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Clinical Impact of APS Selection, Analytical Performance Specifications, in the Diagnosis and Monitoring of Renal Profile

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ABSTRACT

Chronic kidney disease (CKD) is one of the rapidly growing kidney complications in U. S. citizens. The purpose of this study is to affect the calculation of the sigma metric in laboratory settings based on the analytical performance specification (APS), given its influence. In our investigation, we look into various levels of APS and their impact on different test performance metrics. The findings suggest that the appropriate sigma metric calculation emphasizes the laboratory test quality as it is within the laboratory performing the tests. Laboratory performance metrics are key for achieving the testing's precision, accuracy, and control standards. The diagnostic accuracy and reliability depend on how optimally APS values are selected relative to clinically significant target values. This study aims to underscore selectively tailored APS values for clinically specified targets so that not only accuracy but also precision of diagnostics is achieved. Laboratory practices and patient safety are improved by underscoring APS's involvement in sigma metric calculations as a control improvement strategy. It was noted that selecting APS needs integration into the logic of planning clinical laboratory quality management systems.

INTRODUCTION

Chronic kidney disease (CKD) is one of the rapidly growing kidney complications in U. S. citizens. Proper management of CKD is critical and requires timely evaluation, accurate diagnosis, and effective treatment. Hence, advanced medical devices for the treatment of CKD are in high demand (Ceriotti *et al.,* 2024). There are several methods for monitoring CKD, incorporating a range of imaging scan units and analysis systems that provide information about urine and blood and physiometrical, biochemical, and cellular analysis. To test the renal profile, which includes monitoring serum creatinine levels, blood urea nitrogen (BUN), electrolytes, and urine albumin, several tests, and clinical description standards are required to meet analytical sensitivity and specificity needs for acute or chronic kidney issues the patient may have. The profile also estimates losses of urine protein and albumin, which are essential for confirming and differentiating CKD and classifying the stage of the disease syllabus(Brown, 2023; Hegazy, 2024; Onyango *et al.*). Monitoring CKD has a strong clinical focus (Braga & Panteghini, 2021). Notifications sent to clinicians help prevent overworking with checklist activities or unimportant tasks like solving fundamental methodological issues, which assist in controlling the timeline progress and benchmarks like intervals from enrollment and age-based milestones (Ceriotti *et al.,* 2024). Moreover, the calculation of certain essential parameters aids in the prevention of certain crucial pitfalls. This study aims to assess how varying Analytical Performance Specification (APS) values affect sigma metrics. It focuses on improving laboratory quality control by optimizing APS selection for accurate diagnostic outcomes.

Table 1 describes the main renal diseases, their particular features, and the most commonly used methods for their identification.

Table 1: Most relevant kidney diseases

			Diagnostic Methods										
	Kidney Disease	**Characteristics**	**Serum creatinine,**	**BUN,**	**IFGe,**	**Serum electrolytes.**	**urinalysis**	**renal ultrasound**	**Albumin/ creatinine ratio**	**albumin in urine**	**kidney biopsy**	**glucose**	**HbA1c**
1	Acute Kidney Failure	Sudden loss of kidney function, waste accumulation, and blood imbalance. It can be reversed with prompt treatment.	x	x	x	x	x	x					

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2	Chronic Kidney Failure	Progressive and irreversible loss of kidney function, accumulation of fluids, electrolytes, and waste. Dialysis or a kidney transplant may be required in advanced stages.	x		x			x	x				
3	Preeclampsia	Increased blood pressure and kidney damage in pregnant women. Risk of complications for mother and child.	x		x					x			
4	Polycystic Kidney	Hereditary disorder with multiple cysts in the kidneys, enlargement, and kidney dysfunction. It can affect other organs (liver).	x		x			x					
5	Acute Interstitial Nephropathy	Inflammation of the interstitial tissue of the kidney. Often caused by allergic reactions to medications.	x				x				x		
6	Diabetic Nephropathy	Kidney damage due to persistent hyperglycemia in patients with diabetes.			x				x			x	x
7	Hyperuremia	Accumulation of urea in the blood due to impaired renal excretion.	x	x			x						

Table 2 contains primary analytes monitored in renal patients and their relevance, alongside the clinical values and thresholds denoted with the normal values. All these tables together demonstrate how proper APS within nephrology enhances clinical decision-making and assists the laboratories in reporting results that meaningfully impact the patient's care.

Table 2: Permanent monitoring analytes for diagnosis and follow-up of kidney diseases

Analyte	Diagnostic Purpose	Reference Values	Clinical Implications
Albumin in urine or serum	Indicator of kidney damage. Elevated urinary albumin (albuminuria) is an early marker of kidney disease.	Serum: 3.5-5 g/ dL Urine: <30 mg/g CAC	Persistent albuminuria suggests chronic kidney disease (CKD), especially in patients with diabetes or hypertension.
Creatinine	It reflects kidney function. Elevated levels indicate a reduced glomerular filtration rate (GFR).	Serum: 0.6-1.2 mg/ dL (Men) 0.5-1.1 mg/ dL (Women)	An increase suggests acute or chronic renal failure. It is used in estimating the eGFR.
Albumin-Creatinine Ratio (CACU)	Noninvasive tool for assessing albuminuria predicts the risk of CKD and disease progression.	<30 mg/g	Elevated values indicate a greater risk of progressive kidney damage.
BUN (Blood Urea Nitrogen)	Evaluates the kidney's ability to eliminate waste products.	7-20 mg/ dL	Elevated levels (uremia) suggest kidney failure, dehydration, or gastrointestinal bleeding.

