished products.

INTRODUCTION

The dietary supplement industry in the US is booming, with three-quarters of adults considering themselves to be supplement users.[1] Consumption of dietary supplements, which includes vitamin and mineral supplements, represents an annual US expenditure of more than $40 billion. These figures represent an increasing American and worldwide trend, and as a result, the verification and maintenance of both the quality and safety of these products is critically important.

The Dietary Supplement Health and Education Act of 1994 (DSHEA) amended the Federal Food, Drug, and Cosmetic Act to create the regulatory category called dietary supplements. The DSHEA also gave the FDA authority to write current Good Manufacturing Practices (cGMPs) that require manufacturers to evaluate the identity, purity, and composition of their ingredients and finished products. In addition, the DSHEA authorized the establishment of the Office of Dietary Supplements at the National Institutes of Health (NIH ODS). To enable members of the dietary supplement community to improve the accuracy of the measurements required for compliance with these and other regulations, NIST established the Dietary Supplements Laboratory Quality Assurance Program (DSQAP) in collaboration with the NIH ODS in 2007.

The program offers the opportunity for laboratories to assess their in-house measurements of active or marker compounds, nutritional elements, contaminants (toxic elements, pesticides, mycotoxins), and fat- and water-soluble vitamins in foods as well as botanical dietary supplement ingredients and finished products. Reports and certificates of participation are provided and can be used to demonstrate compliance with the cGMPs. In addition, NIST and the DSQAP assist the ODS Analytical Methods and Reference Materials program (AMRM) at the NIH in supporting the development and dissemination of analytical tools and reference materials. In the future, results from exercises of the DSQAP and other related programs could be used by ODS to identify problematic matrices and analytes for which an AOAC INTERNATIONAL Official Method of Analysis would benefit the dietary supplement community.

NIST has experience in the administration of quality assurance programs, but the DSQAP takes a unique approach. In other NIST quality assurance programs, a set of analytes is measured repeatedly over time in the same or similar matrices to demonstrate and improve laboratory performance. In contrast, the wide range of matrices and analytes under the "dietary supplements"

[1] *2017 CRN Consumer Survey on Dietary Supplements.* Council for Responsible Nutrition, Washington, DC.

umbrella means that not every laboratory is interested in every sample or analyte. The constantly changing dietary supplement market, and the enormous diversity of finished products, makes repeated determination of a few target compounds in a single matrix of little use to participants. Instead, participating laboratories are interested in testing in-house methods on a wide variety of challenging, real-world matrices to demonstrate that their performance is comparable to that of the community and that their methods provide accurate results. In an area where there are few generally accepted methods, the DSQAP offers a unique tool for assessment of the quality of measurements, provides feedback about performance, and can assist participants in improving laboratory operations.

This report summarizes the results from the fourteenth exercise of the DSQAP, Exercise N. Fifty-four laboratories responded to the call for participants distributed in May 2017. Samples were shipped to participants in July 2017 and results were returned to NIST by October 2017. This report contains the final data and information that was disseminated to the participants in August 2018.

OVERVIEW OF DATA TREATMENT AND REPRESENTATION

Individualized data tables and certificates are provided to the participants that have submitted data in each study, in addition to this report. Examples of the data tables using NIST data are also included in each section of this report. Community tables and graphs are provided using randomized laboratory codes, with identities known only to NIST and individual laboratories. The statistical approaches are outlined below for each type of data representation.

Statistics

Data tables and graphs throughout this report contain information about the performance of each laboratory relative to that of the other participants in this study and relative to a target around the expected result, if available. All calculations are performed in PROLab Plus (QuoData GmbH, Dresden, Germany).[2] The consensus mean and standard deviation are calculated according to the robust algorithm outlined in ISO 13528:2015(E), Annex C.[3] The algorithm is summarized here in simplified form.

Initial values of the consensus mean, x^*, and consensus standard deviation, s^*, are estimated as

$$x^* = \text{median of } x_i \qquad (i = 1, 2, \ldots, n)$$
$$s^* = 1.483 \times \text{median of } |x_i - x^*| \qquad (i = 1, 2, \ldots, n).$$

These initial values for x^* and s^* are updated by first calculating the expanded standard deviation, δ, as

$$\delta = 1.5 \times s^*.$$

[2] Certain commercial equipment, instruments or materials are identified in this certificate to adequately specify 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.

[3] ISO 13528:2015(E), *Statistical methods for use in proficiency testing by interlaboratory comparisons*, pp. 53-54.

Each x_i is then compared to the expanded range and adjusted to x_i* as described below to reduce the effect of outliers.

If $x_i < x^* - \delta$, then $x_i^* = x^* - \delta$.
If $x_i > x^* + \delta$, then $x_i^* = x^* + \delta$.
Otherwise, $x_i^* = x_i$.

New values of x^*, s^*, and δ are calculated iteratively until the process converges. Convergence is taken as no change from one iteration to the next in the third significant figure of s^* and in the equivalent digit in x^*:

$$x^* = \frac{\sum_{i=1}^{n} x_i^*}{n}$$

$$s^* = 1.134 \times \sqrt{\frac{\sum_{i=1}^{n} (x_i^* - x^*)}{n-1}}.$$

Individualized Data Table

The data in this table is individualized to each participating laboratory and is provided to allow participants to directly compare their data to the summary statistics (consensus or community data as well as NIST certified, reference, or estimated values). The upper left of the data table includes the randomized laboratory code. Tables included in this report are generated using NIST data to protect the identity and performance of participants.

Section 1 of the data table contains the laboratory results as reported, including the mean and standard deviation when multiple values were reported. A blank indicates that NIST does not have data on file for that laboratory for a particular analyte or matrix. An empty box for standard deviation indicates that a single value or a value below the limit of quantification (LOQ) for the participant was reported and therefore that value was not included in the calculation of the consensus data.[3]

Also in Section 1 are two Z-scores. The first Z-score, Z'_{comm}, is calculated with respect to the community consensus value, taking into consideration bias that may result from the uncertainty in the assigned consensus value, using x* and s*:

$$Z'_{comm} = \frac{x_i - x*}{\sqrt{2} s*}$$

The second Z-score, Z_{NIST}, is calculated with respect to the target value (NIST certified, reference, or estimated value), using x_{NIST} and U_{95} (the expanded uncertainty) or s_{NIST} (the standard deviation of NIST measurements):

$$Z_{NIST} = \frac{x_i - x_{NIST}}{2 * U_{95}}$$

or

$$Z_{NIST} = \frac{x_i - x_{NIST}}{2 * s_{NIST}}.$$

The significance of the Z-score and Z'-score is as follows:

- $|Z| < 2$ indicates that the laboratory result is considered to be within the community consensus range (for Z'_{comm}) or NIST target range (for Z_{NIST}).
- $2 < |Z| < 3$ indicates that the laboratory result is considered to be marginally different from the community consensus value (for Z'_{comm}) or NIST target value (for Z_{NIST}).
- $|Z| > 3$ indicates that the laboratory result is considered to be significantly different from the community consensus value (for Z'_{comm}) or NIST target value (for Z_{NIST}).

Section 2 of the data table contains the community results, including the number of laboratories reporting more than a single value for a given analyte[1], the mean value determined for each analyte, and a robust estimate of the standard deviation of the reported values.[4] Consensus means and standard deviations are calculated using the laboratory means; if a laboratory reported a single value or a value below the LOQ, the reported value is not included.[3] Additional information on calculation of the consensus mean and standard deviation can be found in the previous section.

Section 3 of the data table contains the target values for each analyte. When possible, the target value is a certified or reference value determined at NIST. Certified values and the associated expanded uncertainty (U_{95}) have been determined with two independent analytical methods at NIST, or by combination of a single method at NIST and results from collaborating laboratories. Reference values are assigned using NIST values obtained from the average and standard deviation of measurements made using a single analytical method at NIST or by measurements obtained from collaborating laboratories. For both certified and reference values, at least six samples have been tested and duplicate preparations from the sample package have been included, allowing the uncertainty to encompass variability due to inhomogeneity within and between packages. For samples in which a NIST certified or reference value is not available, the analytes may be measured at NIST using an appropriate method. The NIST-assessed value represents the mean of at least three replicates. For materials acquired from another proficiency testing program, the consensus value and uncertainty from the completed round is used as the target range.

Summary Data Table

This data table includes a summary of all reported data for a particular analyte in a particular study. Participants can compare the raw data for their laboratory to data reported by the other participating laboratories or to the consensus data. A blank indicates that the laboratory signed up and received samples for that particular analyte and matrix, but NIST does not have data on file for that laboratory.

Graphs

Data Summary View (Method Comparison Data Summary View)

In this view, individual laboratory data are plotted with the individual laboratory standard deviation (error bars). Laboratories reporting values below the method detection limit (MDL) are shown in this view as downward triangles beginning at the LOQ, reported as quantitation limit (QL) on the graphs. Laboratories reporting values as "below QL" can still be successful in the study if the target value is also below the laboratory QL. The solid blue line represents the consensus mean, and the green shaded area represents the 95 % confidence interval for the

[4] ISO 13528:2015(E), *Statistical methods for use in proficiency testing by interlaboratory comparisons*, Annex C.

consensus mean, based on the standard error of the consensus mean. The red shaded region represents the target zone for "acceptable" performance, which encompasses the NIST certified, reference, or estimated value bounded by twice its uncertainty (U_{95}) or twice its standard deviation. The area between the solid red lines represents the range of tolerance (values that result in an acceptable Z' score, $|Z'| \leq 2$). If the lower limit is below zero, the lower limit has been set to zero. In this view, the relative locations of individual laboratory data and consensus zones with respect to the target zone can be compared easily. In most cases, the target zone and the consensus zone overlap, which is the expected result. Major program goals include reducing the size of the consensus zone and centering the consensus zone about the target value. Analysis of an appropriate reference material as part of a quality control scheme can help to identify sources of bias for laboratories reporting results that are significantly different from the target zone. In the case in which a method comparison is relevant, different colored data points may be used to indicate laboratories that used a specific approach to sample preparation, analysis, or quantitation.

Sample/Sample Comparison View

In this view, the individual laboratory results for one sample (NIST SRM with a certified, reference, or NIST-determined value) are compared to the results for another sample (another NIST SRM with a more challenging matrix, a commercial sample, etc.). The solid red box represents the target zone for the first sample (x-axis) and the second sample (y-axis). The dotted blue box represents the consensus zone for the first sample (x-axis) and the second sample (y-axis). The axes of this graph are centered about the consensus mean values for each sample, to a limit of twice the range of tolerance (values that result in an acceptable Z' score, $|Z'| \leq 2$). Depending on the variability in the data, the axes may be scaled proportionally to better display the individual data points for each laboratory. In some cases, when the consensus and target ranges have limited overlap, the solid red box may only appear partially on the graph. If the variability in the data is high (greater than 100 % relative standard deviation (RSD)), the dotted blue box may also only appear partially on the graph. These views emphasize trends in the data that may indicate potential calibration issues or method biases. One program goal is to identify such calibration or method biases and assist participants in improving analytical measurement capabilities. In some cases, when two equally challenging materials are provided, the same view (sample/sample comparison) can be helpful in identifying commonalities or differences in the analysis of the two materials.

NUTRITIONAL ELEMENTS (Cr) IN MULTIVITAMIN AND CHROMIUM DIETARY SUPPLEMENTS

Study Overview

In this study, participants were provided with NIST SRM 3280 Multivitamin/Multielement Tablets and candidate SRM 3279 Chromium-Containing Solid Oral Dosage Form. Participants were asked to use in-house analytical methods to determine the mass fraction of chromium in each of the matrices and report values in mg/kg, on an as-received basis.

Sample Information

Multivitamin. Participants were provided with one bottle containing 30 multivitamin/multielement tablets. Before use, participants were instructed to grind all tablets, mix the resulting powder thoroughly, and to use a sample size of at least 0.2 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to prepare three samples and report three values from the single bottle provided. The approximate analyte level was not reported to participants prior to the study. The certified value for chromium in SRM 3280 was determined at NIST using instrumental neutron activation analysis (INAA) and X-ray fluorescence spectrometry (XRF). The certified value and uncertainty for chromium is provided in the table below, both on a dry-mass basis and on an as-received basis accounting for moisture of the material (1.37 %).

	Certified Mass Fraction in SRM 3280 (mg/kg)	
Analyte	(dry-mass basis)	(as-received basis)
Chromium (Cr)	93.7 ± 2.7	92.4 ± 2.7

Chromium Supplement. Participants were provided with three packets, each containing approximately 6 g of ground chromium supplement. The commercial tablets were ground, homogenized, and heat-sealed inside 4 mil polyethylene bags which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel each. Before use, participants were instructed to thoroughly mix the contents of the packet and to use a sample size of at least 0.25 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to prepare one sample and report one value from each packet provided. The approximate analyte level was not reported to participants prior to the study. The target value for chromium in candidate SRM 3279 was determined at NIST using inductively coupled plasma mass spectroscopy (ICP-MS). The NIST-determined value and uncertainty for chromium is provided in the table below, on a dry-mass basis and on an as-received basis accounting for moisture of the material (7.53 %).

	NIST-Determined Mass Fraction in Candidate SRM 3279 (mg/kg)	
Analyte	(dry-mass basis)	(as-received basis)
Chromium (Cr)	1310 ± 19	1211 ± 18

Study Results

- Forty-nine laboratories enrolled in this exercise and received samples. Thirty-nine laboratories reported results for the chromium supplement (80 % participation) and 37 laboratories reported results for the multivitamin/multielement tablets (76 % participation).
  - The consensus mean for chromium in the chromium supplement was below the target range, while the consensus mean for chromium in the multivitamin was within the target range.
  - The between-laboratory variability was very good for both the chromium supplement and the multivitamin (5 % RSD and 12 % RSD, respectively).
  - All but one of the laboratories reported using ICP-MS (97 %) as their analytical method for measuring chromium. The remaining laboratory did not specify a method (3 %).

Technical Recommendations

The following recommendations are based on results obtained from the participants in this study.

- As shown in **Figure 3,** many laboratories reported data for chromium in the multivitamin sample that was within the NIST target range for the but was lower than the NIST target range for the chromium supplement.
  - Laboratories that reported the correct value for the multivitamin but a low value for the chromium supplement may have experienced greater difficulty in digestion of the chromium supplement compared with the multivitamin.
  - While sample preparation information from the participants was limited, the use of a small amount of HF and an increase in temperature may be needed for complete digestions required for analysis.
  - A matrix interference may be present in either one or both samples. The use of standard additions may reduce the impact of matrix interferences.
  - A linear calibration curve that surrounds the expected sample concentration values should be used for calculation. This curve should include both the lowest and highest expected concentration values of the sample solutions. Extrapolation of results beyond calibration curves may result in the low values seen in the chromium supplement.
  - Most laboratories had good sample-to-sample variability (< 6 % for multivitamins and < 13 % for chromium supplement). Difficulty in the digestion of samples will cause increased variability between samples, which may explain the greater variability observed for the chromium supplement.
- For both the multivitamin and the chromium supplement, a few laboratories reported data significantly outside of the target and consensus ranges. The use of appropriate quality assurance samples to establish that a method is in control and performing correctly may reduce the likelihood of outlying data. Quality assurance samples can be commercially available reference materials (CRMs, SRMs, or RMs) or prepared in-house.
- All results should be checked closely to avoid calculation errors and to be sure that results are reported in the requested units.

Table 1. Individualized data summary table (NIST) for chromium in multivitamin and chromium supplement.

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Exercise N - May 2017 - Chromium

	Lab Code:	**NIST**	**1. Your Results**				**2. Community Results**			**3. Target**	
Analyte	Sample	Units	x_i	s_i	Z'_{comm}	Z_{NIST}	N	x*	s*	x_{NIST}	U_{95}
Chromium	Multivitamin	mg/kg	1211	18		0.00	39	1159	63	1211	18
Chromium	Cr Supplement	mg/kg	92.4	2.7		0.00	37	92.2	11.5	92.4	2.7

x_i Mean of reported values

s_i Standard deviation of reported values

Z'_{comm} Z'-score with respect to community consensus

Z_{NIST} Z-score with respect to NIST value

N Number of quantitative values reported

x* Robust mean of reported values

s* Robust standard deviation

x_{NIST} NIST-assessed value

U_{95} ±95% confidence interval about the assessed value or standard deviation (s_{NIST})

Table 2. Data summary table for chromium in multivitamin and a chromium supplement. Data points highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Chromium									
		SRM 3279 Chromium-Containing Solid Oral Dosage Form (mg/kg)					SRM 3280 Multivitamin/Multielement Tablets (mg/kg)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				1211	18				92.4	2.7
	N102	1235	1164	1157	1185	43	94.6	94.7	94.6	94.6	0.1
	N103	1142	1115	1198	1152	42	94.0	91.0	87.0	90.7	3.5
	N104	1170	1180	1180	1177	6	88.6	82.0	77.3	82.6	5.7
	N105	1156	1048	1070	1091	57	104.0	94.0	84.0	94.0	10.0
	N106	1170	1200	1210	1193	21	103.0	104.0	100.0	102.3	2.1
	N107	1232	1264	1211	1236	26	86.0	86.4	87.8	86.7	1.0
	N108	1276	1249	1238	1254	20	87.9	86.7	89.1	87.9	1.2
	N110	1201	1244	1248	1231	26	102.0	98.7	87.5	96.1	7.6
	N111	1137	1093	1120	1117	22	113.0	137.0	140.0	130.0	14.8
	N112	1274	1278	1247	1266	17	105.0	109.0	107.0	107.0	2.0
	N113	1.20	1.18	1.21	1.20	0.02	0.094	0.10	0.09	0.092	0.006
	N114	1090	1130	1170	1130	40	73.9	77.8	92.1	81.3	9.6
	N115										
	N116	1172	1177	1191	1180	10	100.4	100.1	101.9	100.8	0.9
	N119	1160	1186	1144	1163	21	95.6	104.3	97.6	99.2	4.6
	N120										
	N121	1161	1162	1139	1154	13	99.3	96.6	95.6	97.2	1.9
	N122	1142	1115	1198	1152	42	94.0	91.0	87.0	90.7	3.5
	N123	1.13	1.10	1.14	1.12	0.02	0.082	0.092	0.087	0.087	0.005
	N124	1125	1132	1132	1130	4	96.6	96.0	111.0	101.2	8.5
	N125										
	N126	1099	1140	1142	1127	24	89.0	94.8	78.5	87.4	8.3
	N127	1156	1098	1132	1129	29	94.8	92.7	91.2	92.9	1.8
	N129	1188	1192	1186	1189	3	89.8	89.2	90.5	89.8	0.7
	N130	1147	1163	1135	1148	14	82.7	93.2	87.7	87.9	5.3
	N131										
	N132	1070	1130	1180	1127	55	93.8	96.7	98.6	96.4	2.4
	N133	986	970	998	985	14	72.2	73.7	77.3	74.4	2.6
	N134	1158	1176	1190	1175	16	75.7	76.9	79.3	77.3	1.8
	N138	1080	1090	1110	1093	15					
	N139	1049	1058	1073	1060	12	92.7	94.2	98.6	95.1	3.0
	N140	1336	1333	1339	1336	3	92.8	93.6	91.4	92.6	1.1
	N141										
	N142	1304	1332	1352	1330	24	118.1	94.7	106.8	106.5	11.7
	N144										
	N145	1150	1110	1160	1140	26	103.0	91.0	90.7	94.9	7.0
	N146										
	N147										
	N148	2097	1470	1025	1530	539	95.2	94.2	94.1	94.5	0.6
	N149	1190	1210	1180	1193	15	111.0	90.4	88.6	96.7	12.4
	N150										
	N151										
	N152	1172	1167	1167	1169	3	103.4	103.1	84.0	96.8	11.1
	N153	1130	1088	1126	1115	23	88.3	80.5	78.9	82.6	5.0
	N154	1101	1151	1234	1162	67	79.8			79.8	
	N155	1170	1160	1130	1153	21	92.8	91.5	90.5	91.6	1.2
	N156	1190	1140	1130	1153	32	74.3	72.4	68.2	71.6	3.1
	N157	1185	1215	1157	1185	29	115.6	109.8	100.4	108.6	7.7
	N158	1147	1127	1131	1135	11	108.4	108.4	110.3	109.0	1.1
Community Results		Consensus Mean			1159		Consensus Mean			92.2	
		Consensus Standard Deviation			63		Consensus Standard Deviation			11.5	
		Maximum			1530		Maximum			130.0	
		Minimum			1.12		Minimum			0.087	
		N			39		N			37	

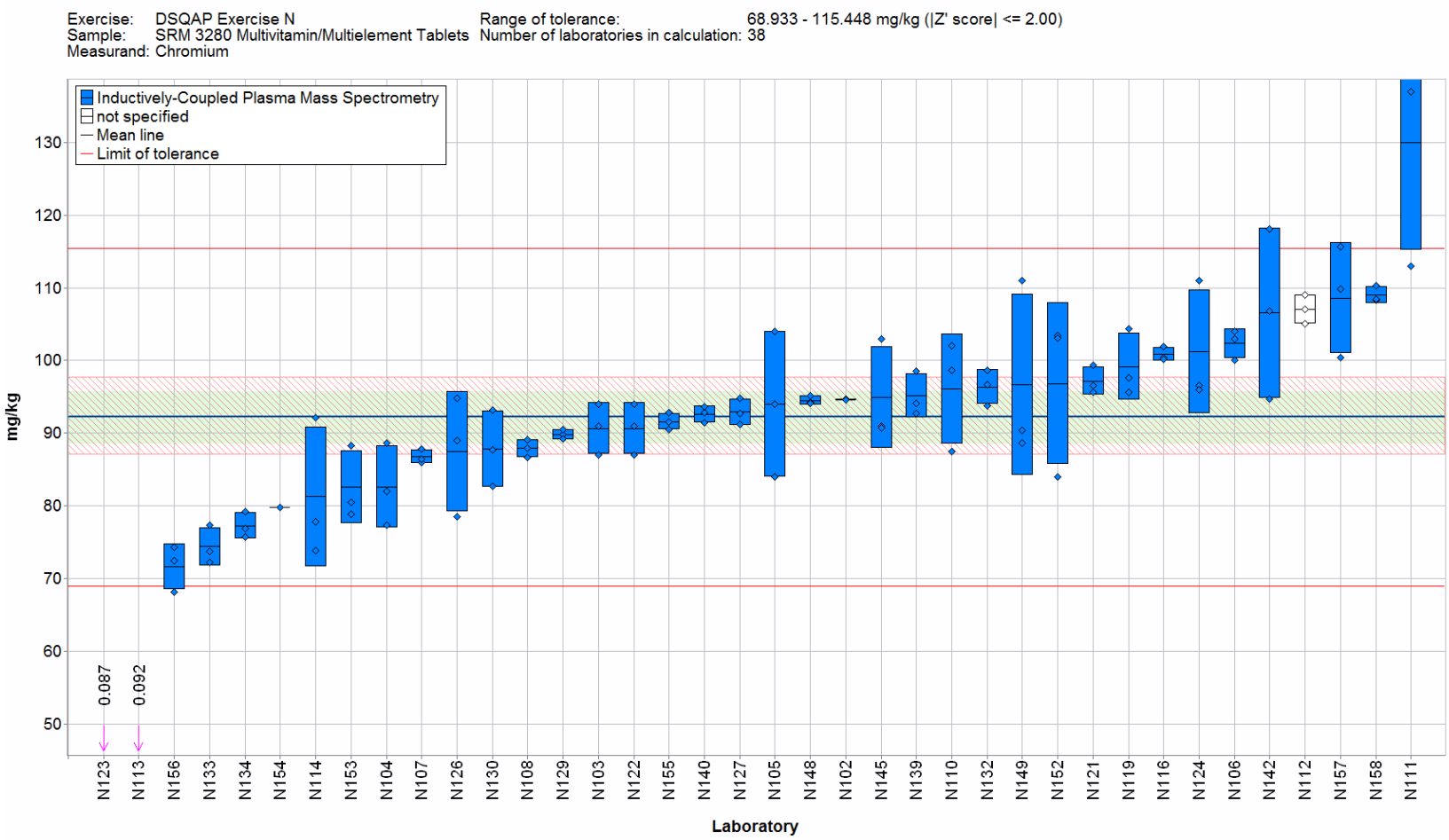

Figure 1. Chromium in SRM 3280 Multivitamin/Multielement Tablets (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

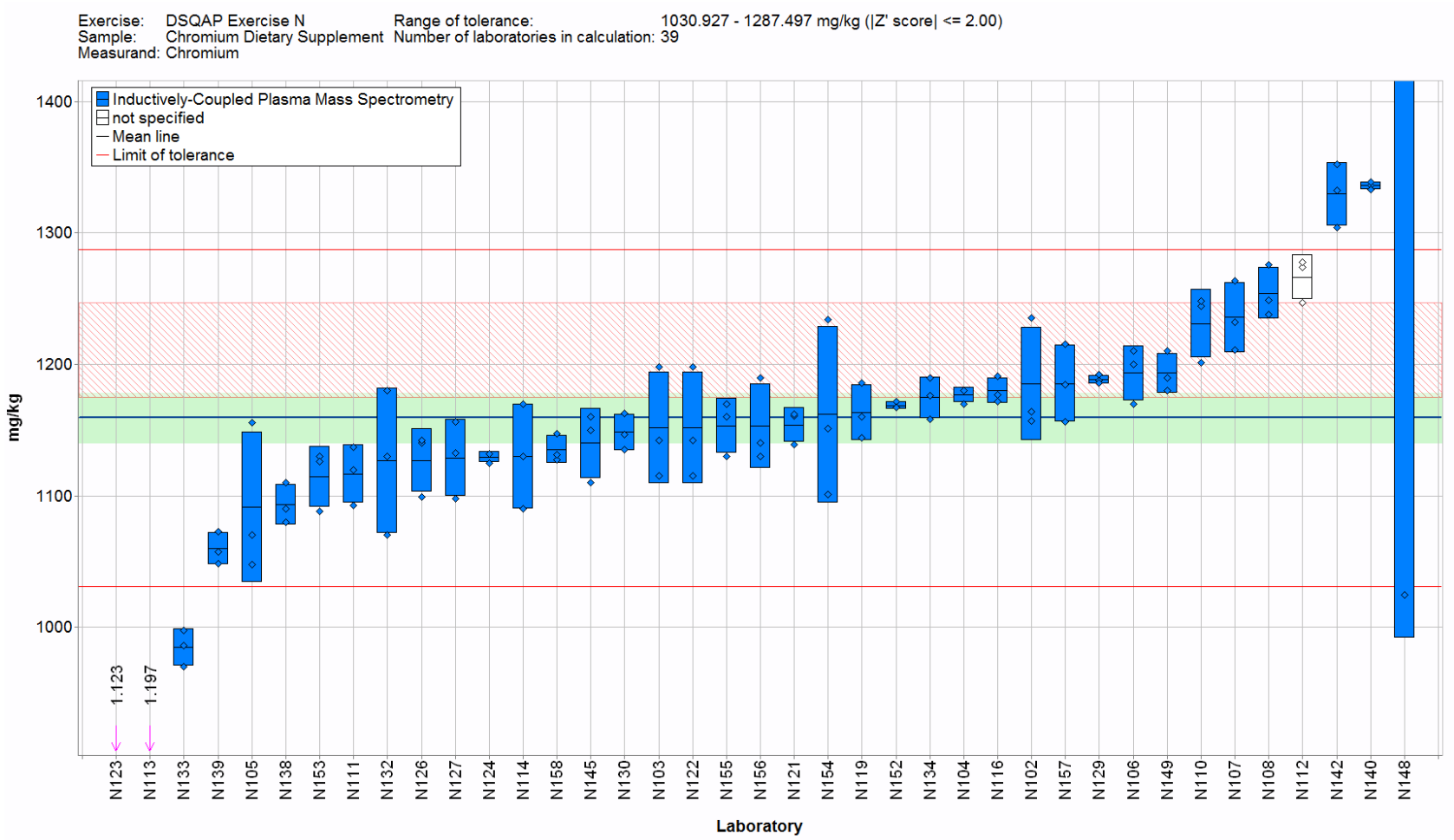

Figure 2. Chromium in candidate SRM 3279 Chromium-Containing Solid Oral Dosage Form (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$.

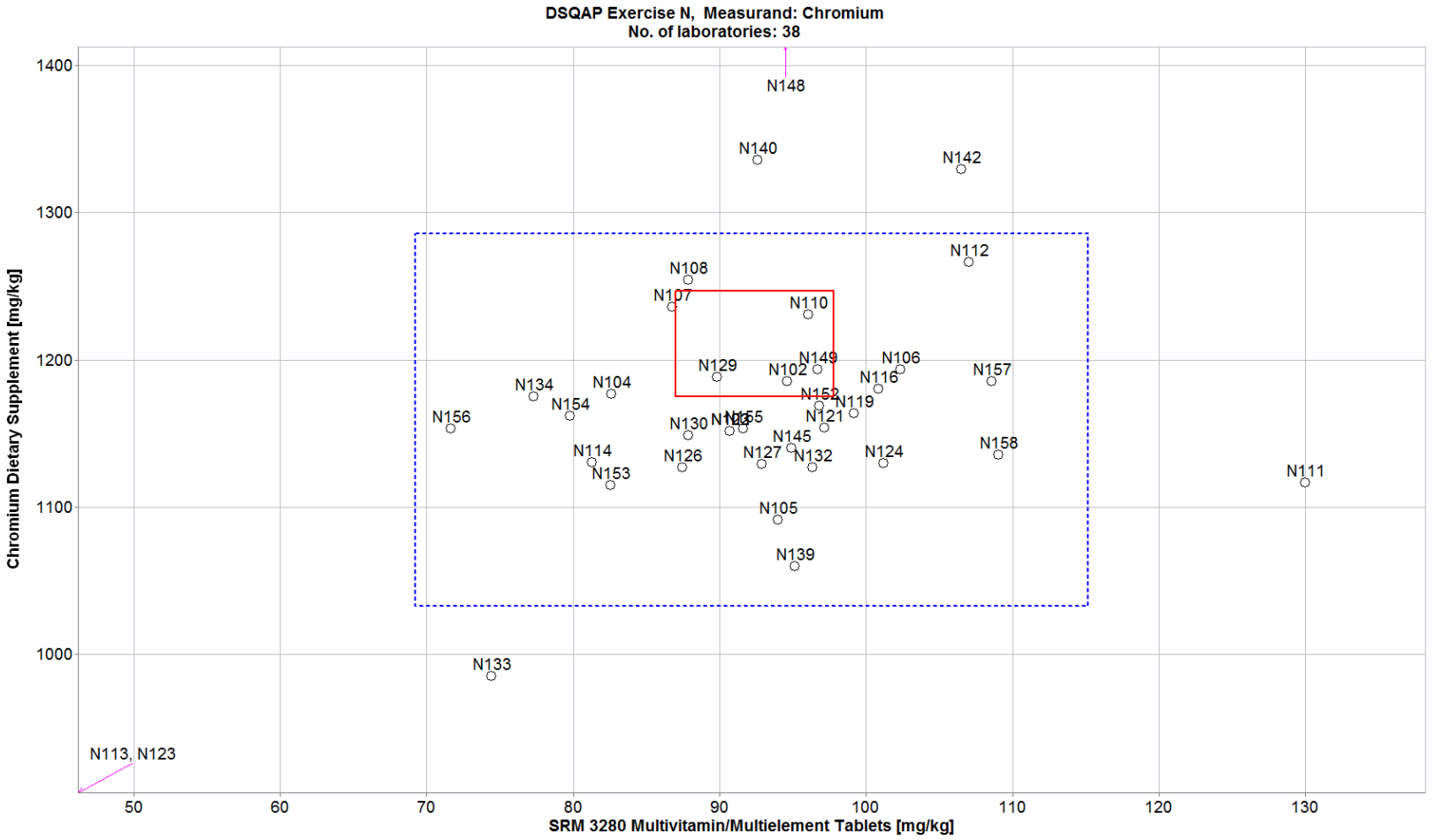

Figure 3. Laboratory means for chromium in SRM 3280 Multivitamin/Multielement Tablets and candidate SRM 3279 Chromium-Containing Solid Oral Dosage Form (sample/sample comparison view). In this view, the individual laboratory mean for one sample (multivitamin) is compared to the mean for a second sample (chromium supplement). The solid red box represents the NIST range of tolerance for the two samples, multivitamin (x-axis) and chromium supplement (y-axis), which encompasses the NIST values bounded by their uncertainties (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$. The dotted blue box represents the consensus range of tolerance for multivitamin (x-axis) and chromium supplement (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

TOXIC ELEMENTS (As, Cd, AND Pb) IN CALCIUM AND GINKGO DIETARY SUPPLEMENTS

Study Overview

In this study, participants were provided with two NIST SRMs, SRM 3532 Calcium-Containing Solid Oral Dosage Form and SRM 3248 Ginkgo-Containing Tablets. Participants were asked to use in-house analytical methods to determine the mass fractions of arsenic (As), cadmium (Cd), and lead (Pb) in each of the matrices and report values in ng/g, on an as-received basis.

Sample Information

Calcium Supplement. Participants were provided with three packets, each containing approximately 10 g of ground calcium supplement. The commercial tablets were ground, homogenized, and heat-sealed inside 4 mil polyethylene bags, which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel. Before use, participants were instructed to thoroughly mix the contents of each packet and use a sample size of at least 0.75 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to report a single value from each packet provided. Approximate analyte levels were not reported to participants prior to the study. The NIST certified value for cadmium in SRM 3532 was determined at NIST by using isotope dilution inductively coupled plasma mass spectrometry (ID ICP-MS). The NIST reference value for lead in SRM 3532 was also determined at NIST by using ID ICP-MS. The NIST-determined value for arsenic in SRM 3532 was estimated at NIST by using ICP-MS and INAA. The NIST values and uncertainties for As, Cd, and Pb are provided in the table below, both on an as-received basis and on a dry-mass basis, accounting for moisture of the material (3.2 %).

	NIST-Determined Mass Fraction in SRM 3532 (ng/g)	
Analyte	(dry-mass basis)	(as-received basis)
Arsenic (As)	365 ± 94	353 ± 91
Cadmium (Cd)	97.9 ± 1.2	94.8 ± 1.2
Lead (Pb)	225 ± 33	218 ± 31

Ginkgo Supplement. Participants were provided with three packets, each containing approximately 1 g of ground Ginkgo supplement. The commercial tablets were ground, homogenized, and heat-sealed inside 4 mil polyethylene bags which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel each. Before use, participants were instructed to thoroughly mix the contents of the packet and to use a sample size of at least 0.75 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to prepare one sample and report one value from each packet provided. The approximate analyte levels were not reported to participants prior to the study. The NIST certified value for lead in SRM 3248 was determined at NIST and at the National Research Council Canada (NRCC) using ID ICP-MS. The NIST reference values for arsenic and cadmium were determined at NIST by INAA and ID ICP-MS, respectively. The NIST values and uncertainties for As, Cd, and Pb are provided in the table below, on a dry-mass basis and on an as-received basis accounting for moisture of the material (4.78 %).

Analyte	NIST-Determined Mass Fraction in SRM 3248 (ng/g) (dry-mass basis)	NIST-Determined Mass Fraction in SRM 3248 (ng/g) (as-received basis)
Arsenic (As)	56.5 ± 4.3	53.8 ± 4.1
Cadmium (Cd)	1.56 ± 0.19	1.49 ± 0.18
Lead (Pb)	775.3 ± 8.9	738.2 ± 8.5

Study Results

- Forty-seven laboratories enrolled in the exercise and received samples to measure arsenic in both supplements. Thirty-three laboratories reported results for arsenic in the calcium supplement (70 % participation). Thirty-two laboratories reported results for arsenic in the ginkgo supplement (68 % participation).
  - The consensus means for arsenic in both materials were within the NIST target ranges. The between-laboratory variability was high for both the calcium supplement and the ginkgo supplement (35 % RSD and 42 % RSD, respectively).
  - All but one of the laboratories reported using ICP-MS (97 %) as their analytical method for measuring arsenic. The remaining laboratory did not specify a method (3 %).
- Forty-nine laboratories enrolled in the exercise and received samples to measure cadmium in both supplements. Thirty-six laboratories reported results for cadmium in the calcium supplement (73 % participation). Sixteen laboratories reported results for cadmium in the ginkgo supplement (33 % participation).
  - The consensus mean for cadmium was below the target range of the calcium supplement with good between-laboratory variability (19 % RSD).
  - The consensus mean for cadmium was above the target range of the ginkgo supplement with very high between-laboratory variability (65 % RSD).
  - All but one of the laboratories reported using ICP-MS (97 %) as their analytical method for measuring cadmium. The remaining laboratory did not specify a method (3 %).
- Forty-nine laboratories enrolled in the exercise and received samples to measure lead in both supplements. Thirty-seven laboratories reported results for lead in the calcium supplement (76 % participation). Thirty-six laboratories reported results for lead in the ginkgo supplement (73 % participation).
  - The consensus mean for lead was within the target range of the calcium supplement with good between-laboratory variability (23 % RSD).
  - The consensus mean for lead was below the target range of the ginkgo supplement, but the consensus range slightly overlapped the target range. The between-laboratory variability was very good for lead in the ginkgo supplement (10 % RSD).
  - All but one laboratory reported using ICP-MS (97 %) as their analytical method for measuring arsenic. The remaining laboratory did not specify a method (3 %).

Technical Recommendations

The following recommendations are based on results obtained from the participants in this study.

- Difficulty in the digestion of samples will cause increased variability between samples. Supplements and tablets can be hard to digest, requiring higher temperatures or the use of a small amount of HF to ensure complete digestion of the materials.
- The high level of Ca in the calcium supplement can cause a buildup on the ICP-MS cones if sample solutions are not diluted. Unfortunately, the analyte of interest is also diluted, and sensitivity is decreased for analytes that are already low in the matrix.
- A difference in reporting units among laboratories is the suspected reason for the occurrence of high between-laboratory variability. Calculation errors may be a cause for incorrect results. Using a quality assurance material (CRM, SRM, RM), or in-house prepared material, to establish that a method is in control will also help find calculation errors. Once a method and quality assurance material appear to be in control, be sure results are reported in the correct units.
- Arsenic is volatile and can be lost during sample preparation. For laboratories experiencing low arsenic values the following may be of help;
  - High temperatures using a vigorous microwave digestion should convert all volatile organoarsenic species to arsenic acid (AsV), at which point subsequent heating will not result in loss of arsenic. Open-beaker digestions should not be used for As analysis and closed-vessel digestions should be opened with care ensuring that no As is lost as a result of inadvertent venting.
  - Extrapolation of samples lying above the calibration curve may result in incorrect results. Ensure calibration curves are linear at the point where sample concentrations are expected to be measured.
- Spectral interferences can make cadmium difficult to measure accurately by ICP-MS, which may be the cause of some of the high QLs reported in the data tables.
  - A scan of the sample before analysis will indicate any potential interferences in the sample that will need to be addressed. High concentrations of certain elements, mainly Mo, Sn, or Zr, are known to cause interferences in the analysis of cadmium by ICP-MS.
  - The high level of Ca compared to Cd in the calcium dietary supplement may also cause interference, especially when using ^{112}Cd $(^{40}Ca_2{}^{16}O)_2$.
  - Examples of molecular interferences include $^{95, 96, 97 \text{ and } 98}Mo^{16}O^+$, $^{94, 95, 96, \text{ and } 97}Mo^{16}O^1H^+$, $^{96}Zr^{16}O^+$, $^{94 \text{ and } 96}Zr^{16}O^1H^+$, $^{40}Ar_2{}^{16}O_2$, $^{40}Ca_2{}^{16}O_2$, or $^{40}Ca_2{}^{16}O_2{}^1H^+$. Examples of elemental isobaric interferences include ^{112}Sn, ^{113}In, and ^{114}Sn.
  - Anion chromatography prior to ICP-MS can reduce interferences. If this is not practical, collision cell technology can be used to remove many of the molecular interferences that may be found in these two materials.
- Analysis of an appropriate number of procedural blanks is always important and can be critical when sample concentrations are near the detection limit, as with cadmium in the ginkgo supplement.
- Lead is easily digested and volatile loss of Pb is not a concern. Digestion with HCl may form a highly insoluble $PbCl_2$ precipitate, so digestion with HNO_3 is recommended.
  - Some laboratories had high sample-to-sample variability (20 % to > 50 %), which may be caused by incomplete sample digestion, matrix interferences, or calibration curves which do not encompass all sample solutions measured.

Calibration curves must be linear and include the lowest and highest values expected to be measured in the sample solutions. Extrapolation of the curve may cause incorrect results.

Table 3. Individualized data summary table (NIST) for arsenic, cadmium, and lead in calcium and ginkgo supplements.

