NEW YORK STATE OF OPPORTUNITY. Department of Health

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May 26, 2016

New York State Soluble Tumor Markers Proficiency Test 5-2016 [1]

Dear Laboratory Director,

This is a summary and critique of the New York State Proficiency Test from May 2016 for Tumor Markers AFP, CA125, CA15-3, CA27.29, CA19-9, CEA, PSA, free PSA and complexed PSA.

Laboratories were challenged with five (5) different coded specimens prepared by Wadsworth Center personnel. Purified analyte preparations were added in varying concentrations to a serum-based matrix, then sterile filtered, aseptically dispensed into sample vials and stored at 4°C until mail-out. All laboratories received the same samples, regardless of whether they tested for one or all of the analytes.

Result evaluation:

Your laboratory's individual results, score(s), previous two PT event scores and overall performance status are on a separate report securely posted on the Department's Health Commerce System site under EPTRS (Electronic Proficiency Test Reporting System). To access the results for your laboratory, please log in to the Electronic Proficiency Test Reporting System homepage at:

https://commerce.health.state.ny.us

Under "My Applications" click on **EPTRS**

Click on **Online Reporting** which will bring you to the "Select Event" page

Scroll down or filter by year under "Submitted/Closed Events" to find the correct survey and click on **Evaluation** in the Scored column.

Laboratory contacts were also sent an email alert indicating the availability of the individual result evaluation report.

This critique with summary tables and graphs is sent by a separate email to the laboratory contacts and will also be posted on the public Wadsworth website at:

http://www.wadsworth.org/regulatory/clep/pt/summaries

Once posted, it can also be accessed by clicking the **Statistical** link from the "Select Event" webpage.

[1] The use of brand and/or trade names in this report does not constitute an endorsement of the products on the part of the Wadsworth Center or the New York State Department of Health.

Please **review, print and sign** your score report within two weeks of notification of release and keep it in your files. You will need it for your next laboratory survey to demonstrate successful participation in the NYS PT program.

For grading purposes, all results were evaluated based on their respective peer group mean (N ≥ 3). This mean was determined with the robust regression followed by outlier identification (ROUT) statistical method, as implemented in GraphPad's Prism®6 software (Harvey J Motulsky and Ronald E Brown, "Detecting outliers when fitting data with nonlinear regression – a new method based on robust nonlinear regression and the false discovery rate," BMC Bioinformatics 7:123 (2006). Available at: http://www.biomedcentral.com/1471-2105/7/123). This method identifies outliers through robust statistical analysis with a nonlinear curve fit of the data, thus removing points that can skew calculations of the mean. For our purposes, the target is the mean determined from the best fit values derived from that analysis while the standard deviation (SD) was calculated by multiplying the standard error of the mean for each individual peer group with the square root of the number of labs in that peer group. Except for AFP, the allowable error and range were determined from the average of the median %CVs for each sample across all methods (see summary tables); allowances for increased scatter at low concentrations were made for some analytes. For AFP only, the allowable error and range were +/- 3SD from your peer group mean. Please note that, unless indicated otherwise, we combined results from different instruments made by the same manufacturer and/or brand into one peer group, except where the linear regression line between the results from two instruments showed a significant ($p<0.01$) deviation from identity.

To help you compare your results to those of your peer group, we have calculated a D/Dmax value and displayed it on your individual report card next to the range for each sample. D/Dmax is a measure of how much your result (x) deviates from your peer group target, **D/Dmax=(x-target)/(maximum allowable error)**, with D being the difference of your result from the target, and Dmax being the **maximal allowable error for your peer group.** In general, an acceptable result has a D/Dmax between –1 and +1. Occasionally, however, due to rounding effects, there may be a small discrepancy between the D/Dmax value and the actual scoring, in which case the actual scoring takes precedence. The closer D/Dmax is to zero, the closer your result was to the target. A negative D/Dmax means that your result was below, and a positive value means your result was above the target. No entry in this place means that your result either had a qualifier (< or >) or was not gradable, in which case there will be an NG in the grade column. **Note: If your D/Dmax is not within +/- 0.66 (approximately +/-2 SD), especially for more than one or two samples, you should carefully check your result(s) since this indicates that they are significantly different from the mean(s) of your peer group.** While this could be an isolated incident, it could also potentially indicate that your assay may not be performing as it should. Furthermore, if your **average D/Dmax is greater than +0.5 or smaller than -0.5,** then your results exhibited a substantial high or low bias compared to the rest of your peer group, suggesting a potentially significant systematic error with your assay. Possible causes could include a calibration drift, reagents that are close to their expiration date, or subtle malfunction of your instrument. We strongly encourage you to take a close look at the run in question as well as others performed around that time and/or with the same reagent lots, and to evaluate if patient results might have been similarly affected.

For all analytes, summary tables give the targets and acceptable ranges for each sample and peer group (if N ≥ 3). We also present graphical comparisons of the results among the different peer groups. In order to compare results between peer groups more easily, average normalized values were calculated for each sample by dividing the individual peer group mean by the median of the means from all peer groups (all method median). The all method medians are used instead of the all lab means to reduce the bias towards methods that are used by a greater proportion of labs. For AFP, PSA and free PSA, we calculated these values relative to the assigned target values (see below) as well as the all method median. Keep in mind when comparing methods that in some of the peer groups the number of results (N) was small. However, the fact that the relative performance for almost all methods has been very constant over the last several years indicates that the results shown reflect the true behavior of each method compared to its peers, at least under the conditions of the NYS Sera and Soluble Tumor Markers Proficiency Test.

Discussion:

CA125 (Table 1, Figure 1): Results were reported by 54 labs using instruments from eight different manufacturers corresponding to seven peer groups with N ≥ 3. The peer group means ranged from 33% below to 17% above the all method median, with Ortho Clinical Diagnostics being the lowest and Abbott Architect being the highest. Over half (57%) of the labs were in the two peer groups that fell at or within +/-6% of the all method median. The different methods used to measure CA125 are still not very well harmonized, and the reference range cut-off value of 35 U/ml may not apply across the board. Indeed, different laboratories reported cut-off values ranging from 16.3 to 35.0 U/ml suggesting that individual laboratories determine their own reference ranges based on their own patient populations. However, an individual lab's reference range does not necessarily correspond to the lab's method's relative performance in the NYS PT. Consequently, baseline levels for serial measurements should be redetermined if there is a change in the method or instrument used.

CA19-9 (Table 2, Figure 2): Results were reported by 32 labs using instruments from six different manufacturers, three with N ≥ 3 for peer group grading. Forty-one percent of all reporting labs used Siemens ADVIA Centaur XP, 38% used either Beckman's Unicel or Access/2, and 9% used the Tosoh ST-AIA method. Similar to what has been seen in past events, results from the Siemens Advia Centaur method were almost two-fold higher than those from Beckman and Tosoh, and the Abbott Architect method results averaged 5.4 times higher than the all method median (data not shown, but used by one lab only).

The MUC1 breast cancer antigen was measured by 49 labs, with 59% using an instrument from one of five manufacturers (two with N=2) to measure **CA15-3** (Table 3, Figure 3), and the remainder using an instrument from one of two manufacturers to measure **CA27.29** (Table 4, Figure 4). Of the methods used for CA15-3, the Beckman Unicel/Access results exhibited a notable negative bias, averaging -31% from the all method medians and Siemens Immulite averaged 16% above the median. **CA27.29** measurements showed a 28% difference between the ADVIA Centaur XP/CP and the Tosoh methods, and the median CA27.29 measurements showed a 1-17% concentration dependent positive bias compared to the corresponding median CA15-3 measurements.

CEA (Table 5, Figure 5): Results were reported by 81 labs using instruments from eight different manufacturers corresponding to eight peer groups comprising from 3 to 21 labs. Tosoh AIA exhibited a high positive bias averaging 63% above the median and Siemens Immulite 2000 exhibited a smaller, though still positive bias of +17%, while the other methods were within +/-10% of the medians suggesting some degree of harmonization among the methods.

For **AFP, PSA and free PSA,** target values were assigned using traceable International Standards. However, for scoring purposes the results were evaluated based on their respective peer group means. For the purpose of method comparison, the tables show the method bias against both the all method medians and the assigned target values, but the graphs show the performance relative only to the assigned targets.

