Wadsworth Center
NEW YORK STATE DEPARTMENT OF HEALTH
Trace Elements Laboratory

TRACE ELEMENTS IN SERUM

Special Report:

Investigation of Serum Selenium in Human and Bovine Matrices

May 8th, 2014

NEW YORK
state department of
HEALTH

Howard A. Zucker, M.D., J.D.
Acting Commissioner of Health

Sue Kelly
Executive Deputy Commissioner

May 8, 2014

NEW YORK STATE PROFICIENCY TESTING PROGRAM *for* TRACE ELEMENTS in SERUM

Dear Laboratory Director,

This report summarizes the results of our investigation of laboratory performance in the **New York State Proficiency Testing (NYS PT) program for Selenium (Se) in Serum**. At the end of 2011, we agreed to join with other Trace Element External Quality Assessment (EQA) programs in using a common PT sample for trace elements in serum and ceased production of our own in-house human serum PT samples. This idea was rooted in the desire to harmonize various aspects of the different international PT programs developed for trace elements (Taylor et al. 2006; Arnaud et al. 2008). The MCA Laboratory of Queen Beatrix Hospital, The Netherlands, which organizes an ISO-accredited Trace Elements EQA scheme in Europe, produced the common PT samples for serum trace elements. The principal goals of using the common PT samples were to obtain lower levels of serum Se (the lowest Se level obtained from North American human serum is ~100 µg/L) and to obtain additional characterization data from the federated European EQA scheme similarly distributing the product. The origin of the material used for the common PT samples was Australian bovine calf serum, which has lower endogenous Se than human-sourced materials. There were no reported issues with the use of this product in EQA schemes for trace element analysis at that time.

In May 2012, we began distributing bovine serum samples for PT Event 2. Bovine samples were again distributed in September 2012 for PT Event 3. In December 2012, a review of participant performance for serum Se showed that one laboratory had been unsuccessful, i.e., failed to achieve the minimum satisfactory score (80% or greater) for two of three consecutive events. As a result of their root cause analysis, the laboratory suggested that the bovine samples might have caused their unsuccessful performance. Since the laboratory had satisfactory performance with the previous human samples, this prompted an internal review of our serum PT program, and more specifically, serum Se. Grading for serum Se was suspended after 2012 PT Event 3 in order to conduct a more detailed study of bovine versus human matrices, and possible polyatomic interferences in plasma mass spectrometry. As part of these studies, we circulated both bovine (non-graded) and human (educational) serum, matched as closely as possible in Se concentrations, for participant analysis by standard mode ICP-MS or DRC/CC-ICP-MS under similar analytical conditions during 2013 PT Events 2 and 3.

1. Performance in the NYS PT Program Since 2006

Performance in the NYS PT program was reviewed to assess the overall acceptability of participant results for both human and bovine PT samples. Overall NYS PT satisfactory performance for human (2006-12) compared to bovine (2012-13) serum for aluminum (Al), copper (Cu), selenium (Se) and zinc (Zn) was reviewed. The trace element-specific graphs (Appendix – Figure 1) show that only serum Se (Figure 1c) appeared to be affected by the change. Overall satisfactory performance for serum Se decreased from 100% for human PT samples (2012 PT Event 1) to 84.7% for bovine PT samples (2012 PT Event 2).

2. Performance for Human and Bovine Serum – standard versus DRC/CC modes

We separated ICP-MS participant data into two broad method categories: standard mode versus use of a collision cell or dynamic reaction cell approach in ICP-MS. A comparison between these two methods with both human and bovine samples is shown (Appendix – Figure 2). The PT sample means for participants analyzing bovine serum Se in standard mode ICP-MS (●) were approximately 10 µg/L greater than the target value. Note that the positive bias for bovine serum analyzed in standard mode (●) is problematic at concentrations below ~50 µg/L, and was a contributing factor to the unsatisfactory PT performance observed. An overall decrease in precision at lower Se concentrations for bovine PT samples analyzed in standard mode (PT Report – Statistical Summary by Method) is observed; a comparison of results obtained for serum Se in both matrices at target values (TV) of approximately 115 - 120 µg/L (Appendix – Figure 3) is shown.

3. Questionnaire Regarding Selenium Method Implementation

A questionnaire was sent to all laboratories participating in the NYS PT program for serum Se, to gain additional information regarding the analytical method implementation used for Se. Table 1 shows the categories addressed, and depth of the questions. Although no clear pattern emerged that could explain the data based on method alone, it was evident that many laboratories implement ICP-MS in different ways (calibration, isotope monitored, internal standard, standard mode, collision cell, reaction cell gas etc.).