National Institute of Standards & Technology

Exercise N - May 2017 - Toxic Elements

	Lab Code:	**NIST**	**1. Your Results**				**2. Community Results**			**3. Target**	
Analyte	Sample	Units	x_i	s_i	Z'_{comm}	Z_{NIST}	N	x*	s*	x_{NIST}	U_{95}
Arsenic	Ca Supplement	ng/g	353	91		0.00	33	324	114	353	91
Arsenic	Ginkgo Tablets	ng/g	54.0	4.1		0.00	32	58.2	24.4	54.0	4.1
Cadmium	Ca Supplement	ng/g	94.8	1.2		0.00	36	85	16	94.8	1
Cadmium	Ginkgo Tablets	ng/g	1.49	0.18		0.00	17	3	2	1.5	0.2
Lead	Ca Supplement	ng/g	218	31		0.00	37	223	51	218	31
Lead	Ginkgo Tablets	ng/g	738	9		0.00	36	712	71	738	9

x_i Mean of reported values

s_i Standard deviation of reported values

Z'_{comm} Z'-score with respect to community consensus

Z_{NIST} Z-score with respect to NIST value

N Number of quantitative values reported

x* Robust mean of reported values

s* Robust standard deviation

x_{NIST} NIST-assessed value

U_{95} ±95% confidence interval about the assessed value or standard deviation (s_{NIST})

Table 4. Data summary table for total arsenic in calcium and ginkgo supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Total Arsenic									
		SRM 3532 Calcium Dietary Supplement (ng/g)					SRM 3248 Ginkgo-Containing Tablets (ng/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				353	91				53.8	4.1
	N102	271	261	265	266	5	44.0	40.0	47.0	43.7	3.5
	N103	313	276	289	293	19	131.0	147.0	150.0	142.7	10.2
	N104	312	310	318	313	4	46.7	46.7	49.3	47.6	1.5
	N105	317	264	285	289	27	< 50	< 50	< 50	< 50	
	N106	370	370	390	377	12	56.0	47.0	58.0	53.7	5.9
	N107	70	74	74	73	3	30.2	28.0	27.7	28.6	1.4
	N108	309	329	302	313	14	52.0	53.0	52.0	52.3	0.6
	N110	706	722	716	714	8	83.6	90.7	85.8	86.7	3.6
	N111	204	228	321	251	62	102.0	102.0	101.0	101.7	0.6
	N112	276	339	296	304	32	72.0	69.0	69.0	70.0	1.7
	N113	292	275	252	273	20	51.0	71.0	60.8	60.9	10.0
	N114	356	358	913	542	321	63.0	45.0	55.0	54.3	9.0
	N115										
	N116										
	N118	172	178	203	184	16	26.5	27.6	23.7	25.9	2.0
	N119	297	304	292	298	6	48.8	46.9	47.6	47.8	1.0
	N120										
	N121	0.310	0.350	0.340	0.333	0.021	0.050	0.050	0.050	0.050	0.000
	N122	313	276	289	293	19	131.0	147.0	150.0	142.7	10.2
	N124	390	380	394	388	8	48.5	50.0	53.6	50.7	2.6
	N125										
	N126	372	371	374	372	2	59.0	59.0	55.0	57.7	2.3
	N127	3890	3160	3987	3679	452	184.6	174.1	173.1	177.3	6.3
	N129	327	307	312	315	11	49.8	50.5	45.2	48.5	2.9
	N130	157	181	161	166	13	59.7	54.9	59.8	58.1	2.8
	N131										
	N132	330	330	340	333	6	60.0	60.0	60.0	60.0	0.0
	N133										
	N134	277	223	220	240	32	48.0	68.0	37.0	51.0	15.7
	N140						52.7	52.5	49.6	51.6	1.7
	N141										
	N142	379	366	377	374	7	51.5	49.2	51.5	50.7	1.4
	N144										
	N145	303	291	368	321	41	43.5	48.0	48.4	46.6	2.721
	N146										
	N147										
	N148	600	512	490	534	58	162.9	165.3	196.8	175.0	18.9
	N149	406	1704	266	792	793	39.2	51.5	54.8	48.5	8.2
	N150										
	N151										
	N152	401	362	421	395	30	233.9	206.7	200.1	213.6	17.9
	N153	441	366	510	439	72	55.0	50.0	50.0	51.7	2.9
	N154	212	186	183	194	16	< 100	< 100	< 100	< 100	
	N155	309	350	340	333	21	52.0	53.0	52.0	52.3	0.6
	N156	330	340	320	330	10	30.0	30.0	38.0	32.7	4.6
	N157	< 660	< 660	< 660	< 660		< 670	< 670	< 670	< 670	
	N158	249	294	276	273	23	42.8	38.0	43.0	41.2	2.8
Community Results		Consensus Mean			325		Consensus Mean			58.2	
		Consensus Standard Deviation			114		Consensus Standard Deviation			24.4	
		Maximum			3679		Maximum			213.6	
		Minimum			0.333		Minimum			0.050	
		N			33		N			32	

Table 5. Data summary table for cadmium in calcium and ginkgo supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Cadmium									
		SRM 3532 Calcium Dietary Supplement (ng/g)					SRM 3248 Ginkgo-Containing Tablets (ng/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				94.8	1.2				1.49	0.18
	N102	66.0	62.0	62.0	63.3	2.3	< 3.00	< 3.00	< 3.00	< 3.00	
	N103	77.0	79.0	73.0	76.3	3.1	3.00	4.00	2.00	3.00	1.00
	N104	100.0	102.0	100.0	100.7	1.2	1.60	1.55	1.32	1.49	0.15
	N105	87.0	82.0	83.0	84.0	2.6	< 50.00	207.00	< 50.00	207.00	
	N106	96.0	97.0	93.0	95.3	2.1	< 10.00	< 10.00	< 10.00	< 10.00	
	N107	12.9	11.7	12.2	12.2	0.6	7.43	6.32	6.64	6.80	0.57
	N108	89.00	89.00	91.00	89.67	1.15	71.00	53.00	1.96	41.99	35.81
	N110	90.7	91.6	93.2	91.8	1.3	1.20	1.90	1.70	1.60	0.36
	N111	111.0	110.0	111.0	110.7	0.6	2.00	2.00	2.00	2.00	0.00
	N112	83.0	84.0	80.0	82.3	2.1	< 10.00	< 10.00	< 10.00	< 10.00	
	N113	93.9	89.4	81.1	88.1	6.5	< 24.90	< 24.90	< 24.90	< 24.90	
	N114	85.0	91.0	112.0	96.0	14.2	< 1.000	2.00	2.00	2.00	0.00
	N115										
	N116										
	N118	58.9	55.9	57.8	57.5	1.5	1.31	1.75	1.54	1.53	0.22
	N119	95.7	98.0	96.2	96.6	1.2					
	N120										
	N121	0.10	0.10	0.10	0.10	0.00	< 0.010	< 0.010	< 0.010	< 0.010	
	N122	77.0	79.0	73.0	76.3	3.1	3.00	4.00	2.00	3.00	1.00
	N123	105.0	98.1	94.1	99.1	5.5					
	N124	95.7	95.2	102.7	97.8	4.2	2.15	1.92	1.94	2.00	0.13
	N125										
	N126	118.0	118.0	123.0	119.7	2.9	1.10	1.50	1.20	1.27	0.21
	N127	92.4	92.0	85.1	89.8	4.1					
	N129	85.8	103.1	93.5	94.1	8.7	2.30	3.18	0.96	2.14	1.12
	N130	90.5	89.0	84.9	88.1	2.9	1.75	2.23	1.90	1.96	0.25
	N131										
	N132	83.0	82.0	85.0	83.3	1.5	2.00	1.00	1.00	1.33	0.58
	N133										
	N134	68.0	70.0	68.0	68.7	1.2	< 10.00	< 10.00	< 10.00	< 10.00	
	N135	75.5	75.0	76.2	75.6	0.6					
	N140	100.4	100.0	102.6	101.0	1.4					
	N141										
	N142	80.7	94.3	98.2	91.1	9.2					
	N144										
	N145	79.3	83.9	79.6	80.9	2.6					
	N146										
	N147										
	N148	54.1	54.2	49.8	52.7	2.5	15.70	17.00	17.20	16.63	0.81
	N149	88.8	82.2	86.3	85.8	3.3	2.36	2.14	1.77	2.09	0.30
	N150										
	N151										
	N152	87.4	90.0	89.9	89.1	1.5	< 20.00	< 20.00	< 20.00	< 20.00	
	N153	110.0	113.0	102.0	108.3	5.7					
	N154	70.0	71.0	68.0	69.7	1.5	< 20.00	< 20.00	< 20.00	< 20.00	
	N155	85.7	87.1	90.7	87.8	2.6	< 0.50	< 0.50	< 0.50	< 0.50	
	N156	74.0	72.0	76.0	74.0	2.0	< 8.00	< 8.00	< 8.00	< 8.00	
	N157	< 660	< 660	< 660	< 660		< 670	< 670	< 670	< 670	
	N158	77.9	78.8	84.2	80.3	3.4	1.18	0.96	0.46	0.87	0.37
Community Results		Consensus Mean			85.3		Consensus Mean			2.59	
		Consensus Standard Deviation			15.8		Consensus Standard Deviation			1.69	
		Maximum			119.7		Maximum			207.00	
		Minimum			0.100		Minimum			0.87	
		N			36		N			17	

Table 6. Data summary table for lead in calcium and ginkgo supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Lead									
		SRM 3532 Calcium Dietary Supplement (ng/g)					SRM 3248 Ginkgo-Containing Tablets (ng/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				218	31				738	8
	N102	214	209	201	208	7	715	696	706	706	10
	N103	241	246	265	251	13	632	641	676	650	23
	N104	270	312	227	270	43	692	692	702	695	6
	N105	182	146	163	164	18	748	680	662	697	45
	N106	270	240	220	243	25	700	720	710	710	10
	N107	247	223	184	218	32	655	629	642	642	13
	N108	214	229	271	238	30	727	689	727	714	22
	N110	266	522	268	352	148	883	934	954	923	37
	N111	252	261	280	264	14	850	844	852	849	4
	N112	255	191	216	221	32	671	675	669	672	3
	N113	191	188	208	196	11	717	717	737	724	12
	N114	177	259	263	233	49	824	768	770	787	32
	N115										
	N116										
	N118	103	106	92	100	8	822	803	821	815	11
	N119	229	304	272	268	38	689	704	701	698	8
	N120										
	N121	0.260	0.290	0.290	0.280	0.017	0.780	0.830	0.770	0.793	0.032
	N122	241	246	265	251	13	632	641	675	649	23
	N123	186	206	195	196	10	804	780	726	770	40
	N124	198	198	302	233	60	688	647	667	668	20
	N125										
	N126	98	186	106	130	49	709	708	689	702	11
	N127	282	232	285	266	29	718	689	674	694	23
	N129	185	171	300	219	71	712	728	685	708	22
	N130	239	324	224	262	54	712	732	715	720	11
	N131										
	N132	180	190	200	190	10	660	680	680	673	12
	N133										
	N134	211	211	213	212	1	711	732	736	726	13
	N135	167	170	168	168	2	501	492	500	498	5
	N140	235	247	236	239	7	780	780	790	783	6
	N141										
	N142	255	244	243	247	7	763	770	773	769	5
	N144										
	N145	229	190	217	212	20	690	774	720	728	43
	N146										
	N147										
	N148	241	206	244	230	21	724	829	934	829	105
	N149	209	221	85	172	75	685	707	711	701	14
	N150										
	N151										
	N152	343	251	210	268.0	68.1	792	773	786	783.5	9.4
	N153	207	291	215	238	46	739	720	673	711	34
	N154	166	169	150	162	10	563	558	559	560	3
	N155	230	240	358	276	71	761	772	772	768	6
	N156	230	230	250	237	12	690	700	690	693	6
	N157	800	730	730	753	40	< 670	< 670	< 670	< 670	
	N158	165	171	168	168	3	584	609	587	593	14
Community Results		Consensus Mean			223		Consensus Mean			712	
		Consensus Standard Deviation			51		Consensus Standard Deviation			71	
		Maximum			753		Maximum			923	
		Minimum			0.280		Minimum			0.793	
		N			37		N			36	

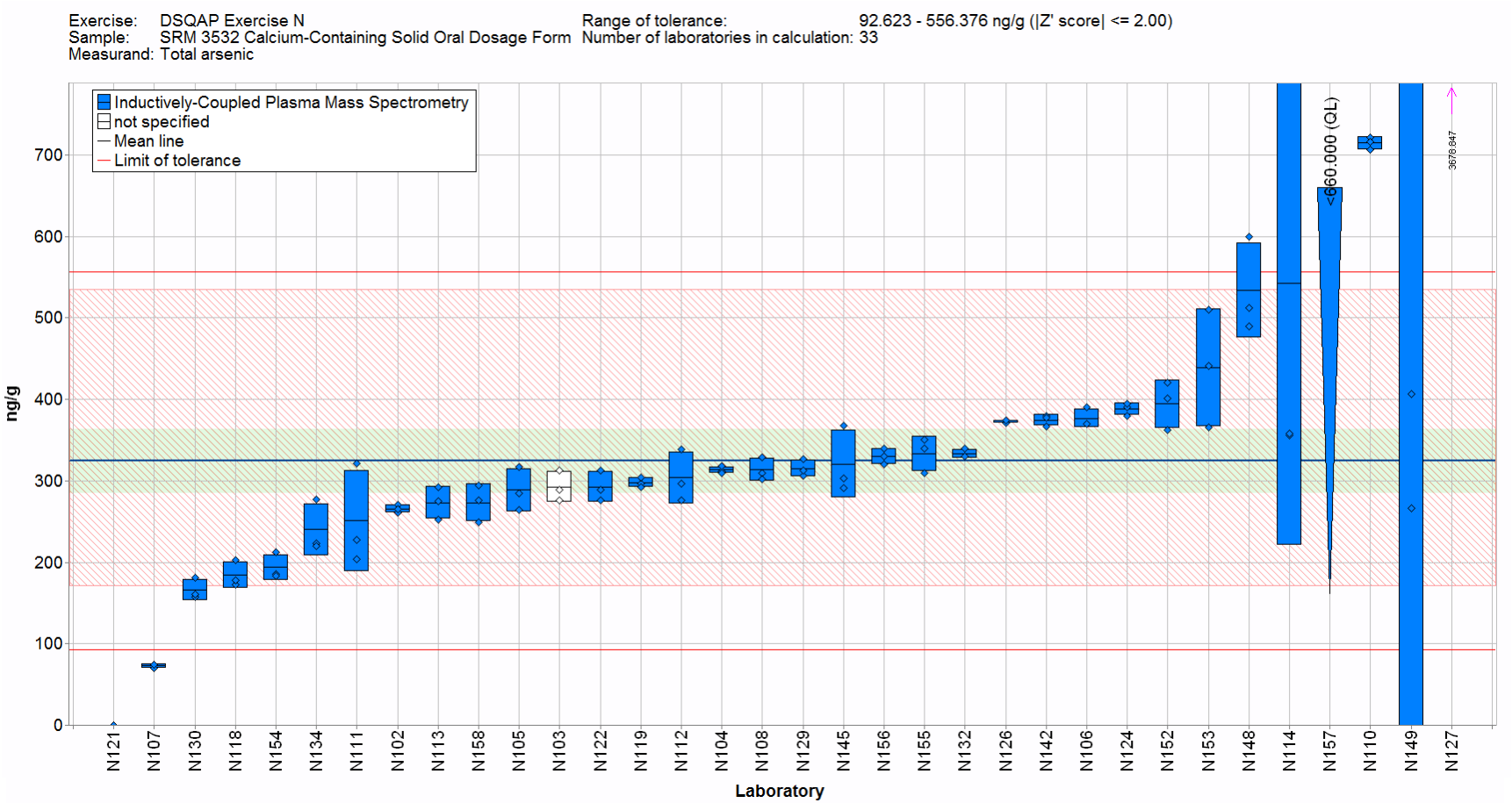

Figure 4. Arsenic in SRM 3532 Calcium-Containing Solid Oral Dosage Form (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$.

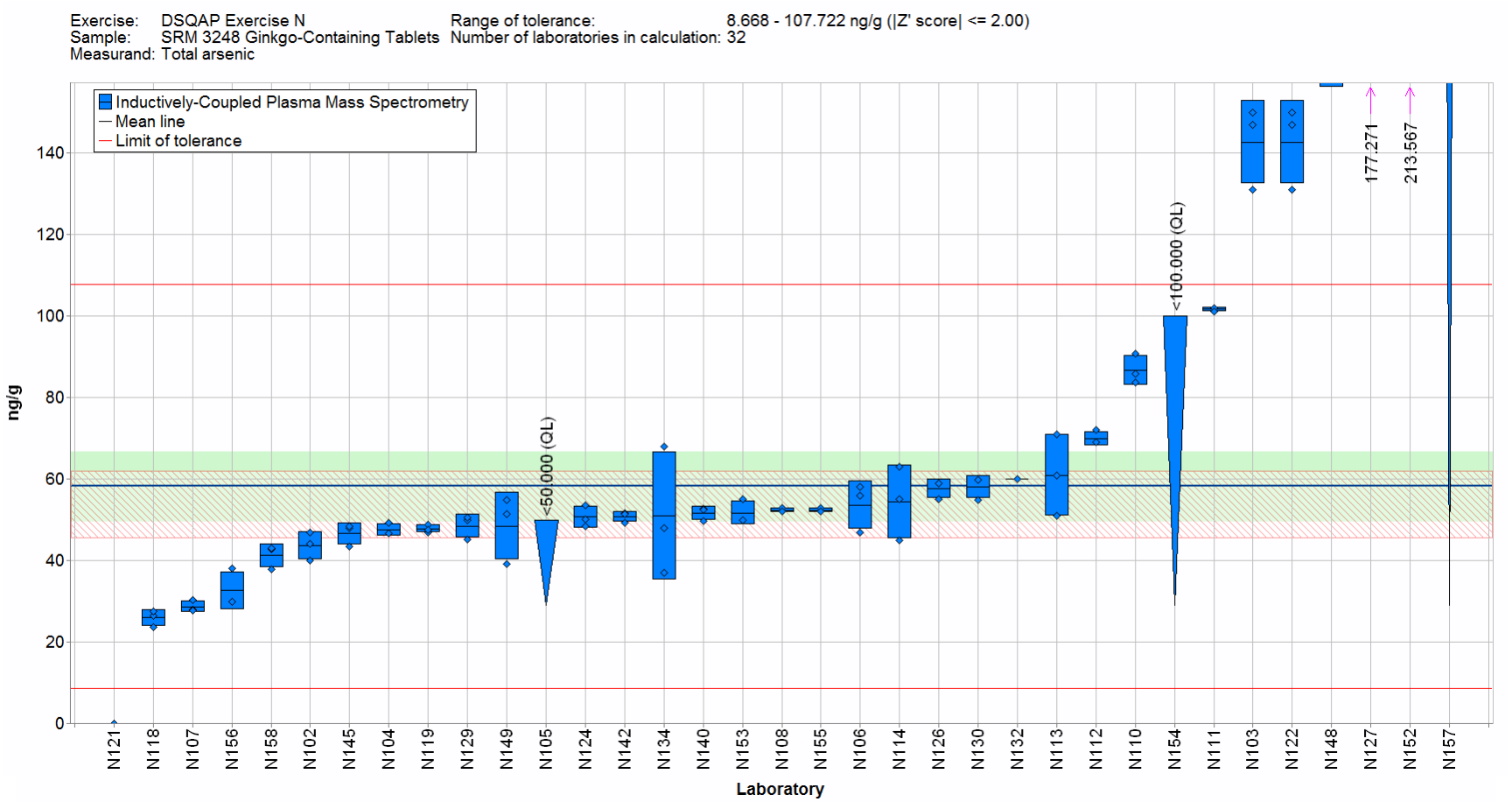

Figure 5. Arsenic in SRM 3248 Ginkgo-Containing Tablets (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST reference value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

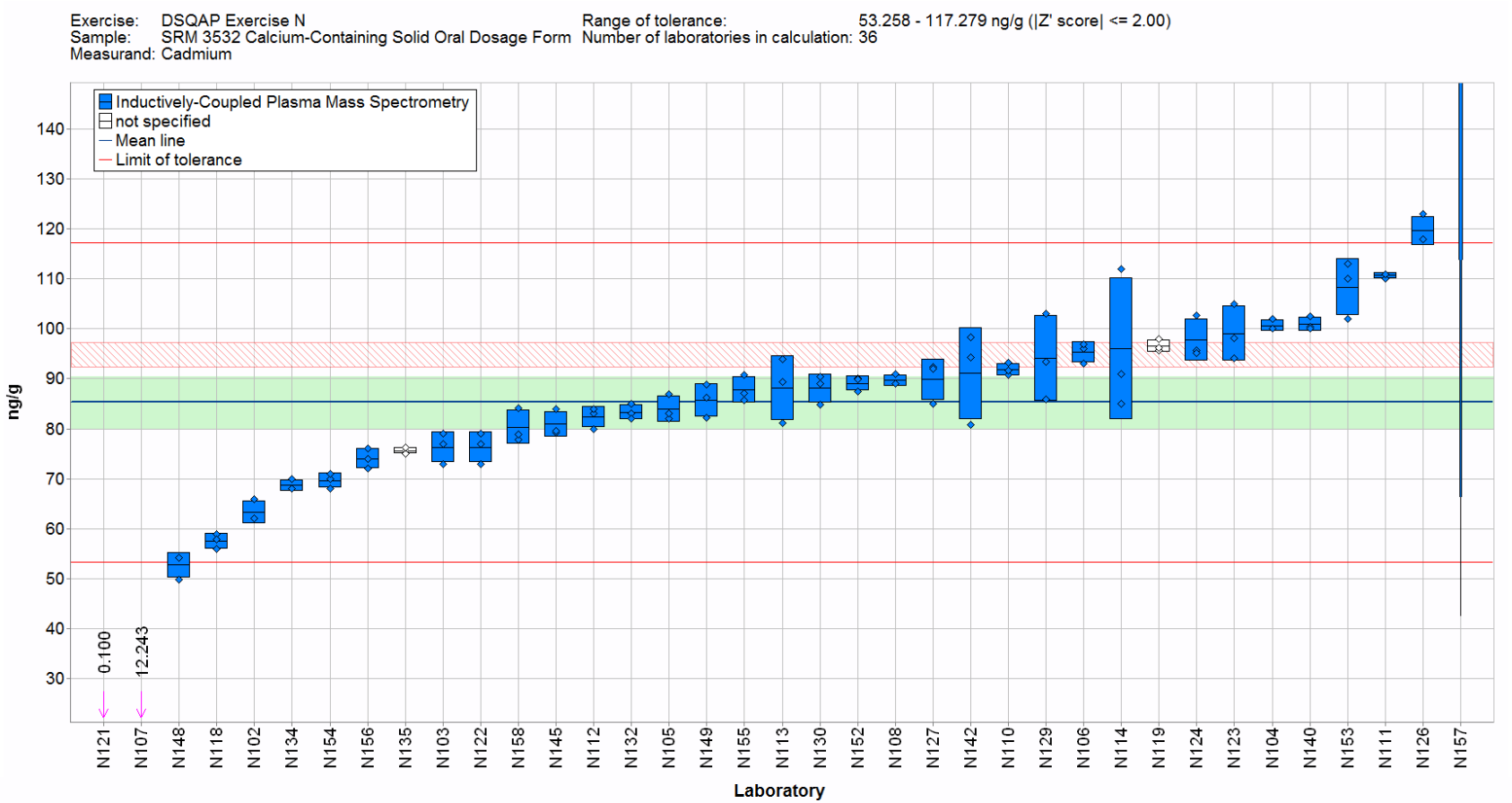

Figure 6. Cadmium in SRM 3532 Calcium-Containing Solid Oral Dosage Form (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

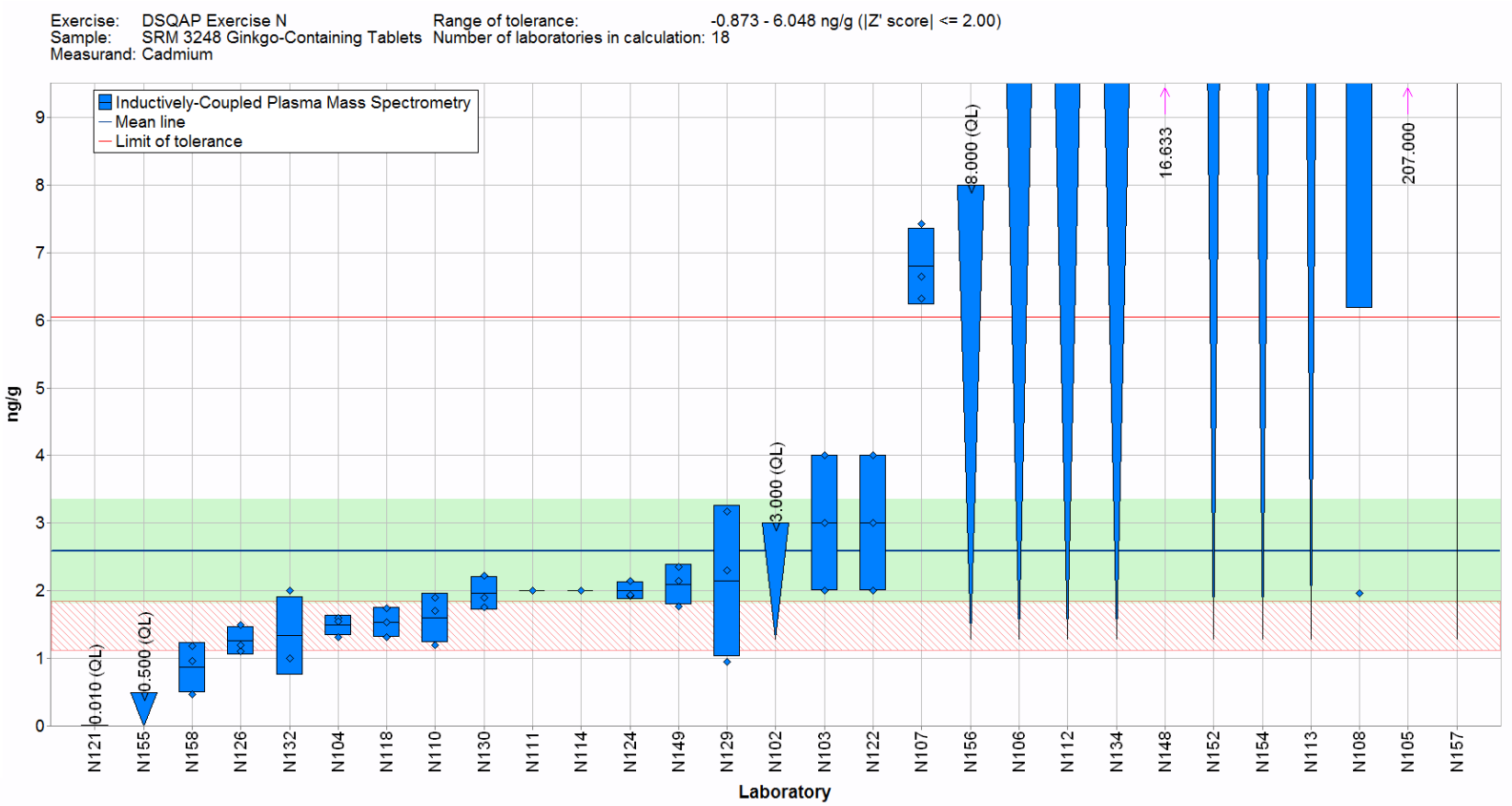

Figure 7. Cadmium in SRM 3248 Ginkgo-Containing Tablets (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set at zero. The red shaded region represents the NIST range of tolerance, which encompasses the NIST reference value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

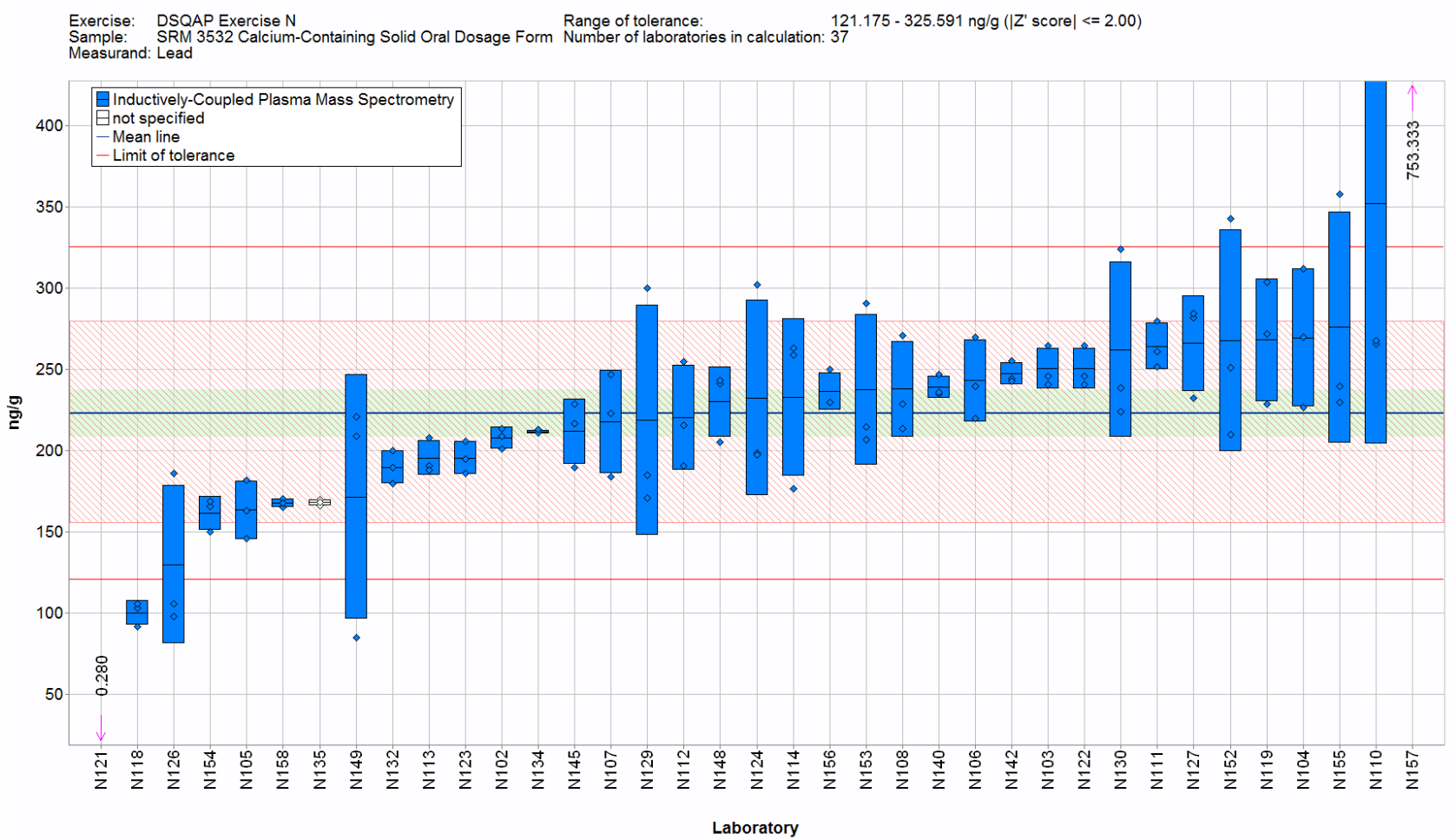

Figure 8. Lead in SRM 3532 Calcium-Containing Solid Oral Dosage Form (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST reference value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

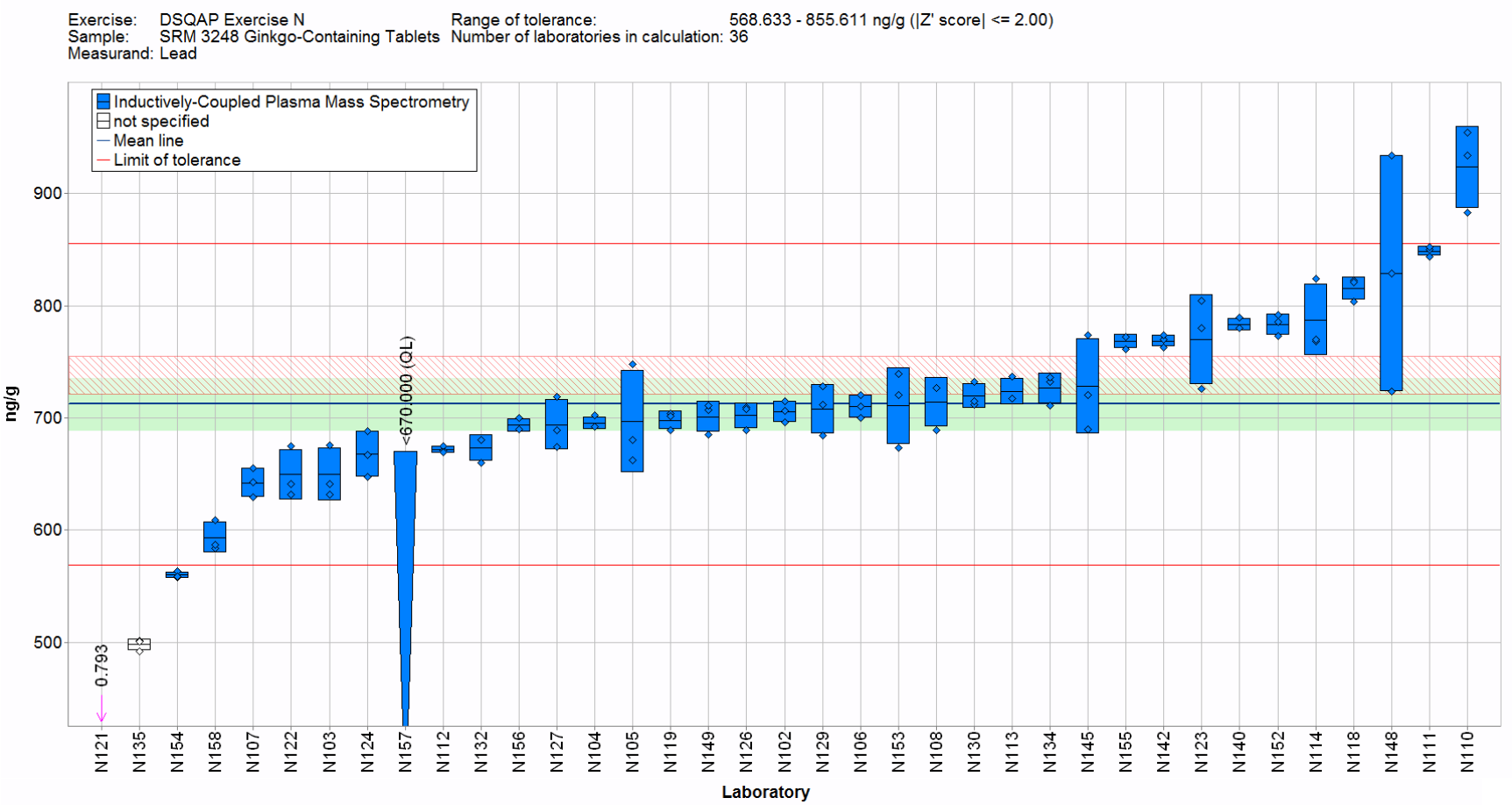

Figure 9. Lead in SRM 3248 Ginkgo-Containing Tablets (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$.

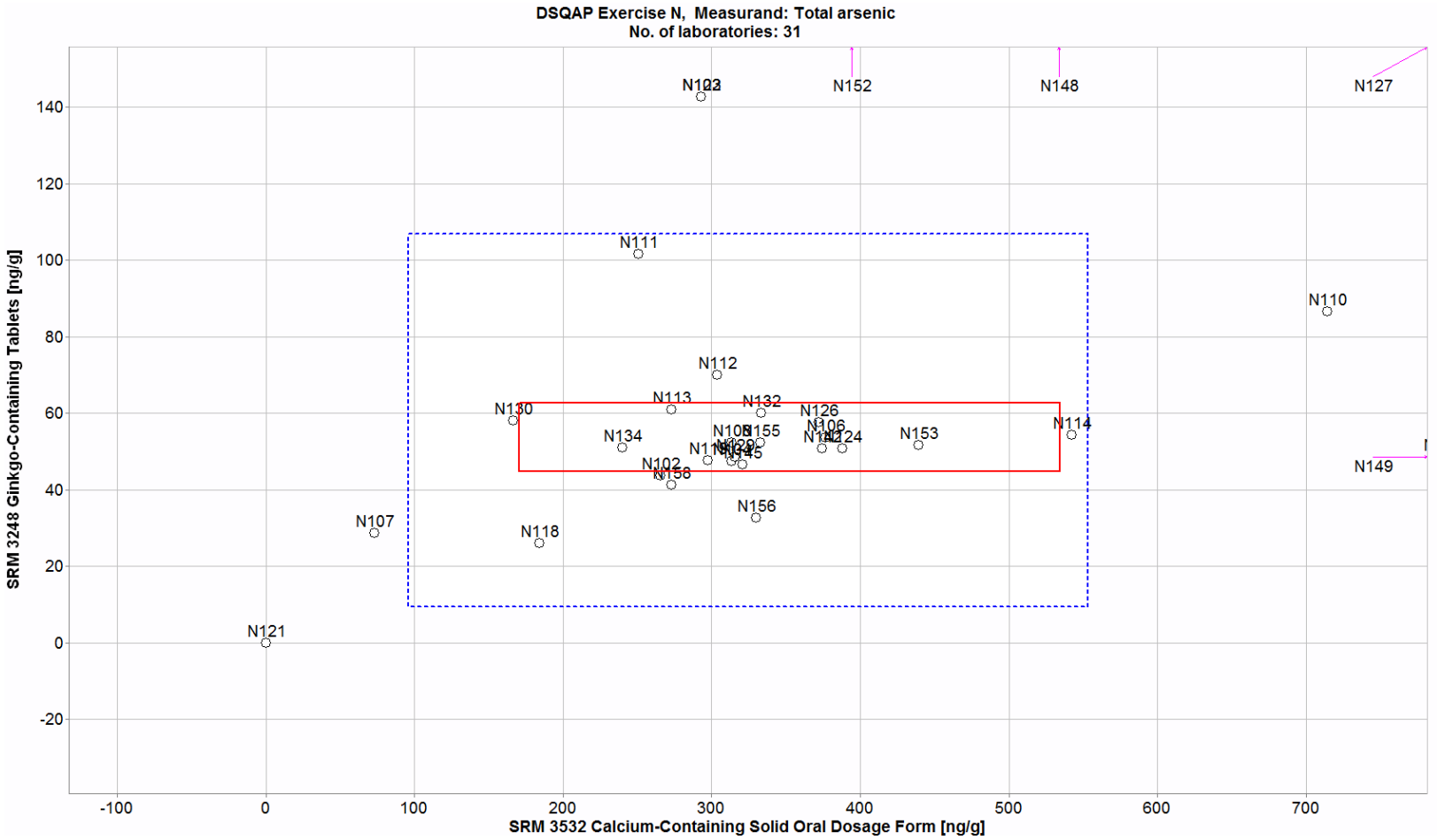

Figure 10. Laboratory means for total arsenic in SRM 3532 Calcium-Containing Solid Oral Dosage Form and SRM 3248 Ginkgo-Containing Tablets (sample/sample comparison view). In this view, the individual laboratory mean for one sample (calcium supplement) is compared to the mean for a second sample (ginkgo tablets). The solid red box represents the NIST range of tolerance for the two samples, calcium supplement (x-axis) and ginkgo tablets (y-axis), which encompasses the NIST values bounded by their uncertainties (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$. The dotted blue box represents the consensus range of tolerance for calcium supplement (x-axis) and ginkgo tablets (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

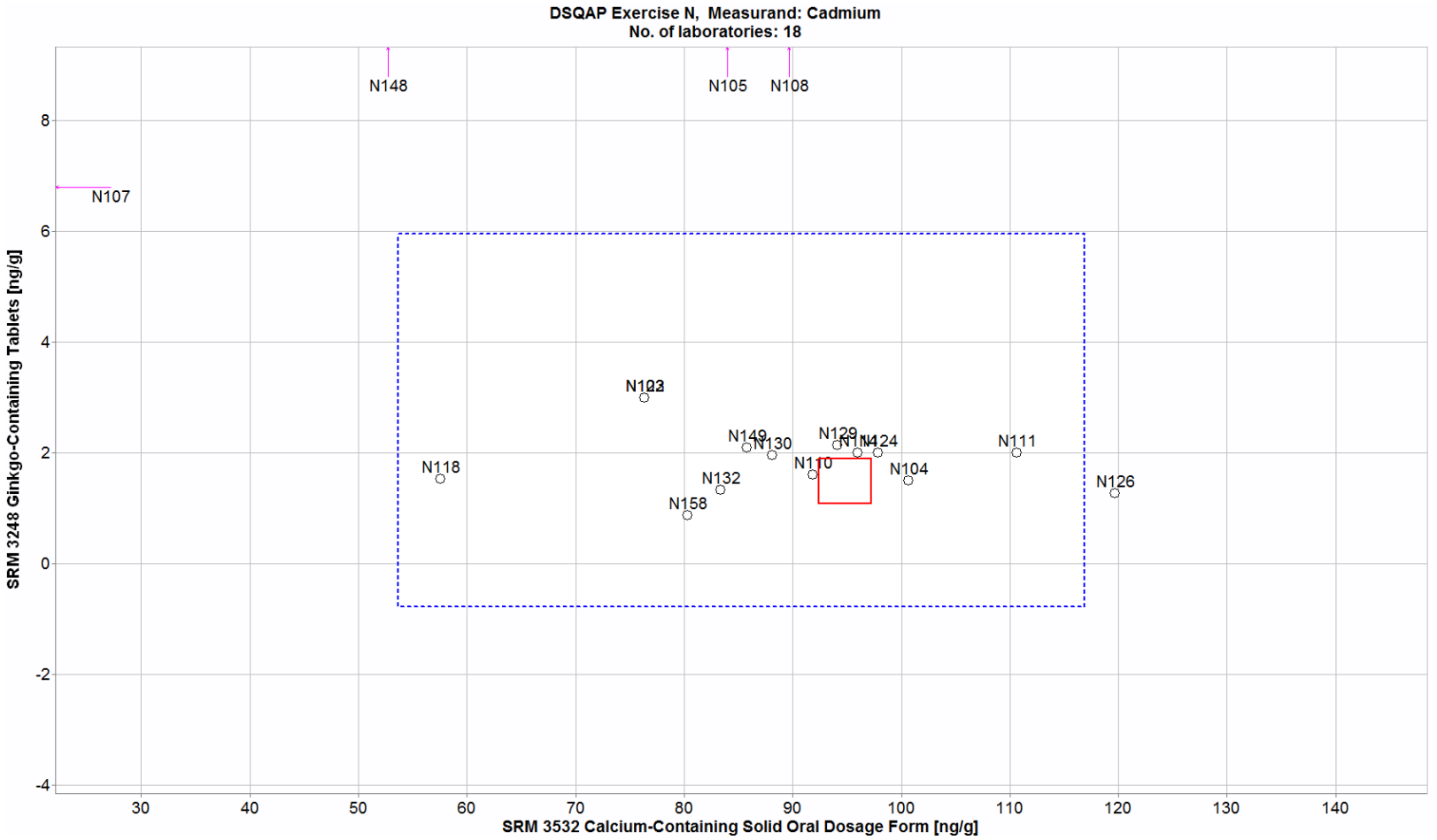

Figure 11. Laboratory means for cadmium in SRM 3532 Calcium-Containing Solid Oral Dosage Form and SRM 3248 Ginkgo-Containing Tablets (sample/sample comparison view). In this view, the individual laboratory mean for one sample (calcium supplement) is compared to the mean for a second sample (ginkgo tablets). The solid red box represents the NIST range of tolerance for the two samples, calcium supplement (x-axis) and ginkgo tablets (y-axis), which encompasses the NIST values bounded by their uncertainties (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$. The dotted blue box represents the consensus range of tolerance for calcium supplements (x-axis) and ginkgo tablets (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

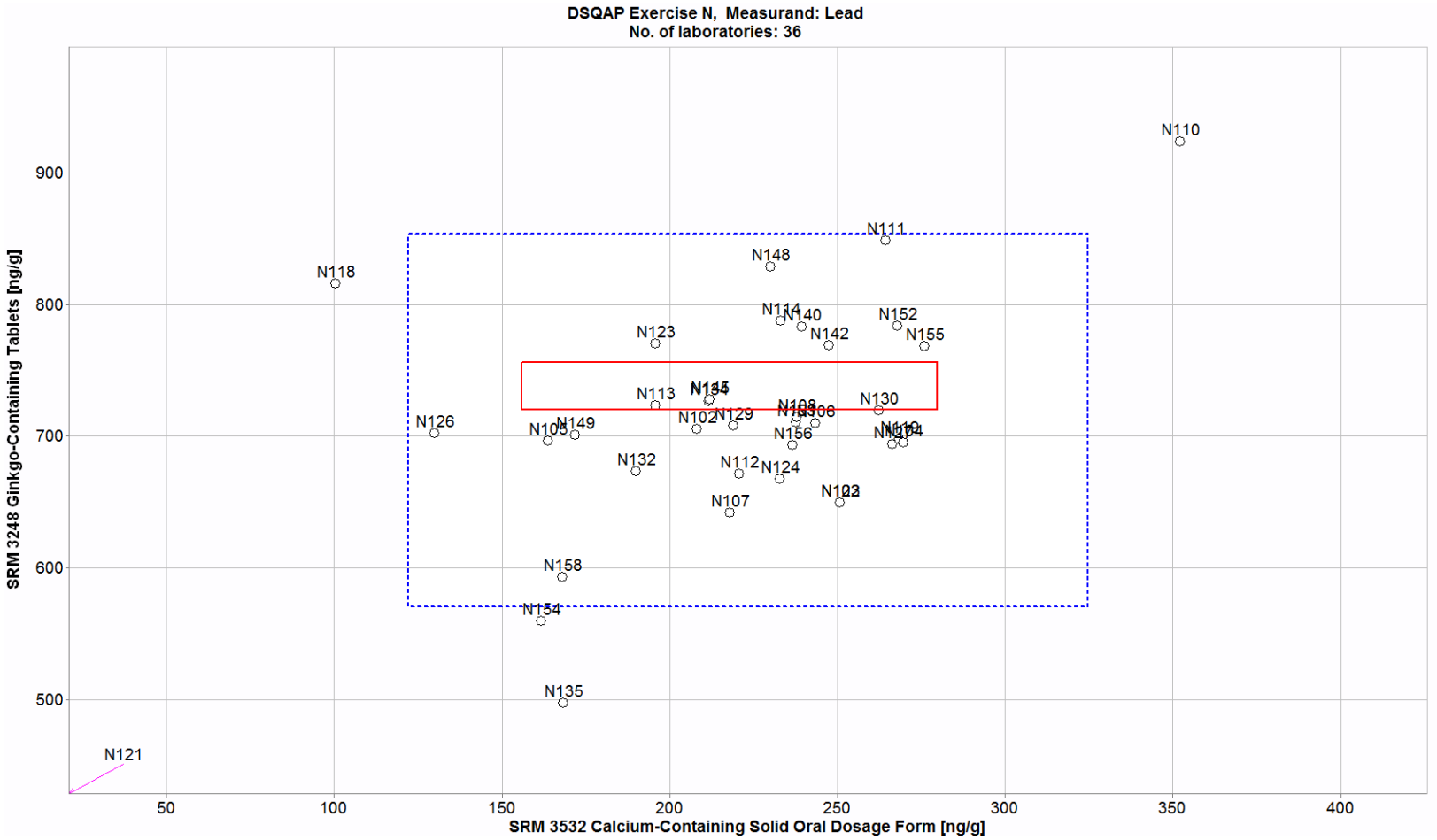

Figure 12. Laboratory means for lead in SRM 3532 Calcium-Containing Solid Oral Dosage Form and SRM 3248 Ginkgo-Containing Tablets (sample/sample comparison view). In this view, the individual laboratory mean for one sample (calcium supplement) is compared to the mean for a second sample (ginkgo tablets). The solid red box represents the NIST range of tolerance for the two samples, calcium supplement (x-axis) and ginkgo tablets (y-axis), which encompasses the NIST values bounded by their uncertainties (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$. The dotted blue box represents the consensus range of tolerance for calcium supplement (x-axis) and ginkgo tablet (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

WATER-SOLUBLE VITAMINS (FOLIC ACID) IN FOODS AND DIETARY SUPPLEMENTS

Study Overview

In this study, participants were provided with two NIST SRMs, SRM 3280 Multivitamin/Multielement Tablets, and SRM 3233 Fortified Breakfast Cereal. Participants were asked to use in-house analytical methods to determine the mass fraction of folic acid in each of the matrices and report values in mg/kg on an as-received basis.

Sample Information

Multivitamin. Participants were provided with one bottle containing 30 multivitamin/multielement tablets. Before use, participants were instructed to grind all tablets, mix the resulting powder thoroughly, and to use a sample size of at least 0.3 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to prepare three samples and report three values from the single bottle provided. The approximate analyte level was not reported to participants prior to the study. The certified value for folic acid in SRM 3280 was determined at NIST using isotope dilution liquid chromatography with tandem mass spectrometry detection (ID-LC-MS/MS) in combination with data from collaborating laboratories. The certified value and uncertainty for folic acid is provided in the table below, both on a dry-mass basis and on an as-received basis accounting for moisture of the material (1.37 %).

	Certified Mass Fraction in SRM 3280 (mg/kg)	
Analyte	(dry-mass basis)	(as-received basis)
Folic Acid	394 ± 22	389 ± 22

Breakfast Cereal. Participants were provided with three packets containing at least 3 g of ground cereal. The commercial cereal was ground, homogenized, and heat-sealed inside 4 mil polyethylene bags which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel each. Before use, participants were instructed to thoroughly mix the contents of each packet and use a sample size of at least 1 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to prepare one sample and report one value from each packet provided. The approximate analyte level was not reported to participants prior to the study. The certified value for folic acid in SRM 3233 was determined at NIST using ID-LC-MS/MS in combination with data from collaborating laboratories. The certified value and uncertainty for folic acid is provided in the table below, both on a dry-mass basis and on an as-received basis accounting for moisture of the material (1.7 %).