AFP (Table 6, Figure 6): Results were reported by 44 labs using instruments from eight different manufacturers corresponding to eight peer groups. Three of the eight methods, used by 45% of the labs, gave results within +/-5% of the target, but averaged 11% lower than the all method median. The remaining five methods averaged 22% above the target (range 14-34%), with the Siemens Centaur method exhibiting the highest positive bias at +34%. Most methods somewhat overestimated AFP levels in our samples, but the overall difference in measurements between most methods is less than 15%, which is a result similar to what has been observed in previous NYS PT events.

PSA (Table 7, Figure 7): Results were reported by 129 labs using instruments from nine manufacturers. Results from two methods, Beckman Unicel/Access and Siemens Dimension (RxL Max Xpand Plus, EXL), were clearly higher than those from the others at 25% and 23% above the target, respectively. Results from the rest of the methods ranged from 5% below the target (Ortho Clinical Diagnostics Vitros ECiECiQ & 5600) to 14% above the target (Abbott Architect and Tosoh AIA). These results are consistent with the known difference in calibration between different methods, using either the Hybritech calibrator or the WHO international standard.

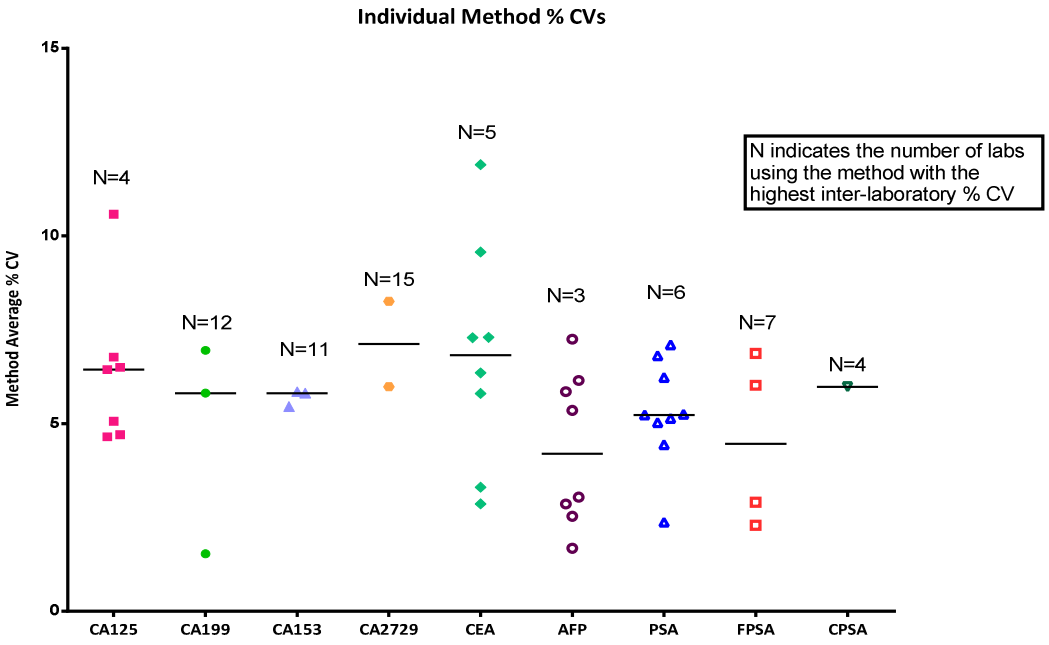
Free PSA (Table 8, Figure 8): Results were reported by 40 labs using instruments from seven manufacturers, but only four had N ≥ 3. The Beckman Unicel/Access calibrated with the Hybritech standards was the method used by the most labs (43%) and results were distinctly higher than those obtained by the other methods (30% higher than the all method medians and 47% higher than the assigned targets). Abbott Architect was 7% above the all method median and 20% above the assigned targets, the Siemens Immulite averaged 7% lower than the all method medians and 6% higher than the assigned targets while the Dimension Vista was 12% below the all method medians and the same as the assigned targets. We calculated % free PSA for each sample using each peer group's respective average PSA and free PSA levels and observed that the differences between methods showed a pattern similar to that of the measured free PSA.

Please note, labs are required to measure and report **free PSA** for **all proficiency test samples** if free PSA

is on their test menu. We understand that this may in some cases be a deviation from a lab's policy in dealing with free PSA and could mean that PT samples are not treated exactly like patient samples.

Finally, only four labs measured **complexed PSA** and all of them used either the Siemens ADVIA-Centaur XP or CP instrument, which exhibited little difference between them and good inter-laboratory agreement, indicated by an average %CV of 5.9% (Table 9).

In conclusion, substantial differences remain between the results obtained with various methods or instruments for some analytes. Furthermore, not all methods appear equally reproducible as indicated by the spread of the average within-method %CVs (see graph below). Most %CVs are <10% but there are some notable outliers, which could at least in part be caused by the low number of labs using that particular method.



Median %CV distribution for each analyte, with individual symbols representing separate peer groups.

While some of the differences between methods may be attributed to the artificial nature of the PT samples, others are more likely due to inherent differences in the assays themselves. We make every effort to minimize the differences that can be attributed to the sample composition and suggest that despite the somewhat artificial nature of the PT samples, the differences between the results obtained by various methods might also be reflected in patient serum samples. Therefore, we encourage labs and physicians to use caution when comparing the results from the same patient measured with different methods on different instruments, since clearly not all methods are equal. For this reason, **we require that the method used be clearly indicated on the patient report** (Oncology Standard OC S1). We also encourage you to educate your physician clients about this potential problem.

We would like to reiterate the following cautionary notes regarding the interpretation of the results from this proficiency test: 1) since some of the assays were done by a small number of labs, the results might be skewed due to a lack of statistical power; 2) it is difficult to make accurate comparisons of results when the % CVs are large; and finally 3) the analyses for PT purposes are done with artificially prepared mixtures of proteins, which may or may not accurately reflect patient derived samples.

Please be aware that even though the Instrument and Reagent fields will usually be pre-populated in

EPTRS based on what was previously entered, it is still necessary to confirm that ALL instruments and reagents have been correctly entered prior to final submission, especially when you changed instruments. That information is critical to evaluate your results within the correct peer group or it could (and has) lead to failure if the two peer groups are substantially different. Furthermore, make sure to only select a qualifier (< or >) when your result is below or above your quantifiable range or you may end up with a technical failure. No changes can be made for incorrect or missing information after the submission deadline.

Note: As per new guidelines from CMS, measuring and reporting results from a second instrument is no longer allowed.

Please note that questions regarding the electronic proficiency testing reporting system (EPTRS) account application process and the entry and submission of proficiency test results can be directed to clepeptrs@health.state.ny.us .

The scheduled date for the remaining 2016 Tumor Marker Proficiency Test event is:

Mail-out date:	**Due date:**
August 30, 2016	September 14, 2016

If you have any questions or wish to discuss topics alluded to in this critique, contact Susanne McHale at susanne.mchale@health.ny.gov (518) 486-5775, or myself at erasmus.schneider@health.ny.gov or (518) 473-4856.