Calcium	Mineral balance indicator. Related to bone and cardiovascular disorders in kidney disease.	8.5-10.5 mg/ dL	Frequent hypocalcemia in advanced CKD due to vitamin D and PTH metabolism alterations.
Phosphorus	Altered in CKD due to decreased renal excretion, it contributes to vascular calcification and bone disorders.	2.5-4.5 mg/ dL	Hyperphosphatemia associated with advanced CKD increases the risk of vascular calcification and cardiovascular disease.
Potassium	Critical indicator of kidney, heart, and muscle function. The kidneys regulate potassium balance.	3.5-5.0 mmol/L	Hyperkalemia can cause serious arrhythmias in renal failure; hypokalemia in early stages may be associated with malnutrition or diuretic use.
Gluco sa	Prolonged hyperglycemia, common in patients with diabetes, can lead to diabetic nephropathy.	Fasting: 70-100 mg/ dL	High blood glucose damages renal capillaries, increasing the risk of CKD in diabetic patients.
Estimated Glomerular Filtration Rate (eGFR)	Calculated from serum creatinine, age, gender, and ethnicity, it assesses overall renal function.	Normal: >90 mL / min/1.73 m^2	A decrease in eGFR (<60 mL / min/1.73 m^2 for more than 3 months) indicates CKD; values <15 mL /min/1.73 m^2 suggest the need for dialysis or kidney transplantation.
Uric Acid	Associated with kidney and metabolic diseases.	3.5-7.2 mg/ dL (Men) 2.6-6.0 mg/ dL (Women)	Hyperuricemia contributes to the progression of CKD and can lead to urate crystal nephropathy.
Electrolytes (Na +, Cl-)	Indicators of hydroelectrolytic balance.	Sodium: 135-145 mmol/L Chlorine: 98-106 mmol/L	Alterations in sodium or chloride reflect imbalances in volumetric status, which are common in kidney patients.
Cystatin C	Sensitive marker of kidney function, less influenced by muscle mass than creatinine.	0.6-1.2 mg/L	Elevation indicates decreased GFR, which is useful in the early diagnosis of CKD.

LITERATURE REVIEW

Defining APS: Clinical and Biological Considerations

Several interrelated elements determine the diagnosis of APS, starting with biological variation. Intra- and interindividual variability explains how much fluctuation in analyte concentrations is considered acceptable without altering clinical conclusion (Braga & Panteghini, 2021). Clinically pertinent reference ranges have also been set for APS, ensuring that methods based in the laboratory can pick up essential variations relative to these limits. For example, in albuminuria testing, low concentrations (often < 30 mg/g CAC) signaling renal impairment must be detected. Without adequate sensitivity, an analytical approach may fail to account for such changes, postponing diagnosis and treatment. In addition to biological considerations, APS is also defined due to the "state of the art" level" in laboratory medicine (Çubukçu *et al.,* 2024). This is the case when one looks at international regulatory standards like CLIA, ISO 15189, or governance documents of some consensus(Ceriotti *et al.,* 2024). These documents furnish a useful starting point for acceptable performance and assist laboratories in ensuring compliance and comparability across institutions are achieved(Çubukçu *et al.,* 2024; Safaa, 2023; Yasser & Yasameen, 2022). Finally, the adequacy of clinical needs is also critical to setting APS because even small changes could be clinically consequential – especially in situations where decisions need to be made regarding therapy. Focusing on some of these instances, incorrect potassium or phosphorus values in patients with renal disease could lead to erroneous prescriptions of dialysis or potassium retention.

Analytical Performance Specifications (APS) in Laboratory Testing

Analytical Performance Specifications (APS), or in simpler terms, the Maximum Permissible Total Error (TEmp), is a standard used in measuring the accuracy and reliability of tests or any medical examination performed in a laboratory. The study (Fischer *et al.,* 2022) introduced TEmp, which blends random and systematic errors, to ascertain some level of performance achievement.

This constructs a barrier so that laboratory results remain clinically relevant by upholding fundamental boundaries. As (Horvath *et al.,* 2024) noted, they are integral in devising evaluation methodologies concerning laboratory techniques in tandem with clinical judgement and logic, especially where precision in measurement can be detrimental to diagnosis and treatment. This is critical in clinical practice, especially for tests that form a basis for understanding renal pathology. The direct laboratory measurement of parameters is accurate, and routine clinical decisions require that APS be met. These measures set the boundaries of control and aid in the simplification of processes in high-level diagnostics, such as renal profiling (Horvath *et al.,* 2015; Rotgers *et al.,* 2023). Lack of precision on predefined performance expectations increases the chances of misinterpretation, thereby heightening the chances of endangering the patients by unnecessarily offering timely but misleading medical interventions (Jones, 2024).

Importance of APS in the Diagnosis and Monitoring of Renal Profiles

Renal function tests typically include measurements of creatinine, albumin, blood urea nitrogen (BUN), and other electrolytes, all of which contain tightly defined clinical reference limits. Subtle fluctuations can profoundly impact the diagnosis and care of renal disorders. For instance, creatinine is critical in estimating the glomerular filtration rate (eGFR) (Horvath *et al.,* 2024). If the allowable total error (TEa) for creatinine is too wide, kidney function may be overestimated or underestimated, resulting in inappropriate renal management. Thus, accomplished renal laboratory practitioners (ACLAP) must provide precise APS to enable actionable clinical decisions. Moreover, quality assessment and method validation rely heavily on APS. During methodological development, APS defines the boundaries of acceptable analytical accuracy, precision, sensitivity, and specificity (Jones, 2024). Techniques such as mass spectrometry or liquid chromatography require rigid performance criteria for reproducible, high-quality outcomes (Shi *et al.,* 2025; Theodorsson, 2024). In the case of cystatin C or microalbuminuria testing, there is a need for sensitive and consistent analytical methods that can accurately identify early renal damage. Thus, stringent laboratory procedures mandated by APS are necessary to respond to clinical requirements for high sensitivity and diagnostic precision.

MATERIALS AND METHODS

Study Design and Data Source

This research was developed using data from a network of 71 clinical laboratories in Colombia. Its main goal was to evaluate the analytical accuracy and reliability of tests pertinent to the diagnosis and follow-up of kidney diseases. In particular, the study concentrated on seven biochemical analytes that are routinely measured in renal profiles: blood urea nitrogen (BUN), albumin, calcium, creatinine, phosphorus, glucose, and potassium. These analytes were included due to their importance in assessing kidney function, the stage of the disease, and the treatment response (Horvath *et al.,* 2015). To maintain clinical applicability, reference values of each parameter were taken from the most recent guidelines of KDIGO Kidney Disease: Improving Global Outcomes (2024). These guidelines set the gold standard for internationally accepted thresholds for interpreting renal biomarkers and make it possible for laboratory performance to be measured against a well-established standard. Having used these benchmarks, it can be hoped that the findings will address practical challenges and demands in kidney disease diagnostics and management.