SUMMARY

Throughout 2013, staff investigated potential problems with the use of bovine calf serum the NYS PT program and concluded that this matrix can be problematic for certain types of inorganic mass spectrometry when analyzing for serum Se at *m/z* 82, especially at low Se concentrations. Participant laboratories measuring ^{82}Se by standard mode ICP-MS experience a significant positive bias for bovine PT samples at low Se concentrations, while laboratories using DRC/CC-ICP-MS do not. Since it is difficult to obtain human sera with low (<100 µg/L) levels of Se, especially in North America, interference at *m/z* 82 cannot be definitively characterized in human matrices at the current time. Nonetheless, we have resumed the use of human serum in the Trace Elements PT program.

Yours sincerely,

Patrick J. Parsons, Ph.D., Chief
Laboratory of Inorganic & Nuclear Chemistry
Deputy Director, Division of Environmental Health

Mary Frances Verostek, Ph.D.
Assistant Section Head, PT Program

cc: CLEP

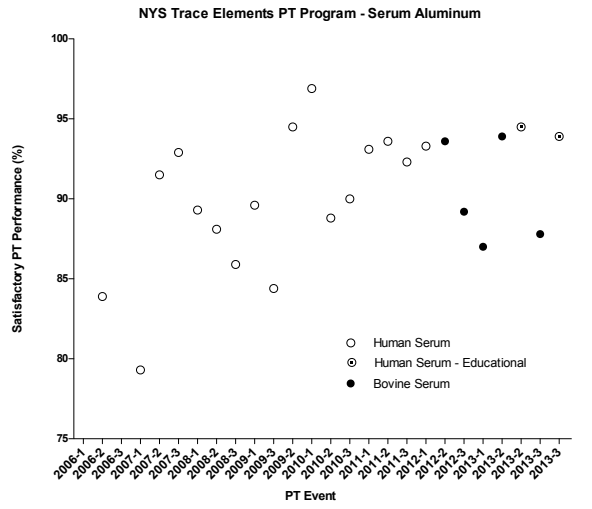
APPENDIX

Figure 1.

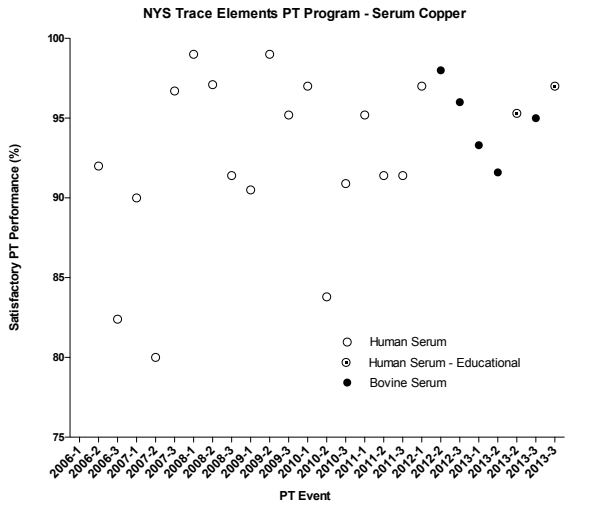
Laboratory performance in the NYS Serum Trace Elements PT program from 2006 – 2013 for (a) aluminum, (b) copper, (c) selenium, and (d) zinc.

Overall satisfactory performance for each analyte for each event is measured by dividing the total number of PT results within the acceptable limits by the total number of PT results submitted. The trace element-specific graphs (Appendix – Figure 1) show that only serum Se (Figure 1c) appeared to be affected by the serum matrix change. The overall satisfactory performance for serum Se decreased from 100% for human PT samples (2012 PT Event 1) to 84.7% for bovine PT samples (2012 PT Event 2). Unsatisfactory PT performance for this event is attributed to 3 of the 17 participants reporting 2 or more of the 5 results outside the acceptable ranges, and 2 participants reporting 1 of the 5 results outside the acceptable ranges. Participant laboratories achieved an overall satisfactory performance for serum Se of 100% and 97.3%, respectively, with the educational human samples circulated for 2013 Events 2 and 3. If graded, overall satisfactory performance for bovine samples for 2013 Events 2 and 3 was 90.7% and 92.0%, respectively, with unsatisfactory PT performance for these events perhaps attributable to the lower levels of Se (SE13-08 and SE13-13) distributed.