Erasmus Schneider, Ph.D.
Director, Oncology Section
Clinical Laboratory Reference System

Table 1: 5-16 NYS Tumor Marker PT Summary for CA 125

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median	
Abbott Architect ABH									
TM301	5	49.9	**40.9**	**58.9**	9.0	6.99		1.21	
TM302	5	26.4	**21.0**	**31.8**	5.4	7.12		1.16	
TM303	5	35.8	**29.4**	**42.2**	6.4	7.43		1.16	
TM304	5	59.6	**48.9**	**70.3**	10.7	5.27		1.14	
TM305	5	33.4	**27.4**	**39.4**	6.0	5.69		1.18	
					mean ±SD	6.50	0.96	1.17	0.02
Beckman Unicel & Access/2 BCU/BCX									
TM301	13	42.9	**35.2**	**50.6**	7.7	4.38		1.04	
TM302	12	23.0	**17.6**	**28.4**	5.4	3.74		1.01	
TM303	13	32.1	**26.3**	**37.9**	5.8	4.58		1.04	
TM304	13	59.2	**48.5**	**69.9**	10.7	5.02		1.14	
TM305	13	30.8	**25.3**	**36.3**	5.5	5.78		1.09	
					mean ±SD	4.70	0.76	1.06	0.05
Roche Elecsys & Cobas BME/BMR									
TM301	4	32.0	**26.2**	**37.8**	5.8	6.50		0.77	
TM302	4	18.2	**12.8**	**23.6**	5.4	6.54		0.80	
TM303	4	24.4	**19.0**	**29.8**	5.4	8.24		0.79	
TM304	4	39.6	**32.5**	**46.7**	7.1	6.24		0.76	
TM305	4	22.8	**17.4**	**28.2**	5.4	6.32		0.81	
					mean ±SD	6.77	0.83	0.79	0.02
Siemens Advia Centaur XP & CP COB/COC									
TM301	18	41.3	**33.9**	**48.7**	7.4	4.36		1.00	
TM302	18	22.7	**17.3**	**28.1**	5.4	4.89		1.00	
TM303	18	30.8	**25.3**	**36.3**	5.5	4.42		1.00	
TM304	18	52.1	**42.7**	**61.5**	9.4	3.99		1.00	
TM305	18	28.2	**22.8**	**33.6**	5.4	5.60		1.00	
					mean ±SD	4.65	0.62	1.00	0.00
Siemens Immulite 2000 DPD									
TM301	5	35.4	**29.0**	**41.8**	6.4	4.63		0.86	
TM302	5	18.1	**12.7**	**23.5**	5.4	5.52		0.80	
TM303	5	26.4	**21.0**	**31.8**	5.4	4.58		0.86	
TM304	5	45.6	**37.4**	**53.8**	8.2	4.10		0.88	
TM305	5	23.9	**18.5**	**29.3**	5.4	6.44		0.85	
					mean ±SD	5.06	0.93	0.85	0.03
Ortho Clinical Diag Vitros 5600 JJF									
TM301	3	26.5	**21.1**	**31.9**	5.4	5.36		0.69	
TM302	3	10.0	**4.6**	**15.4**	5.4	13.10		0.49	
TM303	3	19.0	**13.6**	**24.4**	5.4	9.47		0.66	
TM304	3	40.8	**33.5**	**48.1**	7.3	1.64		0.84	
TM305	3	18.0	**12.6**	**23.4**	5.4	2.61		0.69	
					mean ±SD	6.44	4.81	0.67	0.12
Tosoh AIA TOM									
TM301	4	47.5	**39.0**	**56.1**	8.6	11.01		1.15	
TM302	4	26.7	**21.3**	**32.1**	5.4	13.26		1.18	
TM303	4	35.9	**29.4**	**42.4**	6.5	13.06		1.17	
TM304	4	60.8	**49.9**	**71.7**	10.9	6.25		1.17	
TM305	4	32.8	**26.9**	**38.7**	5.9	9.33		1.16	
					mean ±SD	10.58	2.91	1.16	0.01

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Table 1 (cont.): 5-16 NYS Tumor Marker PT Summary for CA 125

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data	Method Bias Relative to All Method Median

Sample ID	N	All Method Median	Median % CV	Min %CV	Max %CV
TM301	52	41.3	5.36	4.36	11.01
TM302	51	22.7	6.54	3.74	13.26
TM303	52	30.8	7.43	4.42	13.06
TM304	52	52.1	5.02	1.64	6.25
TM305	52	28.2	5.78	2.61	9.33

Average	6.02
Allowable CV %	6.0
Allowable Error if >/= 30 U/ml (+/-) %	18.0
Allowable Error if < 30 U/ml (+/- U/ml)	5.4

Figure 1: CA 125 Method Comparison

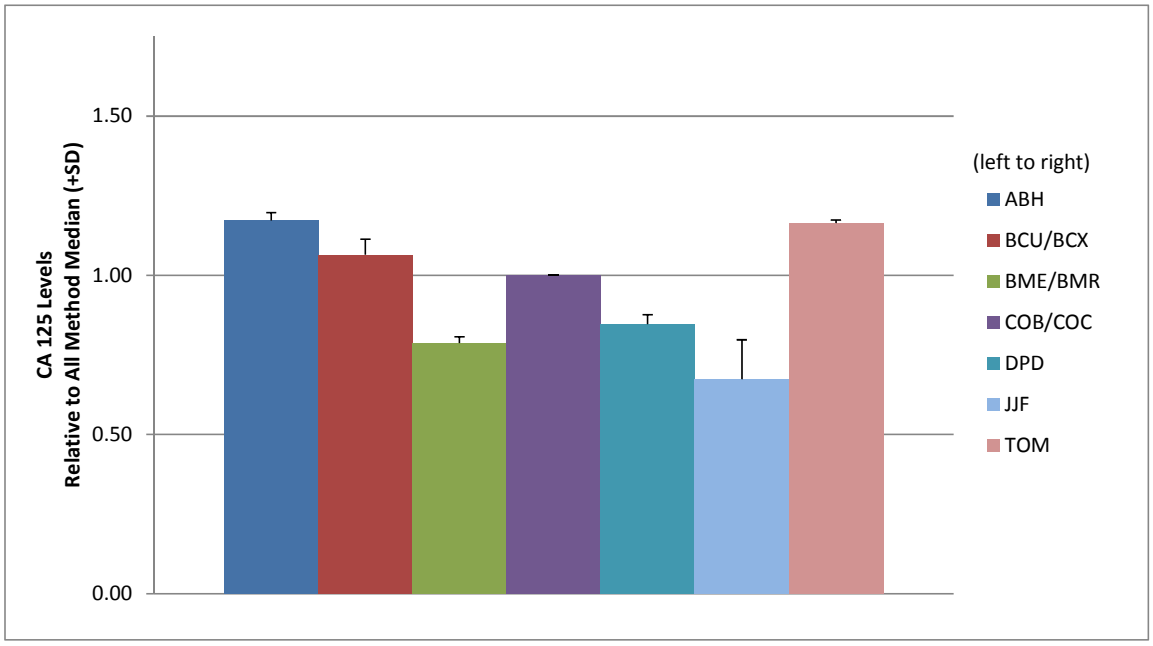

Table 2: 5-16 NYS Tumor Marker PT Summary for CA 19-9

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median	
Beckman Unicel & Access/2 BCU/BCX									
TM301	11	25.9	**21.2**	**30.6**	4.7	3.63		1.00	
TM302	12	47.7	**39.1**	**56.3**	8.6	8.99		1.00	
TM303	12	41.4	**33.9**	**48.9**	7.5	9.83		1.00	
TM304	10	59.1	**48.5**	**69.7**	10.6	2.91		1.00	
TM305	12	33.4	**27.4**	**39.4**	6.0	9.37		1.00	
					mean ±SD	6.95	3.38	1.00	0.00
Siemens Advia Centaur XP COB									
TM301	13	50.1	**41.1**	**59.1**	9.0	5.07		1.93	
TM302	13	96.5	**79.1**	**113.9**	17.4	4.67		2.02	
TM303	13	80.7	**66.2**	**95.2**	14.5	6.23		1.95	
TM304	13	117.2	**96.1**	**138.3**	21.1	6.46		1.98	
TM305	13	61.2	**50.2**	**72.2**	11.0	6.63		1.83	
					mean ±SD	5.81	0.88	1.94	0.07
Tosoh AIA TOM									
TM301	3	23.0	**18.9**	**27.1**	4.1	1.39		0.89	
TM302	3	34.5	**28.3**	**40.7**	6.2	1.54		0.72	
TM303	3	33.6	**27.6**	**39.6**	6.0	1.82		0.81	
TM304	3	40.2	**33.0**	**47.4**	7.2	1.49		0.68	
TM305	3	29.9	**24.5**	**35.3**	5.4	1.40		0.90	
					mean ±SD	1.53	0.17	0.80	0.10

Sample ID	N	All Method Median	Median % CV	Min %CV	Max %CV
TM301	**27**	**25.9**	**3.63**	**1.39**	**5.07**
TM302	**28**	**47.7**	**4.67**	**1.54**	**8.99**
TM303	**28**	**41.4**	**6.23**	**1.82**	**9.83**
TM304	**26**	**59.1**	**2.91**	**1.49**	**6.46**
TM305	**28**	**33.4**	**6.63**	**1.40**	**9.37**
		Average	**4.82**		