Collection and Organization of Performance Specifications

All participating laboratories submitted their analytical performance specifications (PSAs) for the seven targeted analytes. These specifications contained pertinent information on precision, accuracy, total error, and other relevant factors concerning the validation of the method. The gathered PSAs for each analyte were sorted in increasing order from the minimum to the maximum value for each PSA. This ordering facilitated performance threshold comparisons across different laboratories, revealing performance inconsistencies throughout the network. All laboratories were given an equal CV to achieve uniformity in the comparison, and bias was applied as a model across all laboratories. This ensured consistent computation of all relevant KPIs with performance expectation gaps sighted due to methodology differences. This analytic focus aimed to create a norm to highlight the relative position of every participant in the laboratory analytic grade quality competition.

Analysis- Total Error and Sigma Metrics

Total analytical error and sigma metrics were computed for each analyte for all 71 laboratories using the standard model of CV and bias. Total analytical error was calculated using systematic (bias) and random (imprecision) errors, which estimated all test reliability. The sigma metric, a well-understood error assessment tool, was evaluated by measuring the total error against the allowable error limits. The sigma metric scores gave a measurable comparison of analytical performance within each laboratory, stratifying them from low to world-class quality. Laboratories with six and above Sigma scores were deemed to perform excellently, while those below three were flagged for possible improvement. This allowed for a comprehensive analysis of how each laboratory aligns with the benchmarks set by international standards on quality and reliability, highlighting the gaps in analytical reliability focus for essential renal markers.

RESULTS AND DISCUSSION

Results

APS used in the 71 laboratories for each analyte

Table 3: Summary of APS used in the 71 laboratories for each analyte

Analyte	Number of Laboratories	Number of Different APS	Lower APS (%)	Higher APS (%)
BUN	71	23	7.20	10.5
Albumin	57	12	3.40	12.50
Calcium	61	16	2.30	11.01
Creatinine	70	19	4.00	20.00
Phosphorus	56	21	4.90	17.08
Glucose	64	16	5.40	14.20
Potassium	61	16	2.40	18.10

Table 3 shows the Analytical Performance Specifications (APS) study of over 71 laboratories, which showed a marked inconsistency in setting quality thresholds for important renal analytes. Creatinine and phosphorus display the most significant ranges in APS at 4.00% - 20.00% and 4.90% - 17.08%, respectively, demonstrating substandard calibrations that are certain to compromise diagnostic precision. Although BUN, albumin, and calcium display notable deficiencies in variation, the lack of unique APS values is striking. Potassium, which is extremely important as an electrolyte, is alarming at the 2.40% - 18.10% range; this can endanger some critical clinical decisions. This inconsistency indicates poor organization between the laboratories, highlighting the need for uniform standardized APS based on other authoritative frameworks so that patient results are reliable, consistent, and relevant.

Influence of APS

The information in Table 4 illustrates the specific effects

Table 4: Serum albumin: Influence of the selected APS on the calculation of the sigma metric

	Albumin	**g/ dL**	**1.65**				
	APS	**Target Value**	**IQC average**	**CV**	**Bias**	**Analytical Error**	**Sigma Metric**
1	3.40%	3.97	4.02	2.30%	-1.26%	5.05%	0.93
2	3.90%	3.97	4.02	2.30%	-1.26%	5.05%	1.15
3	3.90%	3.97	4.02	2.30%	-1.26%	5.05%	1.15
4	4.07%	3.97	4.02	2.30%	-1.26%	5.05%	1.22
5	4.57%	3.97	4.02	2.30%	-1.26%	5.05%	1.44
6	5.20%	3.97	4.02	2.30%	-1.26%	5.05%	1.71
7	5.36%	3.97	4.02	2.30%	-1.26%	5.05%	1.78
8	5.80%	3.97	4.02	2.30%	-1.26%	5.05%	1.97
9	6.32%	3.97	4.02	2.30%	-1.26%	5.05%	2.20
10	8.00%	3.97	4.02	2.30%	-1.26%	5.05%	2.93
11	10.00%	3.97	4.02	2.30%	-1.26%	5.05%	3.80
12	12.50%	3.97	4.02	2.30%	-1.26%	5.05%	4.89

of selected Analytical Performance Specifications (APS) on sigma for serum albumin. Sigma metric values tend to increase with widening APS even when the coefficients of variation, sigma, and biases are identical. For example, with APS set at 3.40, sigma is 0.93, suggesting poor analytical quality. Yet at 12.50, APS drives the sigma value to 4.89, almost achieving a sigma level indicative of qualitatively acceptable performance. This shows that more relaxed APS can bias performance metrics and hide methodological deficiencies. Thus, defining clinically relevant and uniform APS is vital to ensure effective quality evaluation and patient safety.

The value of the sigma metric for urine albumin in Table 5 shows a marked increase with higher APS (Analytical Performance Specifications), while the coefficient of variation (1.05%) and bias (2.05%) remain constant. With an APS yielding 9.30%, the sigma is already commendable at 6.91 (as noted, 6.0 is the minimum for clinical usefulness). However, with a further increase in APS, reaching 61.87 %, the APS jumps to a staggering 56.97. This proves that overly lenient APS might lead to an illusion of structure polish while hiding severe underlying deficiencies. While appeal appears high, high sigma values are almost meaningless if the APS is not clinically substantiated (Figure 1). This presents the need to ensure that dependable and realistic, evidence-based APS are set to safeguard diagnostic dependability.

Table 6 analyses the relationship between different Analytical Performance Specifications (APS) and the sigma metric for serum BUN. Even though the coefficients