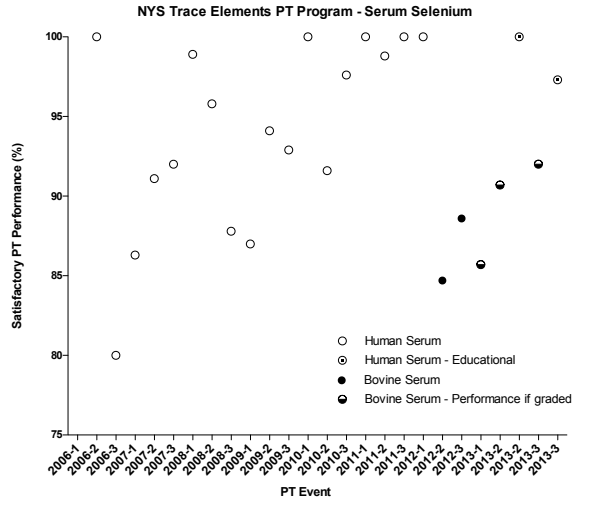
a)



b)



c)



d)

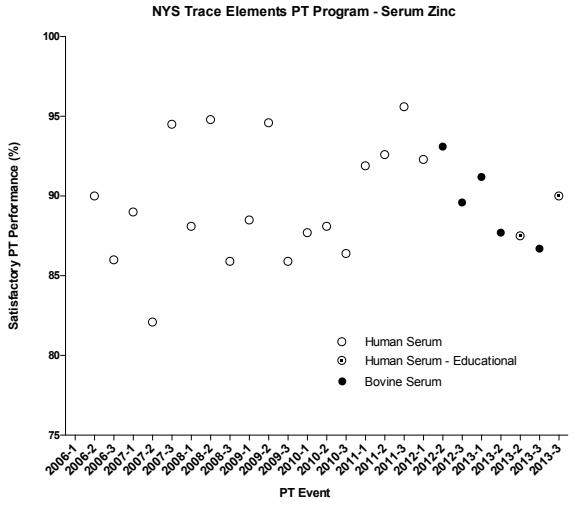


Figure 2.

Review of performance for serum Se in the NYS PT program

Bias for PT samples distributed between 2011 and 2013 is plotted as the difference between the assigned target value and the arithmetic mean obtained from participant data reported as using either standard mode ICP-MS (● bovine; ○ human) or DRC/CC-ICP-MS (■ bovine; □ human) versus the target value. Target values are established using robust statistics, and for recent events, participants are now reporting serum Se by DRC/CC-ICP-MS nearly twice as often as standard mode ICP-MS. Instrument means for participants analyzing bovine serum Se in standard mode (●) were approximately 10 µg/L greater when compared to the target value, while participants analyzing Se by DRC/CC-ICP-MS (■) typically showed a negative bias. Historically, results obtained from participants analyzing Se in human serum, by either DRC/CC-ICP-MS (□) or in standard mode ICP-MS (○), have appeared evenly distributed around the target value. However, Se measurements in human serum by ICP-MS (○) were biased high when compared to DRC/CC-ICP-MS (□) for 2013 Educational Event 2.