	Certified Mass Fraction in SRM 3233 (mg/kg)	
Analyte	(dry-mass basis)	(as-received basis)
Folic Acid	15.1 ± 1.2	14.8 ± 1.2

Study Results

- Thirty-three laboratories enrolled in this exercise and received samples. Sixteen laboratories reported results for folic acid in the cereal (48 % participation) and 25 laboratories reported results for folic acid in multivitamin (76 % participation).

- The consensus mean for folic acid in the multivitamin was within the target range and the between-laboratory variability was very good (9 % RSD).
- The consensus mean for folic acid in the breakfast cereal was below the target range, but the consensus range overlapped the target range. The between-laboratory variability was high (33 % RSD).
- Most laboratories reported using LC with absorbance detection as the analytical method for analysis (65 % for breakfast cereal and 70 % for the multivitamin). Laboratories also reported using a microbiological assay for breakfast cereal (6 %), LC-MS/MS (6 % for cereal and 4 % for the multivitamin), and a USP assay for the multivitamin (4 %). Several laboratories did not report an instrumental approach (24 % for cereal or 15% for multivitamin).

Technical Recommendations

The following recommendations are based on results obtained from the participants in this study.

- Results for the multivitamin tablet were very good. No methods were presented as significantly better or worse than any other. No systematic biases were noted.
  - Some laboratories had high sample-to-sample variability, which may be related to tablet-to-tablet variability if the recommended sample preparation procedure was not followed. The recommended sample preparation procedure included grinding all 30 provided tablets together and sampling from the resulting powder to reduce sample-to-sample variability. Additional variability may have resulted from exposure of the ground powder to light and/or air during sample preparation, if samples were not prepared in rapid succession.
  - The low bias of the consensus results may indicate incomplete extraction of the high concentration of folic acid from the matrix. A subsequent re-extraction of the sample can indicate if measurable amounts of the analyte remain in the matrix following extraction.
- Results for the breakfast cereal were highly variable. However, no methods were presented as significantly better or worse than any other and no systematic biases were noted.
  - The mass fraction of the folic acid in the breakfast cereal was significantly lower than the multivitamin sample. A linear calibration curve which surrounds the expected sample concentration values, including both the lowest and highest expected concentration values of the sample solutions, should be used for calculation. Extrapolation of results beyond calibration curves may result in inaccuracies in sample results.
- Neat folic acid standards are known to contain high levels of water (up to 8 % or more), which would not be detectable by LC-absorbance or LC-MS purity approaches. The purity of reference standards should always be thoroughly characterized in-house to reduce potential bias.
- Some laboratories reported high values for one sample or the other (but not both), which may indicate chromatographic coelutions with matrix components. Because each matrix is different, the chromatographic method should be evaluated to confirm any potential biases resulting from interfering compounds.

Table 7. Individualized data summary table (NIST) for folic acid in multivitamin and breakfast cereal.

National Institute of Standards & Technology

Exercise N - May 2017 - Folic Acid

	Lab Code:	**NIST**	**1. Your Results**				**2. Community Results**			**3. Target**	
Analyte	Sample	Units	x_i	s_i	Z'_{comm}	Z_{NIST}	N	x*	s*	x_{NIST}	U_{95}
Folic Acid	Cereal	mg/kg	14.8	1.2		0.00	16	13	5	14.8	1.2
Folic Acid	Multivitamin	mg/kg	389	22		0.00	25	370	33	389	22

x_i Mean of reported values

s_i Standard deviation of reported values

Z'_{comm} Z'-score with respect to community consensus

Z_{NIST} Z-score with respect to NIST value

N Number of quantitative values reported

x* Robust mean of reported values

s* Robust standard deviation

x_{NIST} NIST-assessed value

U_{95} ±95% confidence interval about the assessed value or standard deviation (s_{NIST})

Table 8. Data summary table for folic acid in multivitamin and in breakfast cereal. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Folic Acid									
		SRM 3233 Fortified Breakfast Cereal (mg/kg)					SRM 3280 Multivitamin/Multielement Tablets (mg/kg)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				14.8	1.2				389	22
	N101						412	398	376	395	18
	N102	10.9	11.0	9.8	10.6	0.7	384	379	371	378	7
	N103										
	N105						410	406	403	406	4
	N107	86.8	88.1	85.4	86.8	1.4	368	335	320	341	25
	N108	10.0	10.0	9.9	10.0	0.0	385	381	380	382	3
	N110	19.1	18.4	19.4	19.0	0.5	385	383	376	381	5
	N111	39.0	44.0	38.0	40.3	3.2	336	321	353	337	16
	N112	15.4	15.7	15.7	15.6	0.2	392	382	359	378	17
	N113	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0
	N115										
	N116	9.2	8.8	8.6	8.8	0.3	355	372	383	370	14
	N117						368	361	373	367	6
	N120										
	N121						292	290	295	292	3
	N122										
	N123	14.5	15.7	14.4	14.9	0.7	335	333	342	337	5
	N124						359	355	358	357	2
	N125										
	N126	10.5	9.1	10.3	10.0	0.7	388	394	409	397	10
	N127	11.4	10.7	11.4	11.2	0.4	384	370	398	384	14
	N129	11.8	12.1	12.1	12.0	0.2	389	390	385	388	3
	N130						354	349	354	353	3
	N132	14.5	14.4	14.4	14.4	0.1	453	439	449	447	7
	N133						378	361	373	371	9
	N138						421	427	426	425	3
	N141										
	N143	15.1	15.1	15.1	15.1	0.0	416	411	412	413	3
	N148	7.8	8.3	8.8	8.3	0.5	376	376	379	377	2
	N150										
	N155	10.2	9.7	9.3	9.7	0.5	354	343	358	352	8
	N157	9.8			9.8		356			356	
	N158						344	325	325	331	11
Community Results		Consensus Mean			12.6		Consensus Mean			370	
		Consensus Standard Deviation			4.9		Consensus Standard Deviation			33	
		Maximum			86.8		Maximum			447	
		Minimum			0.0		Minimum			0	
		N			16		N			25	

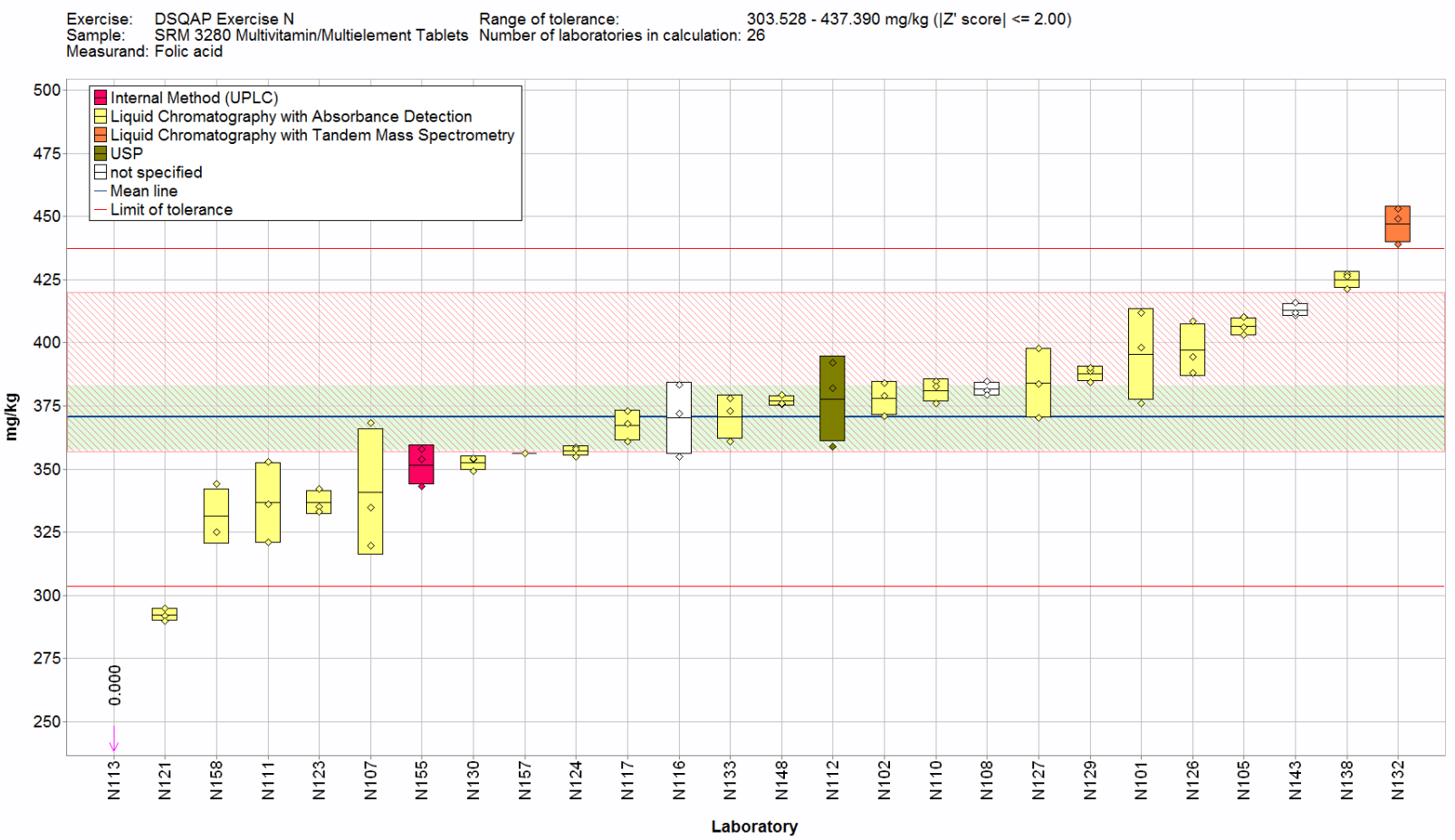

Figure 13. Folic acid in SRM 3280 Multivitamin/Multielement Tablets (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$.

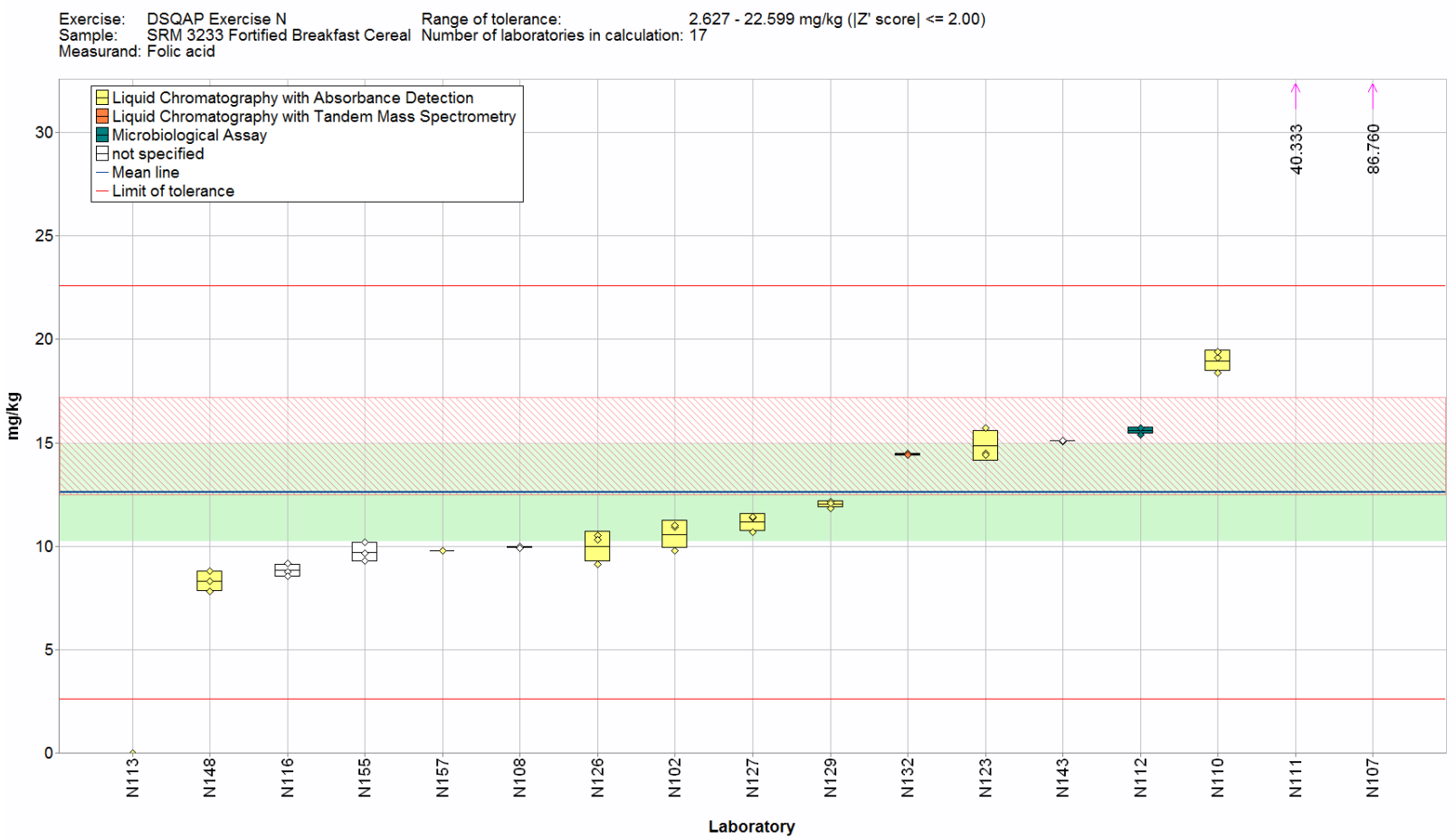

Figure 14. Folic acid in SRM 3233 Fortified Breakfast Cereal (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

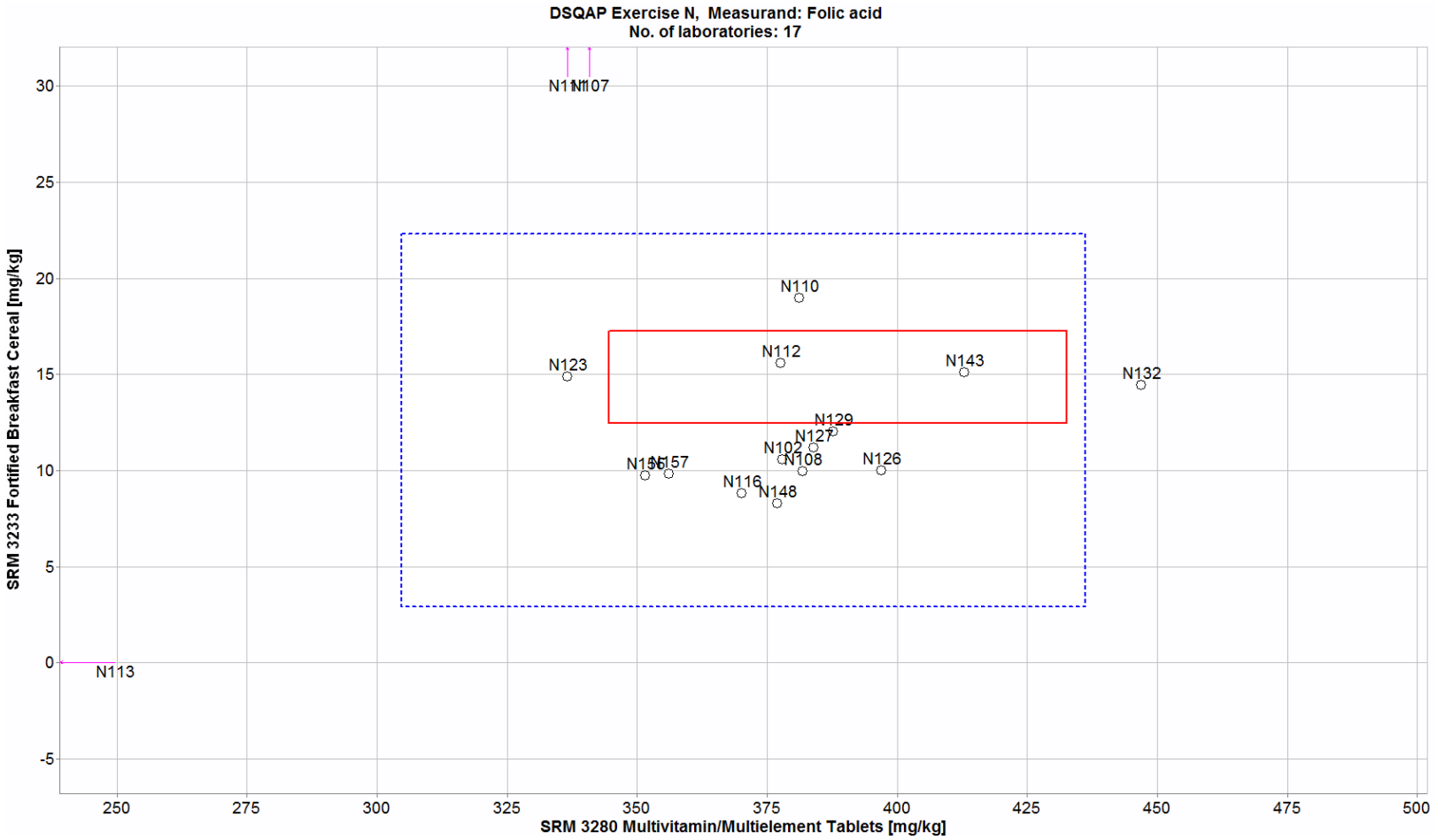

Figure 15. Laboratory means for folic acid in SRM 3280 Multivitamin/Multielement Tablets and SRM 3233 Fortified Breakfast Cereal (sample/sample comparison view). In this view, the individual laboratory mean for one sample (multivitamin) is compared to the mean for a second sample (breakfast cereal). The solid red box represents the NIST range of tolerance for the two samples, multivitamin (x-axis) and breakfast cereal (y-axis), which encompasses the NIST values bounded by their uncertainties (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$. The dotted blue box represents the consensus range of tolerance for multivitamin (x-axis) and breakfast cereal (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

FAT-SOLUBLE VITAMINS (VITAMIN D_2 AND D_3) IN CALCIUM, PROTEIN, AND MULTIVITAMIN DIETARY SUPPLEMENTS

Study Overview

In this study, participants were provided with three NIST SRMs, SRM 3532 Calcium-Containing Solid Oral Dosage Form, SRM 3252 Protein Drink Mix, and SRM 3280 Multivitamin/Multielement Tablets. Participants were asked to use in-house analytical methods to determine the mass fractions of vitamin D_2 and vitamin D_3 in each of the matrices and report values in mg/kg on an as-received basis. SRM 3280 is fortified with vitamin D_2 and SRM 3532 is fortified with vitamin D_3. In addition, the vitamin D content in the protein drink mix is not fortified.

Sample Information

Calcium Supplement. Participants were provided with three packets, each containing approximately 10 g of ground calcium supplement. The commercial tablets were ground, homogenized, and heat-sealed inside 4 mil polyethylene bags, which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel. Before use, participants were instructed to thoroughly mix the contents of each packet and use a sample size of at least 1 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to report a single value from each packet provided. Approximate analyte levels were not reported to participants prior to the study. The reference value for vitamin D_3 in SRM 3532 was determined at NIST using isotope dilution liquid chromatography with tandem mass spectrometry detection (ID-LC-MS/MS). A target value for vitamin D_2 in SRM 3532 has not been determined at NIST. The NIST value and uncertainty for vitamin D_3 is provided in the table below, both on an as-received basis and on a dry-mass basis, accounting for moisture of the material (3.2 %).

	Reference Mass Fraction in SRM 3532 (mg/kg)	
Analyte	(dry-mass basis)	(as-received basis)
Vitamin D_3	1.310 ± 0.033	1.268 ± 0.032

Protein Supplement. Participants were provided with three packets, each containing approximately 10 g of protein powder. The commercial protein powder was ground, homogenized, and heat-sealed inside 4 mil polyethylene bags, which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel. Before use, participants were instructed to thoroughly mix the contents of each packet and to use a sample size of at least 2 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to prepare a single sample and to report a single value from each packet provided. Approximate analyte levels were not reported to participants prior to the study, and target values for these analytes in SRM 3252 have not been determined at NIST.

Multivitamin. Participants were provided with one bottle containing 30 multivitamin/multielement tablets. Before use, participants were instructed to grind all tablets, mix the resulting powder thoroughly, and to use a sample size of at least 0.6 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to prepare three samples and report three values from the single bottle provided. The approximate analyte level was not reported to

participants prior to the study. The reference value for vitamin D_2 in SRM 3280 was determined at NIST using ID-LC-MS. A target value for vitamin D_3 in SRM 3280 has not been determined at NIST. The reference value and uncertainty for vitamin D_2 is provided in the table below, both on a dry-mass basis and on an as-received basis accounting for moisture of the material (1.37 %).

	Reference Mass Fraction in SRM 3280 (mg/kg)	
Analyte	(dry-mass basis)	(as-received basis)
Vitamin D_2	8.6 ± 2.6	8.5 ± 2.6

Study Results

- Twenty-nine laboratories enrolled in this exercise and received samples to measure vitamin D_2 in dietary supplements. Two laboratories reported results for vitamin D_2 in the calcium supplement (7 % participation), seven laboratories reported results for vitamin D_2 in the protein supplement, (24 % participation) and thirteen laboratories reported results for vitamin D_2 in the multivitamin (45 % participation).
  - The consensus mean was within the target range for vitamin D_2 in the multivitamin.
  - The between-laboratory variability ranged from very high in the multivitamin (41 %) to unacceptable in the calcium supplement and the protein supplement (> 100 % and 98 %, respectively).
  - Laboratories reported using LC-absorbance (50 % to 60 % of laboratories) and LC-MS/MS (14 % to 20 % of laboratories) as their analytical approach. Some laboratories did not report the analytical method used.
- Thirty-three laboratories enrolled in this exercise and received samples to measure vitamin D_3 in dietary supplements. Nineteen laboratories reported results for vitamin D_3 in the calcium supplement (58 % participation) and seven laboratories reported results for vitamin D_3 in both the protein supplement and the multivitamin (21 % participation).
  - The consensus mean was below the target range for vitamin D_3 in the protein supplement and the consensus range slightly overlapped the target range.
  - The between-laboratory variability ranged from moderate in the calcium supplement (25 %) to very high in the multivitamin (71 %). The between-laboratory variability was unacceptable in the protein supplement (> 100 %).
  - Laboratories reported using LC-absorbance (58 % to 67 % of laboratories) and LC-MS/MS (10 % to 16 % of laboratories) as their analytical approach. Some laboratories did not report the analytical method used.

Technical Recommendations

The following recommendations are based on results obtained from the participants in this study.

- No analytical method was identified as exceptionally good or problematic. LC-MS/MS and LC-absorbance methods gave very similar results for samples of this type in these concentration ranges.
- Each of these samples only contains one form of vitamin D (either vitamin D_2 or vitamin D_3, but not both). In addition, the vitamin D content in the protein drink mix is not fortified. As a result, many parts of this study yielded low participation rates or many laboratories indicated that the analyte was below their limit of detection.

    - Focusing only on the analyte/matrix pairs that are fortified, the data variability was acceptable. For both vitamin D_2 in the multivitamin and vitamin D_3 in the calcium supplement, the spread of the consensus range was comparable to or smaller than the NIST target range.
    - Because all sample preparation methods are not appropriate for all matrices, some in-house optimization may be necessary when analyzing a new material to confirm that the procedure is appropriate. Because the form of vitamin D present in each material was not specified, all materials should have been screened for vitamin D_2 and vitamin D_3.
- For both vitamin D_2 in the multivitamin and vitamin D_3 in the calcium supplement, some laboratories reported values that were high for both sample/analyte pairs (or low for both).
    - The low measured values may be a result of incomplete extraction of the vitamin D from the sample matrix. To ensure maximum recovery, a subsequent re-extraction of the sample can indicate if measurable amounts of the analyte remain in the matrix following extraction.
    - The high measured values may indicate chromatographic coelutions with matrix components. Because each matrix is different, the chromatographic method should be evaluated to confirm any potential biases resulting from interfering compounds.
    - Due to the potential for contamination in calibration materials, NIST typically determines the concentration of calibration solutions for certain analytes, including vitamin D, with a spectrophotometer and then adjusts for LC purity at the same wavelength. Impurities in calibration materials could be a source of bias when laboratory-determined values are compared to NIST certified values.

Table 9. Individualized data summary table (NIST) for ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3) in dietary supplements.

National Institute of Standards & Technology

Exercise N - May 2017 - Vitamin D

	Lab Code:	**NIST**	**1. Your Results**				**2. Community Results**			**3. Target**	
Analyte	Sample	Units	x_i	s_i	Z'_{comm}	Z_{NIST}	N	x*	s*	x_{NIST}	U_{95}
Ergocalciferol (Vitamin $D_{2)}$	Protein Drink	mg/kg					7	3.12	5.31		
Ergocalciferol (Vitamin $D_{2)}$	Ca Supplement	mg/kg					2	6.85	6.68		
Ergocalciferol (Vitamin $D_{2)}$	Multivitamin	mg/kg	8.5	2.6		0.00	13	7.95	3.24	8.5	2.6
Cholecalciferol (Vitamin $D_{3)}$	Protein Drink	mg/kg					7	0.51	0.56		
Cholecalciferol (Vitamin $D_{3)}$	Ca Supplement	mg/kg	1.27	0.03		0.00	19	1.12	0.28	1.27	0.03
Cholecalciferol (Vitamin $D_{3)}$	Multivitamin	mg/kg					7	6.49	4.59		

x_i Mean of reported values
s_i Standard deviation of reported values
Z'_{comm} Z'-score with respect to communit consensus
x_i Mean of reported values
N Number of quantitative values reported
x* Robust mean of reported values
N Number of quantitative
x_{NIST} NIST-assessed value
U_{95} ±95% confidence interval about the assessed value or standard deviation (s_{NIST})
x_{NIST} NIST-assessed value

Table 10. Data summary table for ergocalciferol (vitamin D_2) in dietary supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ergocalciferol (Vitamin D_2)														
		SRM 3252 Protein Drink Mix (mg/kg)					SRM 3532 Calcium Dietary Supplement (mg/kg)					SRM 3280 Multivitamin/Multielement Tablets (mg/kg)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST														8.5	2.6
	N101						< 0.003	< 0.003	< 0.003	< 0.003		7.40	6.70	5.50	6.53	0.96
	N102															
	N105															
	N107											1.55	1.65	2.15	1.78	0.32
	N108	9.00	8.61	8.50	8.70	0.26						8.61	8.54	8.65	8.60	0.06
	N110	0.50	0.80	0.50	0.60	0.17	3.50	2.90	1.70	2.70	0.92	20.80	18.50	30.00	23.10	6.09
	N111						11.00	10.00	12.00	11.00	1.00					
	N112	1.40	0.35	0.35	0.70	0.61	< 0.001	< 0.001	< 0.001	< 0.001		8.87	8.53	8.72	8.71	0.17
	N113	< 0.00	< 0.00	< 0.00	< 0.00		< 0.00	< 0.00	< 0.00	< 0.00		< 0.000	< 0.000	< 0.000	< 0.000	
	N115															
	N116											6.20	5.82	6.11	6.05	0.20
	N120															
	N122															
	N124											7.96	9.44	8.61	8.67	0.74
	N125															
	N126															
	N127	13.60	14.10	14.40	14.03	0.40										
	N129															
	N130															
	N132	0.19	0.20	0.21	0.20	0.01	< 0.10	< 0.10	< 0.10	< 0.10		7.48	8.18	8.32	7.99	0.45
	N133											6.36	6.17	6.41	6.31	0.13
	N134	0.30	0.28	0.34	0.31	0.03	< 0.20	< 0.20	< 0.20	< 0.20		10.91	9.79	10.40	10.37	0.56
	N141															
	N143											12.74	12.73	12.56	12.68	0.10
	N147															
	N149															
	N155	< 0.25	< 0.25	< 0.25	< 0.25		< 0.25	< 0.25	< 0.25	< 0.25		5.24	3.14	5.60	4.66	1.33
	N157															
	N158	0.18	0.30	0.20	0.23	0.06						7.59	6.00	7.01	6.87	0.80
Community Results		Consensus Mean			3.12		Consensus Mean			6.85		Consensus Mean			7.95	
		Consensus Standard Deviation			5.31		Consensus Standard Deviation			6.68		Consensus Standard Deviation			3.24	
		Maximum			14.03		Maximum			11.00		Maximum			23.10	
		Minimum			0.20		Minimum			2.70		Minimum			1.78	
		N			7		N			2		N			13	

Table 11. Data summary table for cholecalciferol (vitamin D_3) in dietary supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Cholecalciferol (Vitamin D_3)													
		SRM 3252 Protein Drink Mix (mg/kg)					SRM 3532 Calcium Dietary Supplement (mg/kg)					SRM 3280 Multivitamin/Multielement Tablets (mg/kg)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST									1.27	0.03					
	N101						1.02	1.00	1.03	1.02	0.02	< 0.003	< 0.003	< 0.003	< 0.003	
	N102						1.01	1.03	1.02	1.02	0.01					
	N105															
	N107	0.07	0.07	0.07	0.07	0.00	2.21	2.21	2.21	2.21	0.00					
	N108	0.51	0.53	0.52	0.52	0.01	0.44	0.39	0.42	0.42	0.03					
	N110	1.10	1.20	0.60	0.97	0.32	3.30	3.00	2.90	3.07	0.21	14.10	16.30	14.40	14.93	1.19
	N111						11.00	11.00	11.00	11.00	0.00	10.00	8.00	8.00	8.67	1.15
	N112	< 0.001	< 0.001	< 0.001	< 0.001		1.24	1.19	1.05	1.16	0.10	< 0.001	< 0.001	< 0.001	< 0.001	
	N113	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	N115															
	N116						1.13	1.24	1.21	1.19	0.06					
	N119						1.01	1.21	1.13	1.12	0.10					
	N120															
	N121	0.17	0.30	0.20	0.22	0.07	1.07	1.17	1.04	1.09	0.07	6.78	6.08	6.65	6.50	0.37
	N122															
	N124															
	N125															
	N126															
	N127	0.30	0.49	0.60	0.46	0.15	1.06	1.10	1.05	1.07	0.03	5.50	5.20	5.40	5.37	0.15
	N129	1294.30	1460.90	1330.00	1361.73	87.72	0.80	0.79	0.78	0.79	0.01	4.82	4.65	5.09	4.85	0.22
	N130						1.08	1.05	1.16	1.10	0.06	6.84	6.50	6.69	6.68	0.17
	N132						1.15	1.37	1.36	1.29	0.12	< 0.10	< 0.10	< 0.10	< 0.10	
	N133						0.95	1.05	0.89	0.96	0.08					
	N134	< 0.20	< 0.20	< 0.20	< 0.20		1.11	1.10	1.01	1.07	0.06	< 0.20	< 0.20	< 0.20	< 0.20	
	N138															
	N141															
	N143						1.25	1.26	1.23	1.25	0.02					
	N147															
	N149															
	N150															
	N155	< 0.25	< 0.25	< 0.25	< 0.25		< 0.25	< 0.25	< 0.25	< 0.25		< 0.25	< 0.25	< 0.25	< 0.25	
	N157															
	N158						1.14	1.10	1.10	1.11	0.02					
Community Results		Consensus Mean			0.51		Consensus Mean			1.12		Consensus Mean			6.49	
		Consensus Standard Deviation			0.56		Consensus Standard Deviation			0.28		Consensus Standard Deviation			4.59	
		Maximum			1361.73		Maximum			11.00		Maximum			14.93	
		Minimum			0.00		Minimum			0.00		Minimum			0.00	
		N			7		N			19		N			7	

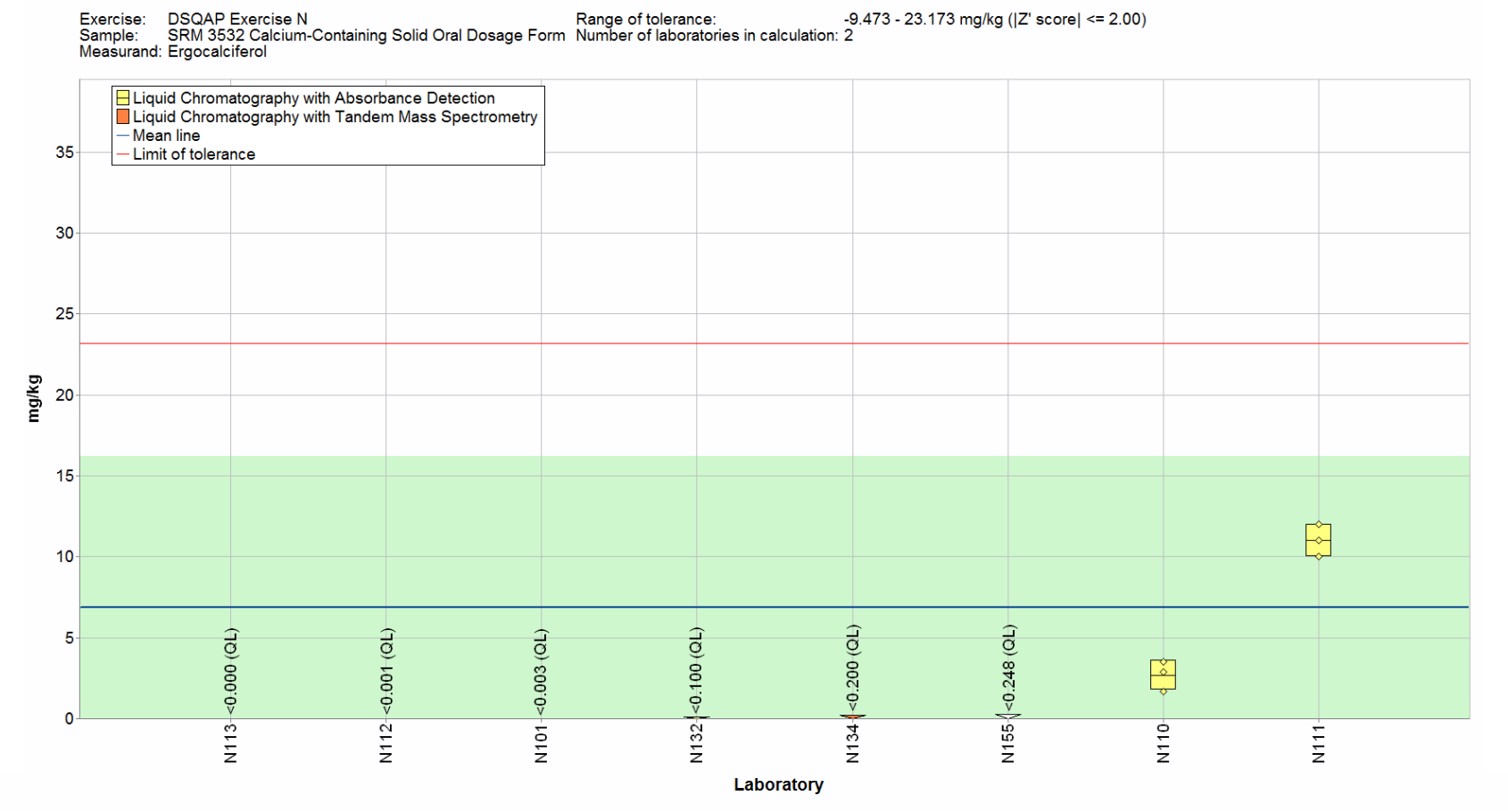

Figure 16. Total ergocalciferol (vitamin D_2) in SRM 3532 Calcium-Containing Solid Oral Dosage Form (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set at zero. A NIST value has not been determined in this material.

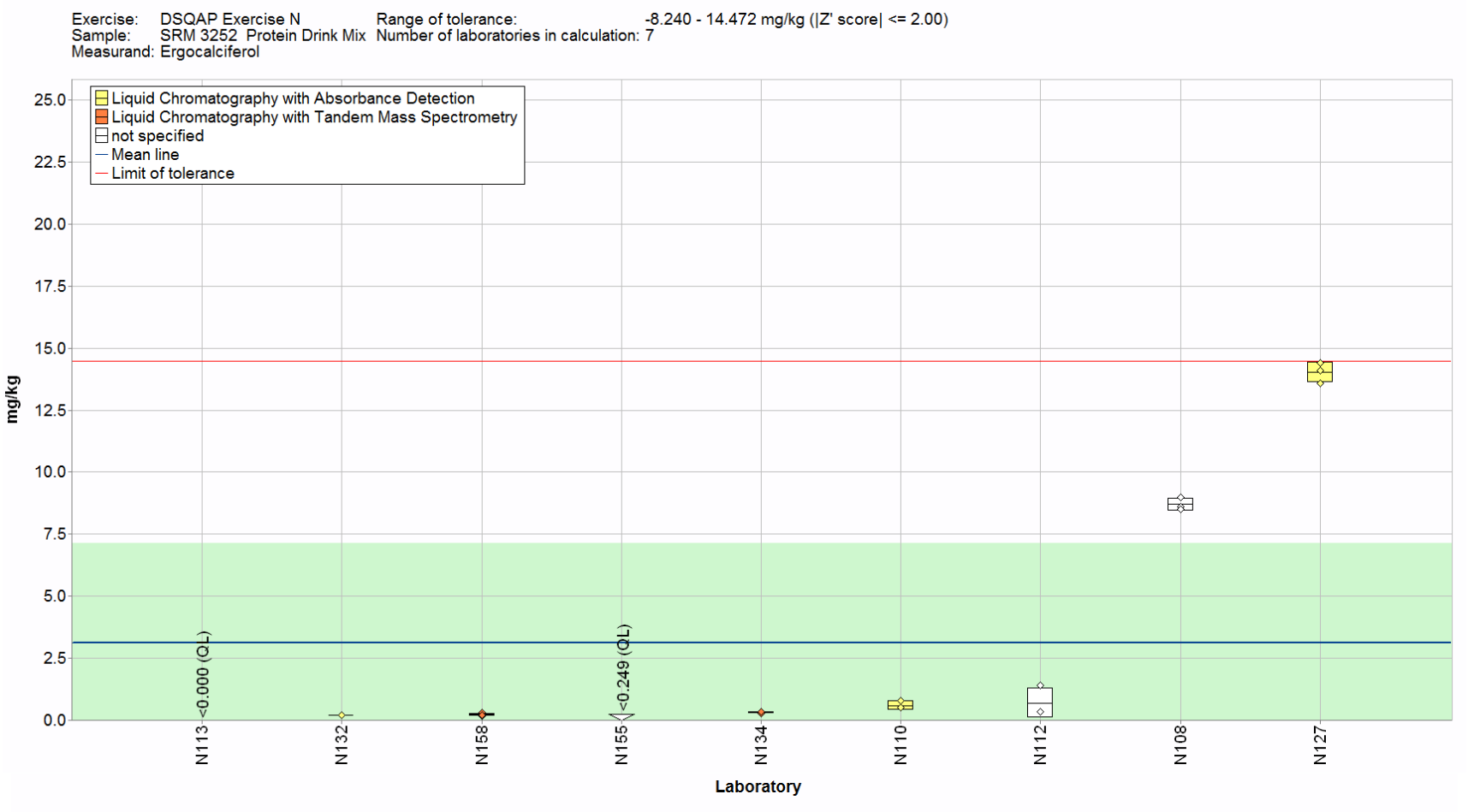

Figure 17. Total ergocalciferol (vitamin D_2) in SRM 3252 Protein Drink Mix (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set at zero. A NIST value has not been determined in this material.