Allowable CV %	**6.0**
Allowable Error if >/= 20 U/ml (+/-) %	**18.0**
Allowable Error if < 20 U/ml (+/- U/ml)	**3.6**

Figure 2: CA 19-9 Method Comparison

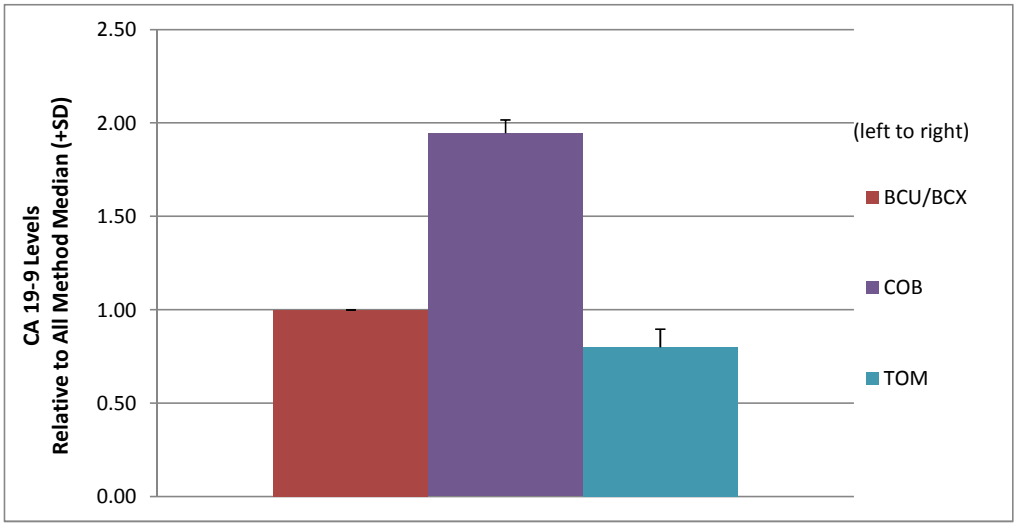

Table 3: 5-16 NYS Tumor Marker PT Summary for CA 15-3

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median	
Beckman Unicel & Access/2 BCU/BCX									
TM301	11	12.5	**10.3**	**14.8**	2.3	3.68		0.69	
TM302	11	20.3	**16.6**	**24.0**	3.7	5.07		0.70	
TM303	11	37.1	**30.4**	**43.8**	6.7	6.17		0.68	
TM304	11	34.8	**28.5**	**41.1**	6.3	7.90		0.69	
TM305	11	40.5	**33.2**	**47.8**	7.3	6.22		0.68	
					mean ±SD	5.81	1.56	0.69	0.01
Siemens Advia Centaur XP & CP COB/COC									
TM301	11	18.4	**15.1**	**21.7**	3.3	7.07		1.01	
TM302	11	30.1	**24.7**	**35.5**	5.4	4.62		1.04	
TM303	11	55.3	**45.3**	**65.3**	10.0	5.48		1.02	
TM304	11	51.5	**42.2**	**60.8**	9.3	5.71		1.02	
TM305	11	60.9	**49.9**	**71.9**	11.0	6.37		1.02	
					mean ±SD	5.85	0.93	1.02	0.01
Siemens Immulite 2000 DPD									
TM301	3	19.8	**16.2**	**23.4**	3.6	4.65		1.09	
TM302	3	32.7	**26.8**	**38.6**	5.9	7.58		1.13	
TM303	3	64.3	**52.7**	**75.9**	11.6	4.79		1.18	
TM304	3	60.6	**49.7**	**71.5**	10.9	7.26		1.20	
TM305	3	70.6	**57.9**	**83.3**	12.7	2.18		1.18	
					mean±SD	5.45	2.51	1.16	0.03

Sample ID	N	All Method Median	Median % CV	Min %CV	Max %CV
TM301	**25**	**18.4**	**4.65**	**3.68**	**7.07**
TM302	**25**	**30.1**	**5.07**	**4.62**	**7.58**
TM303	**25**	**55.3**	**5.48**	**4.79**	**6.17**
TM304	**25**	**51.5**	**7.26**	**5.71**	**7.90**
TM305	**25**	**60.9**	**6.22**	**2.18**	**6.37**
		Average	**5.74**		
		Allowable CV %	**6.0**		
		Allowable Error (+/-) %	**18.0**		

Figure 3: CA 15-3 Method Comparison

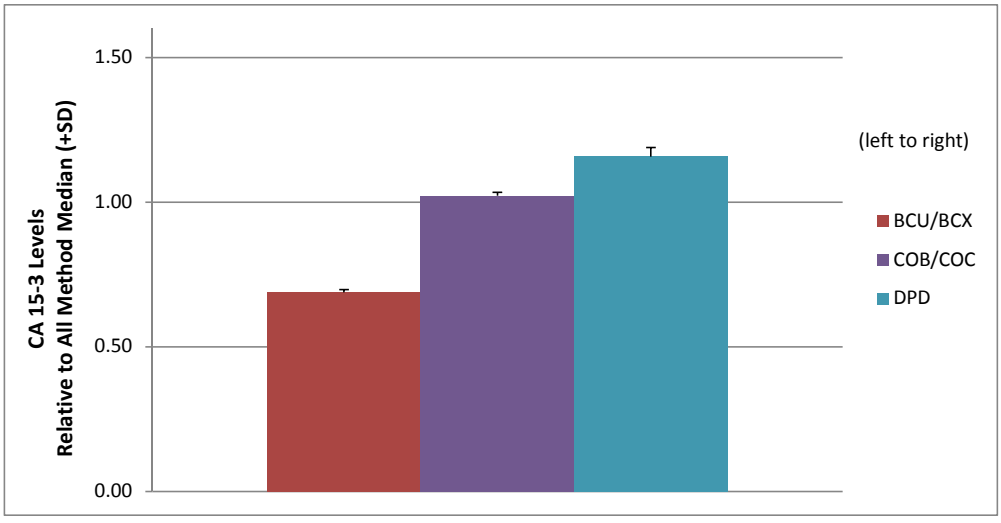

Table 4: 5-16 NYS Tumor Marker PT Summary for CA 27.29

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median	
Siemens Advia Centaur XP & CP COB/COC									
TM301	15	19.1	**11.8**	**26.5**	7.4	12.04		1.03	
TM302	15	36.0	**28.4**	**43.6**	7.6	9.78		1.11	
TM303	15	76.1	**60.1**	**92.1**	16.0	6.61		1.17	
TM304	15	70.9	**56.0**	**85.8**	14.9	6.56		1.17	
TM305	15	85.7	**67.7**	**103.7**	18.0	6.31		1.20	
					mean ±SD	8.26	2.55	1.14	0.07
Tosoh AIA TOM									
TM301	4	18.1	**10.8**	**25.5**	7.4	5.91		0.97	
TM302	4	29.0	**21.7**	**36.4**	7.4	5.34		0.89	
TM303	4	53.6	**42.3**	**64.9**	11.3	7.93		0.83	
TM304	4	49.9	**39.4**	**60.4**	10.5	7.78		0.83	
TM305	4	57.3	**45.3**	**69.3**	12.0	2.91		0.80	
					mean ±SD	5.98	2.05	0.86	0.07

Sample ID	N	All Method Median		Median % CV	Min %CV	Max %CV
TM301	**19**	**18.6**		**8.98**	**5.91**	**12.04**
TM302	**19**	**32.5**		**7.56**	**5.34**	**9.78**
TM303	**19**	**64.9**		**7.27**	**6.61**	**7.93**
TM304	**19**	**60.4**		**7.17**	**6.56**	**7.78**
TM305	**19**	**71.5**		**4.61**	**2.91**	**6.31**
			Average	**7.12**		
			Allowable CV %	**7.0**		
			Allowable Error if >/= 35 U/ml (+/-) %	**21.0**		
			Allowable Error if < 35 U/ml (+/- U/ml)	**7.35**		