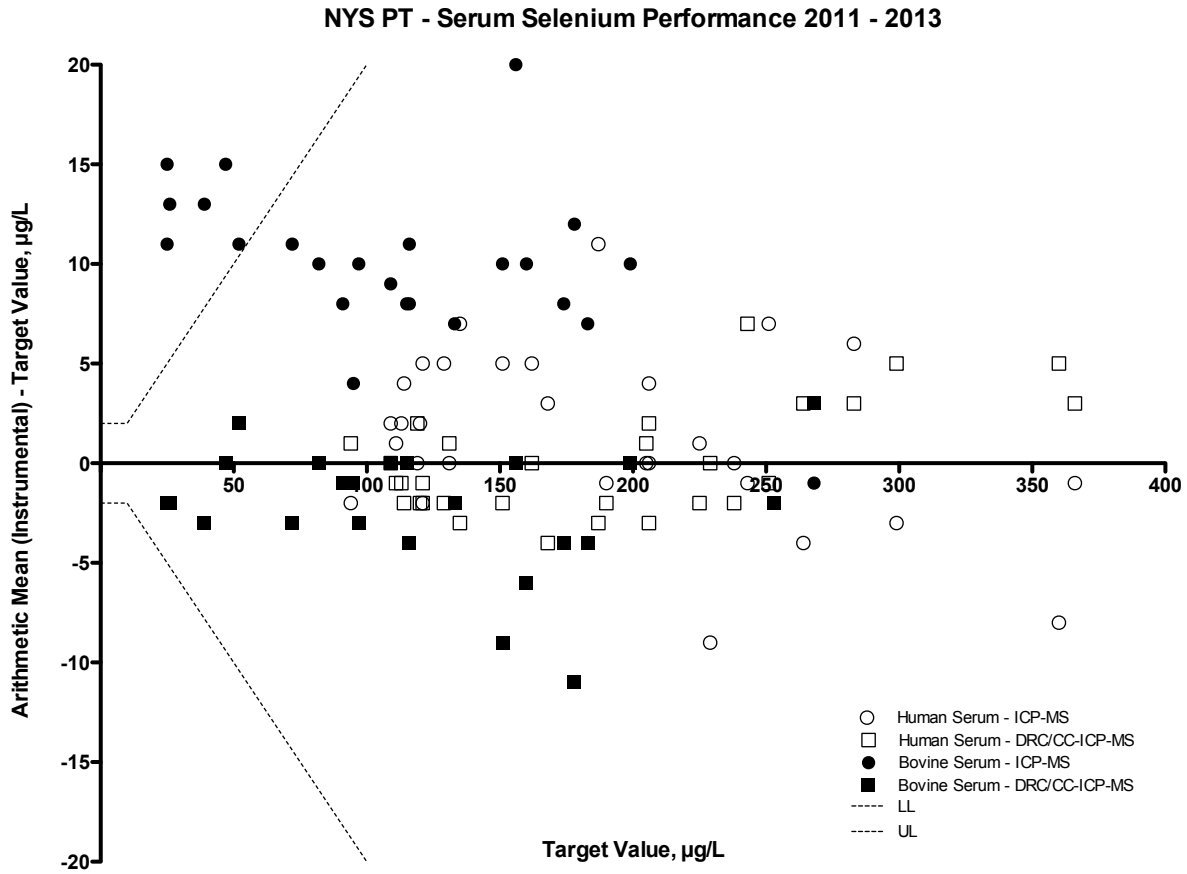


Figure 3.

Review of performance for serum Se in the NYS PT program for matched target values

Human serum samples, selected based upon Se concentrations, were relabeled for distribution with bovine serum samples with similar Se levels for analysis during 2013 PT Events 2 and 3. Serum Se analysis was predominantly performed using either standard mode ICP-MS or DRC/CC-ICP-MS instrumentation, with laboratories monitoring ^{78}Se in either standard or DRC/CC, mode, and ^{82}Se by two standard mode ICP-MS participants. Individual participant results are displayed along with the instrument mean represented by a horizontal line, and the vertical error bars represent ± 1 SD (standard deviation). Serum Se analysis in standard mode ICP-MS for both matrices (●;○) typically produced positively biased results when compared to those obtained by DRC/CC-ICP-MS for either matrix (■;□) (see "Statistical Summary by Method" in individual PT Reports). Bovine serum samples SE13-07 (TV = 116 µg/L) and SE13-15 (TV = 115 µg/L) were the same sample distributed for both performance assessment between 2013 PT Events 2 and 3 (Figure 3a), and, for comparison with human serum samples SE13-17 (TV = 114 µg/L) and SE13-25 (TV = 121 µg/L) in 2013 PT Events 2 and 3 (Figure 3b), respectively.

a)