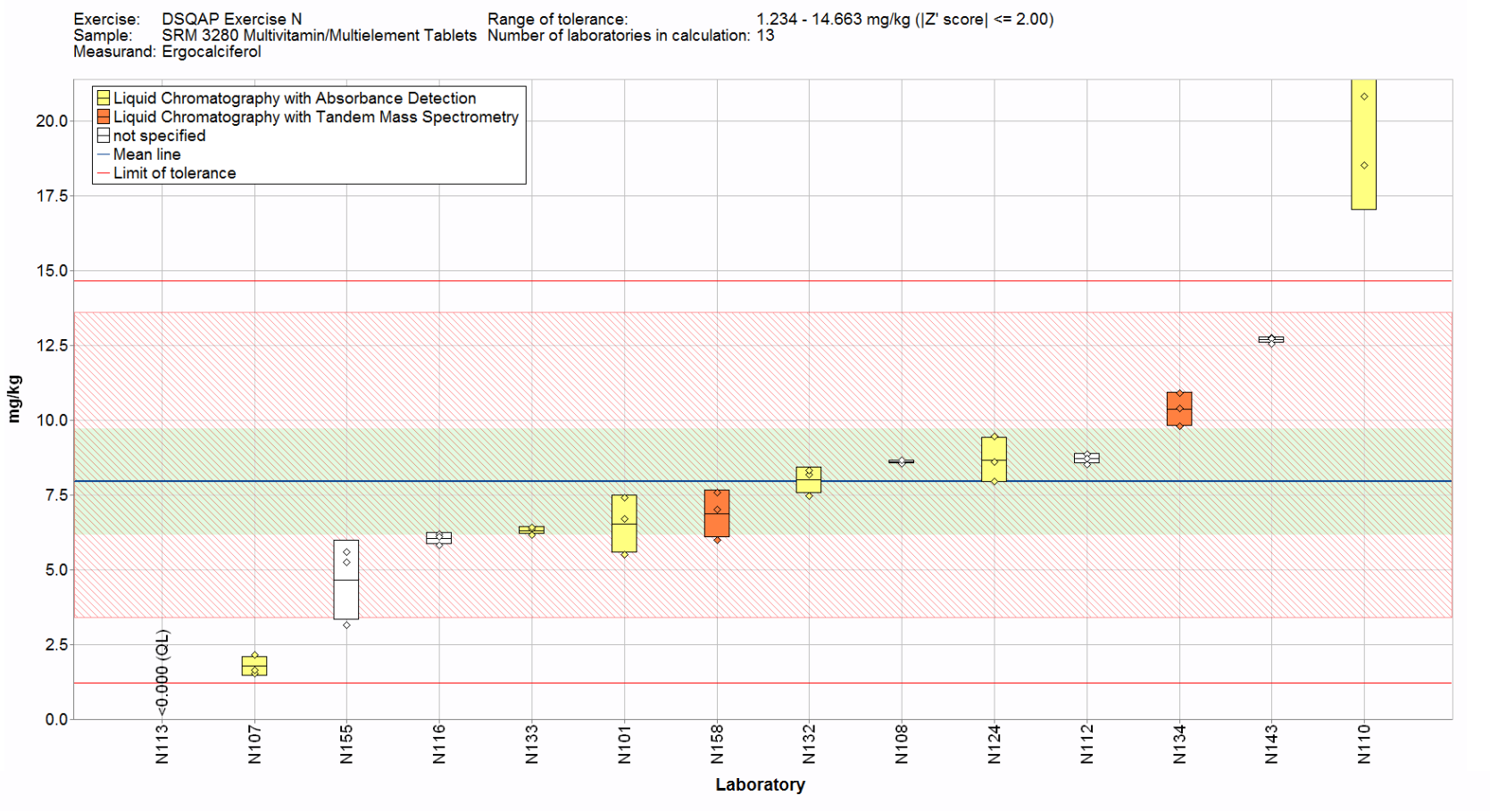

Figure 18. Total ergocalciferol (vitamin D_2) in SRM 3280 Multivitamin/Multielement Tablets (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST reference value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

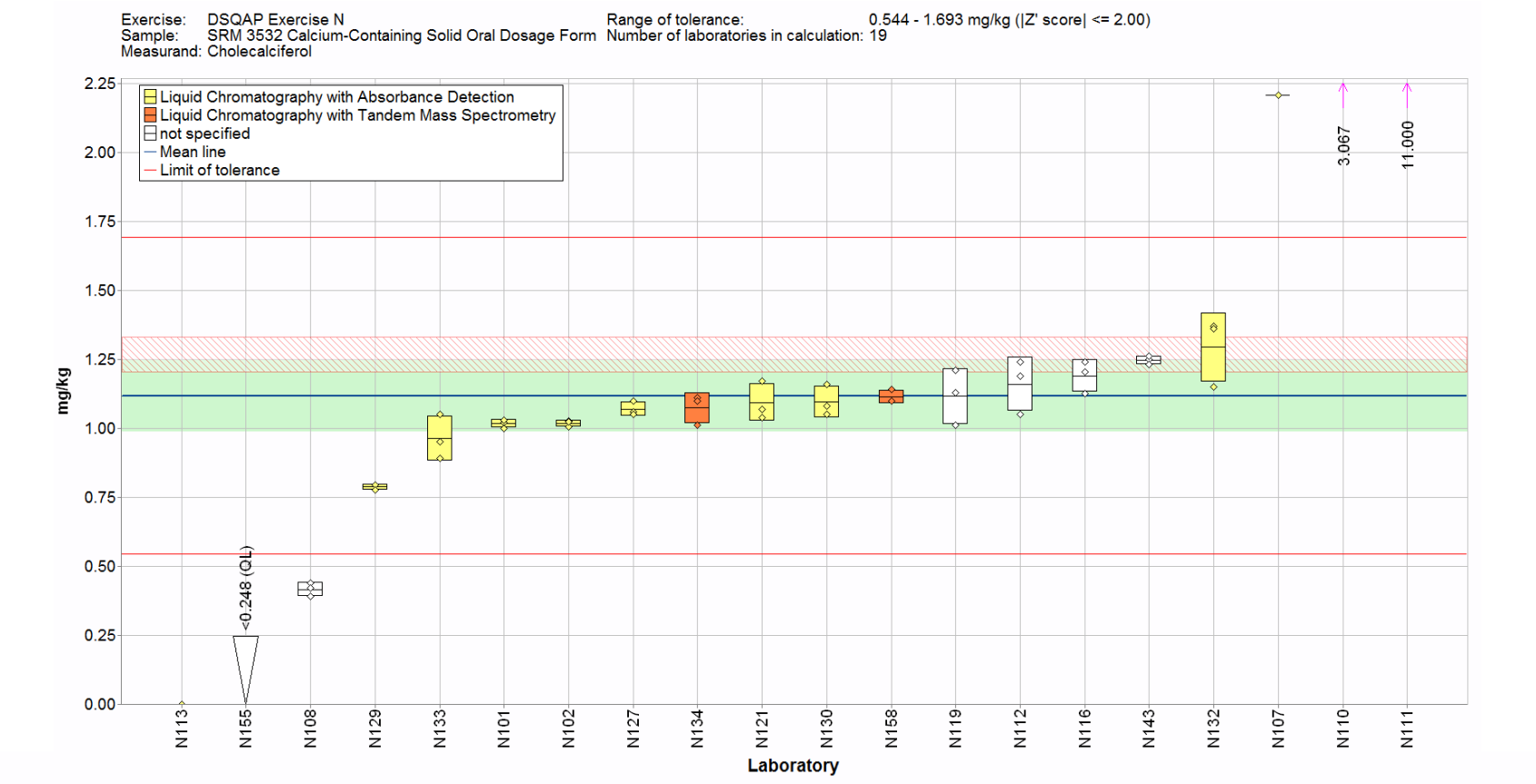

Figure 19. Total cholecalciferol (vitamin D_3) in SRM 3532 Calcium-Containing Solid Oral Dosage Form (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

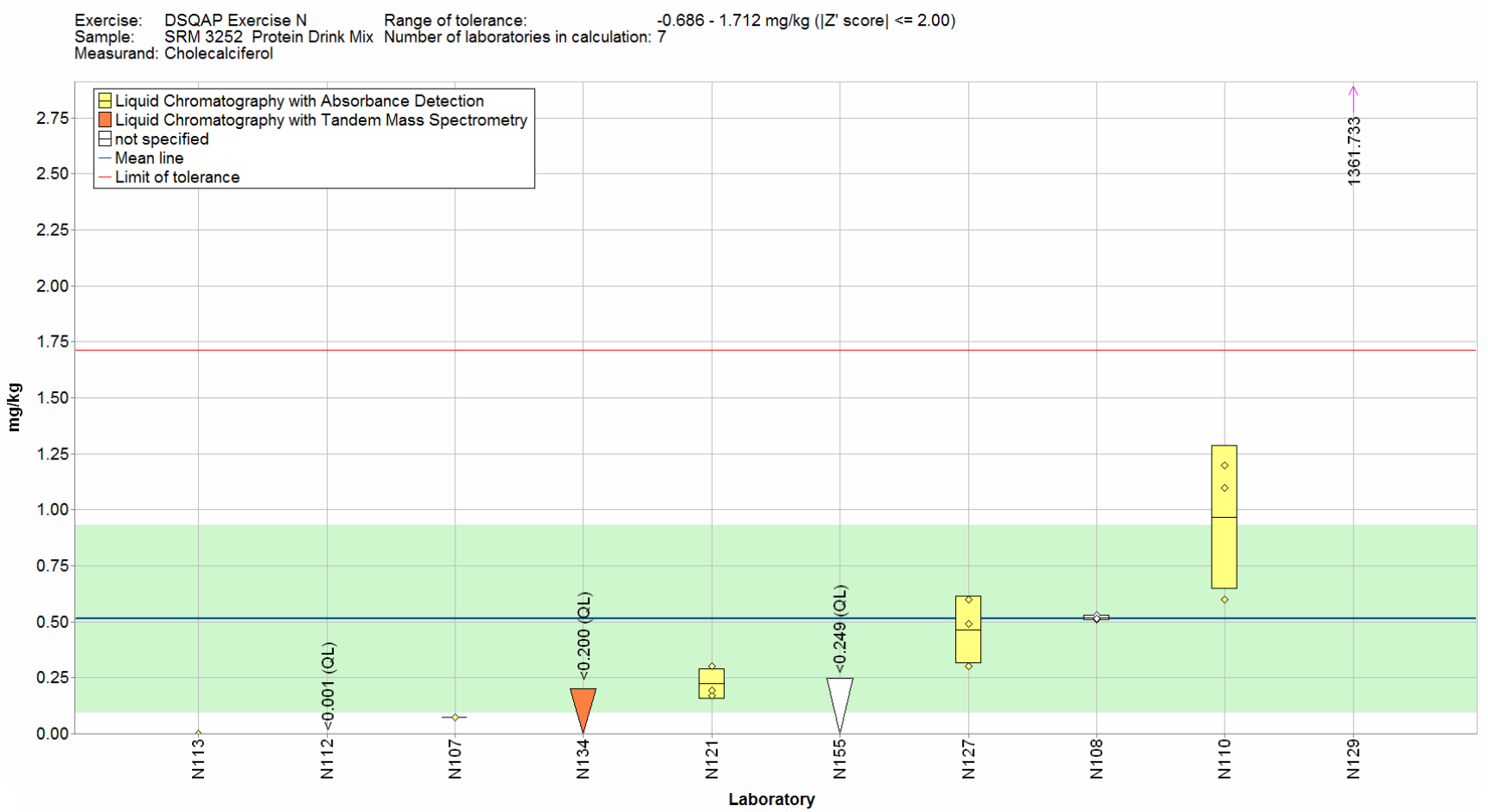

Figure 20. Total cholecalciferol (vitamin D_3) in SRM 3252 Protein Drink Mix (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set at zero. A NIST value has not been determined in this material.

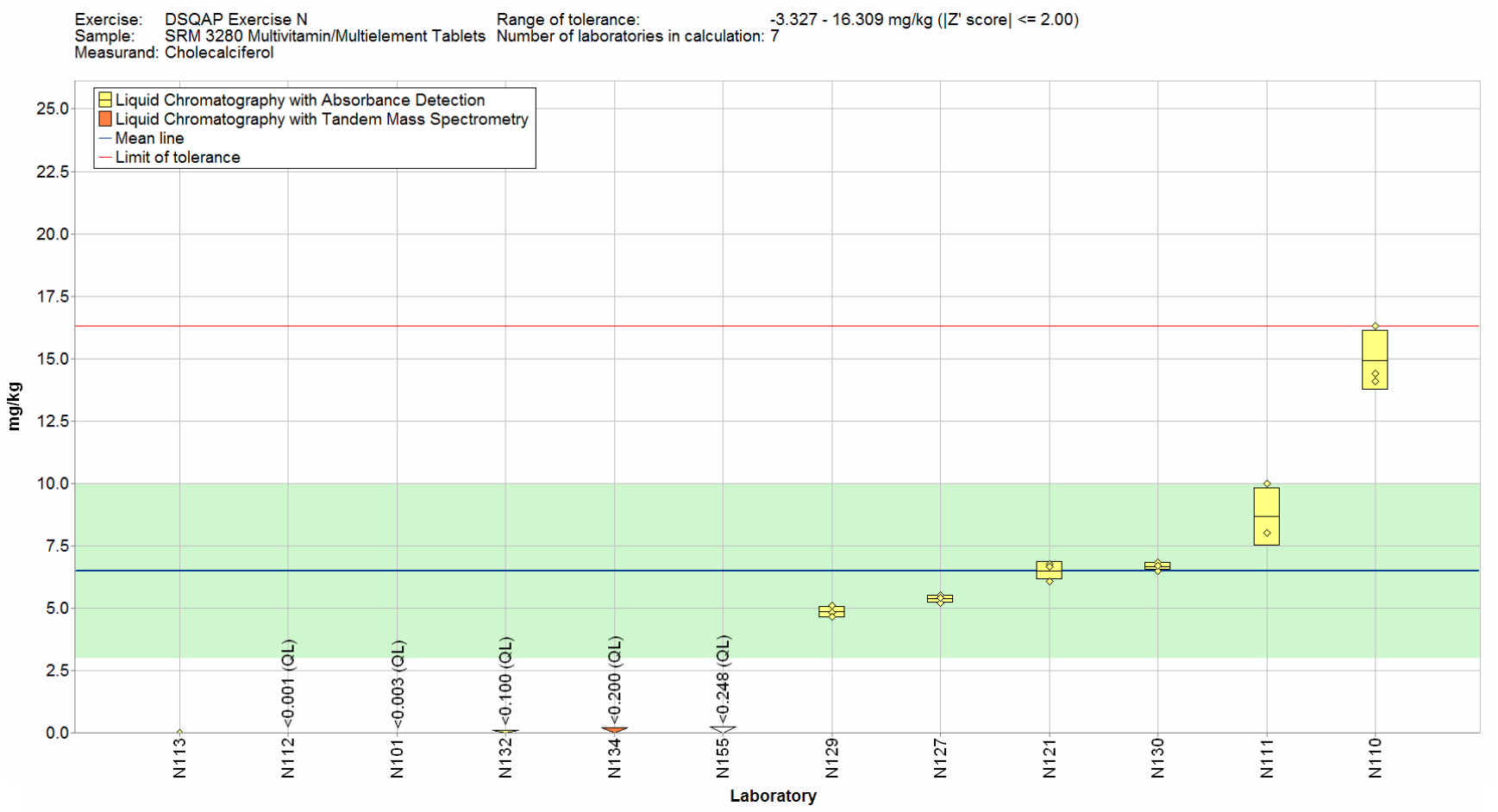

Figure 21. Total cholecalciferol (vitamin D_3) in SRM 3280 Multivitamin/Multielement Tablets (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set at zero. A NIST value has not been determined in this material.

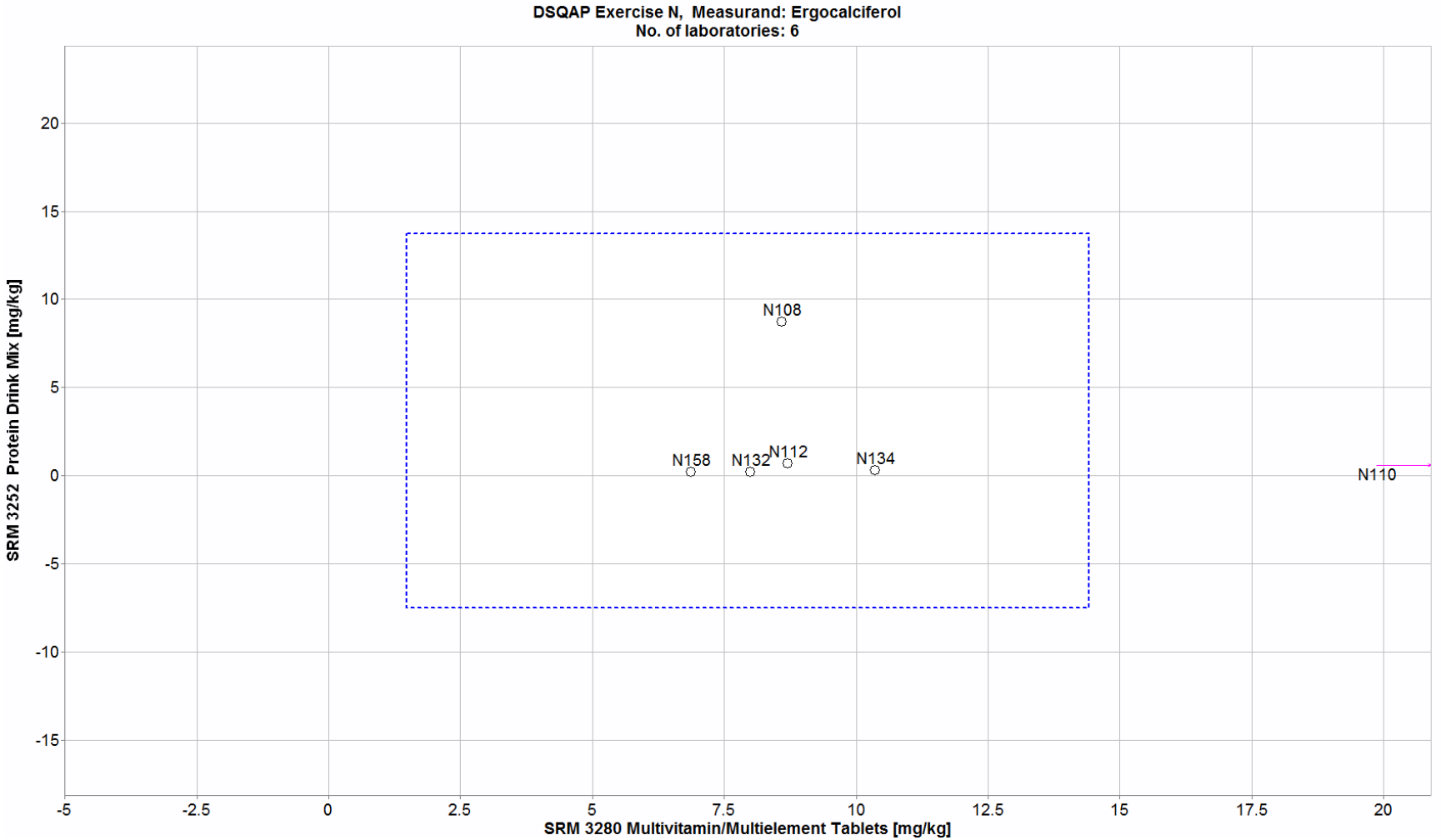

Figure 22. Laboratory means for ergocalciferol (vitamin D_2) in SRM 3280 Multivitamin/Multielement Tablets and SRM 3252 Protein Drink Mix (sample/sample comparison view). In this view, the individual laboratory mean for one sample (multivitamin) is compared to the mean for a second sample (protein supplement). The dotted blue box represents the consensus range of tolerance for multivitamin (x-axis) and protein supplement (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

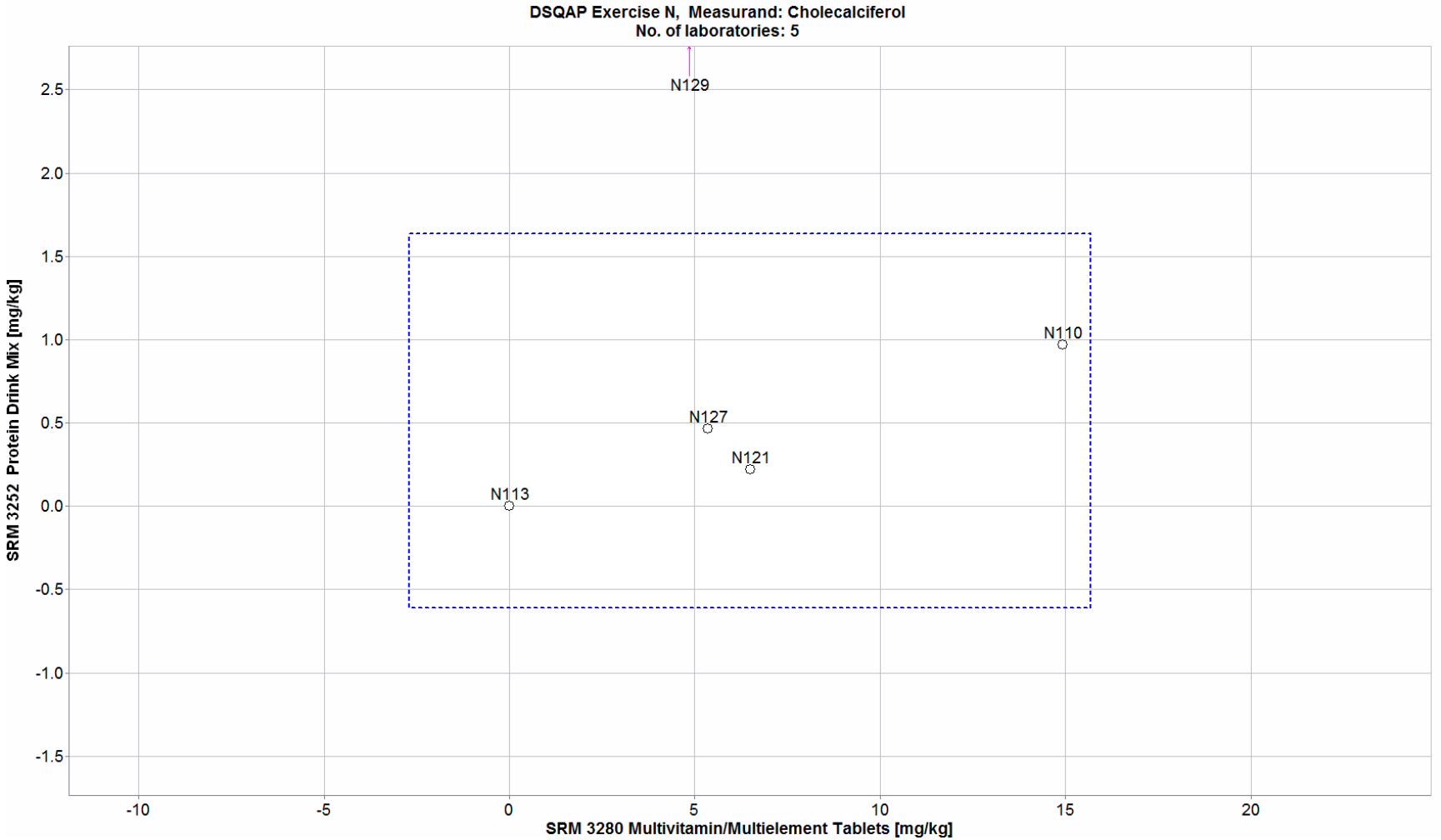

Figure 23. Laboratory means for cholecalciferol (vitamin D_3) in SRM 3280 Multivitamin/Multielement Tablets and SRM 3252 Protein Drink Mix (sample/sample comparison view). In this view, the individual laboratory mean for one sample (multivitamin) is compared to the mean for a second sample (protein supplement). The dotted blue box represents the consensus range of tolerance for multivitamin (x-axis) and protein supplement (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

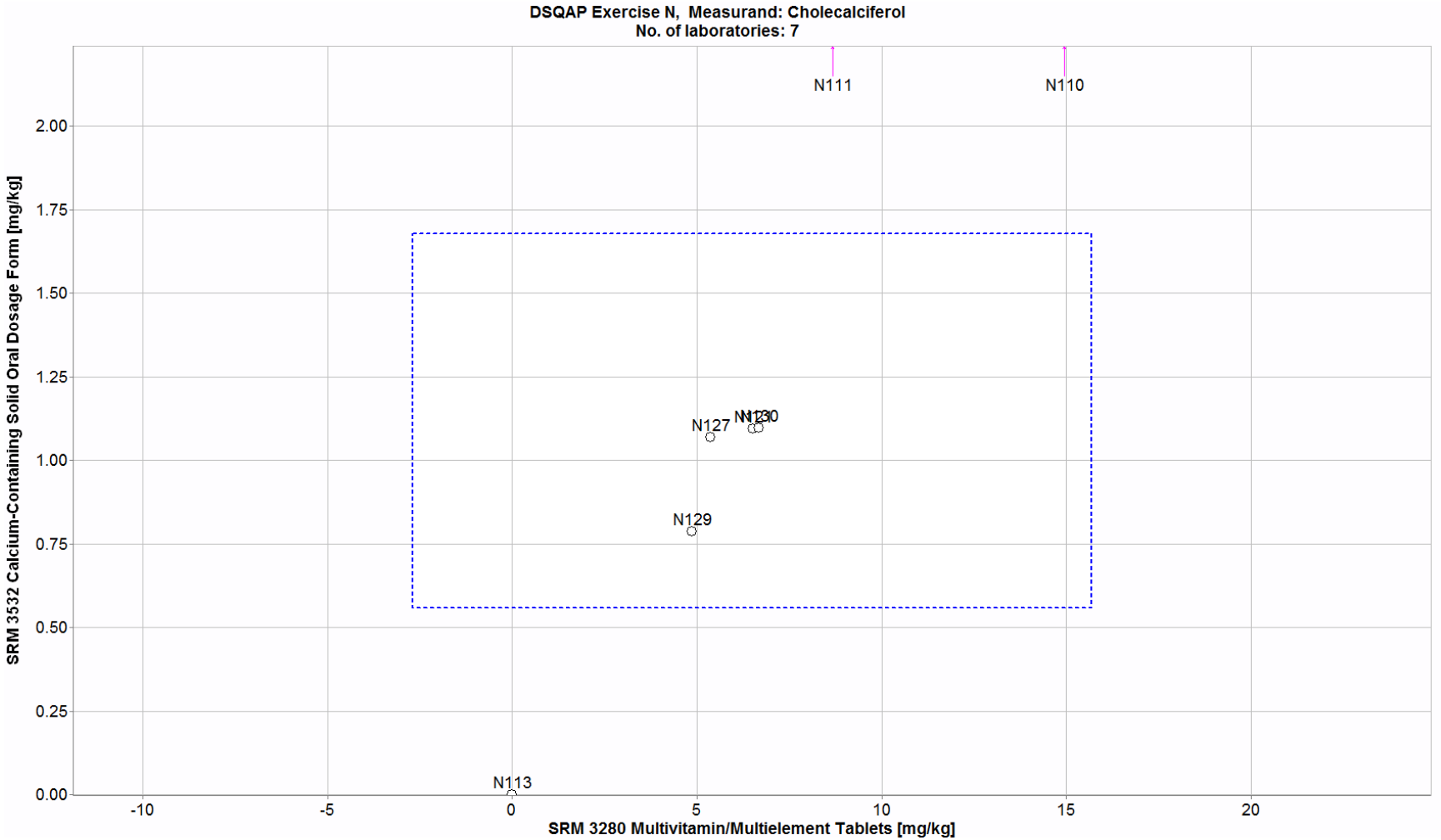

Figure 24. Laboratory means for cholecalciferol (vitamin D_3) in SRM 3280 Multivitamin/Multielement Tablets and SRM 3532 Calcium-Containing Solid Oral Dosage Form (sample/sample comparison view). In this view, the individual laboratory mean for one sample (multivitamin) is compared to the mean for a second sample (calcium supplement). The dotted blue box represents the consensus range of tolerance for multivitamin (x-axis) and calcium supplement (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

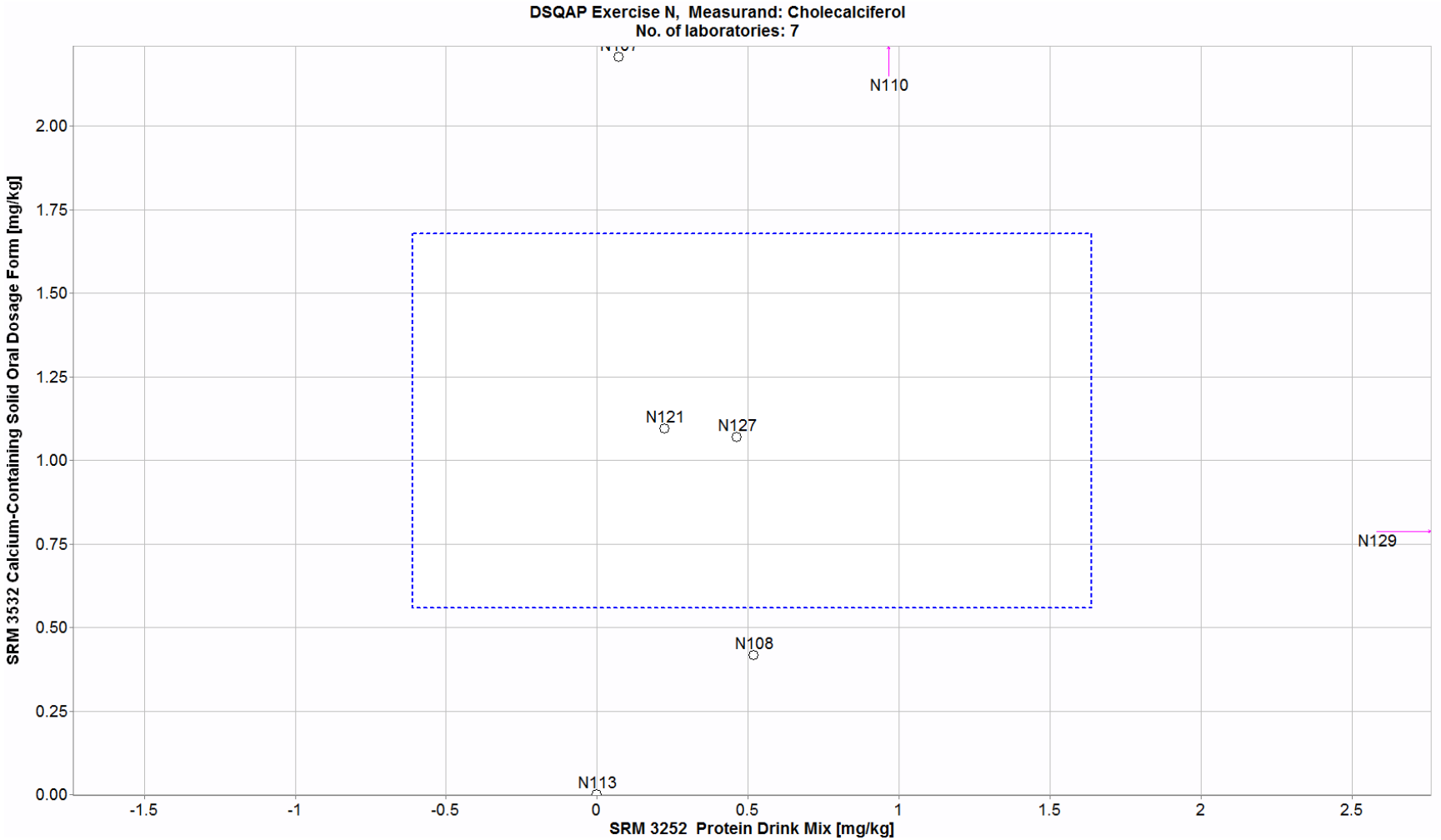

Figure 25. Laboratory means for cholecalciferol (vitamin D_3) in SRM 3252 Protein Drink Mix and SRM 3532 Calcium-Containing Solid Oral Dosage Form (sample/sample comparison view). In this view, the individual laboratory mean for one sample (protein supplement) is compared to the mean for a second sample (calcium supplement). The dotted blue box represents the consensus range of tolerance for protein supplement (x-axis) and calcium supplement (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

FATTY ACIDS IN SAW PALMETTO BERRIES AND BORAGE OIL DIETARY SUPPLEMENTS

Study Overview

In this study, participants were provided with two NIST SRMs, SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit, and SRM 3274-1 Borage (*Borago officinalis*) Oil. Participants were asked to use in-house analytical methods to determine the mass fractions of α-linolenic acid, γ-linolenic acid, linoleic acid, total omega-3 fatty acids, and total omega-6 fatty acids in each of the matrices and report values in mg/g on an as-received basis as fatty acid methyl esters (FAMEs).

Sample Information

Saw Palmetto Berries. Participants were provided with three packets, each containing approximately 6 g of ground berries. The berries were ground, homogenized, and heat-sealed inside 4 mil polyethylene bags, which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel. Before use, participants were instructed to thoroughly mix the contents of each packet and use a sample size of at least 0.5 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to report a single value from each packet provided. Approximate analyte levels were not reported to participants prior to the study. The certified values for α-linolenic acid and linoleic acid in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit were determined at NIST using gas chromatography with flame ionization detection (GC-FID) and GC with mass spectrometric detection (GC-MS). Target values for γ-linolenic acid, total omega-3 fatty acids, and total omega-6 fatty acids in SRM 3250 have not been determined at NIST. The NIST values and uncertainties for α-linolenic acid and linoleic acid are provided in the table below, both on a dry-mass basis as triglycerides, and on an as-received basis as FAMEs[5], accounting for moisture of the material (6.42 %).

	Certified Mass Fraction in SRM 3250 (mg/g)	
Analyte	(dry-mass basis, as triglyceride)	(as-received basis, as FAME)
α-Linolenic Acid	1.94 ± 0.25	1.82 ± 0.24
Linoleic Acid	8.24 ± 0.55	7.75 ± 0.52

Borage Oil. Participants were provided with three ampoules, each containing approximately 1.2 mL of borage oil. The oil was combined with tert-butylhydroquinone (TBHQ), an antioxidant, and packaged under argon into 2 mL amber ampoules. Before use, participants were instructed to thoroughly mix the contents of each ampoule and to use a sample size of at least 0.5 g. Participants were asked to store the material under refrigeration, 0 °C to 4 °C, to prepare a single sample and to report a single value from each ampoule provided. Approximate analyte levels were not reported to participants prior to the study. The certified values for γ-linolenic acid and linoleic acid, and the reference value for α-linolenic acid, in SRM 3274-1 Borage (*Borago officinalis*) Oil were determined at NIST using GC-FID and GC-MS. Target values for total omega-3 fatty acids and total omega-6 fatty acids in SRM 3274-1 have not been determined at NIST. The NIST-determined values and standard deviations are reported in the table below on an as-received basis as triglycerides and as FAMEs.

[5] De Vries, J.W., Kjos, L., Groff L., Martin, B., Cernohous, K., Patel, H., Payne, M., Leichtweis, H., Shay, M., & Newcomer, L. (1999) J. AOAC Int. 82, 1146–1155.

Analyte	NIST-Determined Mass Fraction Values in SRM 3274-1 (mg/g as triglycerides)	(mg/g as FAMEs)
α-Linolenic Acid	1.97 ± 0.11	1.98 ± 0.11
γ-Linolenic Acid	251 ± 24	252 ± 24
Linoleic Acid	374 ± 35	376 ± 35

Study Results

- Thirty laboratories enrolled in the exercise and received samples for some subset of fatty acids in these two samples.
  - For the saw palmetto fruit, the greatest participation was for linoleic acid with 18 laboratories (60 % participation). Half of the laboratories reported results for total omega-6 fatty acids, and approximately 40 % of laboratories reported results for α-linolenic acid and total omega-3 fatty acids. Only three laboratories reported results for γ-linolenic acid (10 % participation).
    - The consensus mean is below the target range for α-linolenic acid and linoleic acid in the saw palmetto fruit.
    - The consensus range for α-linolenic acid does not overlap the target range.
    - The consensus range for linoleic acid slightly overlaps the target range.
    - The between laboratory variability ranged from moderate to unacceptable in the saw palmetto fruit for linoleic acid, α-linolenic acid, and γ-linolenic acid (39 %, 52 %, and > 100 %, respectively).
  - For the borage oil, the greatest participation was also for linoleic acid with 19 laboratories (63 % participation) and γ-linolenic acid with 17 laboratories (59 % participation). Fifteen laboratories reported results for total omega-6 fatty acids (54 % participation), 11 laboratories reported results for α-linolenic acid (40 % participation), and 9 laboratories reported results for total omega-3 fatty acids (32 % participation).
    - The consensus mean is within the target range for α-linolenic acid in the borage oil.
    - The consensus means are below the target range for linoleic acid and γ-linolenic acid in the borage oil.
    - The consensus ranges for linoleic acid, α-linolenic acid, and γ-linolenic acid in the borage oil overlap the target ranges.
    - The between-laboratory variability was good for α-linolenic acid, γ-linolenic acid, linoleic acid, and total omega-6 fatty acids in the borage oil (14 % to 29 %).
    - The between laboratory variability was unacceptable for total omega-3 fatty acids in the borage oil (> 100 %).
  - Most laboratories reported using gas chromatography with flame ionization detection (GC-FID) as their analytical method. One or two laboratories reported using GC-MS as the analytical method.

Technical Recommendations

The following recommendations are based on results obtained from the participants in this study.

- Results for the saw palmetto berries were highly variable. However, no methods were presented as significantly better or worse than any other and no systematic biases were noted.
  - The fatty acids in the saw palmetto berries are challenging to extract and require multiple extraction steps. In past DSQAP exercises, this matrix has proven to be challenging for laboratories, and results are typically below the NIST target ranges.
  - While a laboratory should always evaluate the extraction efficiency for completeness, this particular matrix (saw palmetto berries) does not represent a large portion of the market share and should therefore be treated as an unfamiliar matrix and an example for potential bias.
- Results for the borage oil were good overall. No methods were presented as significantly better or worse than any other and no systematic biases were noted.
  - For most of the fatty acids, the between-laboratory variability was quite good, likely because the sample did not require significant preparation prior to analysis.
  - Wide variability was observed for the total omega-3 fatty acids. The levels of omega-3 fatty acids in borage oil are known to be very low, which likely resulted in the increased variability.
- Note that the two laboratories that reported using GC-MS consistently reported values on the lower end of all laboratories. This trend is not necessarily significant, given that only two laboratories reported using this approach, but worth noting.
- Participants were asked to report concentrations for fatty acids as fatty acid methyl esters (FAMEs). In this case, FAMEs should be used as calibrants or non-esterified fatty acids (e.g., triglycerides) should be carried through the entire sample preparation procedure (hydrolysis and derivatization) to improve quantitation.
  - Knowledge of calibrant response when carried through the derivatization procedure is necessary.
  - Similarly, for those laboratories using GC-MS, quantitation for some compounds may be inaccurate as a result of non-unity response factors from EI fragmentation.

Table 12. Individualized data summary table (NIST) for fatty acids in dietary supplements.

National Institute of Standards & Technology

Exercise N - May 2017 - Fatty Acids

		Lab Code:	**NIST**	**1. Your Results**				**2. Community Results**			**3. Target**	
Analyte	Sample	Units		x_i	s_i	Z'_{comm}	Z_{NIST}	N	x*	s*	x_{NIST}	U_{95}
α-Linolenic Acid (as FAME)	Saw Palmeto (Serenoa repens) Fruit	mg/g		2.08	0.27		0.00	12	0.67	0.37	2.08	0.27
α-Linolenic Acid (as FAME)	Borage (Borago Officinalis) Oil	mg/g		1.98	0.09		0.00	11	2.08	0.29	1.98	0.09
γ-Linolenic Acid (as FAME)	Saw Palmeto (Serenoa repens) Fruit	mg/g						3	0.36	0.60		
γ-Linolenic Acid (as FAME)	Borage (Borago Officinalis) Oil	mg/g		252	23		0.00	17	218	41	252	23
Linoleic Acid (as FAME)	Saw Palmeto (Serenoa repens) Fruit	mg/g		8.85	0.59		0.00	18	5.85	2.28	8.85	0.59
Linoleic Acid (as FAME)	Borage (Borago Officinalis) Oil	mg/g		376	33		0.00	19	340	63	376	33
Total Omega-3 Fatty Acid (as FAME)	Saw Palmeto (Serenoa repens) Fruit	mg/g						10	0.83	0.59		
Total Omega-3 Fatty Acid (as FAME)	Borage (Borago Officinalis) Oil	mg/g						9	13	19		
Total Omega-6 Fatty Acid (as FAME)	Saw Palmeto (Serenoa repens) Fruit	mg/g						14	5.48	1.73		
Total Omega-6 Fatty Acid (as FAME)	Borage (Borago Officinalis) Oil	mg/g						15	550	161		

x_i Mean of reported values
s_i Standard deviation of reported values
Z'_{comm} Z'-score with respect to community consensus
Z_{NIST} Z-score with respect to NIST value
N Number of quantitative values reported
x* Robust mean of reported values
s* Robust standard deviation
x_{NIST} NIST-assessed value
U_{95} ±95% confidence interval about the assessed value or standard deviation (s_{NIST})

Table 13. Data summary table for α-linolenic acid (as FAME) in dietary supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		α-Linolenic Acid (as FAME)									
		SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (mg/g)					SRM 3274-1 Borage (*Borago officinalis*) Oil (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				1.824	0.235				1.98	0.09
	N102						1.93			1.93	
	N103										
	N105										
	N107	1.055	0.875	0.840	0.923	0.115	2.02	1.52	1.92	1.82	0.27
	N108	0.700	0.710	0.700	0.703	0.006	2.05	2.05	2.05	2.05	0.00
	N109	0.356	0.407	0.365	0.376	0.027					
	N110	23.700	23.600	23.900	23.733	0.153	77.30	76.10	76.00	76.47	0.72
	N112	0.700	0.700	0.600	0.667	0.058	2.00	2.00	2.10	2.03	0.06
	N113										
	N115										
	N118	0.649	0.676	0.583	0.636	0.048	1.79	1.80	1.88	1.83	0.05
	N120										
	N121	0.466	0.497	0.511	0.491	0.023	2.30	2.27	2.29	2.29	0.02
	N123										
	N124	2.070	1.570	1.200	1.613	0.437	2.06	2.08	2.06	2.07	0.01
	N125										
	N126										
	N129										
	N130										
	N132	0.550	0.540	0.530	0.540	0.010	1.99	1.99	2.02	2.00	0.02
	N133	0.727	0.740	0.784	0.750	0.030	2.50	2.71	2.33	2.51	0.19
	N136	0.260	0.230	0.340	0.277	0.057					
	N137	0.200	0.200	0.300	0.233	0.058	< 0.000	< 0.000	< 0.000	< 0.000	
	N141										
	N147										
	N150										
	N155										
	N157	< 0.000	< 0.000	< 0.000	< 0.000		< 0.000	< 0.000	< 0.000	< 0.000	
	N158						1.80	1.80	1.80	1.80	0.00
Community Results		Consensus Mean			0.671		Consensus Mean			2.08	
		Consensus Standard Deviation			0.372		Consensus Standard Deviation			0.29	
		Maximum			23.733		Maximum			76.47	
		Minimum			0.233		Minimum			1.80	
		N			12		N			11	

Table 14. Data summary table for γ-linolenic (as FAME) acid in dietary supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		γ-Linolenic Acid (as FAME)									
		SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (mg/g)					SRM 3274-1 Borage (*Borago officinalis*) Oil (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST									252	23
	N102						233			233	
	N103										
	N105	0.950	0.970	0.990	0.970	0.020	2.01	2.60	1.70	2.10	0.46
	N107						260	247	254	254	6
	N108						242	241	241	241	1
	N109										
	N110						128	127	124	126	2
	N112	< 0.100	< 0.100	< 0.100	< 0.100		226	226	226	226	0
	N113										
	N115										
	N118						226	232	225	228	4
	N120										
	N121						234	235	232	234	2
	N123						149	143	147	146	3
	N124	0.030	0.020	0.010	0.020	0.010	237	239	237	237	1
	N125										
	N126										
	N129										
	N130						243	240	241	241	1
	N132						206	203	207	205	2
	N133						270	275	263	269	6
	N136	0.020	0.020	0.210	0.083	0.110	168	171	171	170	2
	N137	< 0.000	< 0.000	< 0.000	< 0.000		237	238	237	237	1
	N141										
	N147										
	N150										
	N155										
	N157	< 0.000	< 0.000	< 0.000	< 0.000		215	221	214	217	4
	N158						239	240	240	240	1
Community Results					0.358		Consensus Mean			218	
		Consensus Standard Deviation			0.603		Consensus Standard Deviation			41	
		Maximum			0.970		Maximum			269	
		Minimum			0.020		Minimum			2.10	
		N			3		N			17	

Table 15. Data summary table for linoleic acid (as FAME) in dietary supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Linoleic Acid (as FAME)									
		SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (mg/g)					SRM 3274-1 Borage (*Borago officinalis*) Oil (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				7.75	0.52				376	33
	N102	1.11			1.11		0.04			0.04	
	N103										
	N105	6.56	6.96	6.76	6.76	0.20	281	283	276	280	4
	N107	6.27	6.24	6.29	6.26	0.02	427	421	401	416	14
	N108	5.80	5.84	5.86	5.83	0.03	371	370	370	370	1
	N109	3.60	3.72	3.41	3.58	0.15					
	N110	23.70	23.60	23.90	23.73	0.15	206	203	200	203	3
	N112	5.80	6.20	5.70	5.90	0.26	353	352	352	352	1
	N113										
	N115										
	N117	6.98	6.95	7.03	6.99	0.04	427	425	428	427	2
	N118	5.64	5.76	5.41	5.60	0.18	370	388	371	376	10
	N120										
	N121	3.62	3.60	3.85	3.69	0.14	366	367	363	365	2
	N123	5.85	5.97	5.92	5.91	0.06	269	258	264	264	6
	N124	18.20	13.29	10.60	14.03	3.85	369	373	369	370	2
	N125										
	N126										
	N129	11.37	11.71	11.49	11.52	0.17	351	356	348	351	4
	N130						371	369	370	370	1
	N132	4.79	4.73	4.74	4.75	0.03	313	309	314	312	3
	N133	5.82	5.71	6.10	5.88	0.20	403	410	392	402	9
	N136	3.97	3.94	4.99	4.30	0.60	265	275	287	275	11
	N137	3.20	3.40	3.60	3.40	0.20	359	357	360	359	2
	N141										
	N147										
	N150										
	N155										
	N157	6.15	6.18	6.23	6.19	0.04	311	320	308	313	6
	N158						364	365	366	365	1
Community Results		Consensus Mean			5.85		Consensus Mean			340	
		Consensus Standard Deviation			2.28		Consensus Standard Deviation			63	
		Maximum			23.73		Maximum			427	
		Minimum			1.11		Minimum			0.04	
		N			18		N			19	

Table 16. Data summary table for total omega-3 fatty acids (as FAMEs) in dietary supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Total Omega-3 Fatty Acids (as FAMEs)									
		SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (mg/g)					SRM 3274-1 Borage (*Borago officinalis*) Oil (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST										
	N103										
	N105										
	N107	1.06	0.87	0.84	0.92	0.12	17.3	15.5	18.2	17.0	1.3
	N108	0.70	0.71	0.70	0.70	0.01	2.1	2.1	2.1	2.1	0.0
	N109										
	N110	23.70	23.60	23.90	23.73	0.15	77.3	76.1	76.0	76.5	0.7
	N112	0.70	0.80	0.70	0.73	0.06	4.0	4.2	4.2	4.1	0.1
	N113										
	N115										
	N118										
	N120										
	N121	0.50	0.51	0.54	0.52	0.02	78.6	79.9	78.2	78.9	0.9
	N123										
	N124	18.23	13.31	10.61	14.05	3.86	2.1	2.1	2.1	2.1	0.0
	N125										
	N126										
	N129										
	N130										
	N132	0.59	0.57	0.56	0.57	0.02	2.1	2.1	2.1	2.1	0.0
	N133	0.93	0.86	0.92	0.90	0.04	2.9	2.9	2.6	2.8	0.2
	N136	0.26	0.23	0.34	0.28	0.06					
	N137	0.20	0.20	0.30	0.23	0.06	< 0.000	< 0.000	< 0.000	< 0.000	
	N141										
	N147										
	N150										
	N155										
	N157	< 0.000	< 0.000	< 0.000	< 0.000		< 0.000	< 0.000	< 0.000	< 0.000	
	N158						3.6	3.7	3.6	3.6	0.1
Community Results		Consensus Mean			0.83		Consensus Mean			12.9	
		Consensus Standard Deviation			0.59		Consensus Standard Deviation			18.9	
		Maximum			23.73		Maximum			78.9	
		Minimum			0.23		Minimum			2.1	
		N			10		N			9	

Table 17. Data summary table for total omega-6 fatty acids (as FAMEs) in dietary supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Total Omega-6 Fatty Acids (as FAMEs)									
		SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (mg/g)					SRM 3274-1 Borage (*Borago officinalis*) Oil (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST										
	N103										
	N105	84.20	94.10	88.50	88.93	4.96	985	990	969	981	11
	N107	6.27	6.24	6.29	6.27	0.03	688	670	657	672	16
	N108	5.80	5.84	5.86	5.83	0.03	612	611	610	611	1
	N109										
	N110	4.66	4.58	4.62	4.62	0.04	325	321	316	321	5
	N112	5.80	6.30	5.80	5.97	0.29	582	581	580	581	1
	N113										
	N115										
	N118										
	N120										
	N121	3.62	3.60	3.85	3.69	0.14	600	602	595	599	4
	N123	5.85	5.97	5.92	5.91	0.06	436	418	428	427	9
	N124	2.07	1.57	1.20	1.61	0.44	606	612	606	608	3
	N125										
	N126										
	N129	11.37	11.71	11.49	11.52	0.17	351	356	348	351	4
	N130										
	N132	4.88	4.80	4.81	4.83	0.04	521	515	524	520	5
	N133	5.98	5.87	6.26	6.04	0.20	705	716	685	702	16
	N136	4.23	4.17	5.32	4.57	0.65	265	275	287	275	11
	N137	3.60	3.80	4.00	3.80	0.20	624	623	625	624	1
	N141										
	N147										
	N150										
	N155										
	N157	6.15	6.18	6.23	6.19	0.04	526	541	522	530	10
	N158						605	608	609	607	2
Community Results		Consensus Mean			5.48		Consensus Mean			550	
		Consensus Standard Deviation			1.73		Consensus Standard Deviation			161	
		Maximum			88.93		Maximum			981	
		Minimum			1.61		Minimum			275	
		N			14		N			15	

