



Educational Discussion: Prostate Specific Antigen Reporting

2017-A Ligand General Survey (K)

Due to a concern about how low-end prostate-specific antigen (PSA) results are reported (e.g., in post-prostatectomy patients), challenge K-02 of K-A 2017 Survey was not spiked with PSA. According to best laboratory practice, participants should have reported 1) a numeric value or 2) a “<” along with a numeric value that corresponded to the laboratory’s lower limit of reporting. In package inserts, each manufacturer provides a limit of detection (LoD) and usually a limit of quantitation (LoQ) to guide laboratories in how they should be reporting low-end PSA results.

Lower Limits of Measurement¹

Limit of Blank (LoB) The highest apparent analyte concentration expected to be found when replicates of a blank sample containing no analyte are tested
($LoB = \text{mean}_{\text{blank}} + 1.65 * SD_{\text{blank}}$).

Limit of Detection (LoD) The lowest analyte concentration likely to be reliably distinguished from the LoB and at which detection is feasible. LoD is determined by utilizing both the measured LoB and test replicates of a sample known to contain a low concentration of analyte
($LoD = LoB + 1.65 * SD_{\text{low concentration sample}}$).

Limit of Quantitation (LoQ) The lowest concentration at which the analyte can not only be reliably detected but at which some predefined goals for bias and imprecision are met. The LoQ may be equivalent to the LoD, or it could be at a much higher concentration.

Because there are no universally accepted guidelines for clinical reporting limits of PSA, we believe there is a significant opportunity for clinical laboratories to harmonize the reporting of low-end PSA results. As laboratories are providing quantitative results, it is our opinion that the LoQ is the most appropriate lower limit of measurement that should be reported. The LoQ included in package inserts tend to be the concentration at which repeated measurements result in a coefficient of variation below some quality target. However, because there are no universally accepted guidelines, this quality target varies from manufacturer to manufacturer, generally ranging from 15% to 30%. Furthermore, the samples used to determine the LoQ may not be patient samples and therefore will not include additional random error that may be present in real samples. Finally, manufacturer



protocols for lower limits of measurement may differ from those recommended above, or from CLSI guideline EP17-A2. Therefore, another reasonable choice is to simply use a clinical lower limit of 0.1 ng/mL.²

With these considerations in mind, we included sample K-02 to be able to evaluate the lower limits of reporting used by laboratories. The table includes the LoD and LoQ values included in package inserts for different manufacturers. We included only peer groups with greater than 30 laboratories in this analysis. We then determined what percentage of laboratories in a given peer group reported a numeric value (with or without a '<') that was below either the manufacturer's 1) LoD or 2) LoQ. For example, if a manufacturer's LoD was 0.05 ng/mL, then laboratories reporting a value of 0.04 ng/mL or lower would be considered to be reporting under the LoD. Because only 2 decimal points were allowed to be reported by participants on the proficiency testing result form, we compared laboratory results to LoDs and LoQs that were truncated to two decimal places. We also included a column displaying what percentage of laboratories reported a value of zero, which is not good laboratory practice as each instrument should have a non-zero lower reportable limit. However, for those peers with an LoD of 0.008 ng/mL, reporting zero may have been reasonable because of the 2 decimal place reporting restriction. As can be seen in the table, a very large percentage of laboratories reported below the LoQ.

We recognize that some laboratories will have determined their own LoD or LoQ, which may differ from their manufacturer's package insert. But in all likelihood, these values will not be very different and typically *higher*, as manufacturer LoD and LoQ calculations may be performed on manufactured samples, and not patient samples that might cause additional dispersion of results.

These Proficiency Testing (PT) samples follow all of the existing CLIA requirements regarding PT processes, i.e., treat these PT samples as you would routine patient samples – both in terms of analysis and reporting. For example, if you report values as <0.1 ng/mL for patients that is how you should report the PT samples. Laboratories are encouraged to review how they report low PSA concentrations and ensure they are in accordance with current recommendations. Lastly, communication with providers about the definitions of lower limits of measurement is essential in appropriately utilizing PSA testing results.



Percentage of Laboratories Reporting Below the Manufacturers' Lower Limits of Measurement

Manufacturer	# Labs	LoD (ng/mL)	LoQ (ng/mL)	Labs reporting the value '0'	Labs reporting under the LoD	Labs reporting under the LoQ
ABBOTT ARCHITECT i	396	0.008	0.05	36.6%	36.6%	69.2%
BECKMAN ACCESS/2	178	0.008	0.019	47.2%	47.2%	47.2%
BECKMAN UNICEL Dxl	339	0.008	0.019	24.8%	24.8%	24.8%
ROCHE e411/ELECSYS	66	0.011	0.03	1.5%	1.5%	71.2%
ROCHE e600 SER/E170	547	0.014	0.03	1.1%	1.1%	75.7%
SIEMENS ADV CNTR XP/XPT	271	0.01	*	1.1%	1.1%	*
SIEMENS DIMENSION VISTA	278	0.01	0.01	0.0%	0.0%	0.0%
SIEMENS DIMENSION HM	129	0.05	0.13	7.0%	19.3%	38.8%
SIEMENS IMMUL 2000/XPi	35	0.045	0.05	2.9%	5.7%	11.4%
VITROS 3600,5600,ECi/ECiQ	273	0.064	0.1	1.5%	4.0%	87.5%

* Siemens Advia Centaur XP/XPT does not provide a LoQ in the package insert
Table includes peer groups with over 30 laboratories

Summary statistics (including all laboratories from all peer groups)

Total: 2,642 responses

Reporting a '<' with a specific number: 1,536 (range 0 to 50.08 ng/mL)

Reporting a numeric between 0.01 and 0.2 ng/mL: 715

Reporting a numeric over 0.2 ng/mL: 16 (range 0.21 ng/mL to 21.76 ng/mL)

Reporting the numeric '0': 327 responses

Reporting '<' without a specific number: 47

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1. Armbruster DA, Pry T. Limit of blank, limit of detection and limit of quantitation. *Clin Biochem Rev.* 2008;29 Suppl 1(August):S49-52. doi:citeulike-article-id:3416410.
2. Penson D. Follow-up surveillance during and after treatment for prostate cancer. *UpToDate Waltham, MA (accessed June 2, 2017).*