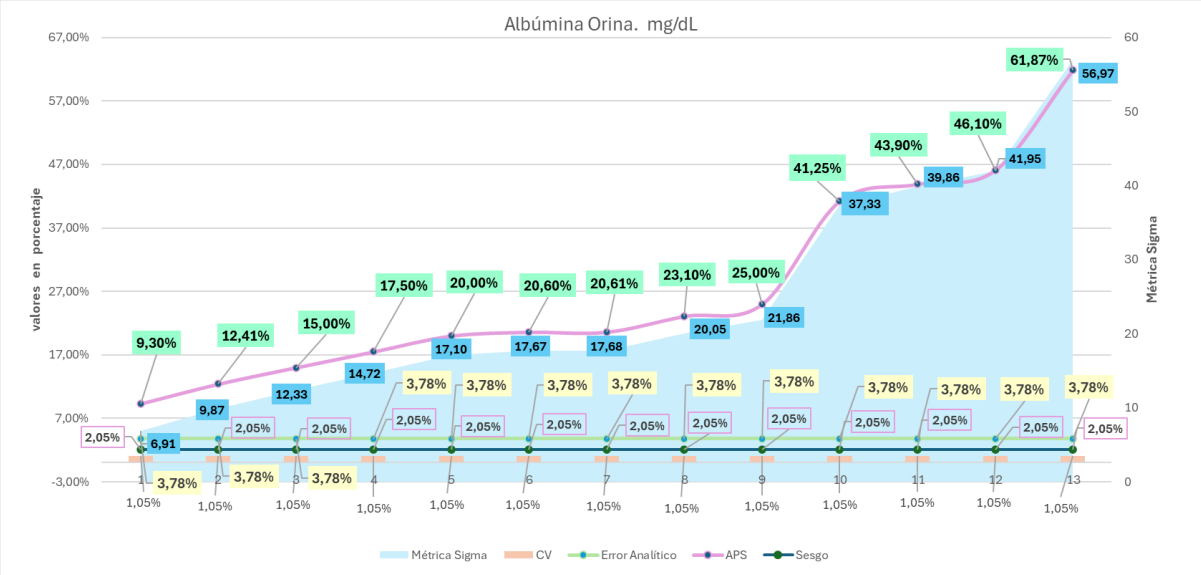

Figure 1: Urine albumin: influence of the selected APS on the calculation of the sigma metric

Table 5: Urine albumin: influence of the selected APS on the calculation of the sigma metric

	Albumin	**mg/ dL**	**1.65**				
Item	**APS**	**Target Value**	**CC average**	**CV**	**Bias**	**Analytical Error**	**Sigma Metric**
1	9.30%	4.88	4.78	1.05%	2.05%	3.78%	6.91
2	12.41%	4.88	4.78	1.05%	2.05%	3.78%	9.87
3	15.00%	4.88	4.78	1.05%	2.05%	3.78%	12.33
4	17.50%	4.88	4.78	1.05%	2.05%	3.78%	14.72
5	20.00%	4.88	4.78	1.05%	2.05%	3.78%	17.10
6	20.60%	4.88	4.78	1.05%	2.05%	3.78%	17.67
7	20.61%	4.88	4.78	1.05%	2.05%	3.78%	17.68
8	23.10%	4.88	4.78	1.05%	2.05%	3.78%	20.05
9	25.00%	4.88	4.78	1.05%	2.05%	3.78%	21.86
10	41.25%	4.88	4.78	1.05%	2.05%	3.78%	37.33
11	43.90%	4.88	4.78	1.05%	2.05%	3.78%	39.86
12	46.10%	4.88	4.78	1.05%	2.05%	3.78%	41.95
13	61.87%	4.88	4.78	1.05%	2.05%	3.78%	56.97

of variation (1.66%) and bias (3.16%) remain static, the sigma metric progressively improves with increasing APS values. When the APS is set at the lowest value of 7.20%, the sigma is 2.43. Although this value indicates underperformance, it is still better than the "acceptable" threshold for high-quality performance. However, as APS increases to 26.60%, the sigma value soars to 14.12, indicating exceptional analytical performance. This trend demonstrates how APS inflation can distort quality measures, leading to the misrepresentation of so-called precise methods as possessing high precision. Hence, the selection of APS requires caution. Too generous limits will enhance sigma values on APS tests set below 7.20% and conceal crucial inaccuracies regarding the accuracy and reliability of the specified test, particularly in primary diagnostic indicators such as BUN (Figure 2).

Table 7 demonstrates the change in the sigma metric for serum calcium based on the differing values of Allowable Error Performance Specifications (APS). Each APS value represents different analytical parameters comprising a constant CV and bias of 0.88% and 0.63%, respectively. Sigma shows increments with an increasing APS. Coupled with an APS of 2.30%, sigma lags at 1.90, depicting poor performance. On the contrary, with an APS cap of 11.01%, sigma makes a tremendous leap to 11.80, suggesting superb analytical quality. This helps reveal that sigma metrics are significantly more responsive to APS values. If the APS value is overly permissive, sigma results may become misleadingly favorable, indicating flawed accuracy and precision (Figure 3). Deductively, selecting clinically credible and evidence-driven APS values becomes essential in calcium testing to guarantee

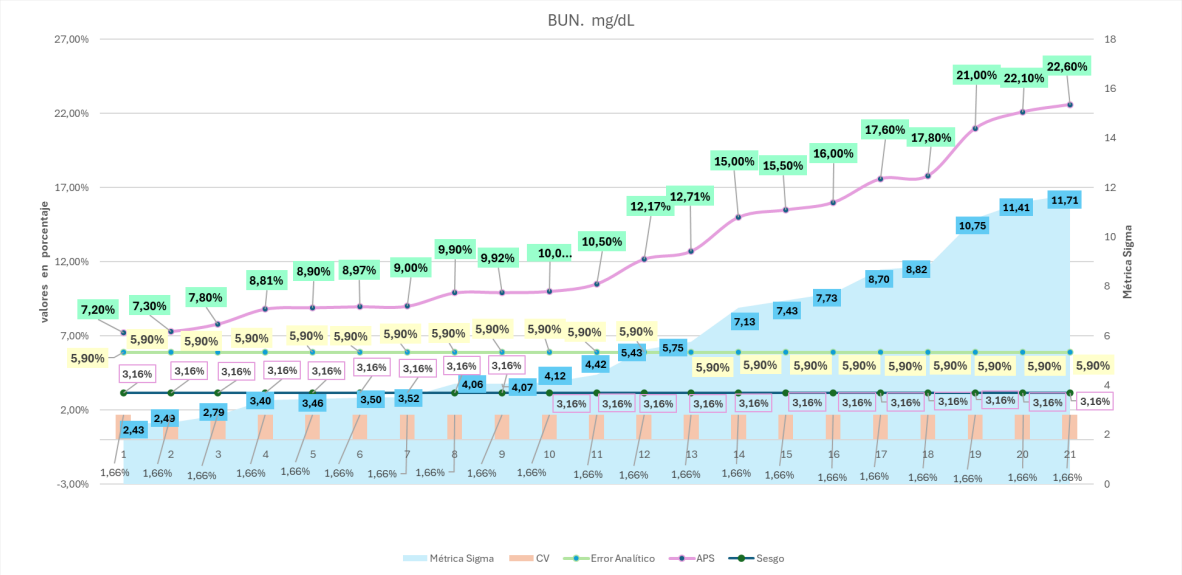

Figure 2: Serum BUN: Influence of the selected APS on the calculation of the sigma metric