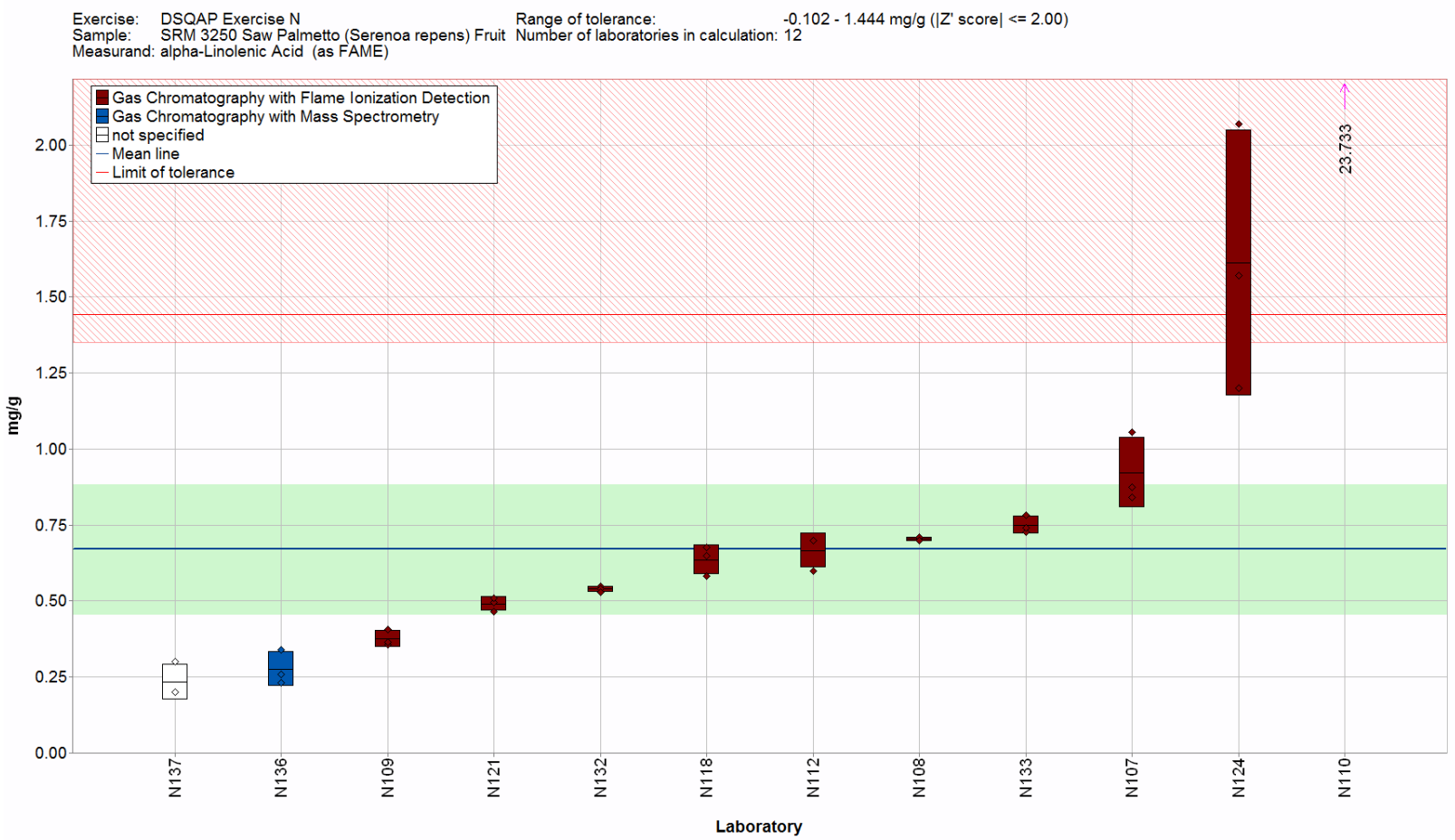

Figure 26. α-Linolenic acid (as FAME) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set a zero. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

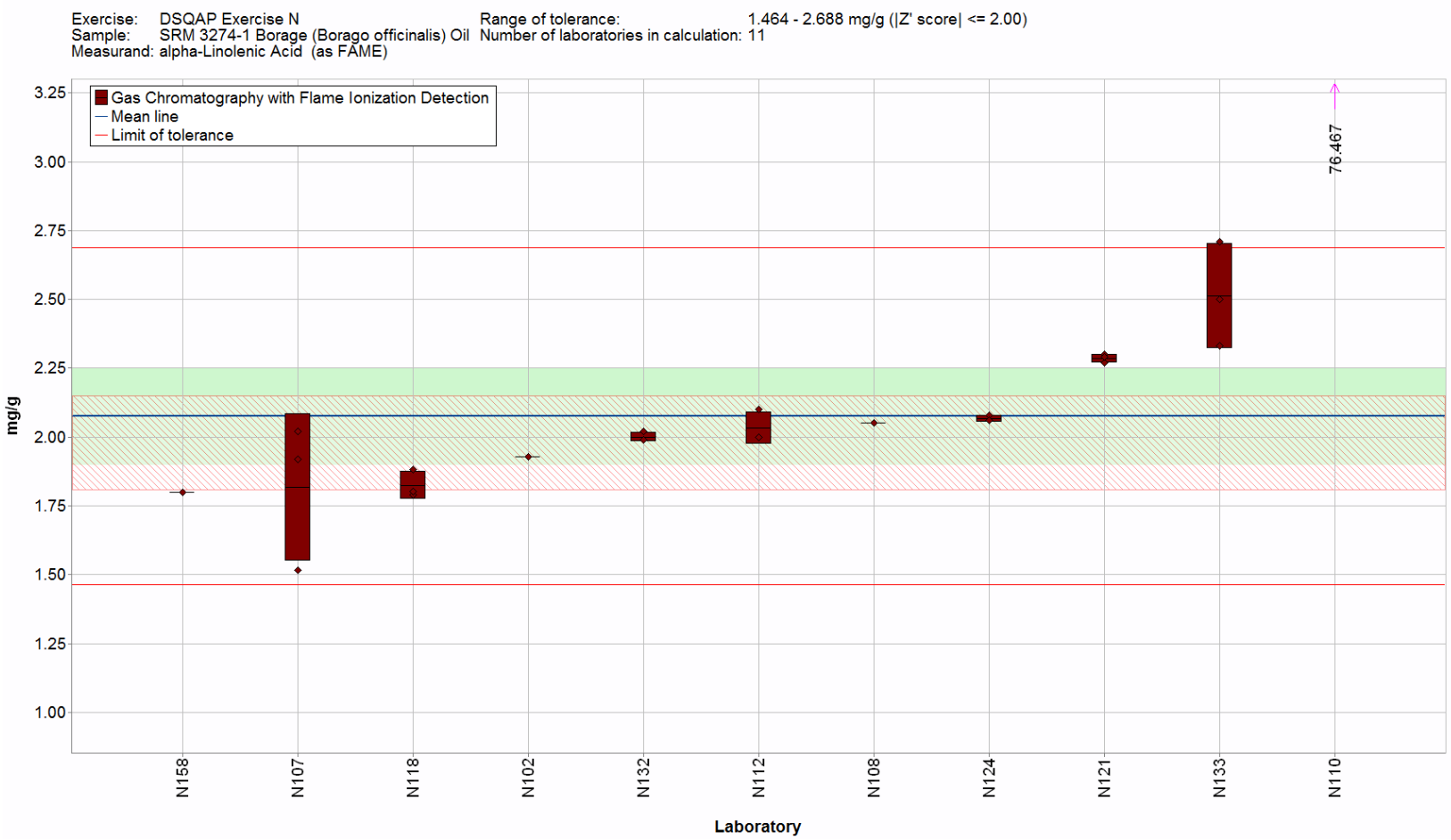

Figure 27. α-Linolenic acid (as FAME) in SRM 3274-1 Borage (*Borago officinalis*) Oil (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST reference value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$.

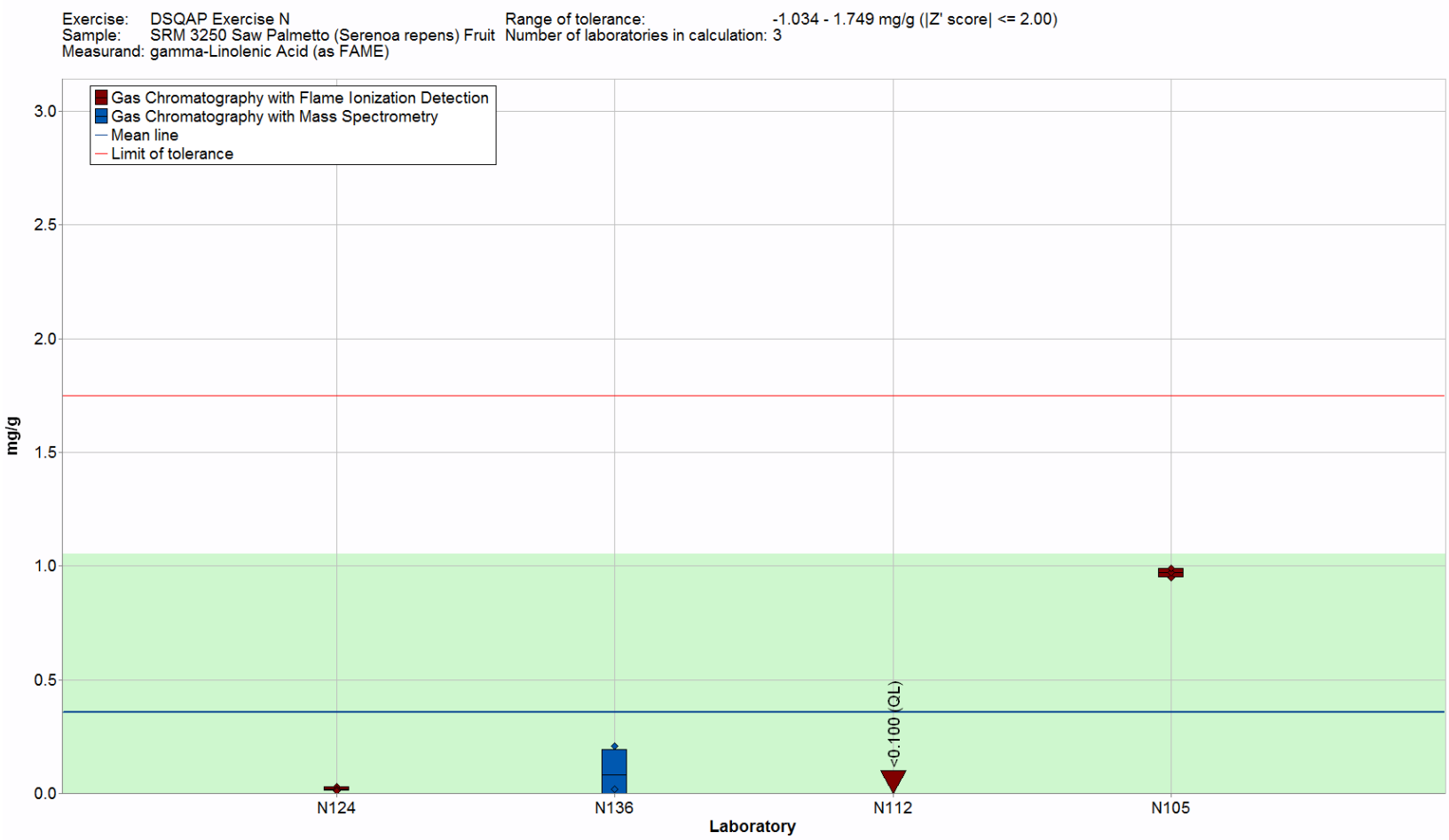

Figure 28. γ-Linolenic acid (as FAME) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set at zero. A NIST value has not been determined in this material.

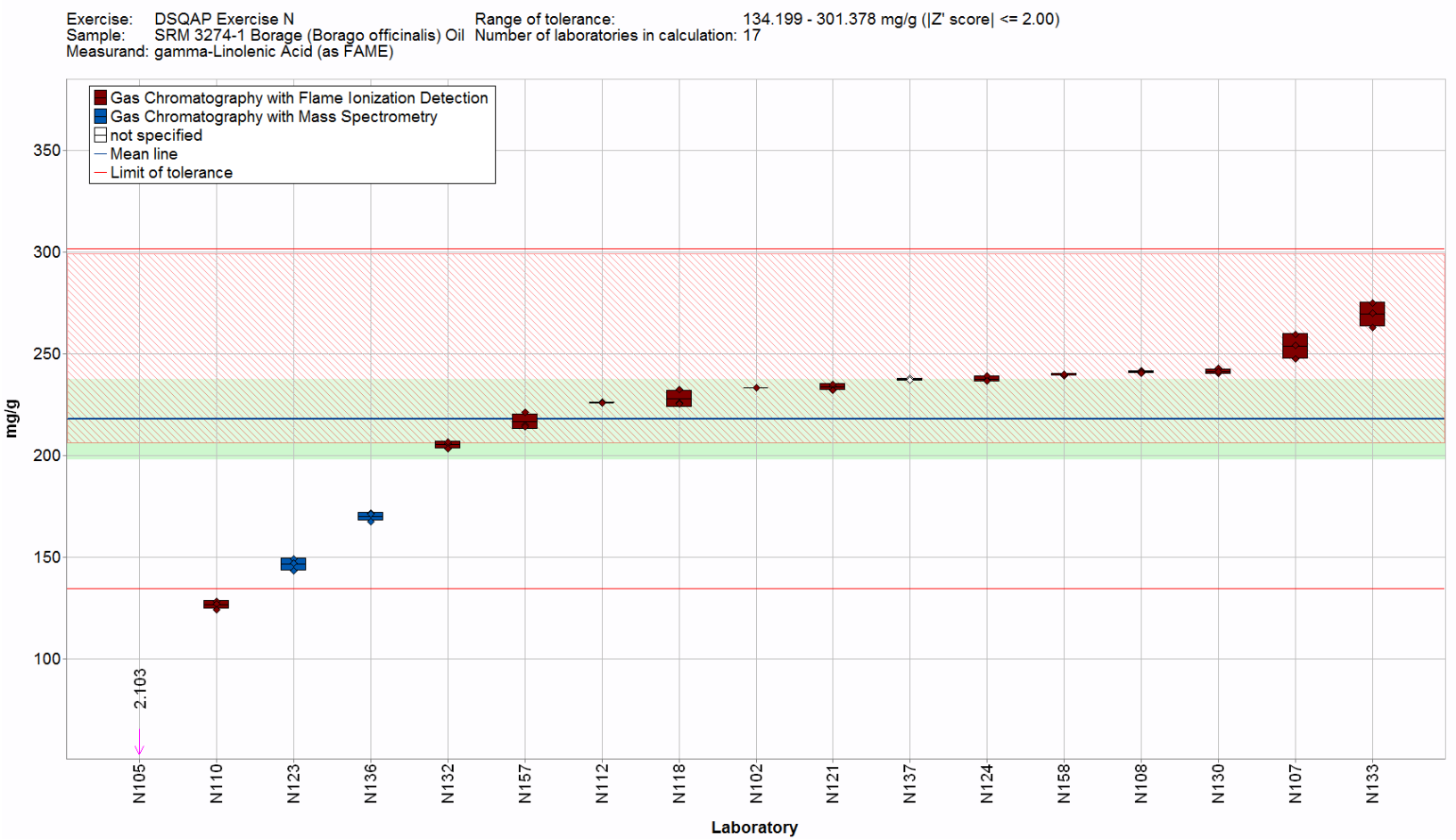

Figure 29. γ-Linolenic acid (as FAME) in SRM 3274-1 Borage (*Borago officinalis*) Oil (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\text{NIST}}| \leq 2$.

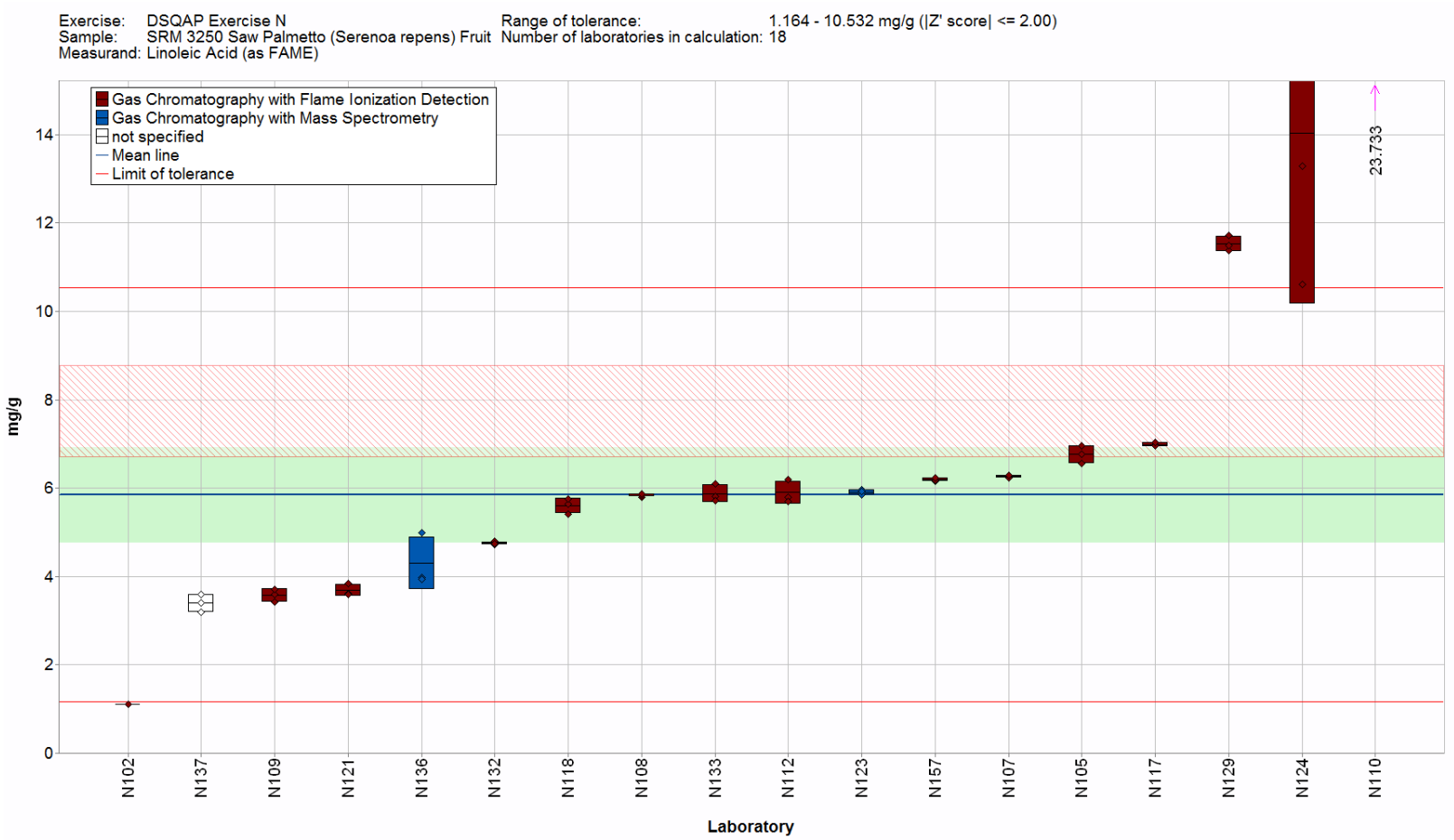

Figure 30. Linoleic acid (as FAME) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

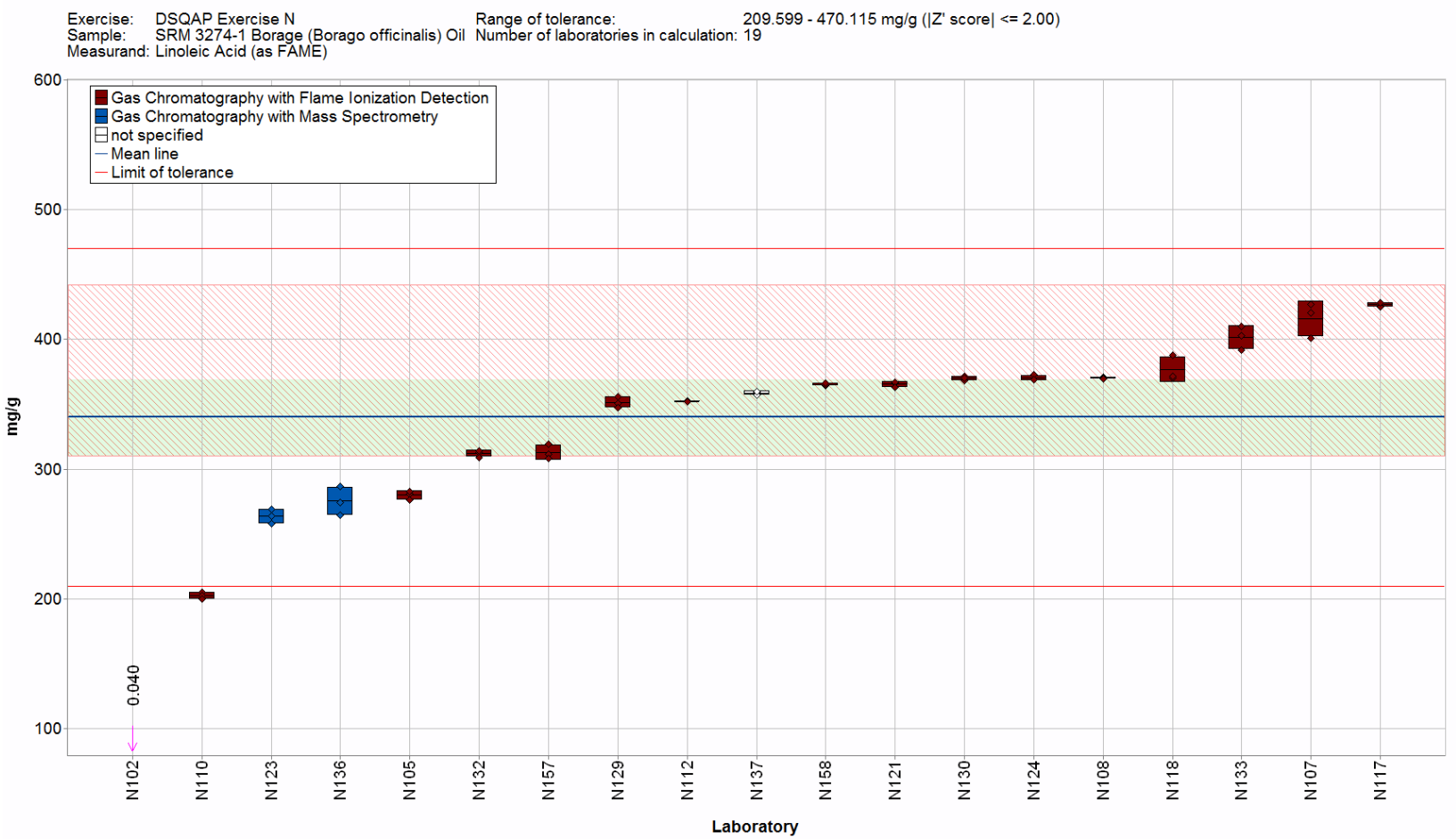

Figure 31. Linoleic acid (as FAME) in SRM 3274-1 Borage (*Borago officinalis*) Oil (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST certified value bounded by twice its uncertainty (U_{95}) and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

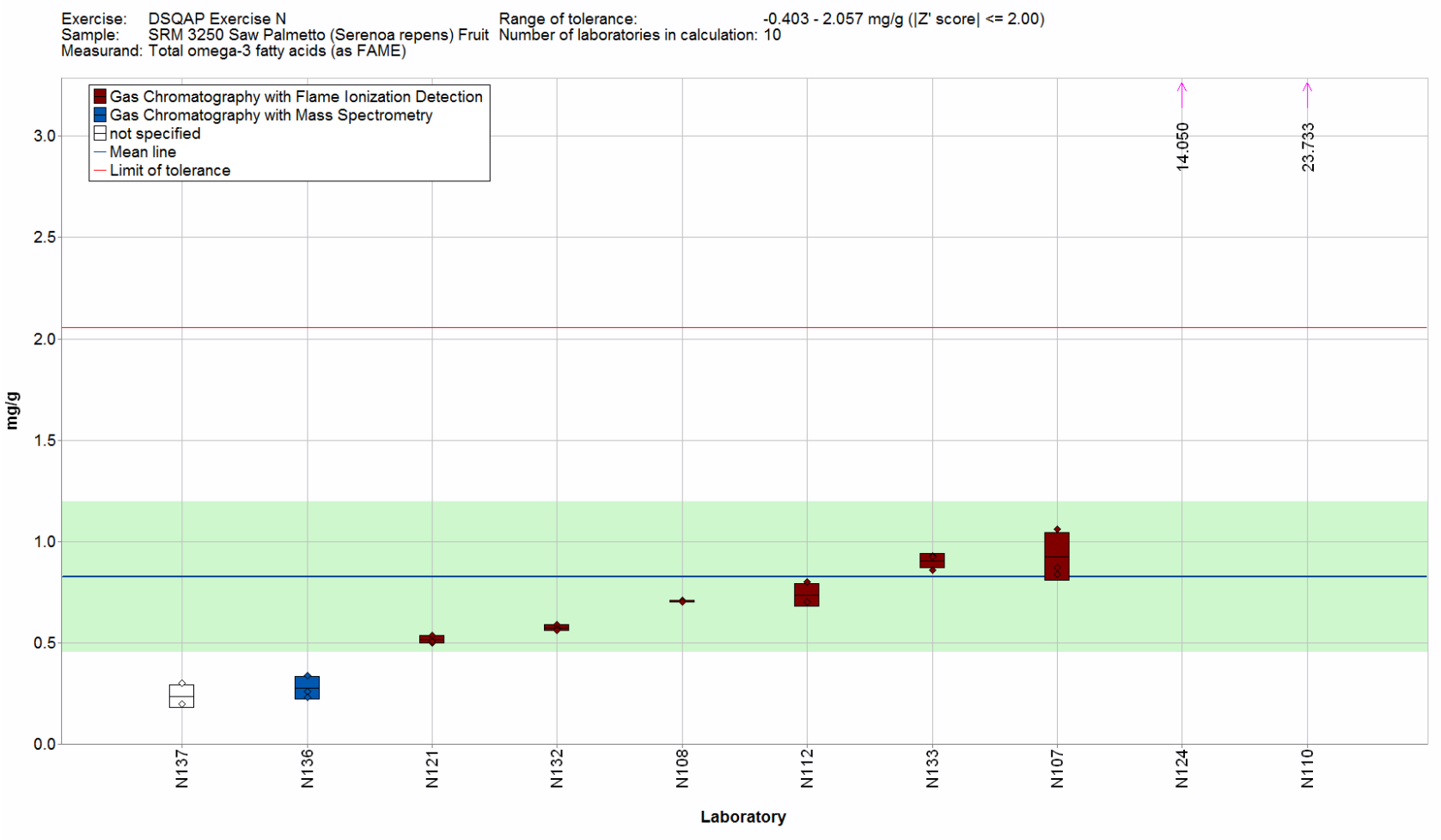

Figure 32. Total omega-3 fatty acids (as FAMEs) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set a zero. A NIST value has not been determined in this material.

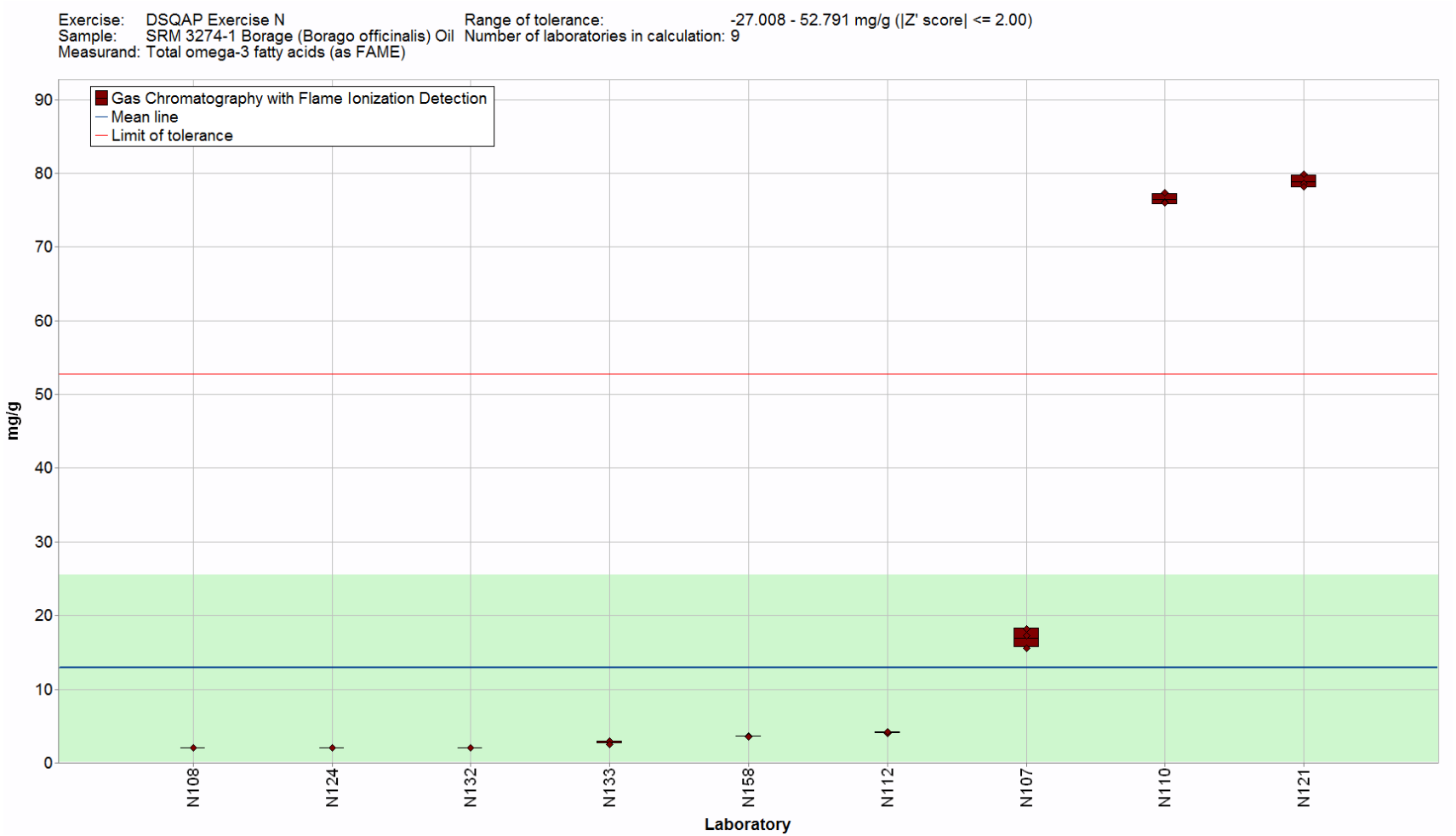

Figure 33. Total omega-3 fatty acids (as FAMEs) in SRM 3274-1 Borage (*Borago officinalis*) Oil (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set a zero. A NIST value has not been determined in this material.

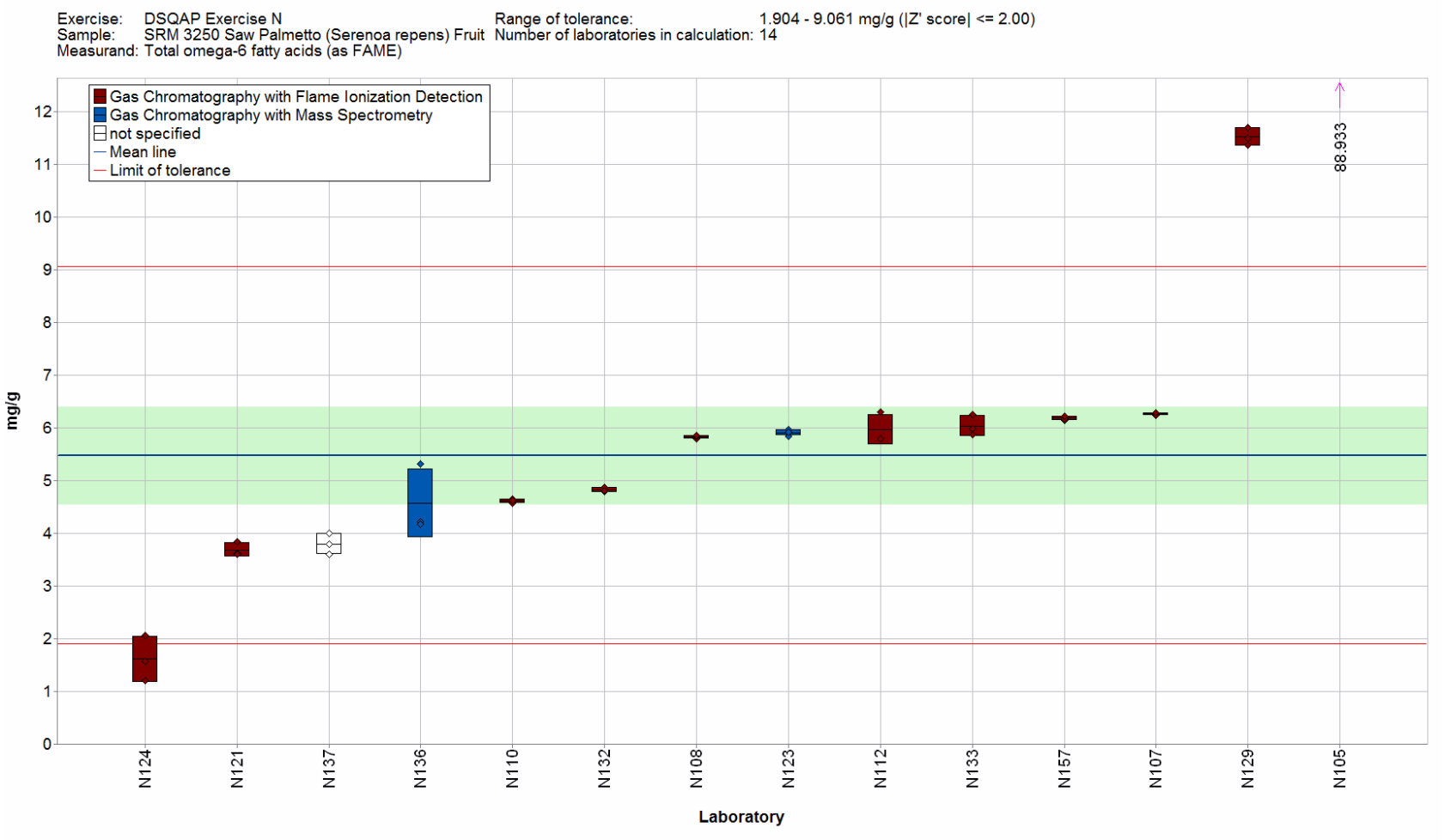

Figure 34. Total omega-6 fatty acids (as FAMEs) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material. A NIST value has not been determined in this material.

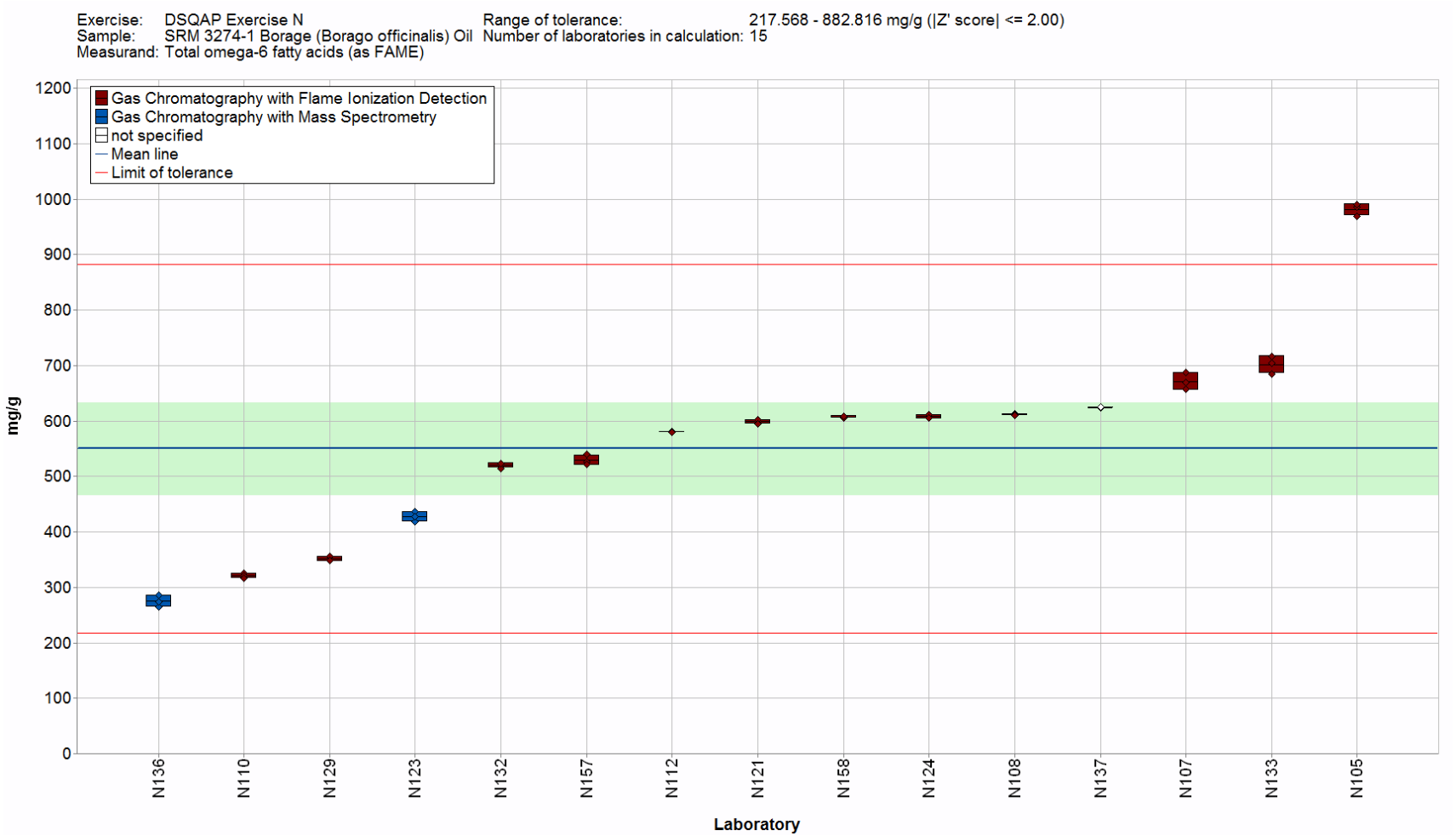

Figure 35. Total omega-6 fatty acid (as FAMEs) in SRM 3274-1 Borage (*Borago officinalis*) Oil (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material.