Figure 4: CA 27.29 Method Comparison

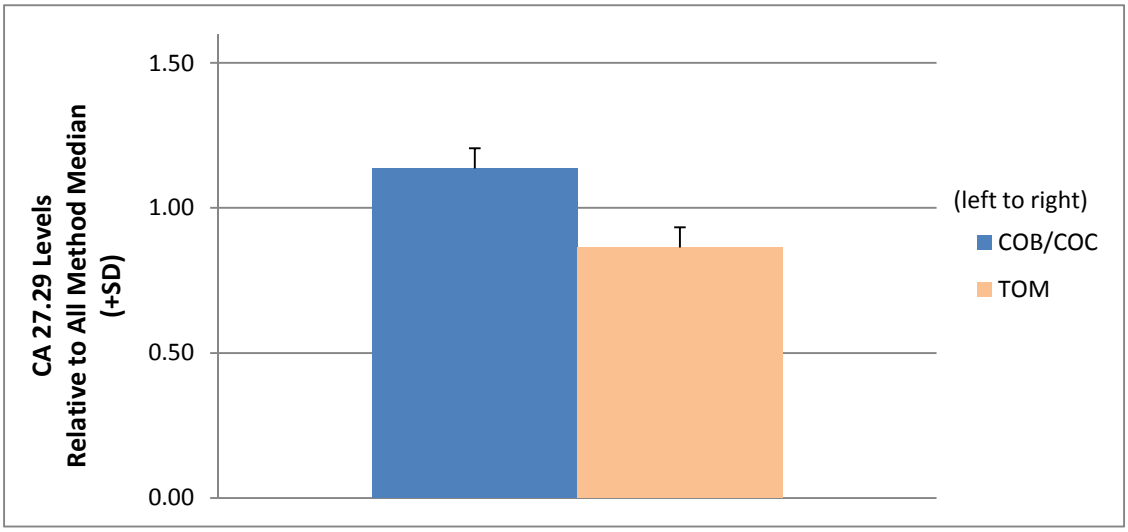

Table 5: 5-16 NYS Tumor Marker PT Summary for CEA

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median	
Abbott Architect ABH									
TM301	9	15.1	**12.4**	**17.8**	2.7	6.23		1.10	
TM302	9	15.1	**12.4**	**17.8**	2.7	5.83		1.10	
TM303	9	11.8	**9.7**	**13.9**	2.1	6.36		1.08	
TM304	9	9.9	**8.1**	**11.7**	1.8	7.78		1.07	
TM305	9	7.0	**5.7**	**8.3**	1.3	5.57		1.10	
					mean ±SD	6.35	0.86	1.09	0.01
Beckman Unicel & Access/2 BCU/BCX									
TM301	21	13.9	**11.4**	**16.4**	2.5	5.61		1.01	
TM302	21	14.1	**11.6**	**16.6**	2.5	5.74		1.03	
TM303	21	10.9	**8.9**	**12.9**	2.0	6.15		1.00	
TM304	21	9.3	**7.6**	**11.0**	1.7	5.05		1.01	
TM305	21	6.5	**5.3**	**7.7**	1.2	6.46		1.02	
					mean ±SD	5.80	0.54	1.01	0.01
Roche Elecsys & Cobas BME/BMR									
TM301	4	13.1	**10.7**	**15.5**	2.4	3.59		0.96	
TM302	4	13.1	**10.7**	**15.5**	2.4	2.82		0.96	
TM303	4	10.2	**8.4**	**12.0**	1.8	2.75		0.94	
TM304	4	8.8	**7.2**	**10.4**	1.6	3.30		0.95	
TM305	4	6.2	**5.1**	**7.3**	1.1	4.03		0.98	
					mean ±SD	3.30	0.54	0.96	0.01
Siemens Advia Centaur XP & CP COB/COC									
TM301	18	13.5	**11.1**	**15.9**	2.4	7.63		0.99	
TM302	18	13.3	**10.9**	**15.7**	2.4	4.81		0.97	
TM303	18	10.5	**8.6**	**12.4**	1.9	7.43		0.96	
TM304	18	8.5	**7.0**	**10.0**	1.5	7.76		0.92	
TM305	18	6.1	**5.0**	**7.2**	1.1	8.85		0.96	
					mean ±SD	7.30	1.50	0.96	0.02
Siemens Immulite 2000 DPD									
TM301	3	17.9	**14.7**	**21.1**	3.2	10.17		1.31	
TM302	3	16.2	**13.3**	**19.1**	2.9	8.09		1.18	
TM303	3	12.4	**10.2**	**14.6**	2.2	3.95		1.14	
TM304	3	10.2	**8.4**	**12.0**	1.8	11.86		1.10	
TM305	3	7.1	**5.8**	**8.4**	1.3	13.80		1.12	
						9.57	3.78	1.17	0.08
Siemens Dimension Vista DUV									
TM301	16	13.1	**10.7**	**15.5**	2.4	2.21		0.96	
TM302	16	13.2	**10.8**	**15.6**	2.4	2.73		0.96	
TM303	16	9.7	**8.0**	**11.4**	1.7	3.20		0.89	
TM304	16	8.1	**6.6**	**9.6**	1.5	2.47		0.88	
TM305	16	5.4	**4.4**	**6.4**	1.0	3.70		0.85	
					mean ±SD	2.86	0.59	0.91	0.05
Ortho Clinical Diag Vitros 5600 JJF									
TM301	6	12.8	**10.5**	**15.1**	2.3	7.27		0.93	
TM302	6	13.1	**10.7**	**15.5**	2.4	5.11		0.96	
TM303	5	10.9	**8.9**	**12.9**	2.0	4.50		1.00	
TM304	6	9.2	**7.5**	**10.9**	1.7	8.04		0.99	
TM305	6	5.9	**4.8**	**7.0**	1.1	11.53		0.93	
						7.29	2.79	0.96	0.03

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Table 5 (cont.): 5-16 NYS Tumor Marker PT Summary for CEA

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median	
Tosoh AIA TOM									
TM301	5	20.2	**16.6**	**23.8**	3.6	21.78		1.47	
TM302	5	21.7	**17.8**	**25.6**	3.9	5.21		1.58	
TM303	5	18.2	**14.9**	**21.5**	3.3	8.19		1.67	
TM304	5	14.9	**12.2**	**17.6**	2.7	6.04		1.61	
TM305	5	11.6	**9.5**	**13.7**	2.1	18.28		1.83	
					mean ±SD	11.90	7.60	1.63	0.13

Sample ID	N	All Method Median	Median % CV	Min %CV	Max %CV
TM301	**82**	**13.7**	**6.75**	**2.21**	**21.78**
TM302	**82**	**13.7**	**5.16**	**2.73**	**8.09**
TM303	**81**	**10.9**	**5.32**	**2.75**	**8.19**
TM304	**82**	**9.3**	**6.90**	**2.47**	**11.86**
TM305	**82**	**6.4**	**7.66**	**3.70**	**18.28**

Average	**6.36**
Allowable CV %	**6.0**
Allowable Error if >/= 5 ng/ml (+/-) %	**18.0**
Allowable Error if < 5 ng/ml (+/- ng/ml)	**0.9**