Table 6: Serum BUN: Influence of the selected APS on the calculation of the sigma metric

	BUN	**mg/ dL**	**1.65**				
Item	**APS**	**Target Value**	**CC average**	**CV**	**Bias**	**Analytical Error**	**Sigma Metric**
1	7.20%	14.55	14.09	1.66%	3.16%	5.90%	2.43
2	7.30%	14.55	14.09	1.66%	3.16%	5.90%	2.49
3	7.80%	14.55	14.09	1.66%	3.16%	5.90%	2.79
4	8.81%	14.55	14.09	1.66%	3.16%	5.90%	3.40
5	8.90%	14.55	14.09	1.66%	3.16%	5.90%	3.46
6	8.97%	14.55	14.09	1.66%	3.16%	5.90%	3.50
7	9.00%	14.55	14.09	1.66%	3.16%	5.90%	3.52
8	9.90%	14.55	14.09	1.66%	3.16%	5.90%	4.06
9	9.92%	14.55	14.09	1.66%	3.16%	5.90%	4.07
10	10.00%	14.55	14.09	1.66%	3.16%	5.90%	4.12
11	10.50%	14.55	14.09	1.66%	3.16%	5.90%	4.42
12	12.17%	14.55	14.09	1.66%	3.16%	5.90%	5.43
13	12.71%	14.55	14.09	1.66%	3.16%	5.90%	5.75
14	15.00%	14.55	14.09	1.66%	3.16%	5.90%	7.13
15	15.50%	14.55	14.09	1.66%	3.16%	5.90%	7.43
16	16.00%	14.55	14.09	1.66%	3.16%	5.90%	7.73
17	17.60%	14.55	14.09	1.66%	3.16%	5.90%	8.70
18	17.80%	14.55	14.09	1.66%	3.16%	5.90%	8.82
19	21.00%	14.55	14.09	1.66%	3.16%	5.90%	10.75
20	22.10%	14.55	14.09	1.66%	3.16%	5.90%	11.41
21	22.60%	14.55	14.09	1.66%	3.16%	5.90%	11.71
22	23.47%	14.55	14.09	1.66%	3.16%	5.90%	12.23
23	26.60%	14.55	14.09	1.66%	3.16%	5.90%	14.12

reliable quality assessments.

Table 8 shows how changing Allowable Performance Specifications (APS) impacts the sigma metric for measuring serum creatinine levels. Under fixed analytical conditions of CV (1.70%) and bias (-1.11%), the sigma metric continues to improve with higher APS values.

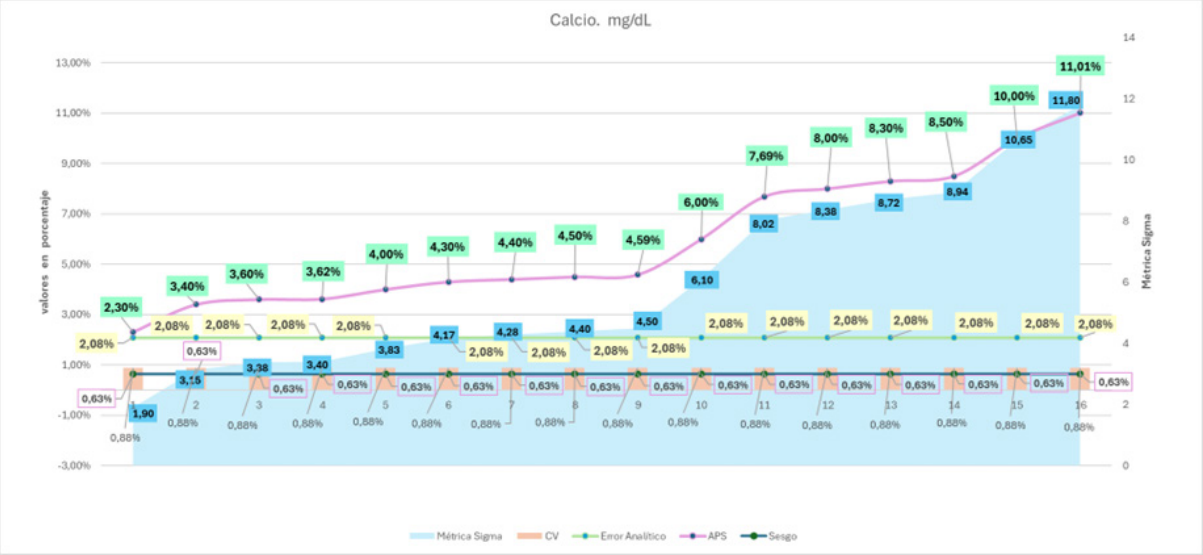

Figure 3: Serum calcium: Influence of the selected PSA on the calculation of the sigma metric

Table 7: Serum calcium: Influence of the selected PSA on the calculation of the sigma metric

	Calcium	mg/ dL	1.65				
Item	**APS**	**Target Value**	**CC average**	**CV**	**Bias**	**Analytical Error**	**Sigma Metric**
1	2.30%	9.53	9.47	0.88%	0.63%	2.08%	1.90
2	3.40%	9.53	9.47	0.88%	0.63%	2.08%	3.15
3	3.60%	9.53	9.47	0.88%	0.63%	2.08%	3.38
4	3.62%	9.53	9.47	0.88%	0.63%	2.08%	3.40
5	4.00%	9.53	9.47	0.88%	0.63%	2.08%	3.83
6	4.30%	9.53	9.47	0.88%	0.63%	2.08%	4.17
7	4.40%	9.53	9.47	0.88%	0.63%	2.08%	4.28
8	4.50%	9.53	9.47	0.88%	0.63%	2.08%	4.40
9	4.59%	9.53	9.47	0.88%	0.63%	2.08%	4.50
10	6.00%	9.53	9.47	0.88%	0.63%	2.08%	6.10
11	7.69%	9.53	9.47	0.88%	0.63%	2.08%	8.02
12	8.00%	9.53	9.47	0.88%	0.63%	2.08%	8.38
13	8.30%	9.53	9.47	0.88%	0.63%	2.08%	8.72
14	8.50%	9.53	9.47	0.88%	0.63%	2.08%	8.94
15	10.00%	9.53	9.47	0.88%	0.63%	2.08%	10.65
16	11.01%	9.53	9.47	0.88%	0.63%	2.08%	11.80

At a low APS of 4.00%, the sigma value is only 1.70, indicative of poor performance. With APS set to 20.00%, the sigma value increases to 11.11, suggesting excellent method capability. This trend demonstrates that the APS directly impacts the sigma metric; lowering the APS limits increases the sigma score. Hence, the APS must be selected with the appropriate degree of stringency to avoid over-inflating the analytical quality (Figure 4). Obsessively hyperbolizing sigma values without the backing of clinical context risks losing sight of actual performance limits in creatinine testing.