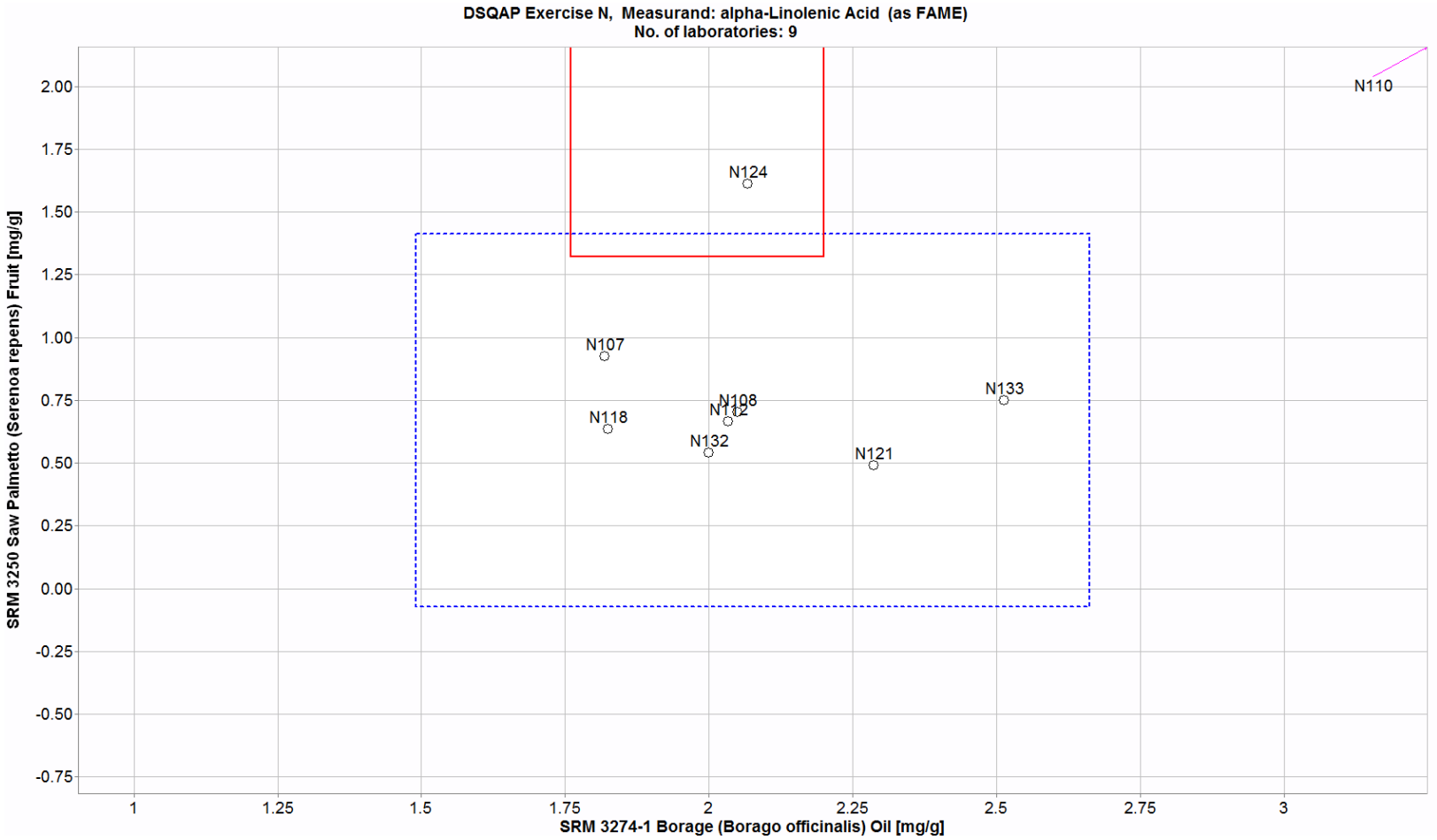

Figure 36. Laboratory means for α-linolenic acid (as FAME) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit, and SRM 3274-1 Borage (*Borago officinalis*) Oil (sample/sample comparison view). In this view, the individual laboratory mean for one sample (saw palmetto fruit) is compared to the mean for a second sample (borage oil). The solid red box represents the NIST range of tolerance for the two samples, borage oil (x-axis) and saw palmetto fruit (y-axis), which encompasses the NIST values bounded by their uncertainties (U_{95}), and represents the range that results in an acceptable Z_{NIST} score, $|Z_{NIST}| \leq 2$. The dotted blue box represents the consensus range of tolerance for borage oil (x-axis) and saw palmetto fruit (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

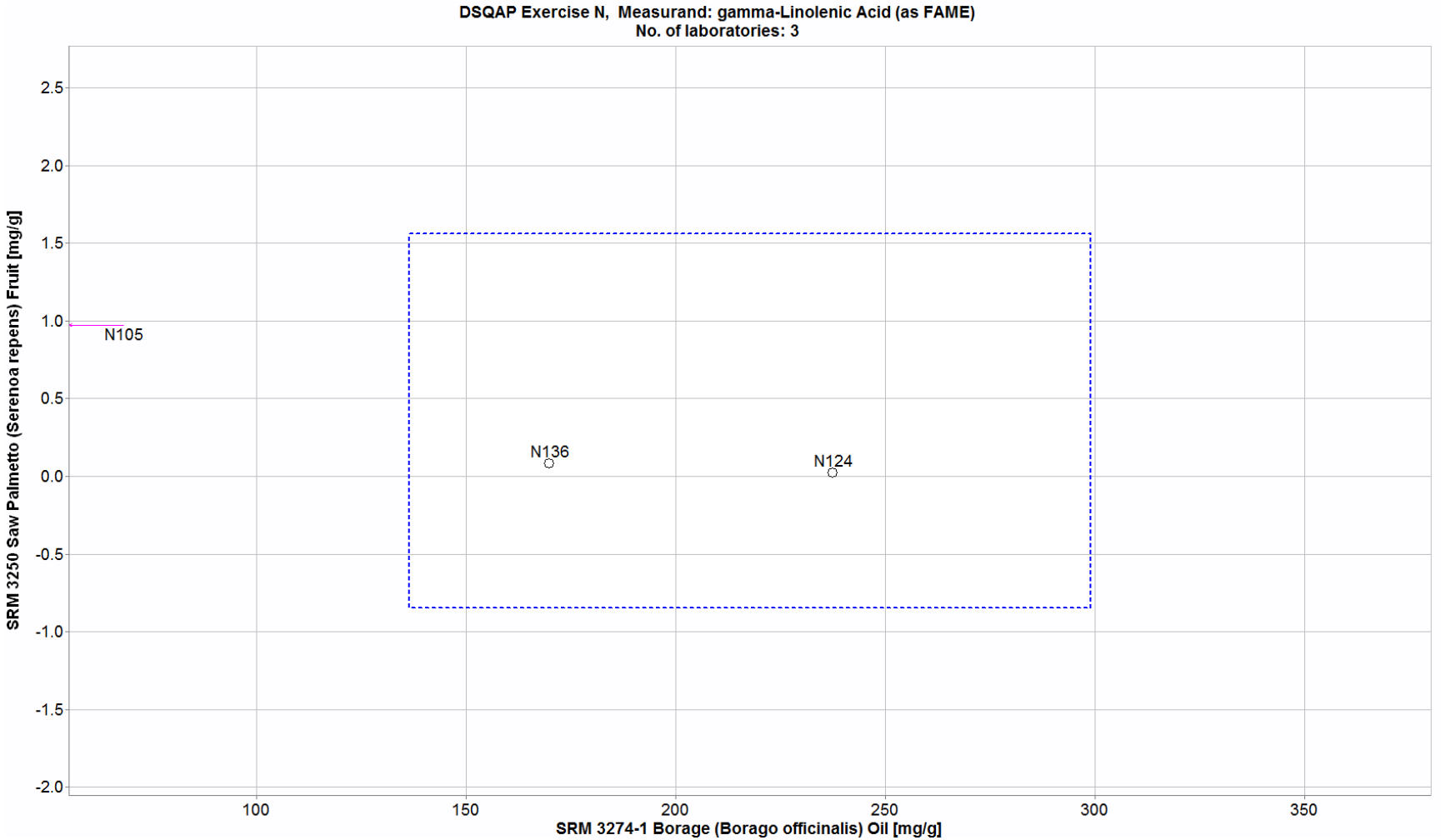

Figure 37. Laboratory means for γ-linolenic acid (as FAME) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit, and SRM 3274-1 Borage (*Borago officinalis*) Oil (sample/sample comparison view). In this view, the individual laboratory mean for one sample (saw palmetto fruit) is compared to the mean for a second sample (borage oil). The dotted blue box represents the consensus range of tolerance for borage oil (x-axis) and saw palmetto fruit (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

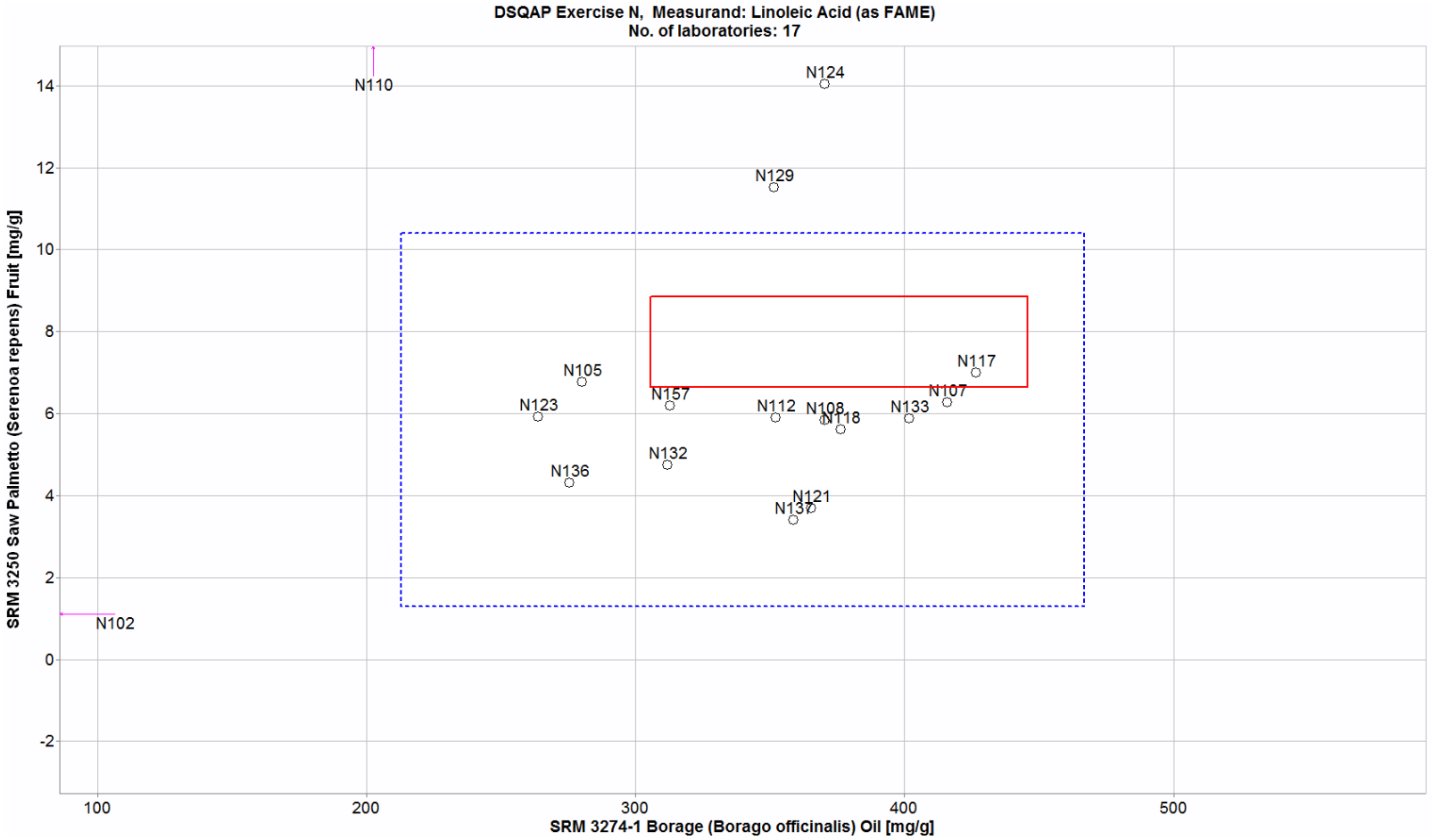

Figure 38. Laboratory means for linolenic acid (as FAME) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit, and SRM 3274-1 Borage (*Borago officinalis*) Oil (sample/sample comparison view). In this view, the individual laboratory mean for one sample (saw palmetto fruit) is compared to the mean for a second sample (borage oil). The solid red box represents the NIST range of tolerance for the two samples, borage oil (x-axis) and saw palmetto fruit (y-axis), which encompasses the NIST values bounded by their uncertainties (U_{95}), and represents the range that results in an acceptable Z_{NIST} score, $|Z_{NIST}| \leq 2$. The dotted blue box represents the consensus range of tolerance for borage oil (x-axis) and saw palmetto fruit (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

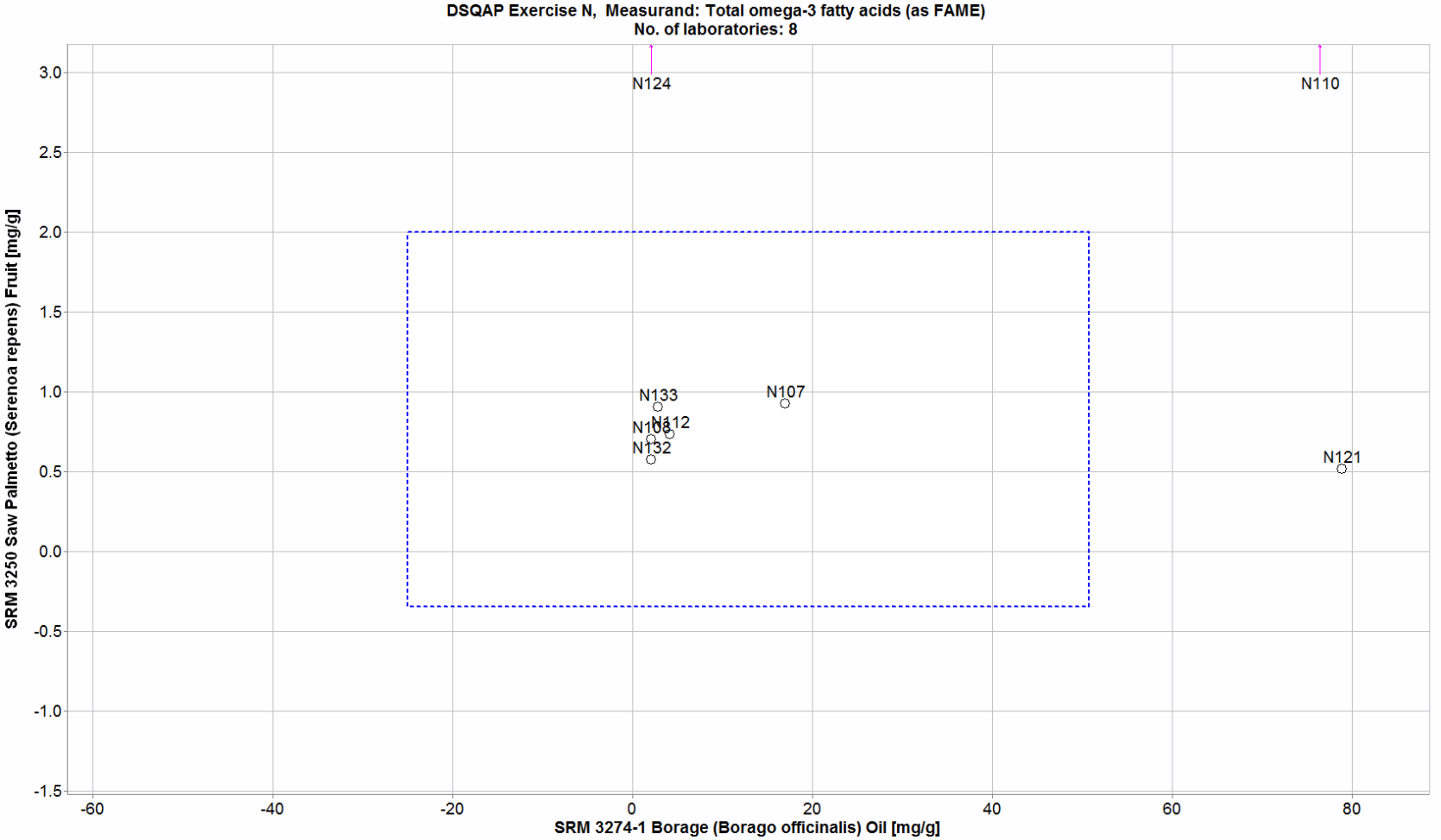

Figure 39. Laboratory means for total omega-3 fatty acids (as FAMEs) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit, and SRM 3274-1 Borage (*Borago officinalis*) Oil (sample/sample comparison view). In this view, the individual laboratory mean for one sample (saw palmetto fruit) is compared to the mean for a second sample (borage oil). The dotted blue box represents the consensus range of tolerance for borage oil (x-axis) and saw palmetto fruit (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

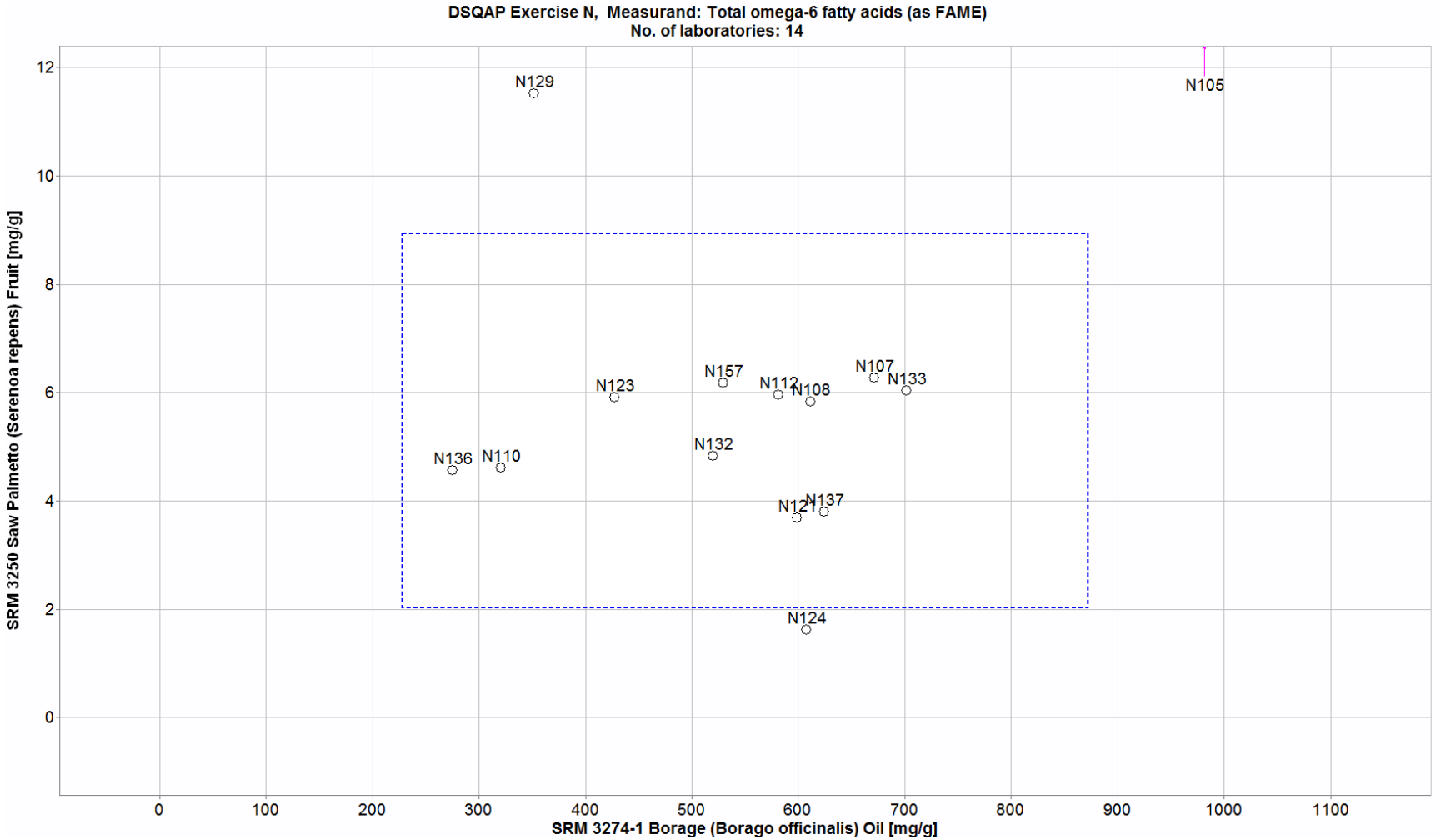

Figure 40. Laboratory means for total omega-6 fatty acids (as FAMEs) in SRM 3250 Saw Palmetto (*Serenoa repens*) Fruit, and SRM 3274-1 Borage (*Borago officinalis*) Oil (sample/sample comparison view). In this view, the individual laboratory mean for one sample (saw palmetto fruit) is compared to the mean for a second sample (borage oil). The dotted blue box represents the consensus range of tolerance for borage oil (x-axis) and saw palmetto fruit (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

GINSENOSIDES IN GROUND ASIAN GINSENG EXTRACT AND RHIZOME BOTANICAL SUPPLEMENTS

Study Overview

In this study, participants were provided with two candidate NIST SRMs, SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome, and SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract. Participants were asked to use in-house analytical methods to determine the mass fractions of ginsenosides Rb1, Rb2, Rc, Rd, Re, Rf, Rg1, and Rg2 in each of the matrices and report values in mg/g on an as-received basis.

Sample Information

Ground Asian Ginseng Rhizome. Participants were provided with three packets, each containing approximately 3 g of ground ginseng rhizome. The rhizomes were ground, homogenized, and heat-sealed inside 4 mil polyethylene bags, which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel. Before use, participants were instructed to thoroughly mix the contents of each packet and use a sample size of at least 1 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to report a single value from each packet provided. Approximate analyte levels were not reported to participants prior to the study. NIST determined values for ginsenosides in candidate SRM 3384 using liquid chromatography with absorbance detection (LC-absorbance). The NIST-determined values and standard deviations are reported in the table below on an as-received basis.

Analyte	NIST-Determined Mass Fraction in SRM 3384 Ginseng Rhizome (mg/g) (as-received basis)
Rb1	15.84 ± 0.26
Rb2	9.30 ± 0.10
Rc	9.03 ± 0.18
Rd	5.16 ± 0.06
Re	6.61 ± 0.14
Rf	1.10 ± 0.12
Rg1	3.94 ± 0.08
Rg2	0.61 ± 0.03

Ground Asian Ginseng Extract. Participants were provided with three packets, each containing approximately 1 g of ground ginseng extract. The extract was ground, homogenized, and heat-sealed inside 4 mil polyethylene bags, which were then sealed inside nitrogen-flushed aluminized plastic bags along with two packets of silica gel. Before use, participants were instructed to thoroughly mix the contents of each packet and use a sample size of at least 0.1 g. Participants were asked to store the material at controlled room temperature, 10 °C to 30 °C, and to report a single value from each packet provided. Approximate analyte levels were not reported to participants prior to the study, and target values for ginsenosides in candidate SRM 3385 have not been determined at NIST.

Study Results

- Twenty-five laboratories enrolled in this exercise and received samples for all analytes. A summary of the participation rates is shown in the table below.

	Number of Laboratories Reporting Results (Percent Participation)	
Analyte	Asian ginseng rhizome	Asian ginseng extract
Rb1	16 (64 %)	16 (64 %)
Rb2	15 (60 %)	16 (64 %)
Rc	15 (60 %)	16 (64 %)
Rd	15 (60 %)	16 (64 %)
Re	15 (60 %)	16 (64 %)
Rf	13 (52 %)	13 (52 %)
Rg1	16 (64 %)	16 (64 %)
Rg2	8 (33 %)	8 (33 %)

- The consensus means for most ginsenosides in the Asian ginseng rhizome were below the target ranges and the consensus ranges did not overlap with the target ranges (see table below). The exceptions were ginsenosides Rf and Rg2. The between-laboratory variability is also summarized below, and ranged from good for Rb1 in the Asian ginseng extract (11 %) to very high for Rg2 in the Asian ginseng rhizome (90 %).

		Between-Laboratory Variability	
Analyte	Position of Consensus and Target in Asian ginseng rhizome	Asian ginseng rhizome	Asian ginseng extract
Rb1	Consensus mean *below* target range Consensus range *does not overlap* target range	16 %	11 %
Rb2	Consensus mean *below* target range Consensus range *does not overlap* target range	34 %	21 %
Rc	Consensus mean *below* target range Consensus range *does not overlap* target range	20 %	19 %
Rd	Consensus mean *below* target range Consensus range *does not overlap* target range	29 %	21 %
Re	Consensus mean *below* target range Consensus range *does not overlap* target range	11 %	13 %
Rf	Consensus mean *within* target range Consensus range *overlaps* target range	30 %	26 %
Rg1	Consensus mean *below* target range Consensus range *does not overlap* target range	18 %	16 %
Rg2	Consensus mean *above* target range Consensus range *overlaps* target range	90 %	64 %

- Most laboratories reported using LC with absorbance detection as their analytical method. One laboratory reported using an internal method (UPLC).

Technical Recommendations

The following recommendations are based on results obtained from the participants in this study.

- Most laboratories reported values below the NIST-determined value for most ginsenosides in the Asian ginseng rhizome samples. The low measured values may be a result of incomplete extraction of the ginsenosides from the sample matrix. To ensure maximum recovery, a subsequent re-extraction of the sample can indicate if measurable amounts of the analyte remain in the matrix following extraction.
- The sample/sample comparison graphs for nearly all of the ginsenosides demonstrate an upward trend, indicating a potential calibration issue. Whenever possible, a matched component should be used to quantify each of the ginsenosides. Calibrant purity should be carefully evaluated to identify and account for possible biases.
- When viewing **Figures 57** through **64**, an increasing trend in the sample/sample comparison data may be attributed to a potential calibration issue or greater difficulty with sample preparation of one sample over the second sample. This trend is very noticeable in ginsenosides Rb1, Rb2, Rd, and Re, and noticeable to a lesser degree in ginsenosides Rc, Rf, and Rg2. No noticeable trend in the data was observed for ginsenosides Rg1.

Table 18. Individualized data summary table (NIST) for ginsenosides in botanical supplements.

National Institute of Standards & Technology

Exercise N - May 2017 - Ginsenosides

		Lab Code: NIST	**1. Your Results**				**2. Community Results**			**3. Target**	
Analyte	Sample	Units	x_i	s_i	Z'_{comm}	Z_{NIST}	N	x*	s*	x_{NIST}	U_{95}
Ginsenoside Rb1	Ginseng Rhizome	mg/g	15.84	0.26		0.00	16	9.38	1.53	15.84	0.26
Ginsenoside Rb1	Ginseng Extract	mg/g					16	34.2	3.9		
Ginsenoside Rb2	Ginseng Rhizome	mg/g	9.30	0.10		0.00	15	6.12	2.08	9.30	0.10
Ginsenoside Rb2	Ginseng Extract	mg/g					16	20.1	4.3		
Ginsenoside Rc	Ginseng Rhizome	mg/g	9.03	0.18		0.00	15	6.56	1.28	9.03	0.18
Ginsenoside Rc	Ginseng Extract	mg/g					16	26.8	5.0		
Ginsenoside Rd	Ginseng Rhizome	mg/g	5.16	0.06		0.00	15	3.18	0.91	5.16	0.06
Ginsenoside Rd	Ginseng Extract	mg/g					16	14.9	3.2		
Ginsenoside Re	Ginseng Rhizome	mg/g	6.61	0.14		0.00	15	5.06	0.58	6.61	0.14
Ginsenoside Re	Ginseng Extract	mg/g					16	17.0	2.2		
Ginsenoside Rf	Ginseng Rhizome	mg/g	1.10	0.12		0.00	13	1.05	0.32	1.10	0.12
Ginsenoside Rf	Ginseng Extract	mg/g					13	2.92	0.77		
Ginsenoside Rg1	Ginseng Rhizome	mg/g	3.94	0.08		0.00	16	3.12	0.56	3.94	0.08
Ginsenoside Rg1	Ginseng Extract	mg/g					16	6.27	1.03		
Ginsenoside Rg2	Ginseng Rhizome	mg/g	0.61	0.03		0.00	8	1.15	1.04	0.61	0.03
Ginsenoside Rg2	Ginseng Extract	mg/g					8	4.43	2.85		

x_i Mean of reported values

s_i Standard deviation of reported values

Z'_{comm} Z'-score with respect to community consensus

Z_{NIST} Z-score with respect to NIST value

N Number of quantitative values reported

x* Robust mean of reported values

s* Robust standard deviation

x_{NIST} NIST-assessed value

U_{95} ±95% confidence interval about the assessed value or standard deviation (s_{NIST})

Table 19. Data summary table for ginsenoside Rb1 in botanical supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ginsenoside Rb1									
		Ginseng Rhizome (mg/g)					Ginseng Extract (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				15.84	0.26					
	N105	10.50	10.90	10.50	10.63	0.23	37.3	37.8	37.7	37.6	0.3
	N107	10.34	10.68	10.52	10.51	0.17	37.6	37.8	38.2	37.9	0.3
	N108	6.36	6.34	6.09	6.26	0.15	27.5	26.7	26.8	27.0	0.5
	N109	8.78	8.66	8.94	8.79	0.14	35.0	34.7	35.0	34.9	0.2
	N110	7.73	7.46	7.60	7.60	0.14	32.0	31.8	31.3	31.7	0.4
	N111										
	N115										
	N117	7.85	7.84	7.26	7.65	0.34	30.4	30.1	28.4	29.6	1.1
	N118	9.44	9.46	9.33	9.41	0.07	32.0	34.5	31.9	32.8	1.5
	N120										
	N121	9.61	9.52	9.50	9.54	0.06	33.9	34.2	33.9	34.0	0.2
	N122										
	N124	13.48	13.61	13.49	13.53	0.07	44.6	44.7	44.4	44.6	0.2
	N125										
	N128	10.06	10.03	9.96	10.02	0.05	34.1	33.8	33.3	33.7	0.4
	N129										
	N130	9.32	9.56	9.37	9.42	0.13	35.7	34.3	34.0	34.7	0.9
	N131	13.18	13.34	13.25	13.26	0.08	47.8	48.2	47.2	47.7	0.5
	N132	9.73	9.48	9.60	9.60	0.13	34.7	34.8	34.7	34.7	0.1
	N134	8.41	8.11	7.92	8.15	0.25	29.9	30.4	30.0	30.1	0.3
	N141										
	N146										
	N154	9.18	9.34	9.18	9.23	0.09	33.8	33.3	33.1	33.4	0.3
	N155	9.00	9.21	9.09	9.10	0.11	33.5	33.7	33.8	33.7	0.2
	N158										
Community Results		Consensus Mean			9.38		Consensus Mean			34.2	
		Consensus Standard Deviation			1.53		Consensus Standard Deviation			3.9	
		Maximum			13.53		Maximum			47.7	
		Minimum			6.26		Minimum			27.0	
		N			16		N			16	

Table 20. Data summary table for ginsenoside Rb2 in botanical supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ginsenoside Rb2									
		Ginseng Rhizome (mg/g)					Ginseng Extract (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				9.30	0.20					
	N105	5.36	5.87	5.63	5.62	0.26	19.8	20.9	18.6	19.8	1.2
	N107	8.64	9.04	8.80	8.83	0.20	28.5	27.6	28.5	28.2	0.5
	N108	1.17	1.11	1.07	1.12	0.05	5.8	5.5	5.0	5.4	0.4
	N109						19.0	18.9	19.0	19.0	0.1
	N110	4.47	4.47	4.50	4.48	0.02	17.3	17.4	17.2	17.3	0.1
	N111										
	N115										
	N117	5.13	4.84	5.76	5.24	0.47	18.0	17.7	17.3	17.7	0.4
	N118	9.51	9.63	9.74	9.63	0.11	24.1	24.2	24.4	24.3	0.1
	N120										
	N121	6.53	6.65	6.39	6.52	0.13	22.9	22.1	22.3	22.4	0.4
	N122										
	N124	7.84	7.88	7.82	7.84	0.03	24.2	23.9	23.9	24.0	0.1
	N125										
	N128	6.47	6.53	6.46	6.49	0.04	21.5	21.4	21.2	21.4	0.2
	N129										
	N130	5.37	5.54	5.37	5.43	0.10	19.4	19.0	18.8	19.1	0.3
	N131	8.85	8.85	8.85	8.85	0.00	29.7	21.3	29.9	27.0	4.9
	N132	5.76	5.58	5.65	5.66	0.09	18.8	19.6	19.3	19.2	0.4
	N134	4.38	4.51	4.42	4.44	0.07	15.7	15.9	16.0	15.9	0.2
	N141										
	N146										
	N154	4.81	4.85	4.84	4.83	0.02	16.3	16.0	16.1	16.1	0.1
	N155	5.28	5.39	5.35	5.34	0.06	18.1	18.7	18.7	18.5	0.3
	N158										
Community Results		Consensus Mean			6.12		Consensus Mean			20.1	
		Consensus Standard Deviation			2.08		Consensus Standard Deviation			4.3	
		Maximum			9.63		Maximum			28.2	
		Minimum			1.12		Minimum			5.4	
		N			15		N			16	

Table 21. Data summary table for ginsenoside Rc in botanical supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ginsenoside Rc									
		Ginseng Rhizome (mg/g)					Ginseng Extract (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				9.03	0.18					
	N105	6.20	6.40	6.08	6.23	0.16	27.5	28.0	27.5	27.7	0.3
	N107	7.44	7.58	7.44	7.49	0.08	27.8	28.0	28.3	28.1	0.3
	N108	5.57	5.37	5.59	5.51	0.12	27.7	27.2	29.0	28.0	0.9
	N109						34.0	33.9	33.5	33.8	0.3
	N110	5.66	5.61	5.70	5.66	0.05	26.1	26.0	25.9	26.0	0.1
	N111										
	N115										
	N117	7.86	6.80	7.07	7.24	0.55	24.7	23.2	23.9	23.9	0.8
	N118	5.44	5.52	5.37	5.44	0.07	19.7	19.4	19.3	19.5	0.2
	N120										
	N121	7.73	7.69	7.60	7.67	0.07	31.2	30.3	30.5	30.7	0.5
	N122										
	N124	9.94	9.95	9.87	9.92	0.04	36.9	36.7	36.3	36.6	0.3
	N125										
	N128	7.10	7.10	7.09	7.09	0.01	28.2	28.0	27.9	28.1	0.2
	N129										
	N130	5.60	5.74	5.56	5.63	0.09	23.9	23.4	23.3	23.5	0.4
	N131	6.12	6.12	6.16	6.13	0.02	24.3	25.0	24.1	24.5	0.5
	N132	6.92	6.65	6.69	6.75	0.15	29.3	29.7	28.5	29.2	0.6
	N134	5.38	5.49	5.92	5.60	0.28	23.1	23.7	22.8	23.2	0.4
	N141										
	N146										
	N154	9.68	9.75	9.66	9.70	0.05	30.2	29.8	29.8	29.9	0.2
	N155	5.00	5.08	5.06	5.05	0.04	18.4	18.8	18.7	18.6	0.2
	N158										
Community Results		Consensus Mean			6.56		Consensus Mean			26.8	
		Consensus Standard Deviation			1.28		Consensus Standard Deviation			5.0	
		Maximum			9.92		Maximum			36.6	
		Minimum			5.05		Minimum			18.6	
		N			15		N			16	

Table 22. Data summary table for ginsenoside Rd in botanical supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ginsenoside Rd									
		Ginseng Rhizome (mg/g)					Ginseng Extract (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				5.16	0.06					
	N105	2.58	2.64	2.91	2.71	0.18	13.9	14.2	13.7	13.9	0.3
	N107	3.75	3.75	3.65	3.72	0.06	16.8	16.7	16.7	16.7	0.0
	N108	5.86	5.60	5.74	5.74	0.13	27.7	27.6	25.5	26.9	1.2
	N109						18.9	18.7	18.8	18.8	0.1
	N110	2.26	2.22	2.25	2.24	0.02	12.7	12.8	12.8	12.8	0.1
	N111										
	N115										
	N117	2.38	2.04	2.53	2.32	0.25	12.1	13.0	11.5	12.2	0.8
	N118	3.15	3.37	3.27	3.26	0.11	14.3	15.1	14.8	14.8	0.4
	N120										
	N121	2.83	2.88	2.87	2.86	0.03	14.5	13.9	13.8	14.1	0.4
	N122										
	N124	4.54	4.57	4.55	4.55	0.01	18.9	18.6	19.0	18.8	0.2
	N125										
	N128	4.25	4.21	4.15	4.20	0.05	17.5	17.5	17.2	17.4	0.2
	N129										
	N130	2.59	2.62	2.53	2.58	0.05	11.2	11.0	11.0	11.1	0.2
	N131	3.94	3.96	3.84	3.91	0.06	17.4	17.6	17.2	17.4	0.2
	N132	2.78	2.71	2.72	2.74	0.04	13.9	13.9	13.9	13.9	0.0
	N134	2.71	2.74	3.53	2.99	0.46	12.8	12.7	12.9	12.8	0.1
	N141										
	N146										
	N154	2.40	2.45	2.43	2.43	0.03	12.0	11.9	12.3	12.1	0.2
	N155	2.64	2.67	2.68	2.66	0.02	12.4	12.6	12.5	12.5	0.1
	N158										
Community Results		Consensus Mean			3.18		Consensus Mean			14.9	
		Consensus Standard Deviation			0.91		Consensus Standard Deviation			3.2	
		Maximum			5.74		Maximum			26.9	
		Minimum			2.24		Minimum			11.1	
		N			15		N			16	

Table 23. Data summary table for ginsenoside Re in botanical supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ginsenoside Re									
		Ginseng Rhizome (mg/g)					Ginseng Extract (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				6.61	0.14					
	N105	5.35	5.56	5.34	5.42	0.12	17.3	17.6	17.6	17.5	0.2
	N107	5.05	5.03	5.00	5.03	0.02	17.1	16.8	17.1	17.0	0.2
	N108	1.38	1.20	0.97	1.19	0.20	2.9	2.5	2.3	2.6	0.3
	N109						17.5	17.3	17.5	17.4	0.1
	N110	4.42	4.41	4.42	4.42	0.01	17.2	17.2	16.9	17.1	0.2
	N111										
	N115										
	N117	5.38	5.62	5.68	5.56	0.16	18.6	17.2	17.9	17.9	0.7
	N118	5.26	5.29	5.32	5.29	0.03	17.5	17.9	17.1	17.5	0.4
	N120										
	N121	5.11	5.15	5.19	5.15	0.04	17.0	16.9	16.9	16.9	0.1
	N122										
	N124	5.84	5.92	5.91	5.89	0.04	19.9	20.0	19.8	19.9	0.1
	N125										
	N128	4.66	4.67	4.67	4.67	0.00	15.1	15.0	14.7	14.9	0.2
	N129										
	N130	4.63	4.74	4.59	4.65	0.08	15.7	15.2	15.1	15.3	0.3
	N131	6.15	6.17	6.22	6.18	0.04	20.7	20.9	20.4	20.6	0.3
	N132	4.88	5.01	5.11	5.00	0.12	19.8	20.0	19.9	19.9	0.1
	N134	5.88	5.16	4.61	5.22	0.64	14.5	14.6	13.8	14.3	0.4
	N141										
	N146										
	N154	4.64	4.74	4.66	4.68	0.05	15.8	15.8	15.4	15.7	0.2
	N155	4.57	4.65	5.06	4.76	0.26	15.4	15.4	17.1	16.0	1.0
	N158										
Community Results		Consensus Mean			5.06		Consensus Mean			17.0	
		Consensus Standard Deviation			0.58		Consensus Standard Deviation			2.2	
		Maximum			6.18		Maximum			20.6	
		Minimum			1.19		Minimum			2.6	
		N			15		N			16	

Table 24. Data summary table for ginsenoside Rf in botanical supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ginsenoside Rf									
		Ginseng Rhizome (mg/g)					Ginseng Extract (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				1.10	0.12					
	N105	0.89	0.93	0.93	0.92	0.03	2.62	2.59	2.65	2.62	0.03
	N107	0.80	0.85	0.80	0.82	0.03	2.62	2.62	2.58	2.61	0.02
	N108	1.06	1.07	0.83	0.99	0.14	3.43	3.45	3.52	3.47	0.04
	N109										
	N110	1.42	1.35	1.25	1.34	0.09	4.39	4.80	4.68	4.62	0.21
	N111										
	N115										
	N117	1.64	1.41	1.42	1.49	0.13	3.43	3.60	2.83	3.29	0.40
	N118	1.75	1.61	1.58	1.64	0.09	3.72	3.14	4.15	3.67	0.51
	N120										
	N121										
	N122										
	N124	1.28	1.25	1.24	1.26	0.02	3.63	3.41	3.35	3.46	0.15
	N125										
	N128	1.19	1.22	1.21	1.21	0.02	3.50	3.51	3.43	3.48	0.04
	N129										
	N130	0.95	0.98	0.76	0.90	0.12	1.99	1.92	2.06	1.99	0.07
	N131										
	N132	0.78	0.75	0.74	0.76	0.02	2.16	2.51	2.57	2.41	0.22
	N134	0.80	0.77	0.72	0.77	0.04	2.16	2.03	2.05	2.08	0.07
	N141										
	N146										
	N154	0.82	0.84	0.82	0.83	0.01	2.33	2.38	2.31	2.34	0.04
	N155	0.86	0.87	0.87	0.87	0.01	2.49	2.41	2.45	2.45	0.04
	N158										
Community Results		Consensus Mean			1.05		Consensus Mean			2.92	
		Consensus Standard Deviation			0.32		Consensus Standard Deviation			0.77	
		Maximum			1.64		Maximum			4.62	
		Minimum			0.76		Minimum			1.99	
		N			13		N			13	

Table 25. Data summary table for ginsenoside Rg1 in botanical supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ginsenoside Rg1									
		Ginseng Rhizome (mg/g)					Ginseng Extract (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				3.94	0.08					
	N105	3.47	3.60	3.50	3.52	0.07	6.88	7.22	1.31	5.14	3.32
	N107	2.92	2.90	2.86	2.89	0.03	6.30	6.23	6.23	6.25	0.04
	N108	3.74	4.18	4.33	4.08	0.31	13.84	14.04	15.99	14.62	1.19
	N109	2.73	2.68	2.79	2.73	0.06	6.27	6.22	6.25	6.25	0.03
	N110	2.51	2.51	2.55	2.52	0.02	6.46	6.45	6.70	6.54	0.14
	N111										
	N115										
	N117	2.74	2.52	3.29	2.85	0.40	5.61	5.98	6.36	5.98	0.38
	N118	3.01	3.34	3.19	3.18	0.16	7.13	7.00	7.25	7.13	0.13
	N120										
	N121	2.68	2.71	2.63	2.67	0.04	5.62	5.46	5.64	5.57	0.10
	N122										
	N124	3.66	3.72	3.71	3.69	0.03	7.85	7.85	7.85	7.85	0.00
	N125										
	N128	3.07	3.07	3.09	3.08	0.01	6.41	6.37	6.27	6.35	0.07
	N129										
	N130	2.66	2.77	2.63	2.69	0.07	5.33	5.33	5.20	5.29	0.08
	N131	3.70	3.70	3.74	3.71	0.02	6.63	6.68	6.54	6.62	0.07
	N132	2.77	2.76	2.81	2.78	0.03	7.14	7.14	7.13	7.14	0.01
	N134	4.25	4.26	4.05	4.19	0.12	4.62	4.57	5.15	4.78	0.32
	N141										
	N146										
	N154	2.57	2.59	2.57	2.58	0.01	5.44	5.38	5.20	5.34	0.12
	N155	3.01	3.02	3.01	3.01	0.01	6.30	6.27	6.26	6.28	0.02
	N158										
Community Results		Consensus Mean			3.12		Consensus Mean			6.27	
		Consensus Standard Deviation			0.56		Consensus Standard Deviation			1.03	
		Maximum			4.19		Maximum			14.62	
		Minimum			2.52		Minimum			4.78	
		N			16		N			16	

Table 26. Data summary table for ginsenoside Rg2 in botanical supplements. Data highlighted in red have been flagged as potential outliers (e.g., difference from reference value, Grubb and/or Cochran) by the NIST software package.

		Ginsenoside Rg2									
		Ginseng Rhizome (mg/g)					Ginseng Extract (mg/g)				
	Lab	A	B	C	Avg	SD	A	B	C	Avg	SD
Individual Results	NIST				0.61	0.03					
	N105	3.47	3.60	3.50	3.52	0.07	6.88	7.22	7.31	7.14	0.23
	N107	0.68	0.63	0.60	0.63	0.04	2.54	2.55	2.53	2.54	0.01
	N108	2.54	2.39	2.44	2.46	0.08	16.30	15.88	14.97	15.72	0.68
	N109										
	N110	0.82	0.74	0.74	0.77	0.05	3.91	3.90	3.87	3.89	0.02
	N111										
	N115										
	N118	1.14	1.23	1.14	1.17	0.05	5.83	6.00	6.05	5.96	0.11
	N120										
	N121										
	N122										
	N124										
	N125										
	N128	< 1.000	< 1.000	< 1.000	< 1.000		< 1.000	< 1.000	< 1.000	< 1.000	
	N129										
	N130										
	N131										
	N132										
	N134	0.43	0.35	0.35	0.38	0.04	2.40	2.54	2.59	2.51	0.10
	N141										
	N146										
	N154	0.54	0.54	0.54	0.54	0.00	2.50	2.47	2.37	2.45	0.07
	N155	0.61	0.48	0.49	0.53	0.07	2.23	2.28	2.29	2.27	0.03
	N158										
Community Results		Consensus Mean			1.15		Consensus Mean			4.43	
		Consensus Standard Deviation			1.04		Consensus Standard Deviation			2.85	
		Maximum			3.52		Maximum			15.72	
		Minimum			0.38		Minimum			2.27	
		N			8		N			8	

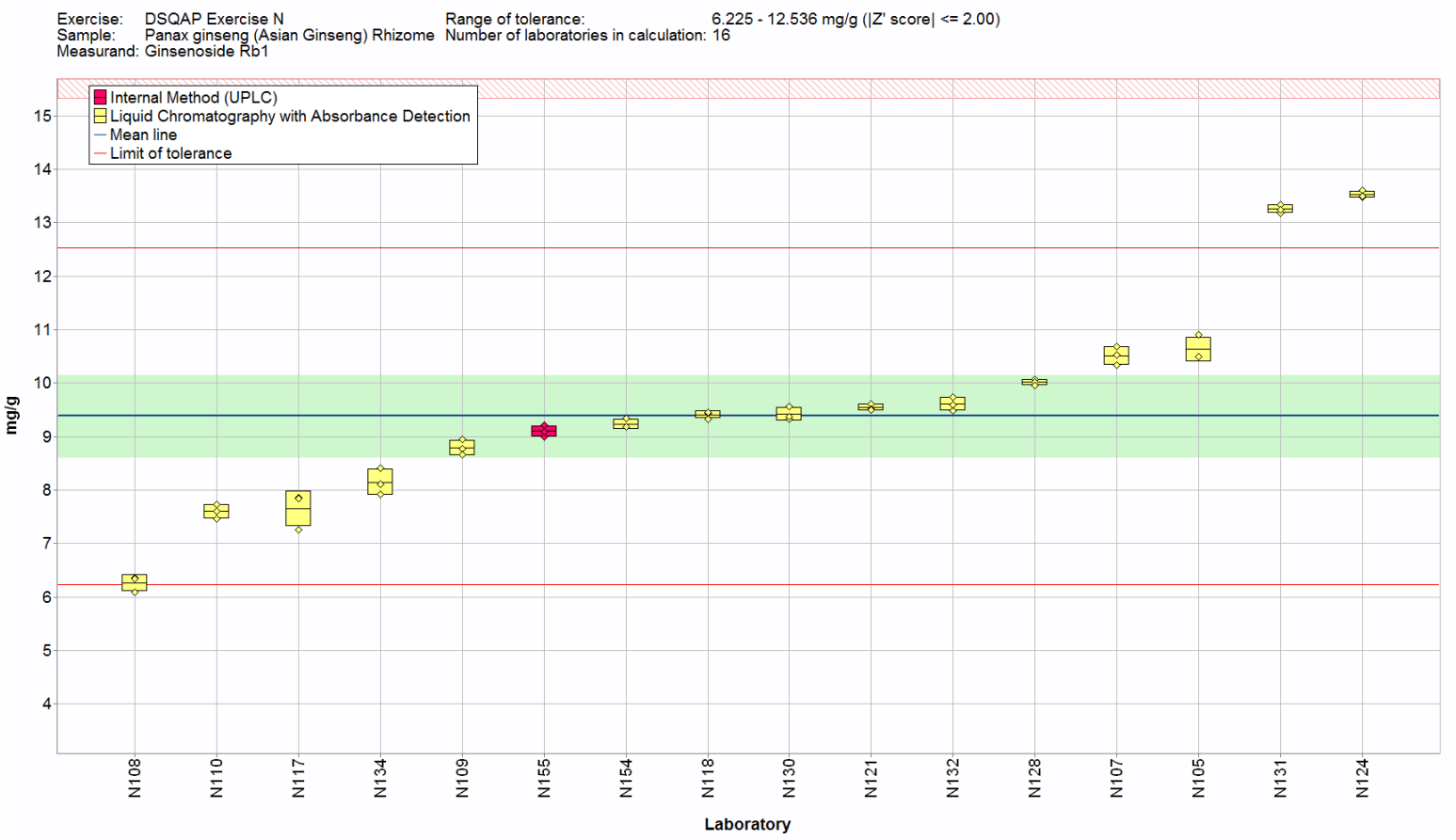

Figure 41. Ginsenoside Rb1 in candidate SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean, and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region (mostly off-chart) represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its standard deviation and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

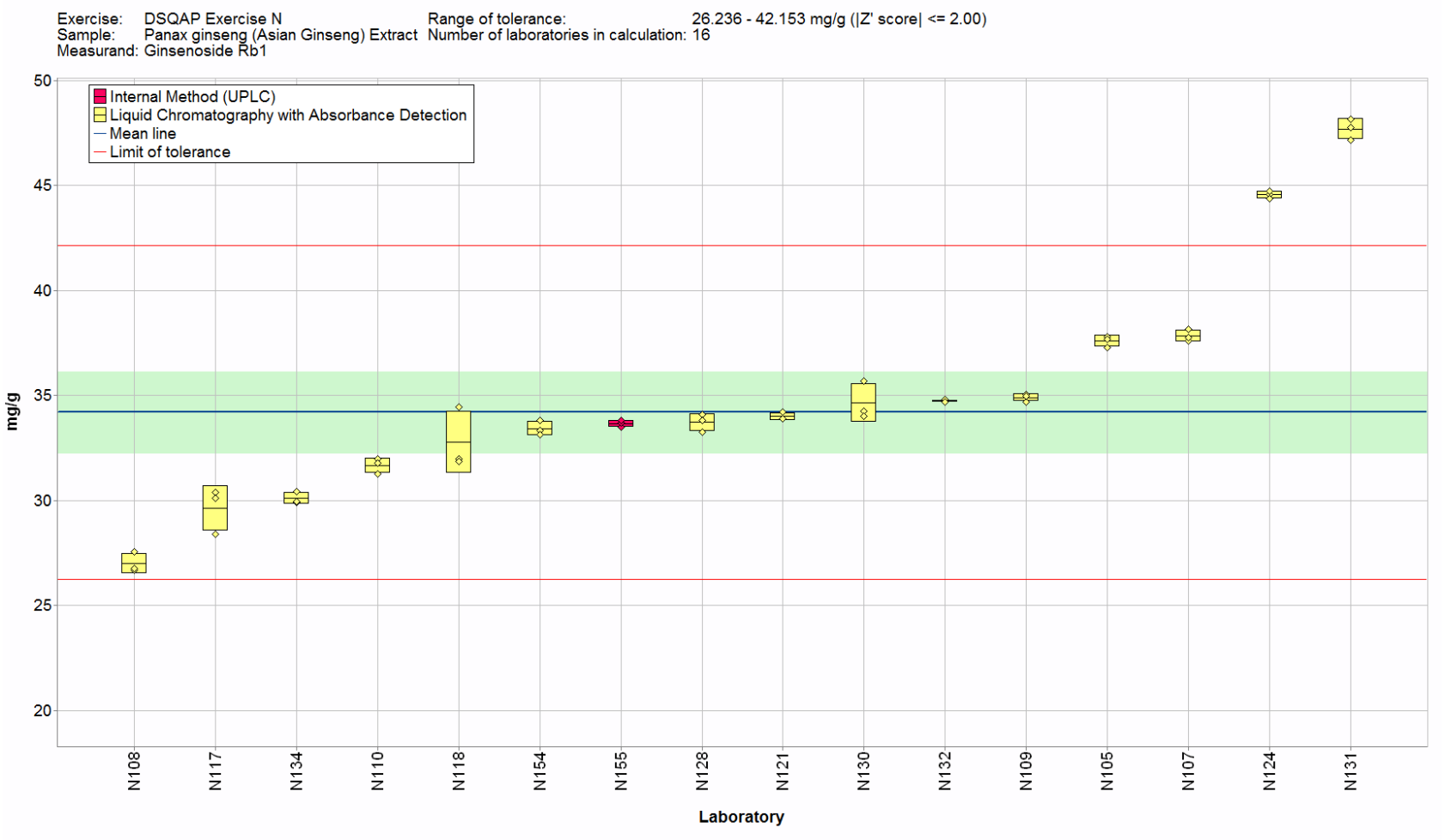

Figure 42. Ginsenoside Rb1 in candidate SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material.