Figure 5: CEA Method Comparison

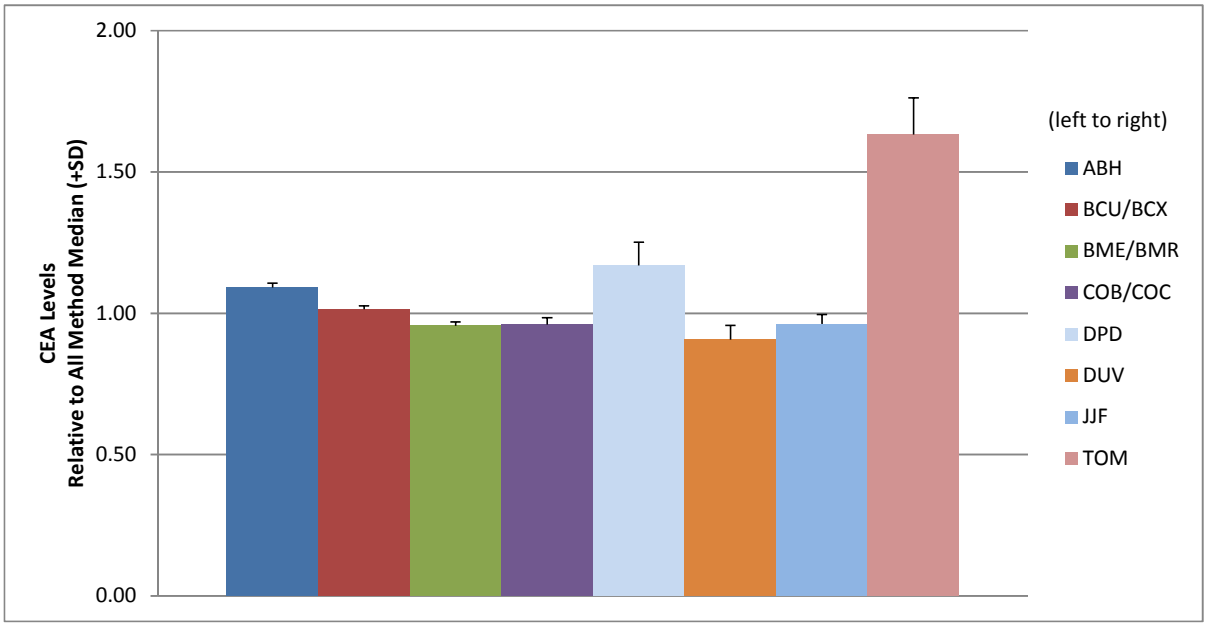

Table 6: 5-16 NYS Tumor Marker PT Summary for AFP

Method Method Code Sample ID	N	Target (Mean)	Lower Limit Based on 3SD	Upper Limit Based on 3SD	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median		Method Bias Relative to IS Target	
Abbott Architect ABH											
TM301	4	5.8	**4.7**	**6.9**	1.1	6.55		0.83		1.00	
TM302	4	15.5	**15.2**	**15.8**	0.3	0.65		0.90		1.03	
TM303	4	25.8	**24.4**	**27.2**	1.4	1.86		0.93		1.05	
TM304	4	37.3	**34.5**	**40.1**	2.8	2.52		0.93		1.05	
TM305	4	49.5	**45.4**	**53.6**	4.1	2.75		0.95		1.06	
					mean ±SD	2.86	2.22	0.91	0.05	1.04	0.03
Beckman Unicel & Access/2 BCU/BCX											
TM301	12	6.0	**5.0**	**7.0**	1.0	5.50		0.86		1.04	
TM302	12	14.8	**11.5**	**18.1**	3.3	7.50		0.86		0.99	
TM303	12	24.0	**19.5**	**28.5**	4.5	6.29		0.86		0.98	
TM304	12	33.8	**29.2**	**38.4**	4.6	4.50		0.85		0.96	
TM305	12	44.5	**37.2**	**51.8**	7.3	5.48		0.85		0.96	
					mean ±SD	5.85	1.12	0.86	0.01	0.98	0.03
Siemens Advia Centaur XP & CP COB/COC											
TM301	13	8.6	**7.0**	**10.3**	1.7	6.40		1.23		1.49	
TM302	13	20.4	**16.7**	**24.1**	3.7	6.08		1.18		1.36	
TM303	13	31.8	**25.8**	**37.8**	6.0	6.29		1.14		1.30	
TM304	13	45.0	**36.5**	**53.5**	8.5	6.29		1.13		1.27	
TM305	13	58.9	**48.8**	**69.0**	10.1	5.70		1.13		1.27	
					mean ±SD	6.15	0.27	1.16	0.04	1.34	0.09
Siemens Immulite 1000 & 2000 DPB/DPD											
TM301	3	7.0	**5.2**	**8.8**	1.8	8.71		1.00		1.21	
TM302	3	19.0	**11.7**	**26.3**	7.3	12.84		1.10		1.26	
TM303	3	29.8	**25.0**	**34.6**	4.8	5.40		1.07		1.22	
TM304	3	42.2	**35.7**	**48.7**	6.5	5.14		1.06		1.19	
TM305	3	54.9	**48.1**	**61.7**	6.8	4.13		1.05		1.18	
					mean ±SD	7.25	3.57	1.06	0.04	1.21	0.03
Siemens Dimension Vista DUV											
TM301	4	6.3	**6.0**	**6.6**	0.3	1.59		0.90		1.09	
TM302	4	15.6	**14.2**	**17.0**	1.4	2.95		0.90		1.04	
TM303	4	25.3	**24.4**	**26.2**	0.9	1.19		0.91		1.03	
TM304	4	36.2	**34.3**	**38.1**	1.9	1.71		0.91		1.02	
TM305	4	46.6	**45.3**	**48.0**	1.4	0.97		0.89		1.00	
					mean ±SD	1.68	0.77	0.90	0.01	1.04	0.03
Ortho Clinical Diag Vitros 5600 JJF											
TM301	3	7.1	**5.4**	**8.8**	1.7	8.17		1.01		1.23	
TM302	3	17.4	**14.7**	**20.1**	2.7	5.17		1.01		1.16	
TM303	3	28.1	**24.0**	**32.2**	4.1	4.91		1.01		1.15	
TM304	3	40.4	**34.8**	**46.0**	5.6	4.63		1.01		1.14	
TM305	3	52.8	**46.7**	**58.9**	6.1	3.84		1.01		1.14	
					mean±SD	5.35	1.66	1.01	0.00	1.16	0.04
Tosoh AIA TOM											
TM301	3	7.0	**6.0**	**8.0**	1.0	4.57		1.00		1.21	
TM302	3	17.1	**15.9**	**18.3**	1.2	2.34		0.99		1.14	
TM303	3	27.6	**25.7**	**29.5**	1.9	2.32		0.99		1.13	
TM304	3	39.5	**38.2**	**40.8**	1.3	1.06		0.99		1.12	
TM305	3	51.4	**47.8**	**55.0**	3.6	2.35		0.99		1.11	
					mean ±SD	2.53	1.27	0.99	0.01	1.14	0.04

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Table 6 (cont.): 5-16 NYS Tumor Marker PT Summary for AFP

Sample ID	N	All Method Median	IS based Target	SD	Median % CV	Min %CV	Max %CV	All Method Median/ IS Target
TM301	44	7.0	5.8	0.68	5.95	1.59	8.71	1.21
TM302	44	17.3	15.0	2.61	4.10	0.65	12.84	1.15
TM303	44	27.9	24.5	4.52	4.09	1.19	6.29	1.14
TM304	44	40.0	35.4	6.57	4.02	1.06	6.29	1.13
TM305	44	52.1	46.5	8.52	3.64	0.97	5.70	1.12
				Average	4.36		mean ±SD	1.15 0.04