Table 9 shows how different levels of Allowable Performance Specifications (APS) might impact the sigma metric pertaining to serum phosphorus. With constant analytical conditions--CV of 0.61% and bias of -0.54%--sigma increases proportionately with APS. At an APS value of 4.90, sigma is already high at 7.14, indicating excellent analytical performance. As APS increases to 17.08%, sigma skyrockets to 27.11, which indicates extremely high method capability. This data suggests that growing APS significantly increases the sensitivity of the sigma metric and the APS chosen. While high sigma values might suggest high reliability, if APS is overly permissive, the sigma value will likely overestimate

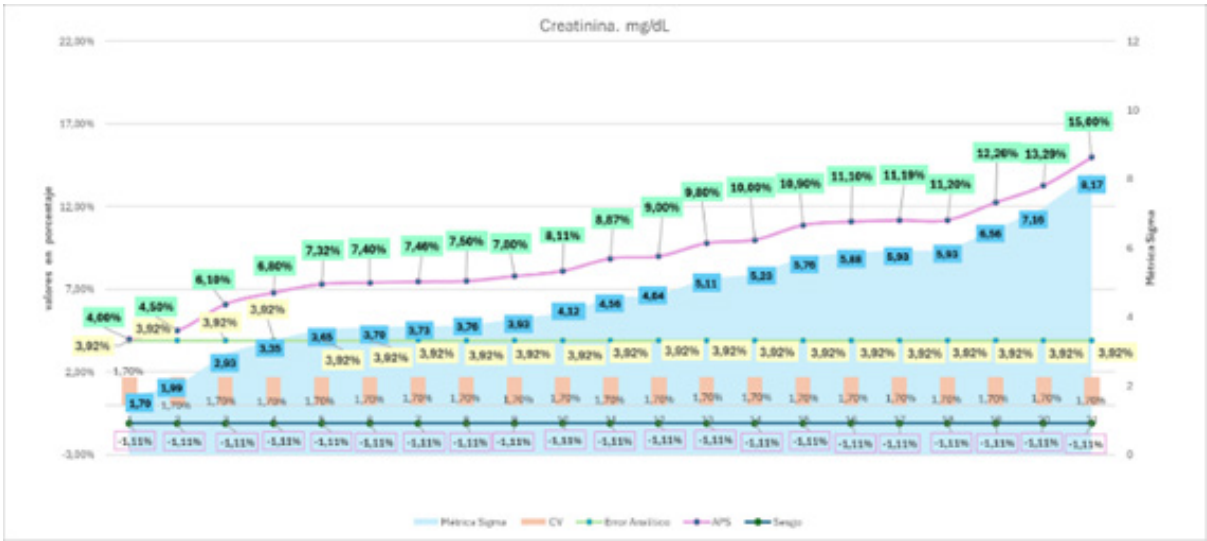

Figure 4: Serum creatinine: Influence of the selected PSA on the calculation of the sigma metric

Table 8: Serum creatinine: Influence of the selected PSA on the calculation of the sigma metric

Item	APS (%)	Target Value	CC Average	CV (%)	Bias (%)	Analytical error (%)	Sigma Metric
1	4.00	1.8	1.82	1.70	-1.11	3.92	1.70
2	4.50	1.8	1.82	1.70	-1.11	3.92	1.99
3	6.10	1.8	1.82	1.70	-1.11	3.92	2.93
4	6.80	1.8	1.82	1.70	-1.11	3.92	3.35
5	7.32	1.8	1.82	1.70	-1.11	3.92	3.65
6	7.40	1.8	1.82	1.70	-1.11	3.92	3.70
7	7.46	1.8	1.82	1.70	-1.11	3.92	3.73
8	7.50	1.8	1.82	1.70	-1.11	3.92	3.76
9	7.80	1.8	1.82	1.70	-1.11	3.92	3.93
10	8.11	1.8	1.82	1.70	-1.11	3.92	4.12
11	8.87	1.8	1.82	1.70	-1.11	3.92	4.56
12	9.00	1.8	1.82	1.70	-1.11	3.92	4.64
13	9.80	1.8	1.82	1.70	-1.11	3.92	5.11
14	10.00	1.8	1.82	1.70	-1.11	3.92	5.23
15	10.90	1.8	1.82	1.70	-1.11	3.92	5.76
16	11.10	1.8	1.82	1.70	-1.11	3.92	5.88
17	11.19	1.8	1.82	1.70	-1.11	3.92	5.93
18	11.20	1.8	1.82	1.70	-1.11	3.92	5.93
19	12.26	1.8	1.82	1.70	-1.11	3.92	6.56
20	13.29	1.8	1.82	1.70	-1.11	3.92	7.16
21	15.00	1.8	1.82	1.70	-1.11	3.92	8.17
22	20.00	1.8	1.82	1.70	-1.11	3.92	11.11

the actual performance of the analyzed method (Figure 5). Therefore, selecting clinically appropriate APS is important in evaluative assessments of quality.