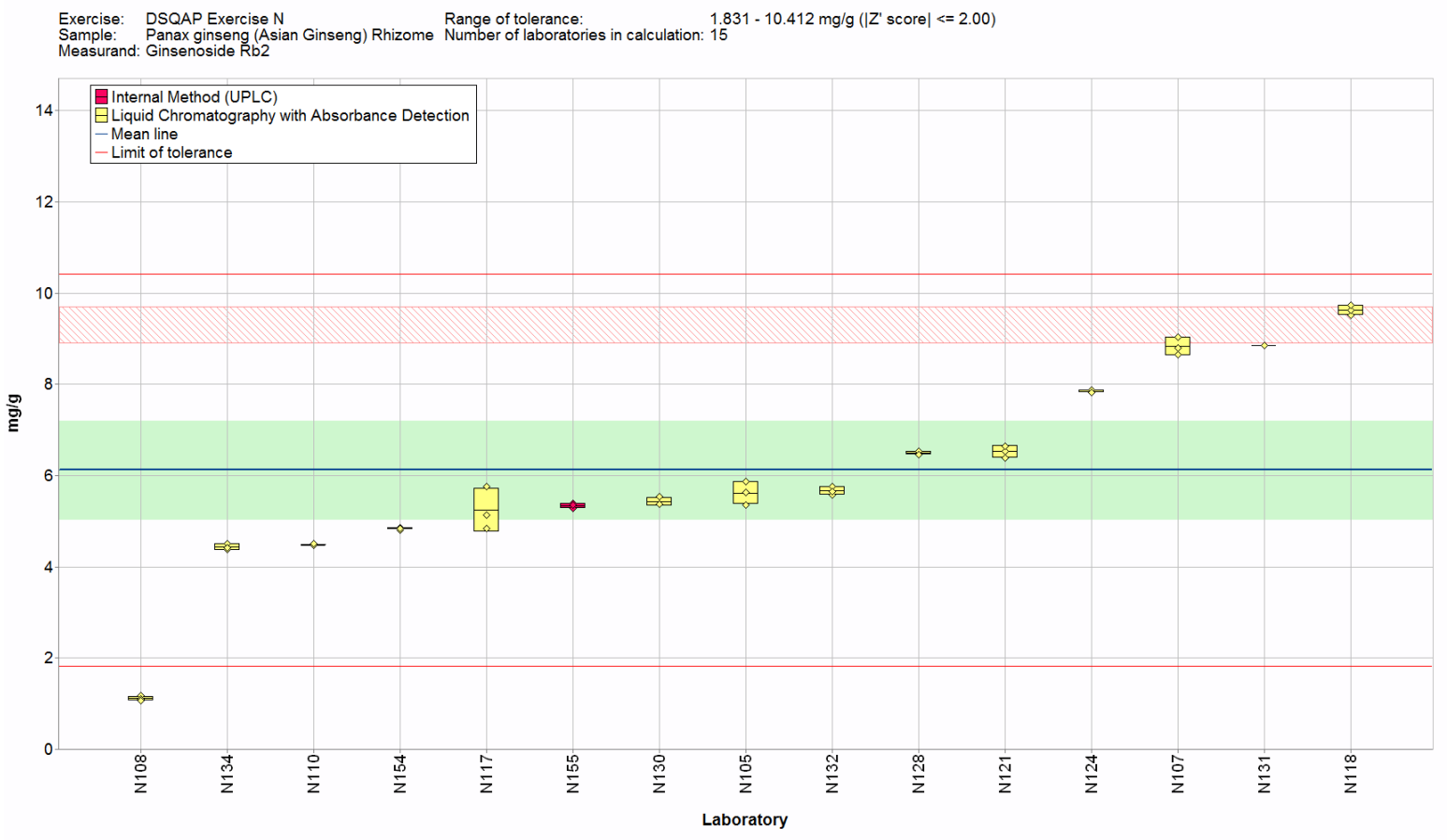

Figure 43. Ginsenoside Rb2 in candidate SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean, and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its standard deviation and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

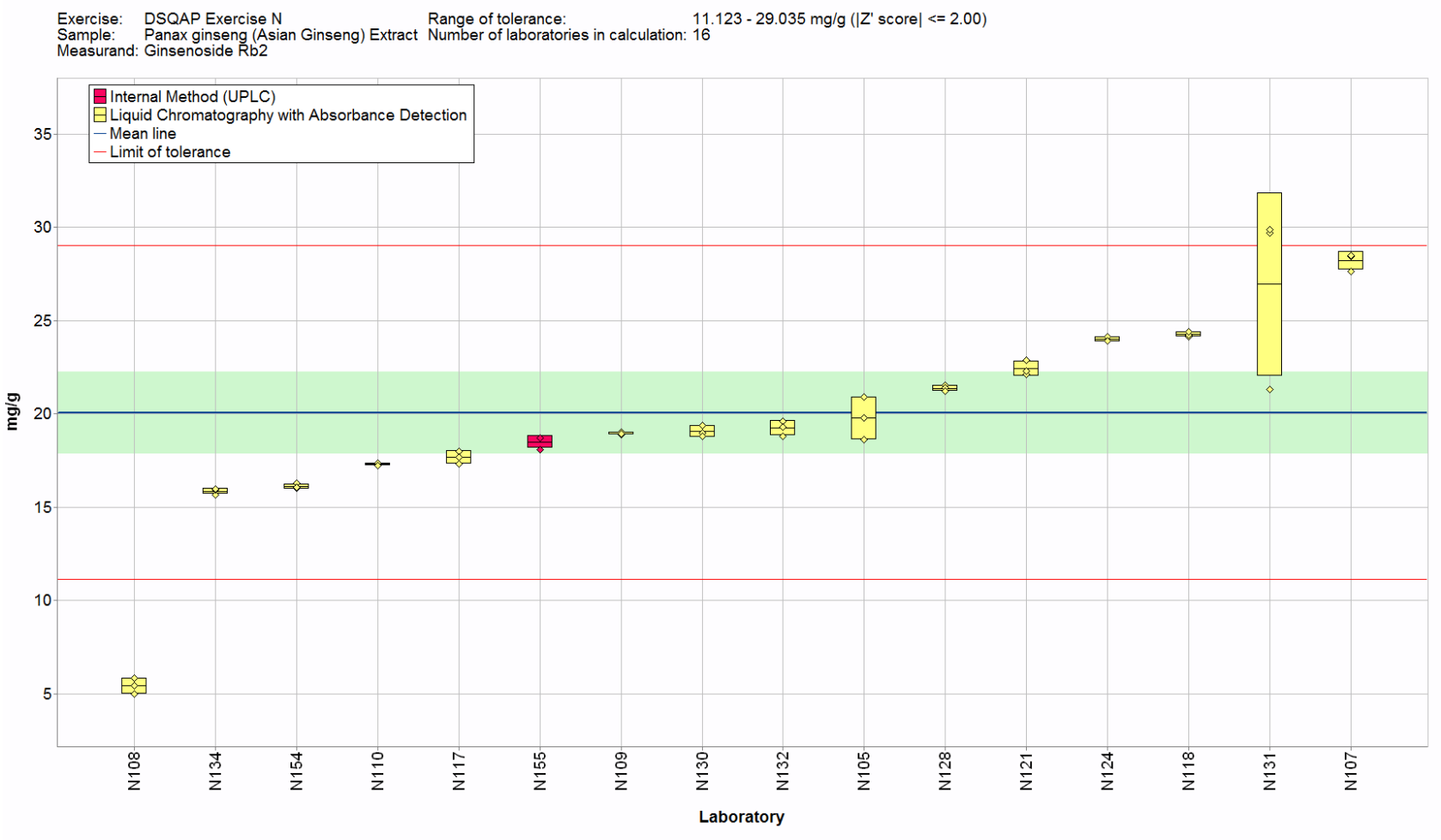

Figure 44. Ginsenoside Rb2 in candidate SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material.

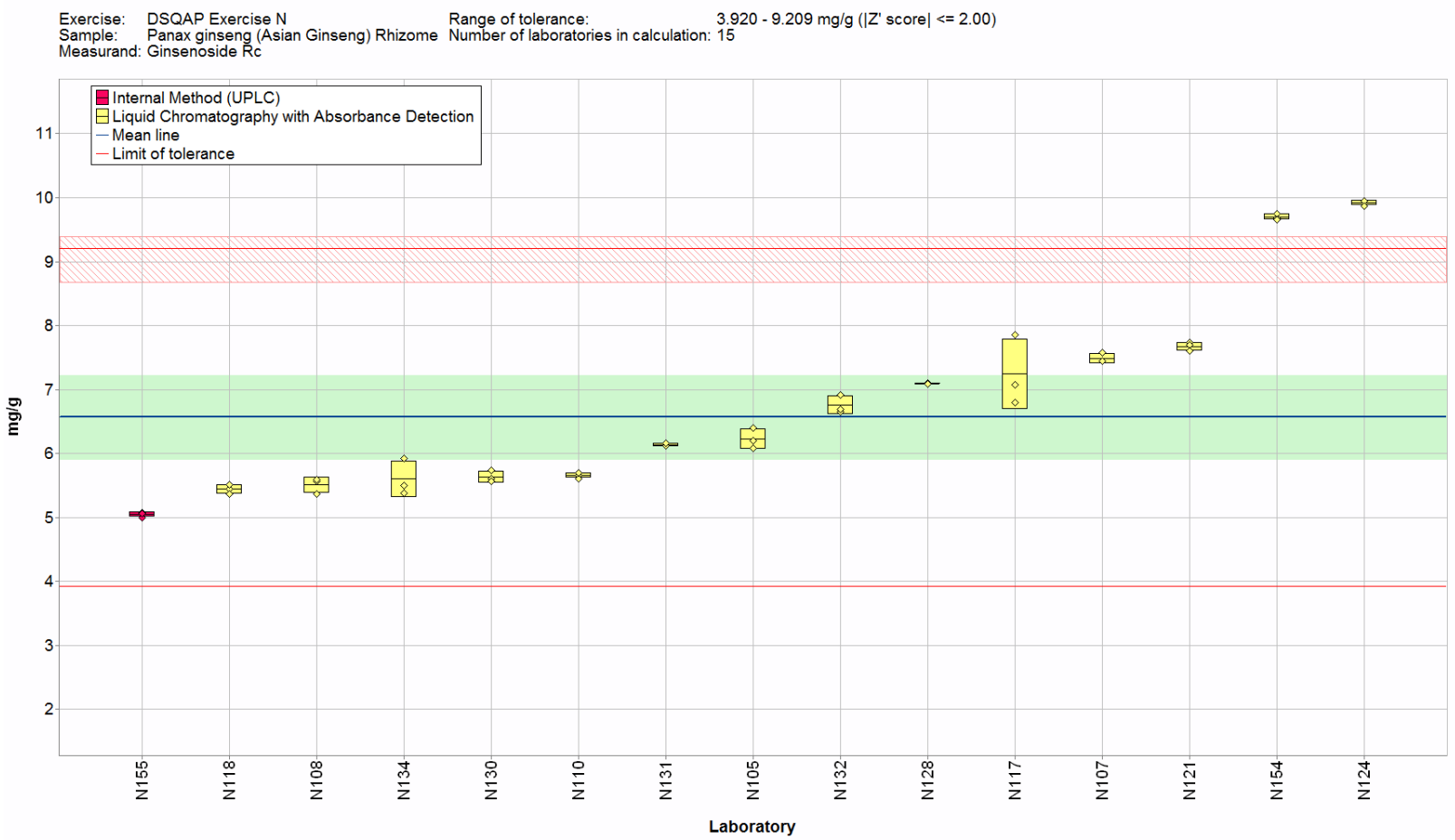

Figure 45. Ginsenoside Rc in candidate SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its standard deviation and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

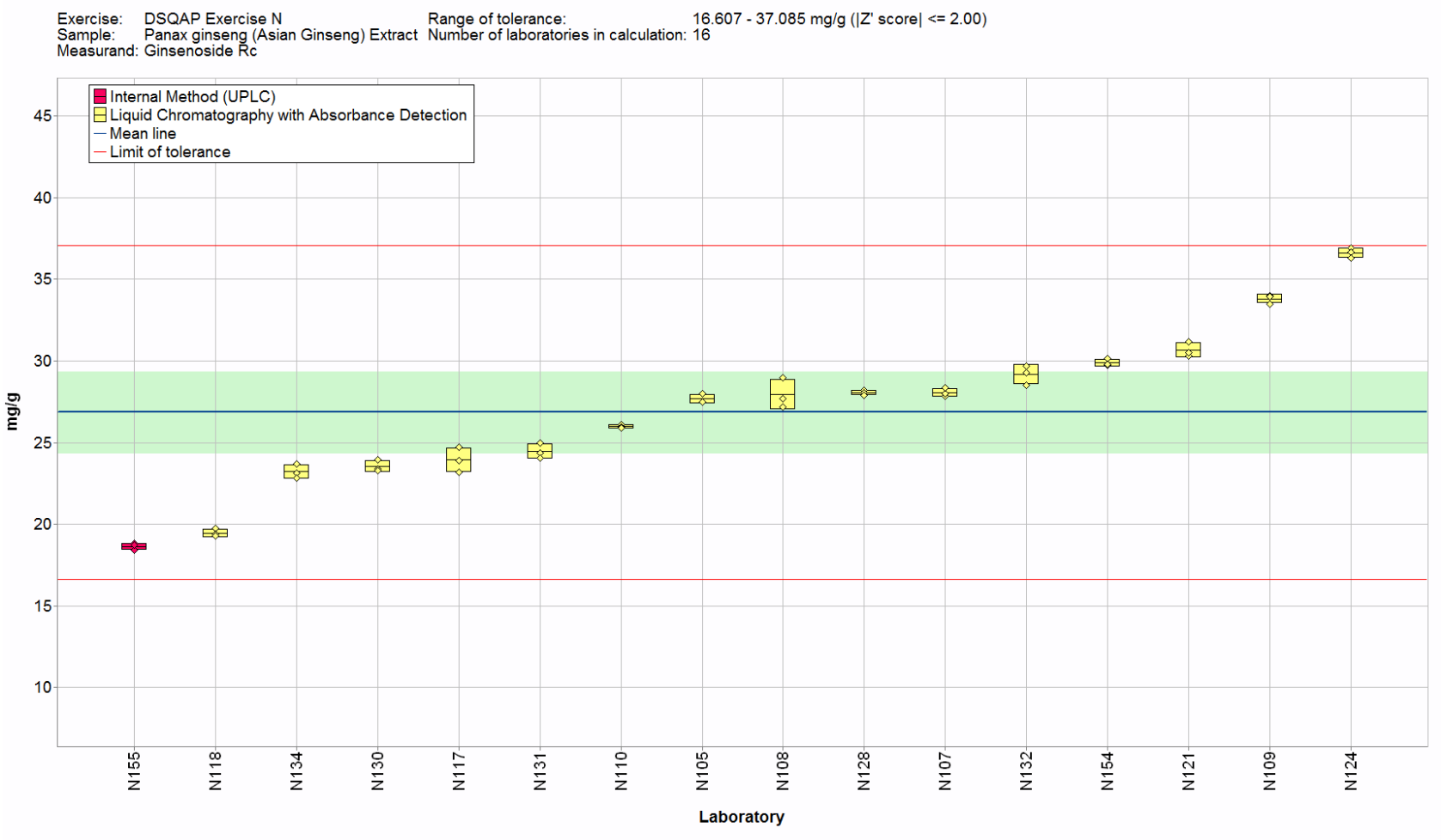

Figure 46. Ginsenoside Rc in candidate SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material.

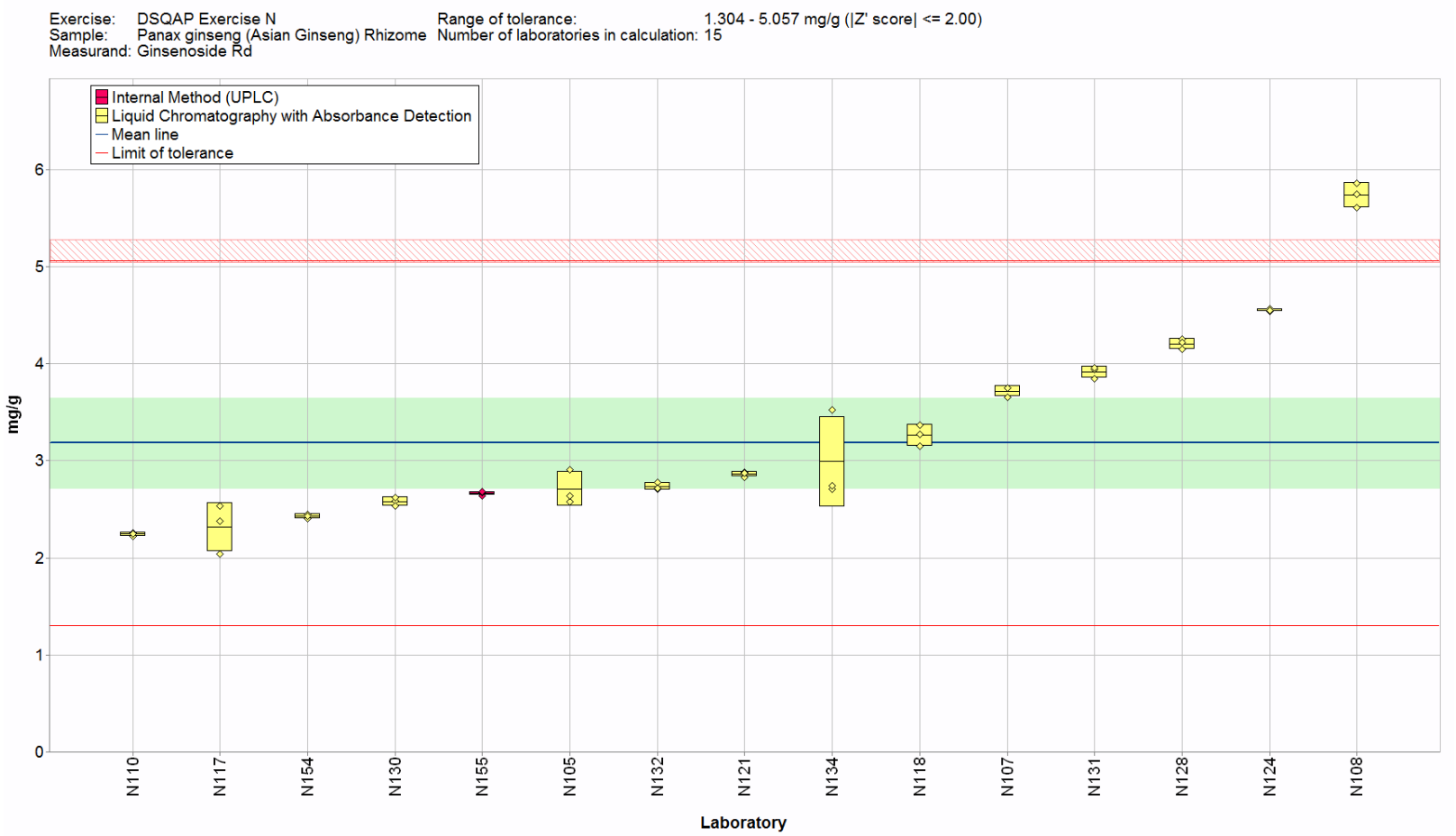

Figure 47. Ginsenoside Rd in candidate SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its standard deviation and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

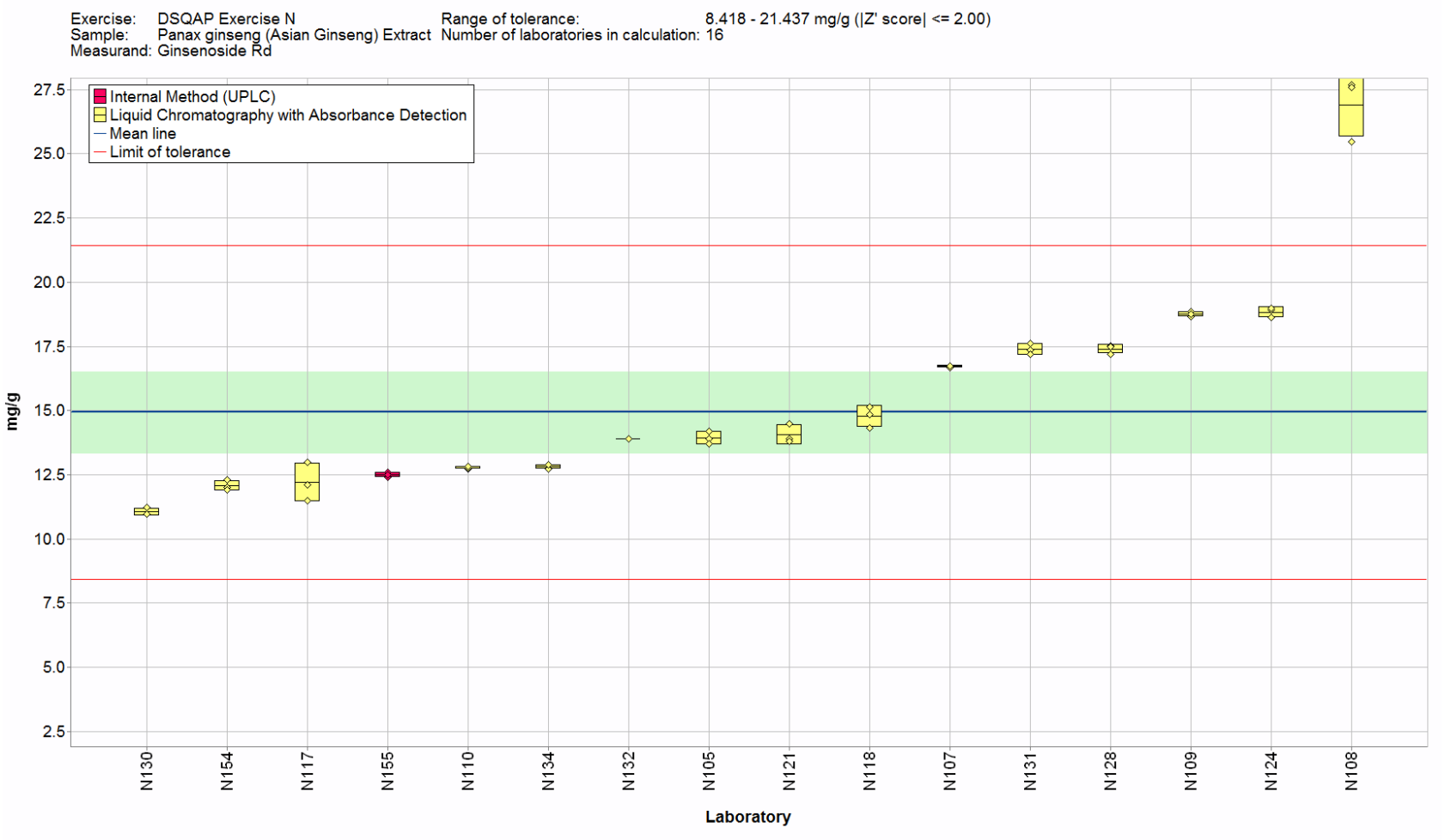

Figure 48. Ginsenoside Rd in candidate SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material.

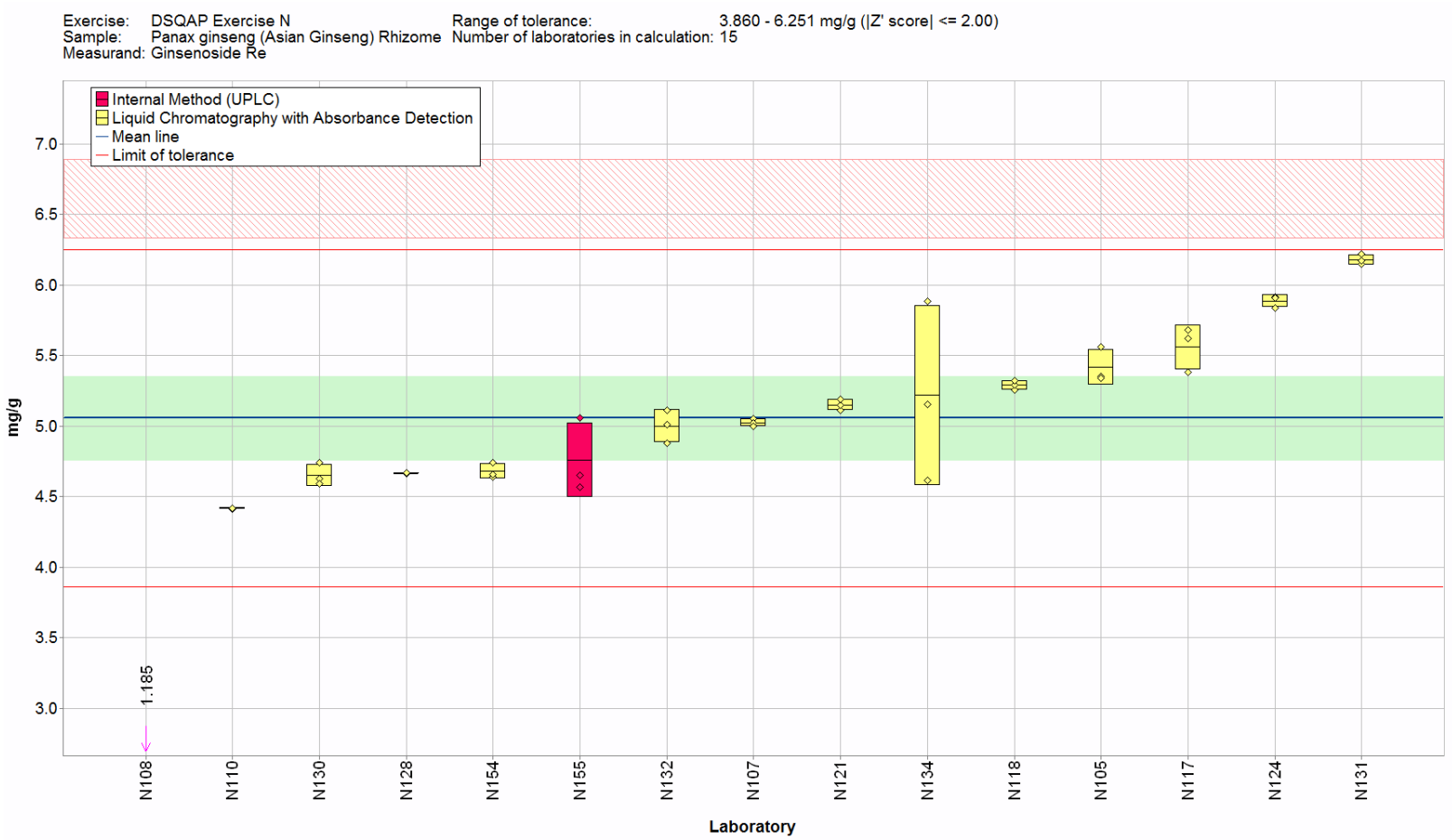

Figure 49. Ginsenoside Re in candidate SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its standard deviation and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

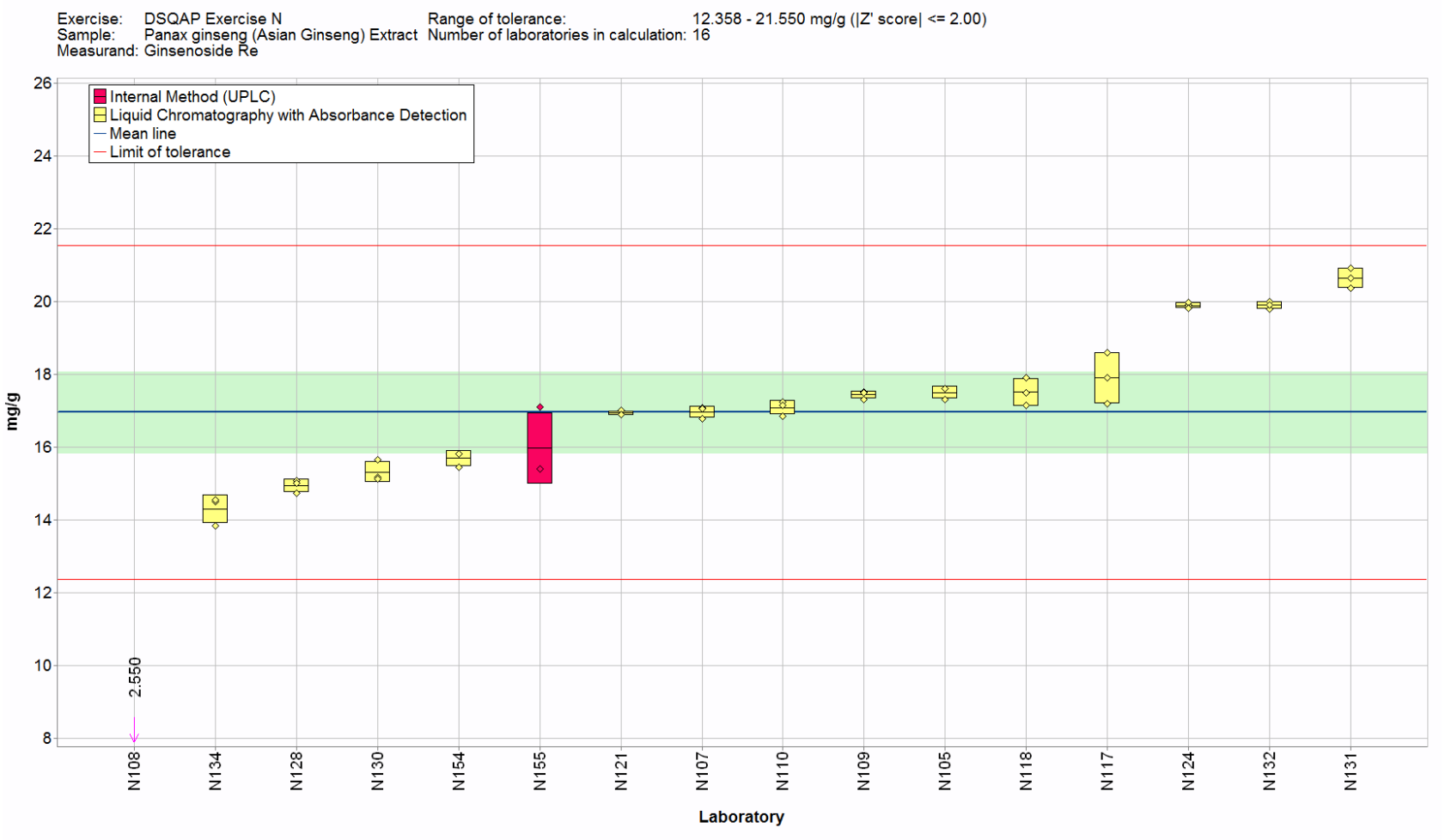

Figure 50. Ginsenoside Re in candidate SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material.

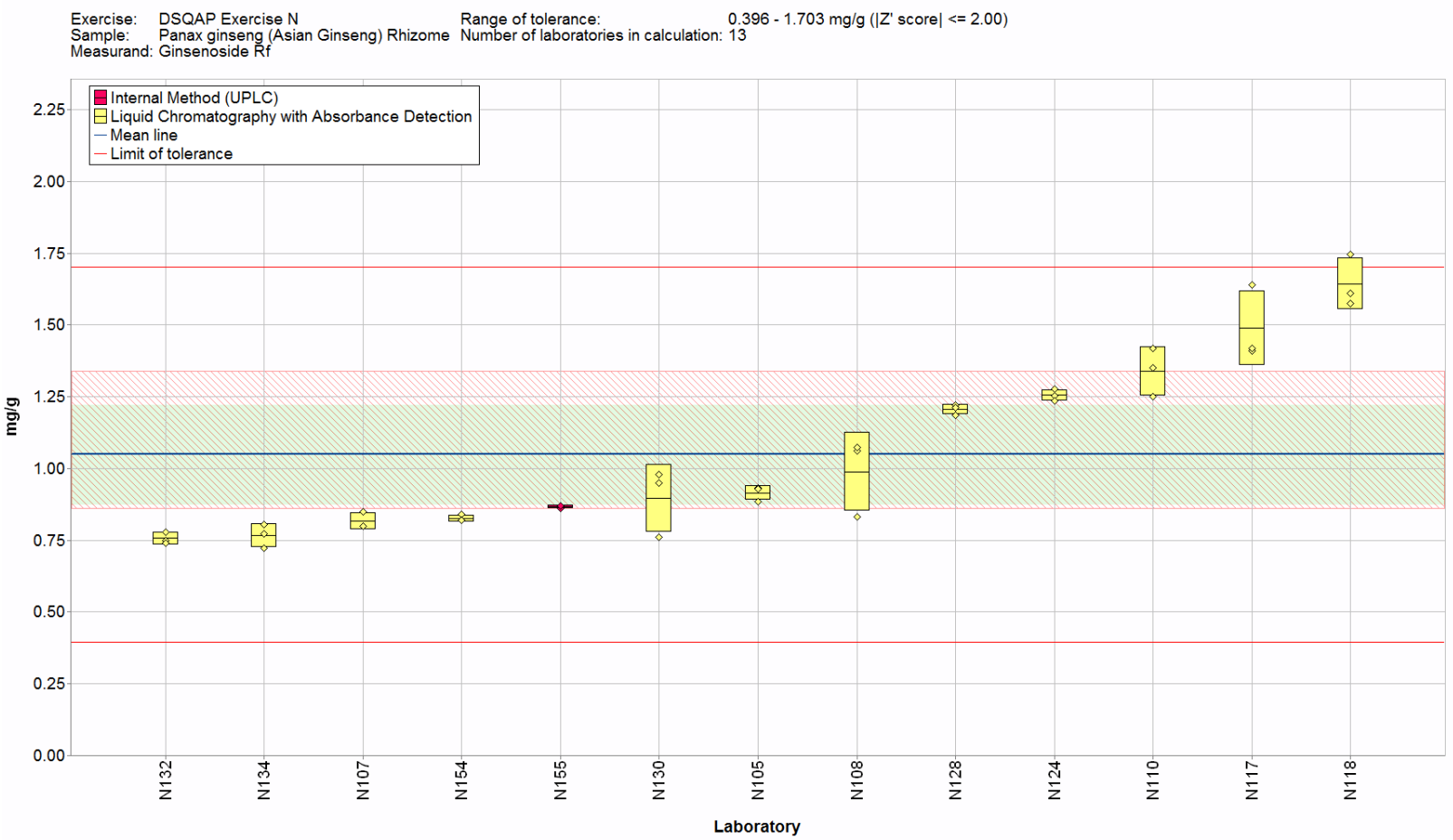

Figure 51. Ginsenoside Rf in candidate SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its standard deviation and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

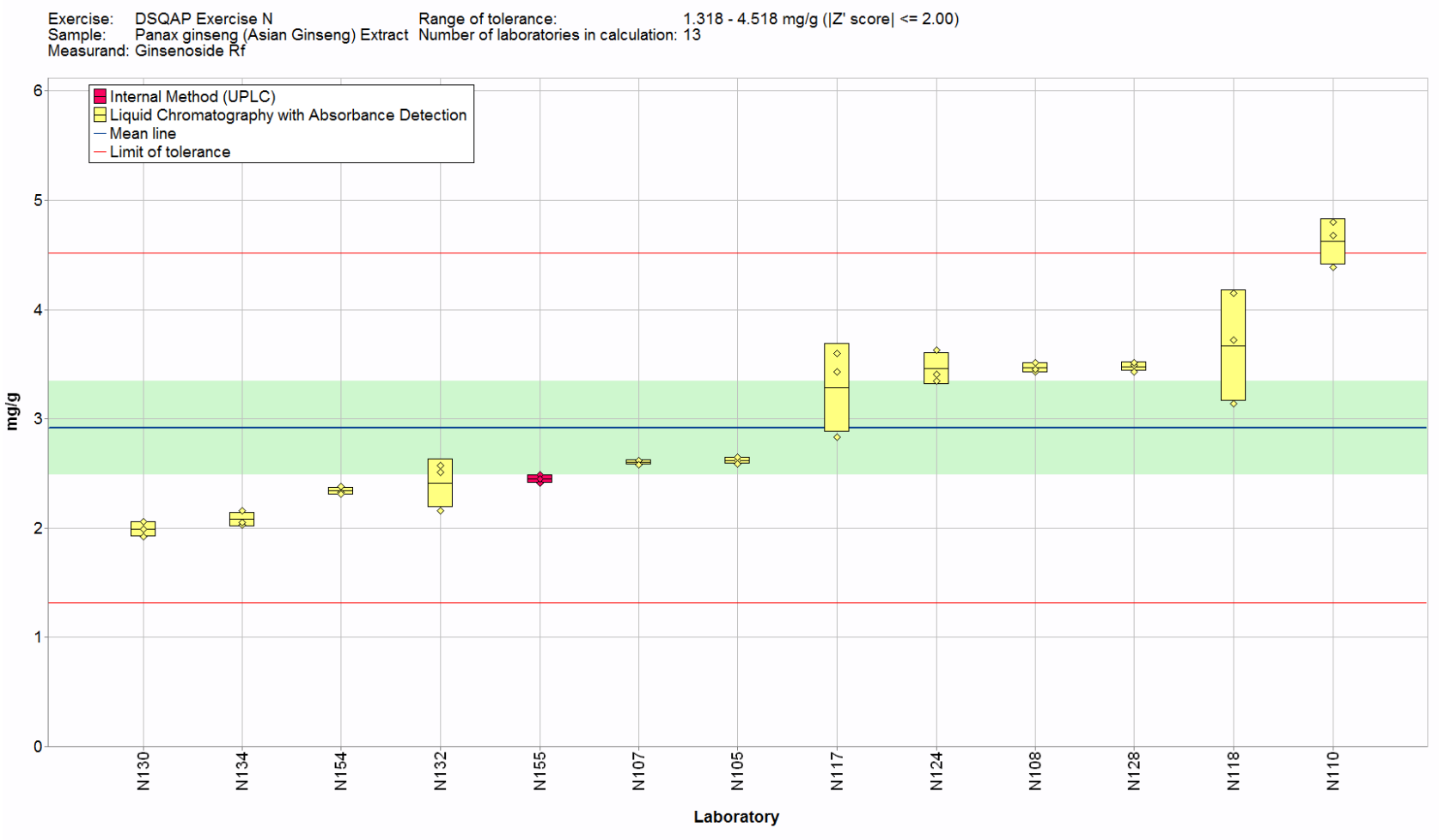

Figure 52. Ginsenoside Rf in candidate SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material.

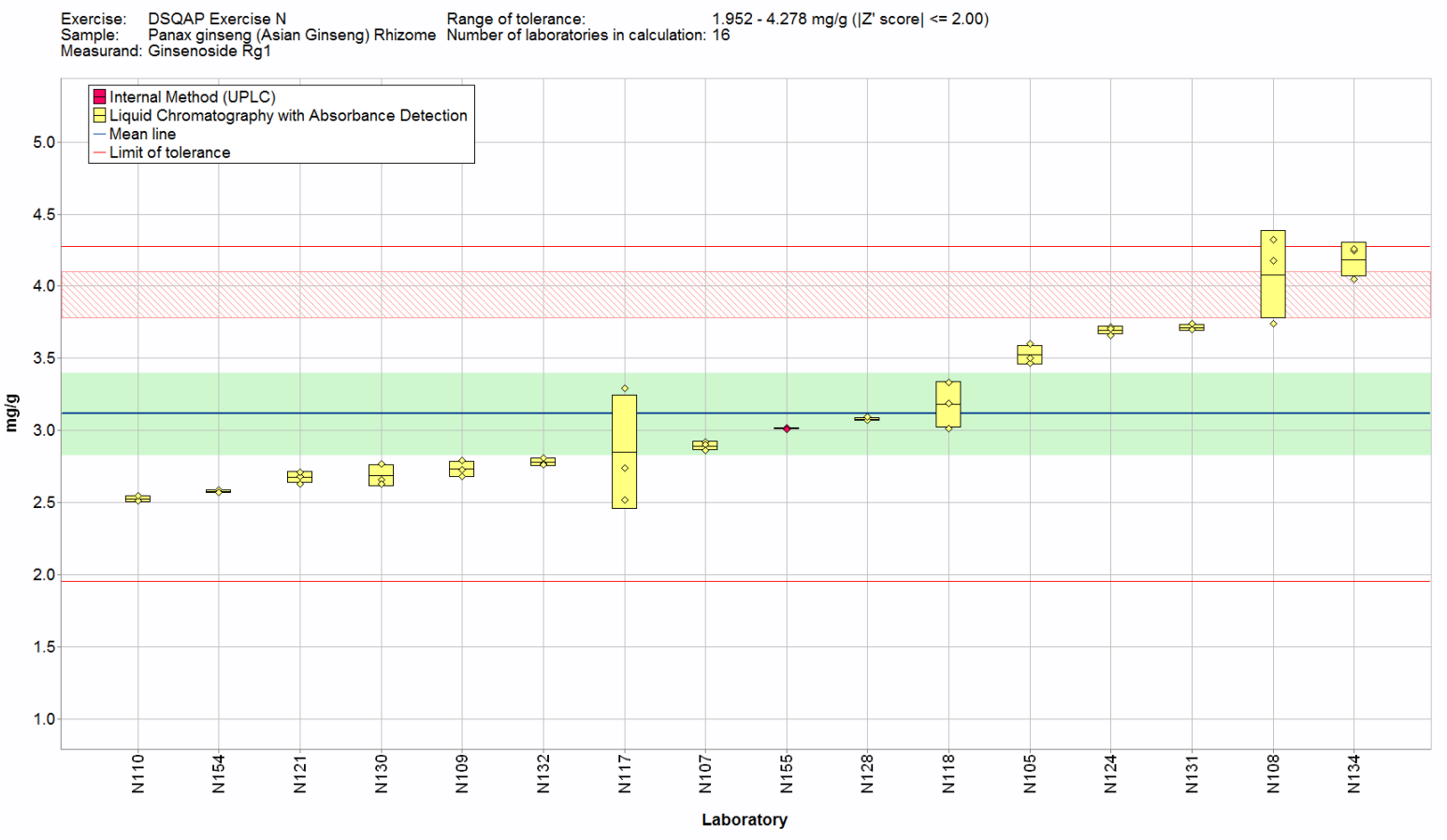

Figure 53. Ginsenoside Rg1 in candidate SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its standard deviation and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

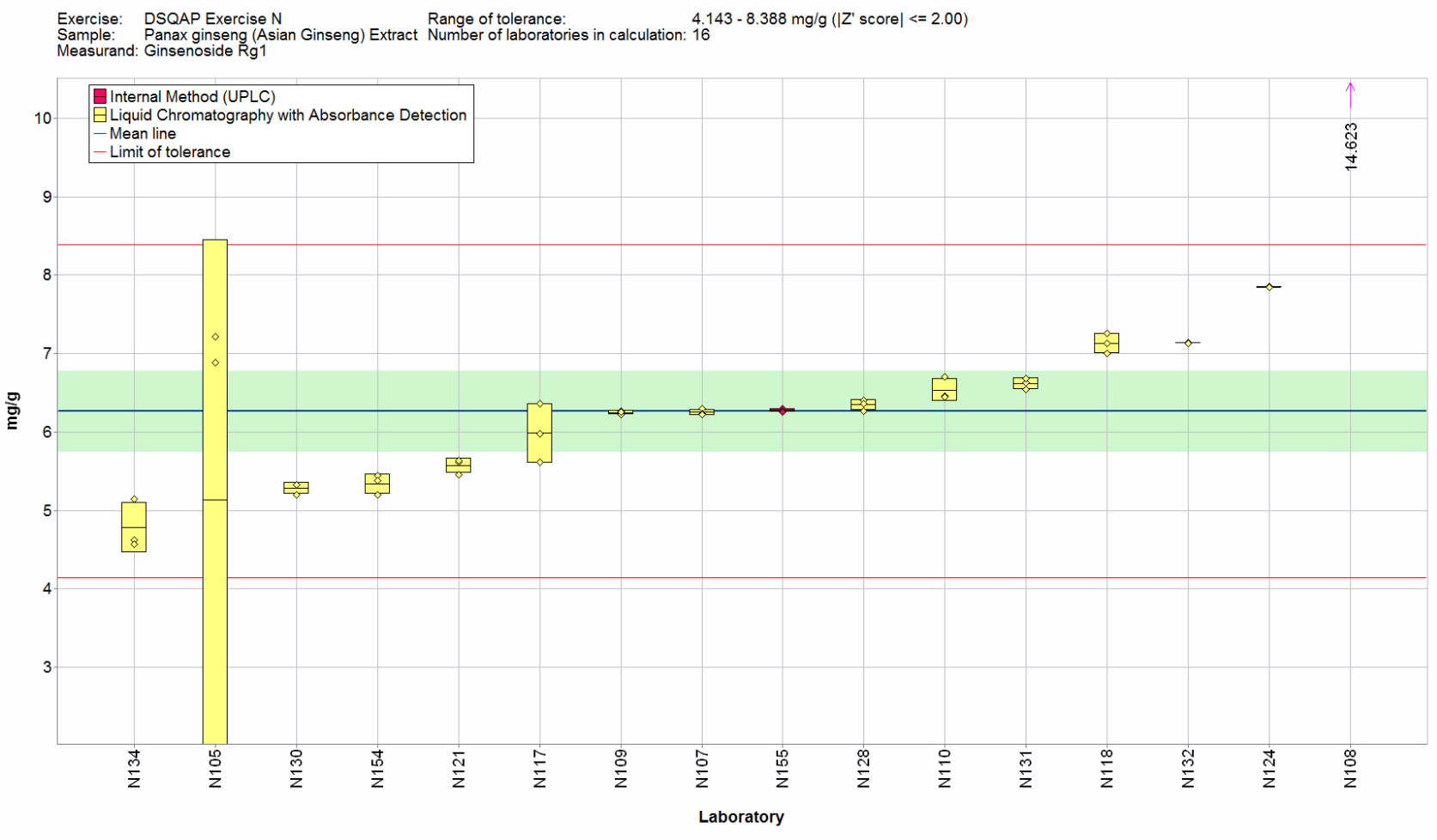

Figure 54. Ginsenoside Rg1 in SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red lines represent the consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$. A NIST value has not been determined in this material.