Allowable Error = +/-3SD

Figure 6: AFP Method Comparison

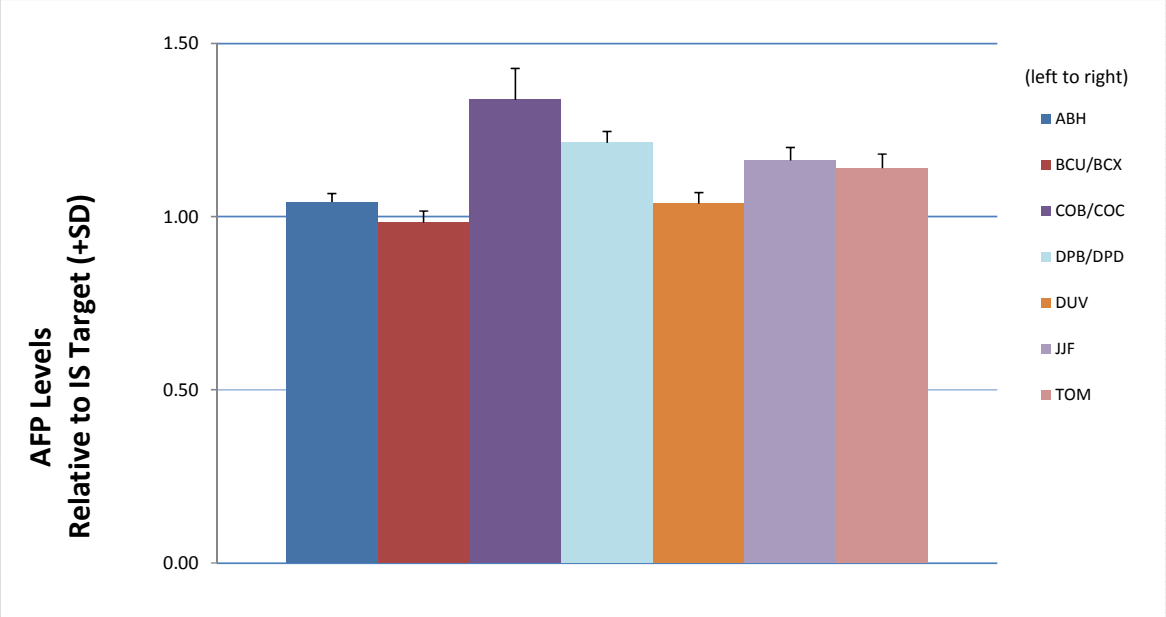

Table 7: 5-16 NYS Tumor Marker PT Summary for PSA

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median		Method Bias Relative to IS Target	
Abbott Architect ABH											
TM301	12	12.99	**10.65**	**15.33**	2.34	3.23		1.01		1.14	
TM302	12	10.25	**8.41**	**12.10**	1.85	3.80		1.01		1.16	
TM303	12	6.85	**5.62**	**8.08**	1.23	4.23		1.00		1.15	
TM304	12	3.91	**3.21**	**4.61**	0.70	4.60		1.01		1.16	
TM305	12	0.79	**0.65**	**0.93**	0.14	6.33		1.00		1.08	
					mean ±SD	4.44	1.17	1.01	0.01	1.14	0.03
Beckman Unicel & Access/2 (Hybritech Calibration) BCU/BCX (HYB)											
TM301	32	14.46	**11.86**	**17.06**	2.60	5.67		1.12		1.27	
TM302	32	11.32	**9.28**	**13.36**	2.04	4.68		1.12		1.28	
TM303	32	7.56	**6.20**	**8.92**	1.36	5.69		1.11		1.26	
TM304	32	4.23	**3.47**	**4.99**	0.76	4.96		1.09		1.25	
TM305	32	0.85	**0.70**	**1.00**	0.15	4.71		1.08		1.16	
					mean ±SD	5.14	0.50	1.10	0.02	1.25	0.05
Roche Elecsys & Cobas BME/BMR											
TM301	10	12.61	**10.34**	**14.88**	2.27	5.31		0.98		1.11	
TM302	10	9.81	**8.04**	**11.58**	1.77	4.49		0.97		1.11	
TM303	10	6.63	**5.44**	**7.82**	1.19	5.28		0.97		1.11	
TM304	10	3.77	**3.09**	**4.45**	0.68	4.77		0.97		1.12	
TM305	10	0.78	**0.64**	**0.92**	0.14	6.41		0.99		1.07	
					mean ±SD	5.25	0.74	0.98	0.01	1.10	0.02
Siemens Advia Centaur XP & CP COB/COC											
TM301	23	11.60	**9.51**	**13.69**	2.09	6.03		0.90		1.02	
TM302	22	8.91	**7.31**	**10.51**	1.60	4.38		0.88		1.01	
TM303	23	6.02	**4.94**	**7.10**	1.08	5.81		0.88		1.01	
TM304	23	3.45	**2.83**	**4.07**	0.62	4.35		0.89		1.02	
TM305	22	0.72	**0.59**	**0.85**	0.13	5.56		0.91		0.99	
					mean ±SD	5.23	0.81	0.89	0.01	1.01	0.01
Siemens Immulite 1000, 2000 - Original Pack DPB, DPD (DP5)											
TM301	6	12.52	**10.27**	**14.77**	2.25	3.67		0.97		1.10	
TM302	6	9.53	**7.81**	**11.25**	1.72	6.82		0.94		1.08	
TM303	6	6.43	**5.27**	**7.59**	1.16	7.93		0.94		1.08	
TM304	6	3.69	**3.03**	**4.35**	0.66	11.38		0.95		1.09	
TM305	5	0.70	**0.57**	**0.83**	0.13	5.71		0.89		0.96	
					mean ±SD	7.10	2.86	0.94	0.03	1.06	0.06
Siemens Dimension RxL Max, Xpand Plus, EXL DUD/DUX											
TM301	13	14.42	**11.82**	**17.02**	2.60	4.16		1.12		1.26	
TM302	13	11.03	**9.04**	**13.02**	1.99	3.90		1.09		1.25	
TM303	13	7.44	**6.10**	**8.78**	1.34	5.11		1.09		1.24	
TM304	13	4.18	**3.43**	**4.93**	0.75	5.02		1.07		1.24	
TM305	13	0.86	**0.71**	**1.01**	0.15	6.98		1.09		1.18	
					mean±SD	5.03	1.21	1.09	0.02	1.23	0.03
Siemens Dimension Vista DUV											
TM301	17	12.98	**10.64**	**15.32**	2.34	2.23		1.01		1.14	
TM302	17	10.20	**8.36**	**12.04**	1.84	2.25		1.01		1.15	
TM303	17	6.82	**5.59**	**8.05**	1.23	2.49		1.00		1.14	
TM304	17	3.89	**3.19**	**4.59**	0.70	2.31		1.00		1.15	
TM305	17	0.79	**0.65**	**0.93**	0.14	2.53		1.00		1.08	
					mean ±SD	2.37	0.14	1.00	0.00	1.13	0.03

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Table 7 (cont.): 5-16 NYS Tumor Marker PT Summary for PSA

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median		Method Bias Relative to IS Target	
Ortho Clinical Diag Vitros ECi/ECiQ & 5600 JJC/JJF											
TM301	11	11.19	**9.18**	**13.20**	2.01	5.81		0.87		0.98	
TM302	11	8.60	**7.05**	**10.15**	1.55	5.93		0.85		0.97	
TM303	10	5.90	**4.84**	**6.96**	1.06	5.42		0.87		0.99	
TM304	11	3.43	**2.81**	**4.05**	0.62	6.71		0.88		1.01	
TM305	11	0.59	**0.48**	**0.70**	0.11	10.17		0.75		0.81	
					mean ±SD	6.81	1.94	0.84	0.05	0.95	0.08
Tosoh AIA TOM											
TM301	5	12.88	**10.56**	**15.20**	2.32	4.74		1.00		1.13	
TM302	5	10.10	**8.28**	**11.92**	1.82	6.73		1.00		1.14	
TM303	5	6.83	**5.60**	**8.06**	1.23	6.15		1.00		1.14	
TM304	5	3.91	**3.21**	**4.61**	0.70	6.14		1.01		1.16	
TM305	5	0.81	**0.66**	**0.96**	0.15	7.41		1.03		1.11	
					mean ±SD	6.23	0.99	1.01	0.01	1.14	0.02

Sample ID	N	All Method Median	IS based Target	SD		Median % CV	Min %CV	Max % CV		All Method Median/ IS Target	
TM301	**129**	**12.88**	**11.40**	**0.67**		**4.74**	**2.23**	**6.03**		**1.13**	
TM302	**128**	**10.10**	**8.85**	**0.58**		**4.49**	**2.25**	**6.82**		**1.14**	
TM303	**128**	**6.82**	**5.98**	**0.29**		**5.42**	**2.49**	**7.93**		**1.14**	
TM304	**129**	**3.89**	**3.38**	**0.15**		**4.96**	**2.31**	**11.38**		**1.15**	
TM305	**127**	**0.79**	**0.73**	**0.08**		**6.33**	**2.53**	**10.17**		**1.08**	
					Average	**5.19**			mean ±SD	**1.13**	0.03
					Allowable CV %	**6.00**					
					Allowable Error (+/-)%	**18.0**					