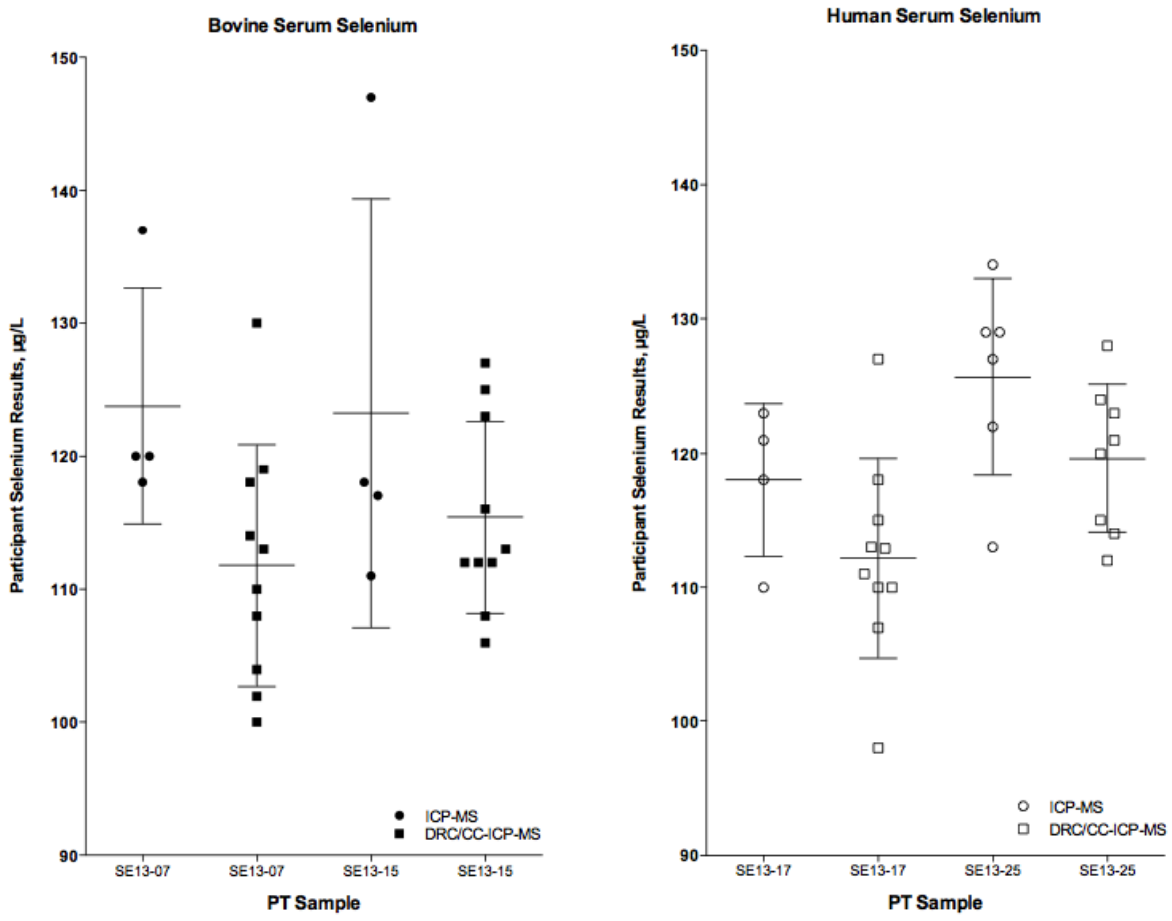


Table 1.

Variability in participant laboratory methodology for serum Se measurements.

Serum Concerns	Serum Matrix	• Human • Animal (equine, porcine, caprine, bovine, etc.)
	Challenge Levels	• > 90 µg/L for human serum (United States) • > 25 µg/L for bovine serum (Australian fetal calf)
Analytical Considerations	Calibration	• Matrix-matched, aqueous
	Dilution	
	Base Serum	• Se concentration (> 90 µg/L endogenous Se?) • Matrix (human/animal)
	QCs	• Human/animal/aqueous
	Internal standard selection	
Implementation of Instrumental Parameters	Se isotope	• ^{78}Se, ^{80}Se, ^{82}Se
	Instrument Mode	• Standard, DRC/CC
	DRC/CC reaction gas	• CH_4, NH_3
	Correction equation used?	

References

Arnaud, J., J. P. Weber, C. W. Weykamp, P. J. Parsons, J. Angerer, E. Mairiaux, O. Mazarrasa, S. Valkonen, A. Menditto, M. Patriarca, and A. Taylor. 2008. Quality Specifications for the Determination of Copper, Zinc, and Selenium in Human Serum or Plasma: Evaluation of an Approach Based on Biological and Analytical Variation. *Clinical Chemistry* 54 (11):1892-1899.

Taylor, Andrew, Jurgen Angerer, Josiane Arnaud, Francoise Claeys, Robert L. Jones, Olav Mazarrasa, Eric Mairiaux, Antonio Menditto, Patrick J. Parsons, Marina Patriarca, Alain Pineau, Sinikka Valkonen, Jean-Philippe Weber, and Cas Weykamp. 2006. Occupational and environmental laboratory medicine: A network of EQAS organisers. *Accreditation and Quality Assurance* 11 (8-9):435-439.