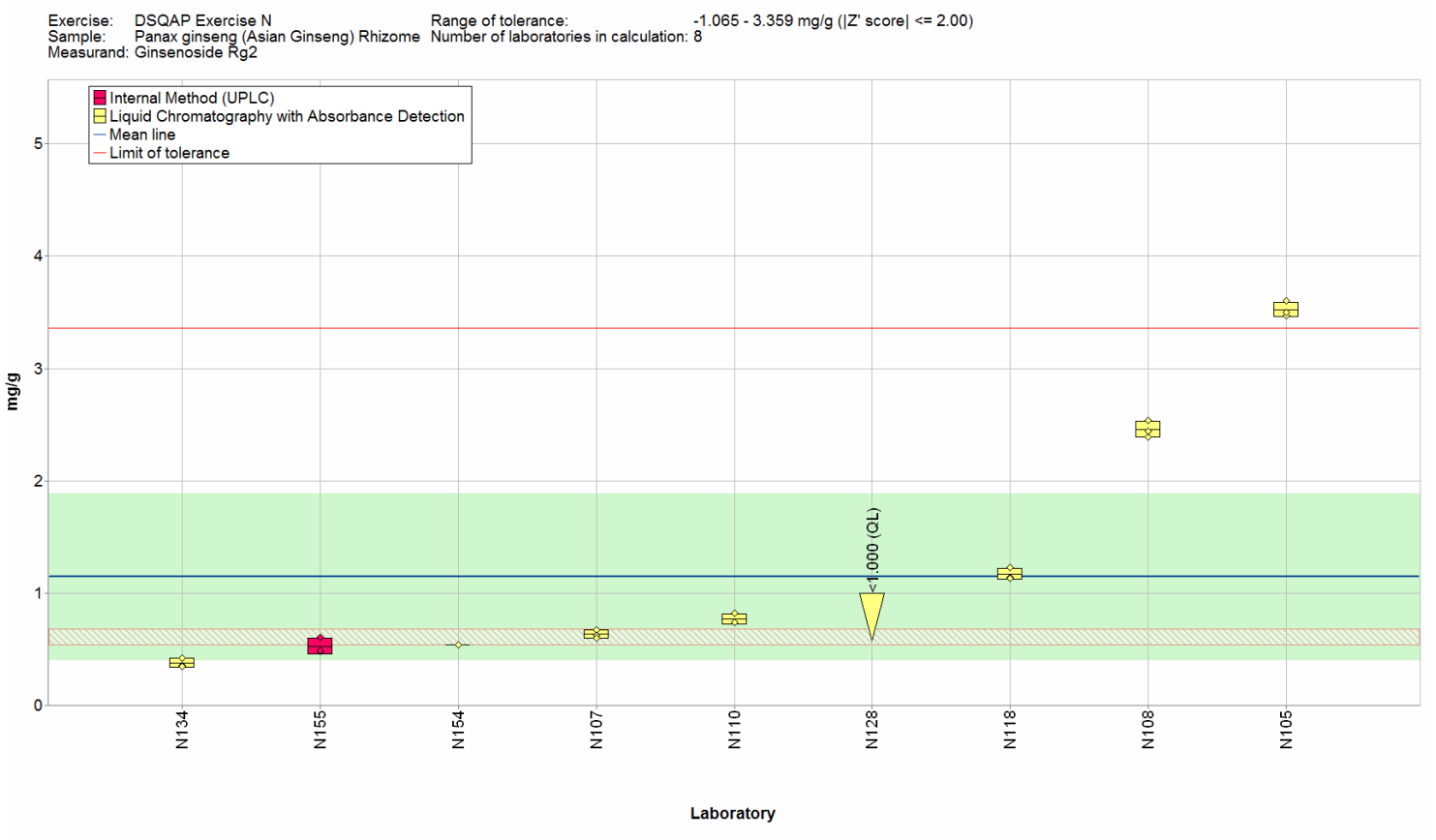

Figure 55. Ginsenoside Rg2 in candidate SRM 3384 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Rhizome (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set at zero. The red shaded region represents the NIST range of tolerance, which encompasses the NIST-determined value bounded by twice its standard deviation and represents the range that results in an acceptable Z_{NIST} score, $|Z_{\mathrm{NIST}}| \leq 2$.

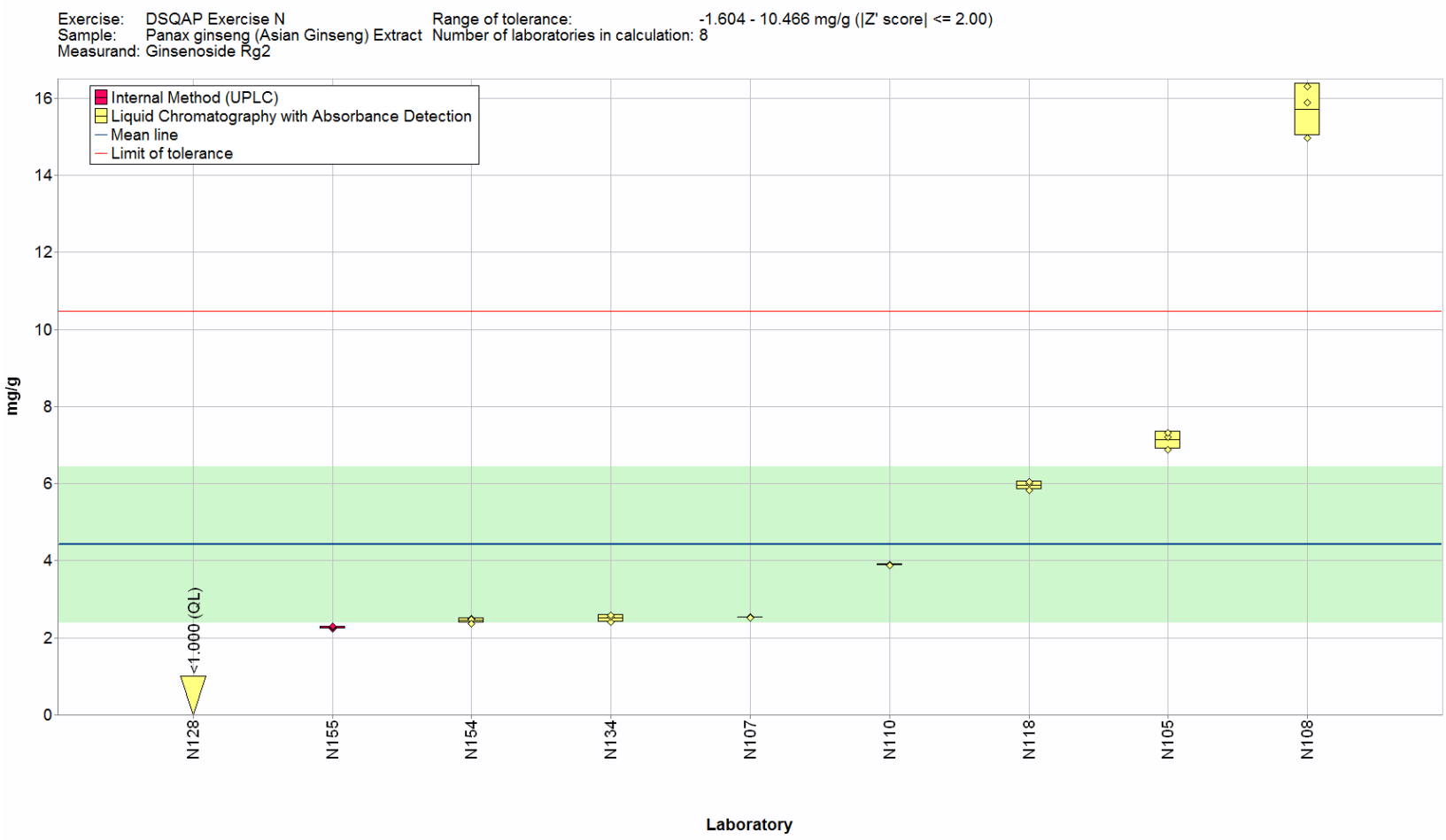

Figure 56. Ginsenoside Rg2 in candidate SRM 3385 Ground Asian Ginseng (*Panax ginseng* C.A. Meyer) Extract (data summary view – analytical method). In this view, individual laboratory data are plotted (diamonds) with the individual laboratory standard deviation (rectangle). The color of the data point represents the analytical method employed. Laboratory data shown as a triangle indicates that a "less than" result was submitted, and the base of the triangle is displayed at the reported laboratory detection limit. The solid blue line represents the consensus mean and the green shaded region represents the 95 % confidence interval for the consensus mean. The solid red line represents the upper consensus range of tolerance, calculated as the values above and below the consensus mean that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$, with the lower range set at zero. A NIST value has not been determined in this material.

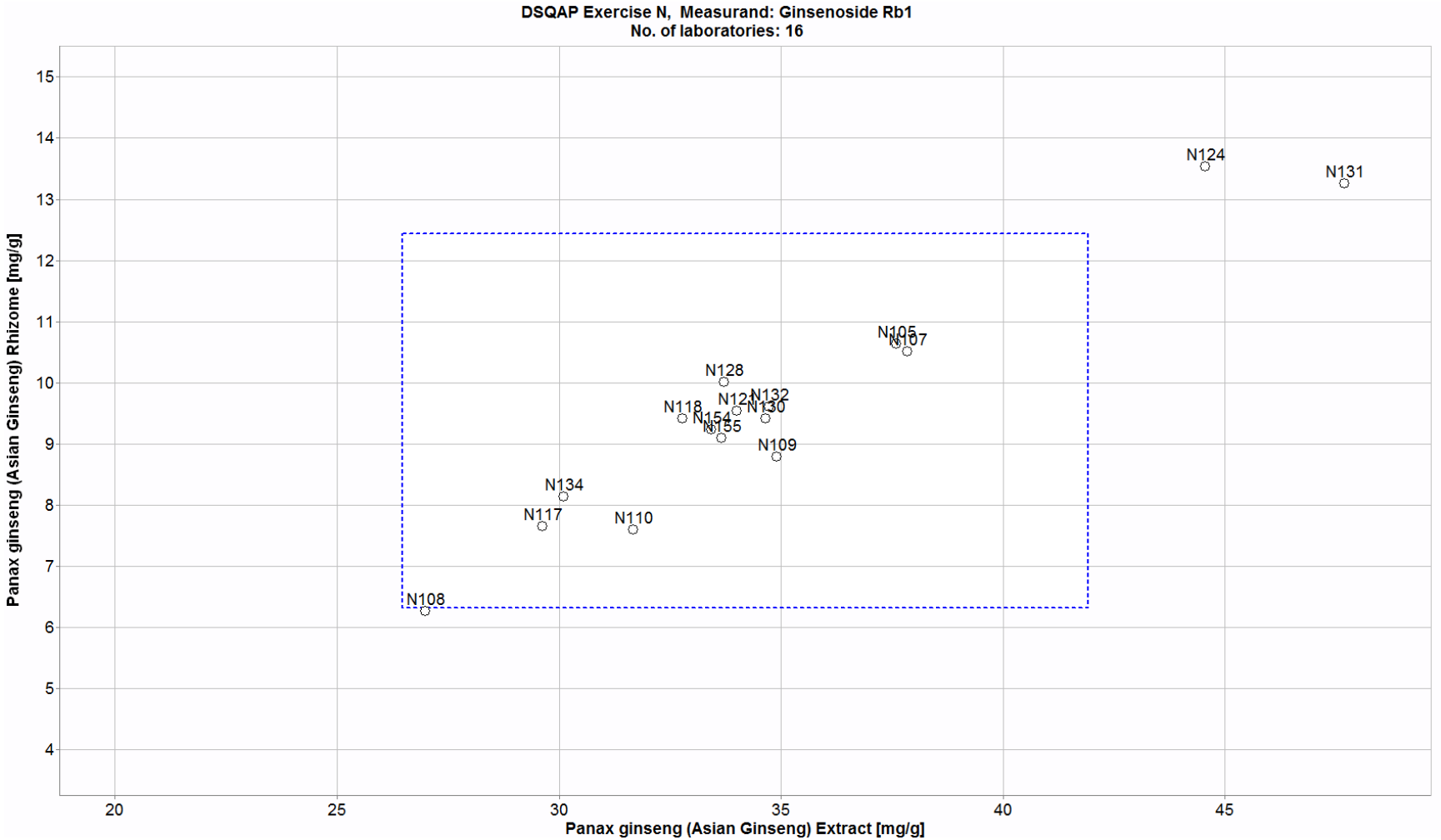

Figure 57. Laboratory means for ginsenoside Rb1 in Asian ginseng rhizome and Asian ginseng extract (sample/sample comparison view). In this view, the individual laboratory mean for one sample (rhizome) is compared to the mean for a second sample (extract). The dotted blue box represents the consensus range of tolerance for Asian ginseng extract (x-axis) and Asian ginseng rhizome (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

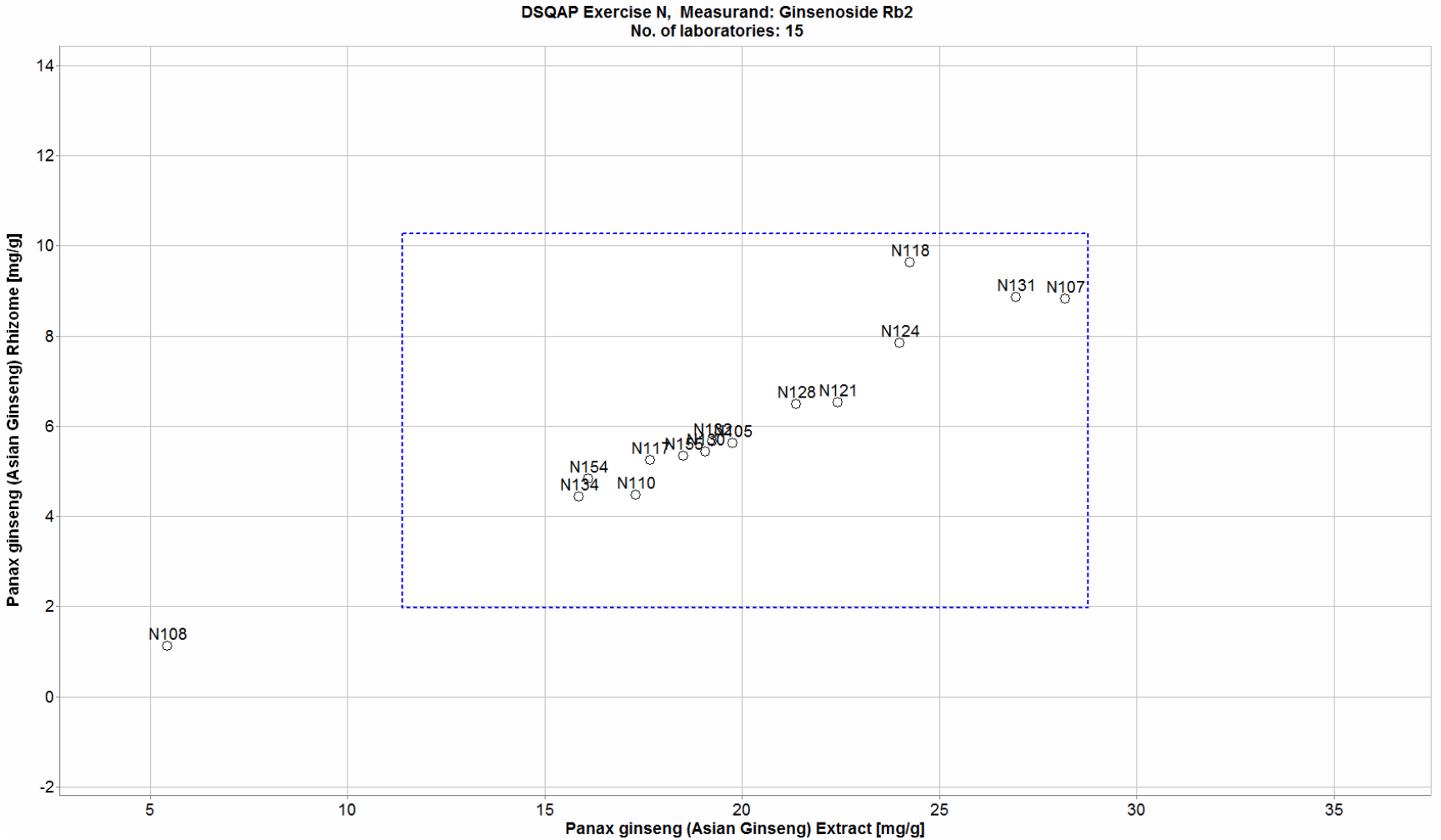

Figure 58. Laboratory means for ginsenoside Rb2 in Asian ginseng rhizome and Asian ginseng extract (sample/sample comparison view). In this view, the individual laboratory mean for one sample (rhizome) is compared to the mean for a second sample (extract). The dotted blue box represents the consensus range of tolerance for Asian ginseng extract (x-axis) and Asian ginseng rhizome (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

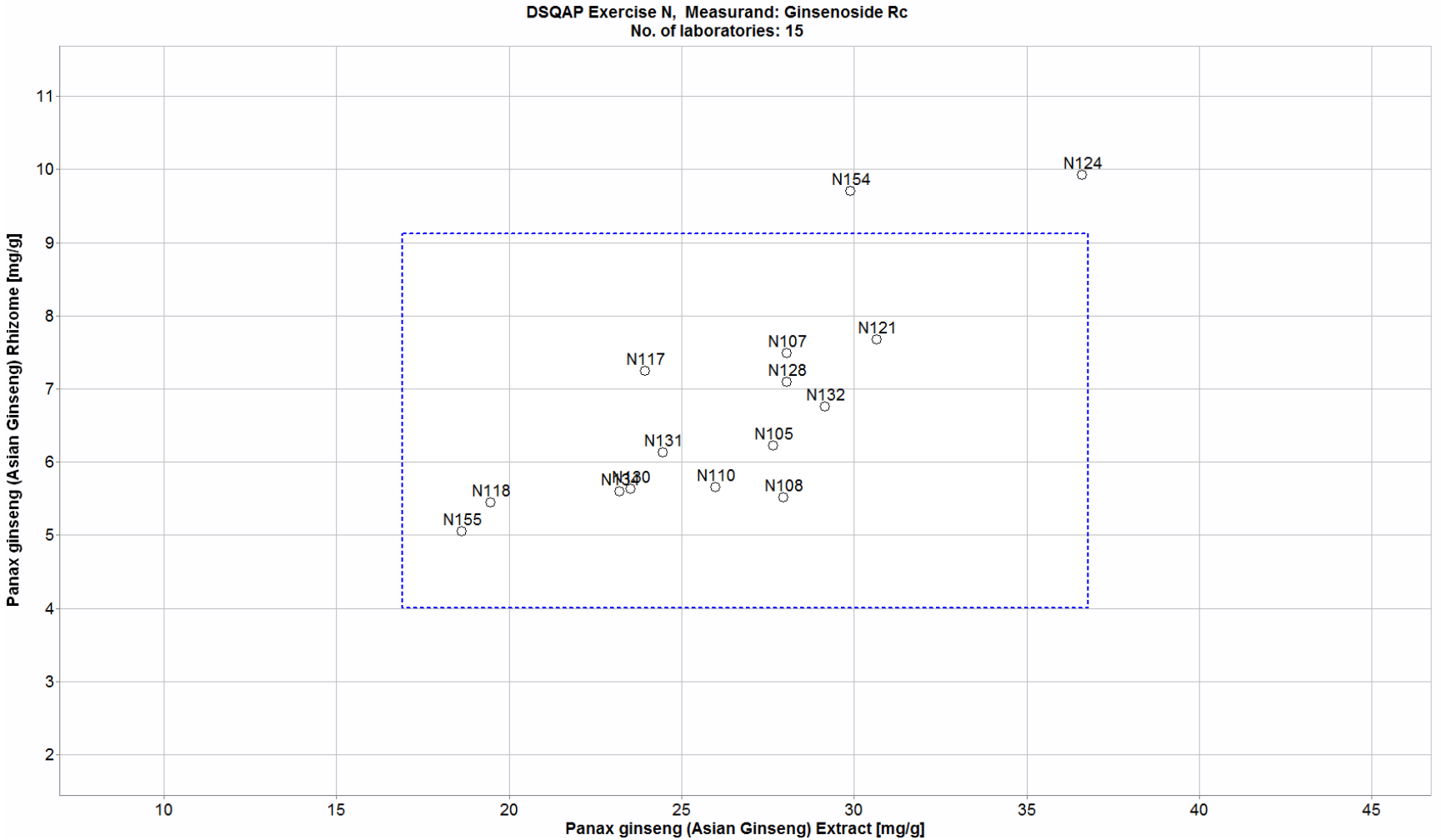

Figure 59. Laboratory means for ginsenoside Rc in Asian ginseng rhizome and Asian ginseng extract (sample/sample comparison view). In this view, the individual laboratory mean for one sample (rhizome) is compared to the mean for a second sample (extract). The dotted blue box represents the consensus range of tolerance for Asian ginseng extract (x-axis) and Asian ginseng rhizome (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

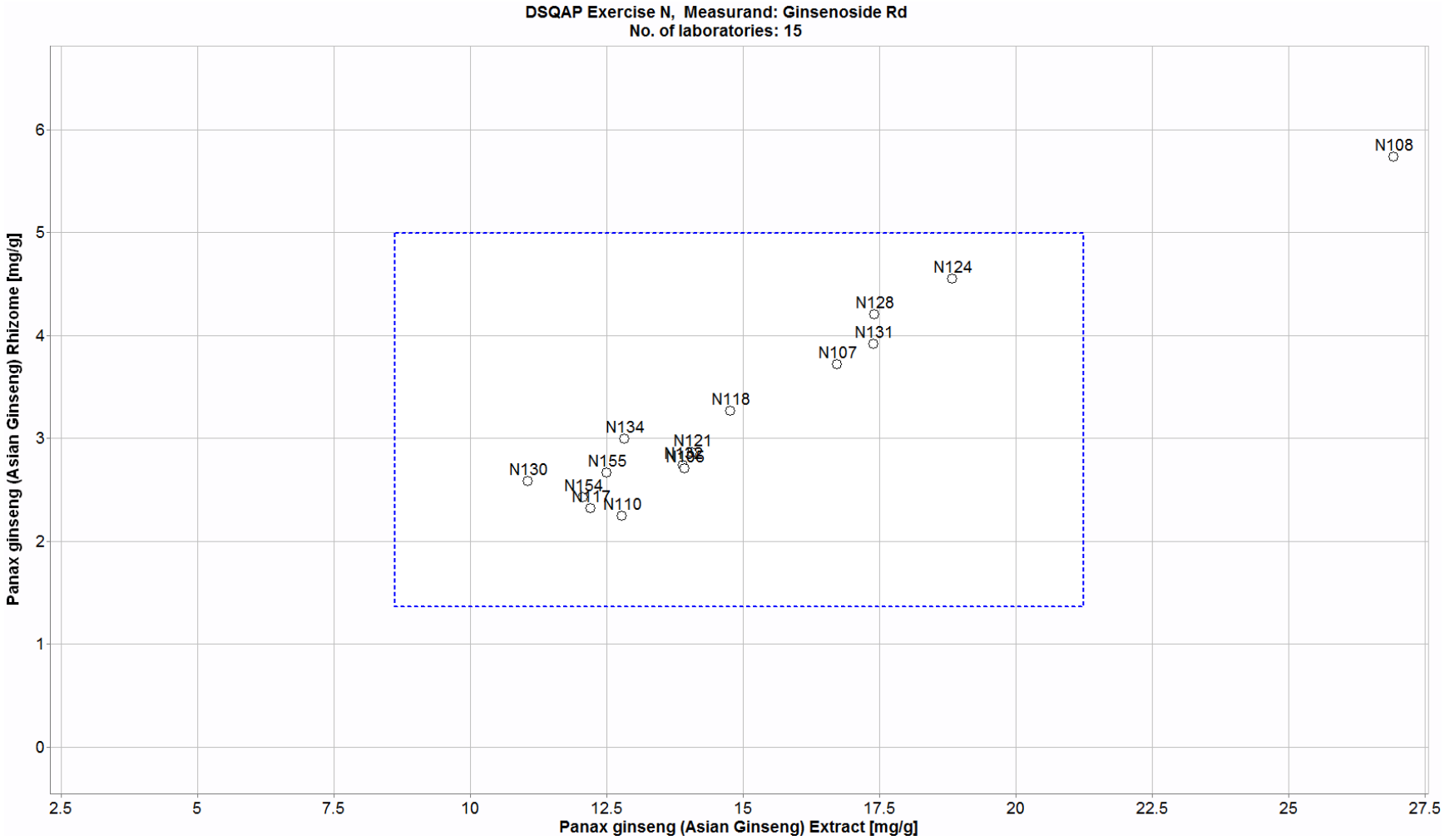

Figure 60. Laboratory means for ginsenoside Rd in Asian ginseng rhizome and Asian ginseng extract (sample/sample comparison view). In this view, the individual laboratory mean for one sample (rhizome) is compared to the mean for a second sample (extract). The dotted blue box represents the consensus range of tolerance for Asian ginseng extract (x-axis) and Asian ginseng rhizome (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

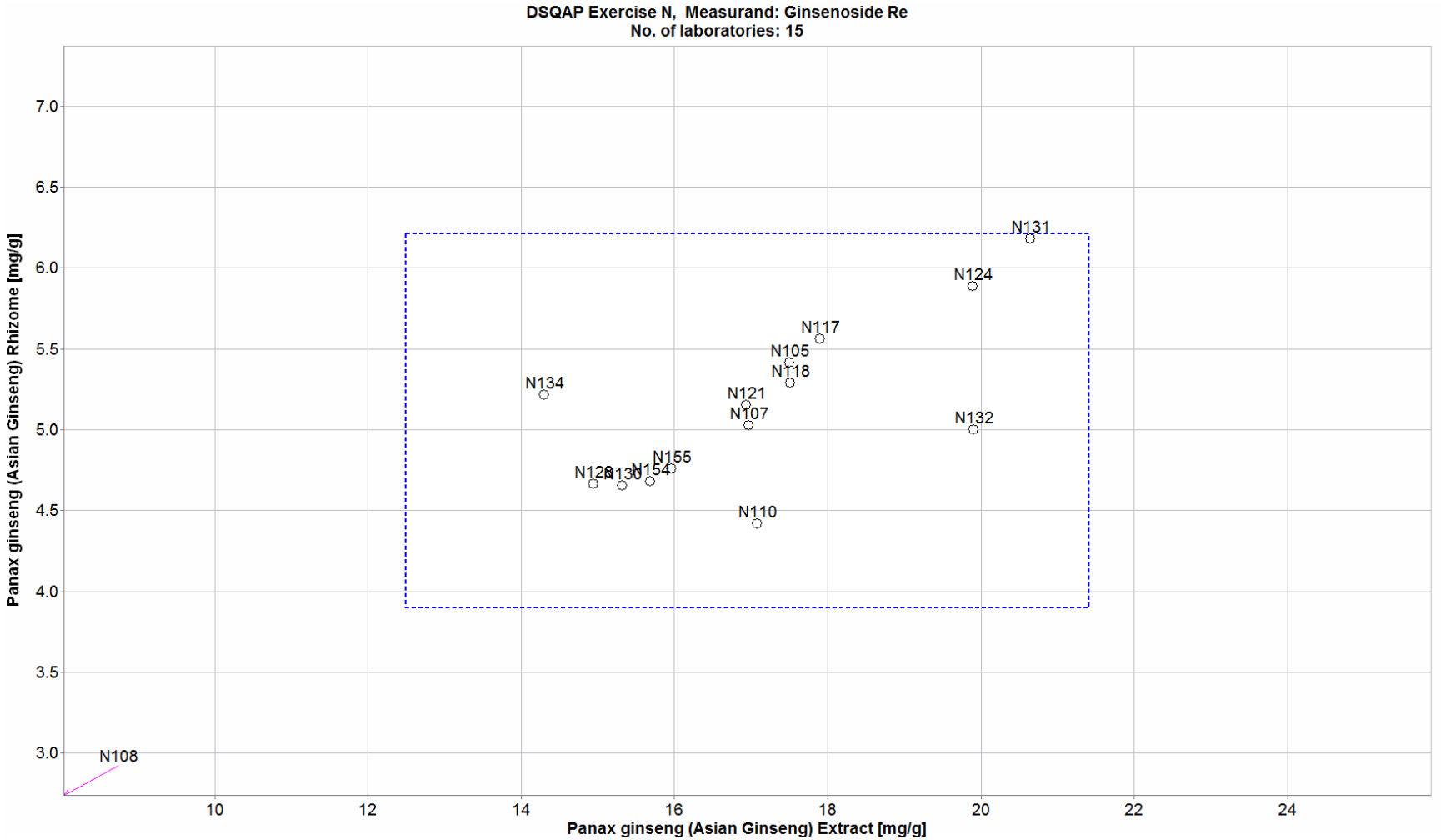

Figure 61. Laboratory means for ginsenoside Re in Asian ginseng rhizome and Asian ginseng extract (sample/sample comparison view). In this view, the individual laboratory mean for one sample (rhizome) is compared to the mean for a second sample (extract). The dotted blue box represents the consensus range of tolerance for Asian ginseng extract (x-axis) and Asian ginseng rhizome (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

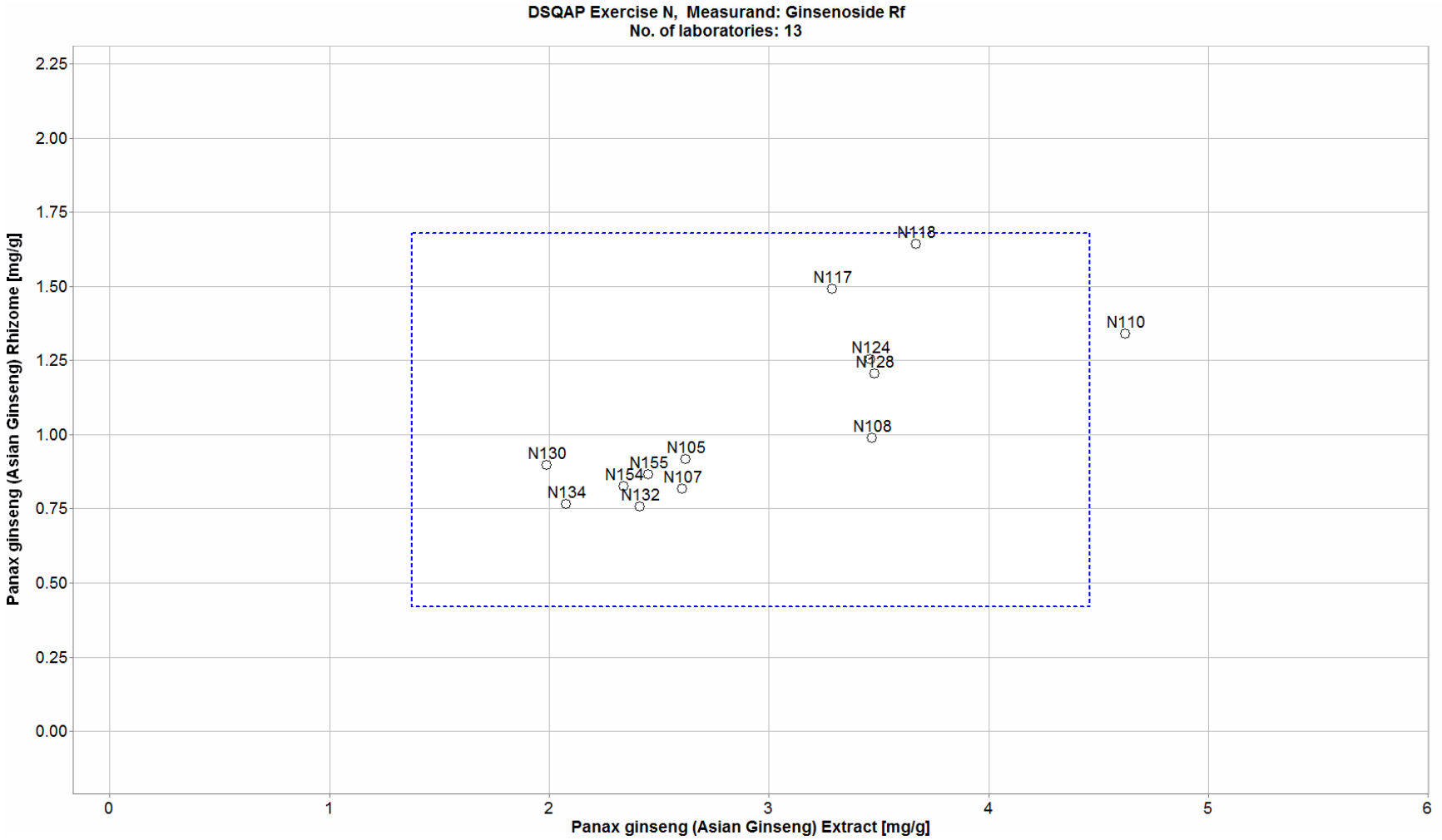

Figure 62. Laboratory means for ginsenoside Rf in Asian ginseng rhizome and Asian ginseng extract (sample/sample comparison view). In this view, the individual laboratory mean for one sample (rhizome) is compared to the mean for a second sample (extract). The dotted blue box represents the consensus range of tolerance for Asian ginseng extract (x-axis) and Asian ginseng rhizome (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

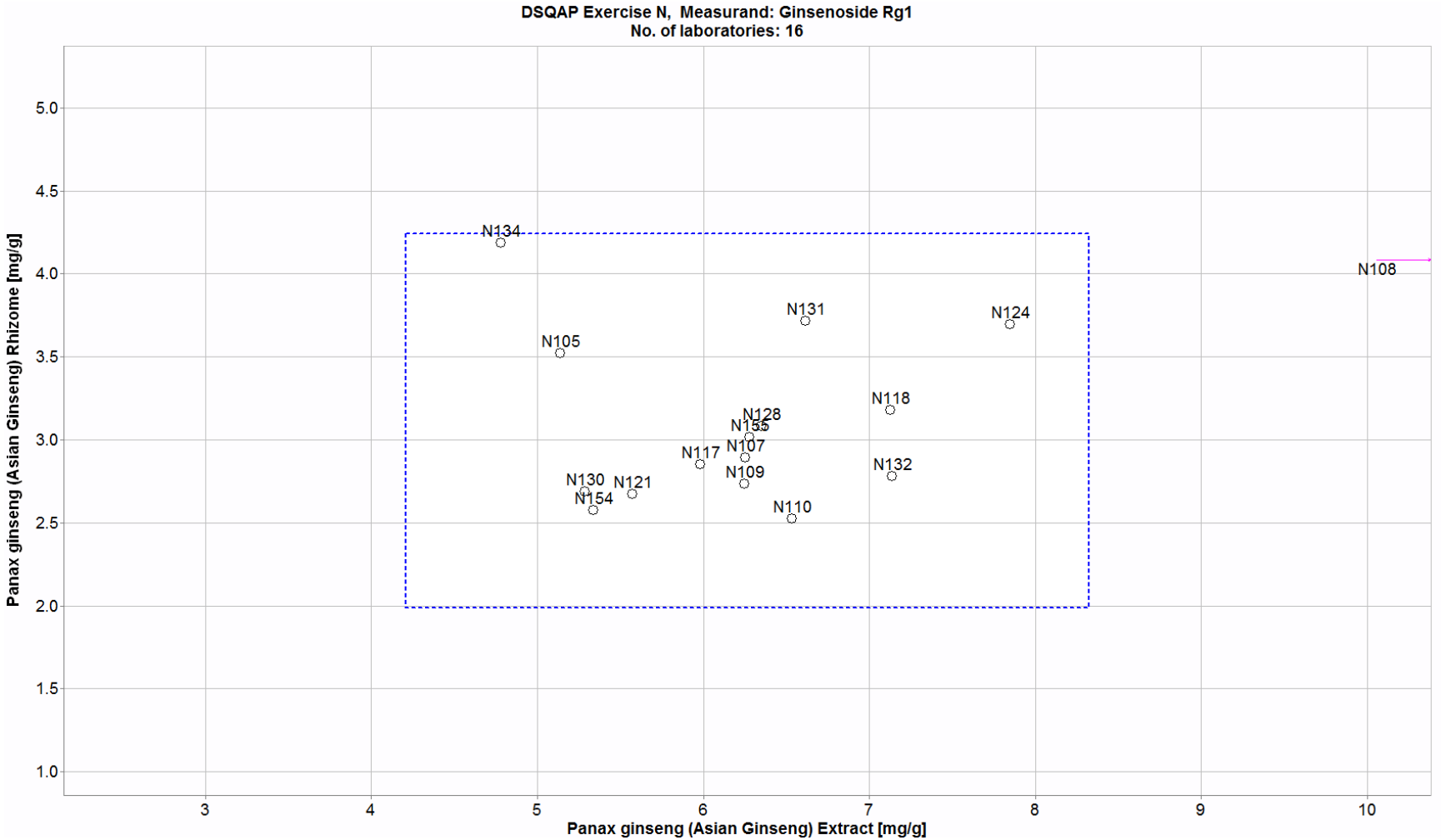

Figure 63. Laboratory means for ginsenoside Rg1 in Asian ginseng rhizome and Asian ginseng extract (sample/sample comparison view). In this view, the individual laboratory mean for one sample (rhizome) is compared to the mean for a second sample (extract). The dotted blue box represents the consensus range of tolerance for Asian ginseng extract (x-axis) and Asian ginseng rhizome (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.

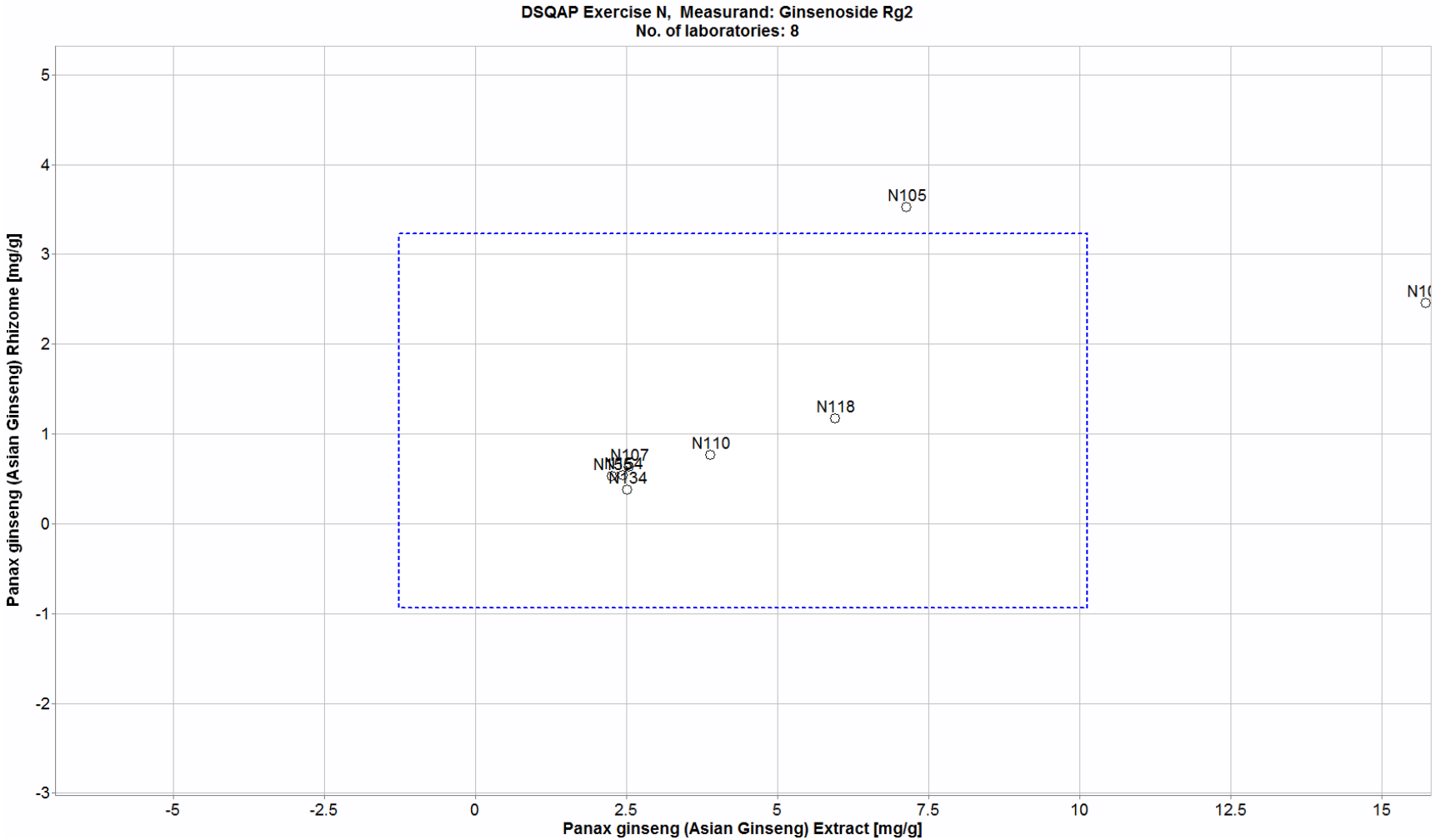

Figure 64. Laboratory means for ginsenoside Rg2 in Asian ginseng rhizome and Asian ginseng extract (sample/sample comparison view). In this view, the individual laboratory mean for one sample (rhizome) is compared to the mean for a second sample (extract). The dotted blue box represents the consensus range of tolerance for Asian ginseng extract (x-axis) and Asian ginseng rhizome (y-axis), calculated as the values above and below the consensus means that result in an acceptable Z'_{comm} score, $|Z'_{comm}| \leq 2$.