Figure 7: PSA Method Comparison

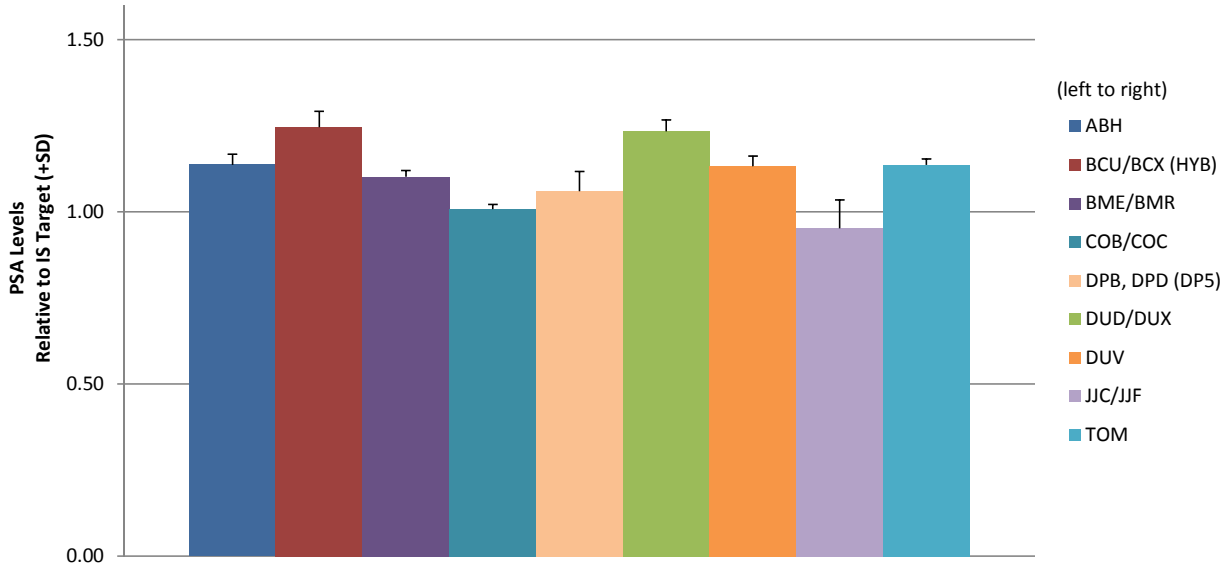

Table 8: 5-16 NYS Tumor Marker PT Summary for Free PSA

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median		Method Bias Relative to IS Target		% free PSA (calculated)
Abbott Architect ABH												
TM301	5	1.70	**1.39**	**2.01**	0.31	3.65		1.09		1.20		13.1%
TM302	5	1.26	**1.03**	**1.49**	0.23	4.21		1.10		1.19		12.3%
TM303	5	0.82	**0.67**	**0.97**	0.15	3.54		1.09		1.16		12.0%
TM304	5	0.45	**0.36**	**0.54**	0.09	3.11		1.05		1.16		11.5%
TM305	4	0.09	**0.00**	**0.18**	0.09	0.00		1.00		1.29		11.4%
					mean ±SD	2.90	1.67	1.07	0.04	1.20	0.05	
Beckman Unicel & Access/2 (Hybritech Calibration) BCU/BCX (HYB)												
TM301	17	1.90	**1.56**	**2.24**	0.34	6.05		1.22		1.34		13.1%
TM302	17	1.47	**1.21**	**1.73**	0.26	4.22		1.28		1.39		13.0%
TM303	16	1.01	**0.83**	**1.19**	0.18	2.28		1.35		1.43		13.4%
TM304	17	0.56	**0.46**	**0.66**	0.10	5.89		1.30		1.45		13.2%
TM305	17	0.12	**0.03**	**0.21**	0.09	11.67		1.33		1.72		14.1%
					mean ±SD	6.02	3.51	1.30	0.05	1.47	0.15	
Siemens Immulite 2000 DPD												
TM301	7	1.42	**1.16**	**1.68**	0.26	5.35		0.91		1.00		11.3%
TM302	7	1.04	**0.85**	**1.23**	0.19	6.35		0.90		0.98		10.9%
TM303	7	0.68	**0.56**	**0.80**	0.12	6.32		0.91		0.96		10.6%
TM304	7	0.41	**0.32**	**0.50**	0.09	6.34		0.95		1.06		11.1%
TM305	7	0.09	**0.00**	**0.18**	0.09	10.00		1.00		1.29		12.9%
					mean ±SD	6.87	1.80	0.93	0.04	1.06	0.13	
Siemens Dimension Vista DUV												
TM301	7	1.34	**1.10**	**1.58**	0.24	2.39		0.86		0.95		10.3%
TM302	7	1.01	**0.83**	**1.19**	0.18	2.38		0.88		0.96		9.9%
TM303	7	0.68	**0.56**	**0.80**	0.12	2.50		0.91		0.96		10.0%
TM304	7	0.38	**0.29**	**0.47**	0.09	4.21		0.88		0.98		9.8%
TM305	5	0.08	**0.00**	**0.17**	0.09	0.00		0.89		1.15		10.1%
					mean ±SD	2.29	1.50	0.88	0.02	1.00	0.08	

Sample ID	N	All Method Median	IS based Targ	SD		Median % CV	All Method Median/ IS Target		% free PSA calculated from IS Targets	Measured %fPSA
TM301	**36**	**1.56**	**1.41**	**0.10**		**4.50**	**1.10**		**12.4%**	**12.0%**
TM302	**36**	**1.15**	**1.06**	**0.07**		**4.21**	**1.09**		**11.9%**	**11.5%**
TM303	**35**	**0.75**	**0.70**	**0.04**		**3.02**	**1.06**		**11.8%**	**11.5%**
TM304	**36**	**0.43**	**0.39**	**0.02**		**5.05**	**1.11**		**11.4%**	**11.4%**
TM305	**33**	**0.09**	**0.07**	**0.01**		**5.00**	**1.29**		**9.5%**	**12.2%**
							mean	±SD		
					Average	**4.36**	**1.13**	0.09		

Allowable CV %	**6.0**
Allowable Error if >/= 0.5 ng/ml (+/-)%	**18.0**
Allowable Error if < 0.5 ng/ml (+/- ng/ml)	**0.09**

Figure 8: Free PSA Method Comparison

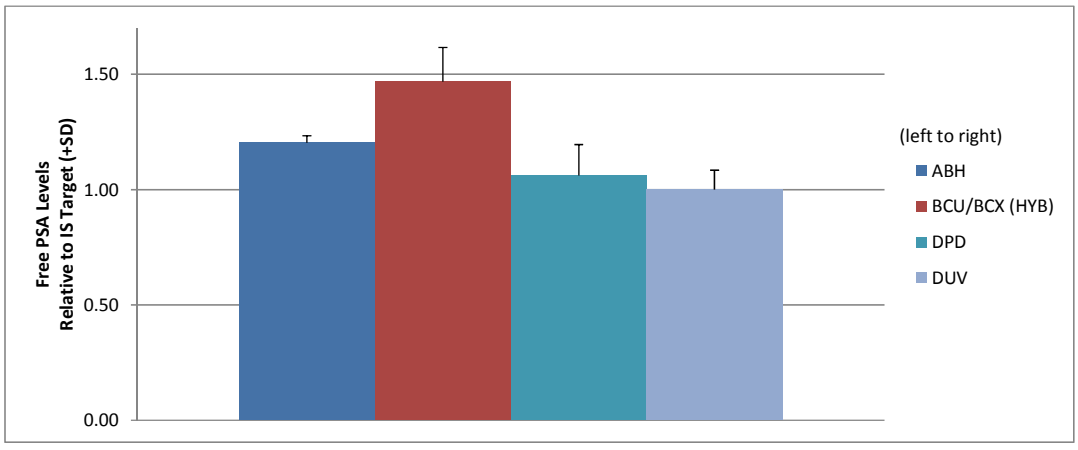

Table 9: 5-16 NYS Tumor Marker PT Summary for Complexed PSA

Method Method Code Sample ID	N	Target (Mean)	Lower Limit	Upper Limit	Dmax (+/-)	%CV of Raw Data		Method Bias Relative to All Method Median	
Siemens Advia Centaur XP & CP COB/COC									
TM301	4	10.4	**8.5**	**12.3**	1.9	9.23		1.00	
TM302	4	8.3	**6.8**	**9.7**	1.5	0.97		1.00	
TM303	4	5.7	**4.7**	**6.7**	1.0	6.87		1.00	
TM304	4	3.2	**2.6**	**3.8**	0.6	12.81		1.00	
TM305	3	0.6	**0.5**	**0.7**	0.1	0.00		1.00	
					mean ±SD	5.98	5.45	1.00	0.00

Sample ID	N	All Method Median		Median % CV
TM301	**4**	**10.4**		**9.23**
TM302	**4**	**8.3**		**0.97**
TM303	**4**	**5.7**		**6.87**
TM304	**4**	**3.2**		**12.81**
TM305	**3**	**0.6**		**0.00**
			Average	**7.47**
			Allowable CV %	**6.0**
			Allowable Error (+/-)%	**18.0**