Table 10 illustrates how differing Allowable Performance Specifications (APS) affect the serum glucose sigma metric. The analytical conditions, CV=1.02% and bias of 0.40% were held constant, yet the APS incremented the sigma metric substantially. At 5.40 APS, the sigma metric value was 4.91, aligning with acceptable methodology performance benchmarks. Also, APS values above 5.40 APS enhanced the sigma metric significantly, achieving 13.53 for APS14.20. This data indicates that higher APS

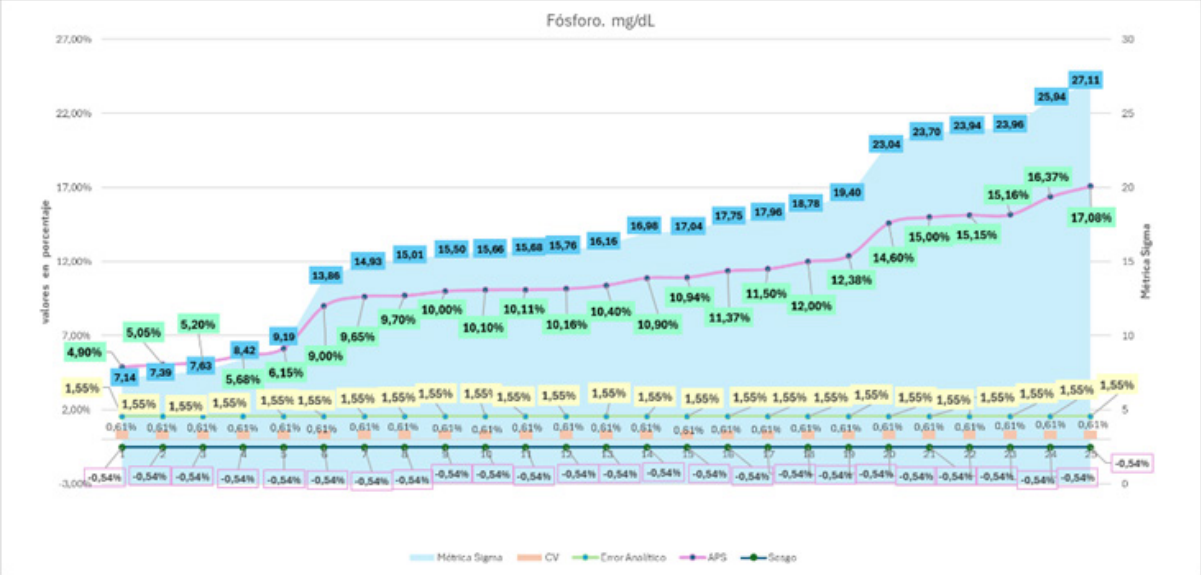

Figure 5: Serum phosphorus: Influence of the selected PSA on the calculation of the sigma metric

Table 9: Serum phosphorus: Influence of the selected PSA on the calculation of the sigma metricc

	Phosphorus	**mg/ dL**	**1.65**				
Item	**APS**	**Target Value**	**CC average**	**CV**	**Bias**	**Analytical Error**	**Sigma Metric**
1	4.90%	3.67	3.69	0.61%	-0.54%	1.55%	7.14
2	5.05%	3.67	3.69	0.61%	-0.54%	1.55%	7.39
3	5.20%	3.67	3.69	0.61%	-0.54%	1.55%	7.63
4	5.68%	3.67	3.69	0.61%	-0.54%	1.55%	8.42
5	6.15%	3.67	3.69	0.61%	-0.54%	1.55%	9.19
6	9.00%	3.67	3.69	0.61%	-0.54%	1.55%	13.86
7	9.65%	3.67	3.69	0.61%	-0.54%	1.55%	14.93
8	9.70%	3.67	3.69	0.61%	-0.54%	1.55%	15.01
9	10.00%	3.67	3.69	0.61%	-0.54%	1.55%	15.50
10	10.10%	3.67	3.69	0.61%	-0.54%	1.55%	15.66
11	10.11%	3.67	3.69	0.61%	-0.54%	1.55%	15.68
12	10.16%	3.67	3.69	0.61%	-0.54%	1.55%	15.76
13	10.40%	3.67	3.69	0.61%	-0.54%	1.55%	16.16
14	10.90%	3.67	3.69	0.61%	-0.54%	1.55%	16.98
15	10.94%	3.67	3.69	0.61%	-0.54%	1.55%	17.04
16	11.37%	3.67	3.69	0.61%	-0.54%	1.55%	17.75
17	11.50%	3.67	3.69	0.61%	-0.54%	1.55%	17.96
18	12.00%	3.67	3.69	0.61%	-0.54%	1.55%	18.78
19	12.38%	3.67	3.69	0.61%	-0.54%	1.55%	19.40
20	14.60%	3.67	3.69	0.61%	-0.54%	1.55%	23.04
21	15.00%	3.67	3.69	0.61%	-0.54%	1.55%	23.70
22	15.15%	3.67	3.69	0.61%	-0.54%	1.55%	23.94
23	15.16%	3.67	3.69	0.61%	-0.54%	1.55%	23.96
24	16.37%	3.67	3.69	0.61%	-0.54%	1.55%	25.94
25	17.08%	3.67	3.69	0.61%	-0.54%	1.55%	27.11

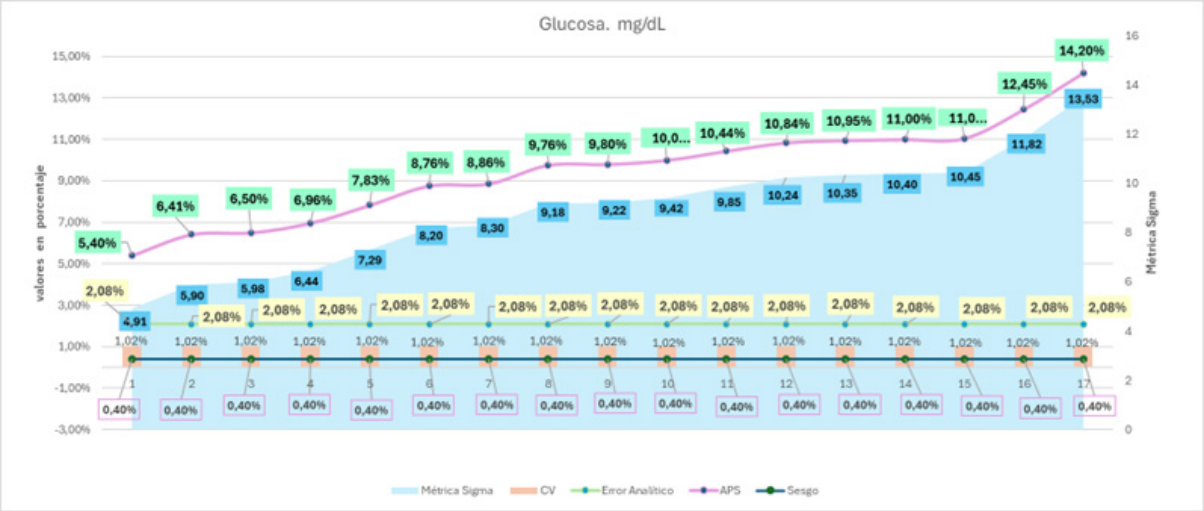

Figure 6: Serum glucose: Influence of the selected PSA on the calculation of the sigma metric

Table 10: Serum glucose: Influence of the selected PSA on the calculation of the sigma metric

	Glucose	mg/ dL	1.65				
Item	**APS**	**Target Value**	**CC average**	**CV**	**Bias**	**Analytical Error**	**Sigma Metric**
1	5.40%	80.85	80.53	1.02%	0.40%	2.08%	4.91
2	6.41%	80.85	80.53	1.02%	0.40%	2.08%	5.90
3	6.50%	80.85	80.53	1.02%	0.40%	2.08%	5.98
4	6.96%	80.85	80.53	1.02%	0.40%	2.08%	6.44
5	7.83%	80.85	80.53	1.02%	0.40%	2.08%	7.29
6	8.76%	80.85	80.53	1.02%	0.40%	2.08%	8.20
7	8.86%	80.85	80.53	1.02%	0.40%	2.08%	8.30
8	9.76%	80.85	80.53	1.02%	0.40%	2.08%	9.18
9	9.80%	80.85	80.53	1.02%	0.40%	2.08%	9.22
10	10.00%	80.85	80.53	1.02%	0.40%	2.08%	9.42
11	10.44%	80.85	80.53	1.02%	0.40%	2.08%	9.85
12	10.84%	80.85	80.53	1.02%	0.40%	2.08%	10.24
13	10.95%	80.85	80.53	1.02%	0.40%	2.08%	10.35
14	11.00%	80.85	80.53	1.02%	0.40%	2.08%	10.40
15	11.05%	80.85	80.53	1.02%	0.40%	2.08%	10.45
16	12.45%	80.85	80.53	1.02%	0.40%	2.08%	11.82
17	14.20%	80.85	80.53	1.02%	0.40%	2.08%	13.53

values relax the criteria for performance evaluation and inflate the sigma metrics (Figure 6). Even though sigma values above six suggest world-class quality, these results highlight the need to establish clinically relevant APS to avert invalid conclusions regarding assay performance, thereby ensuring meaningful quality assurance in laboratory practice.

Table 11 depicts how the Allowable Performance Specifications (APS) impact the sigma metric for potassium serum levels. The consequatur of variance remains the same at 1.08%, with a diminutive negative bias of -0.53%, leading to a constant analytical error of 2.31%. When APS is set to a low value of 2.40%, the sigma metric is only 1.73, which shows poor analytical performance. With a further increase in APS, the sigma metric optimizes to 16.27 but marks the looming APS level at 18.10%. This data corroborates that the APS range profoundly impacts shed value, yielding less APS needing more enhancement to achieve desired lower bound metrics. So, minimum defect metrics perception should be arbitrarily flexible in exposing corresponding EPS gauging for evaluating system performance. (Figure 7) Thoughtful choice of APS is crucial because it directly influences methodology evaluation while retaining value

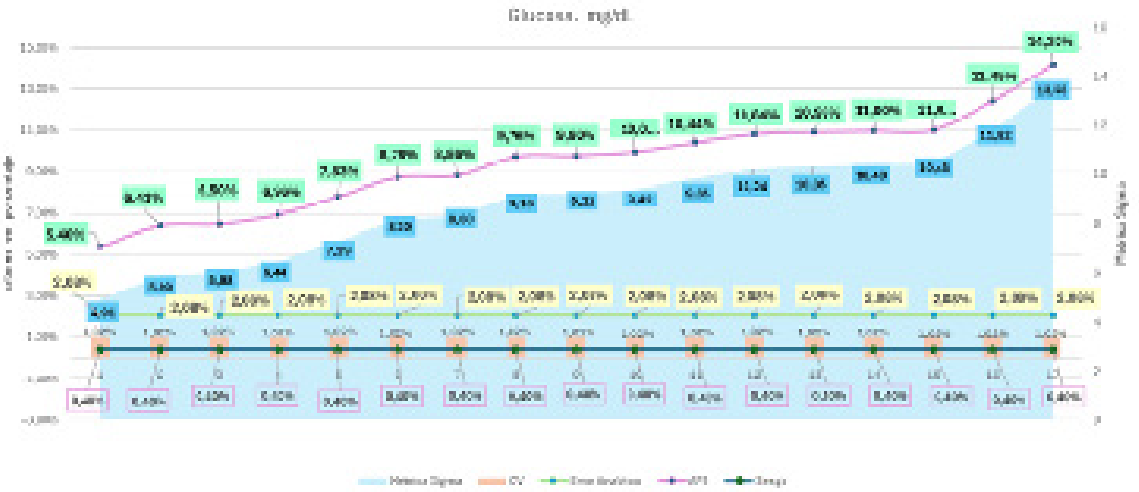

Figure 7: Serum potassium: Influence of the selected PSA on the calculation of the sigma metric

Table 11: Serum potassium: Influence of the selected PSA on the calculation of the sigma metric

	Potassium	mEq/L	1.65				
Item	**APS**	**Target Value**	**CC average**	**CV**	**Bias**	**Analytical Error**	**Sigma Metric**
1	2.40%	3.8	3.82	1.08%	-0.53%	2.31%	1.73
2	2.90%	3.8	3.82	1.08%	-0.53%	2.31%	2.20
3	4.50%	3.8	3.82	1.08%	-0.53%	2.31%	3.68
4	4.73%	3.8	3.82	1.08%	-0.53%	2.31%	3.89
5	4.80%	3.8	3.82	1.08%	-0.53%	2.31%	3.96
6	4.85%	3.8	3.82	1.08%	-0.53%	2.31%	4.00
7	5.30%	3.8	3.82	1.08%	-0.53%	2.31%	4.42
8	5.42%	3.8	3.82	1.08%	-0.53%	2.31%	4.53
9	5.52%	3.8	3.82	1.08%	-0.53%	2.31%	4.62
10	6.00%	3.8	3.82	1.08%	-0.53%	2.31%	5.07
11	6.16%	3.8	3.82	1.08%	-0.53%	2.31%	5.22
12	7.27%	3.8	3.82	1.08%	-0.53%	2.31%	6.24
13	7.30%	3.8	3.82	1.08%	-0.53%	2.31%	6.27
14	8.40%	3.8	3.82	1.08%	-0.53%	2.31%	7.29
15	8.41%	3.8	3.82	1.08%	-0.53%	2.31%	7.30
16	18.10%	3.8	3.82	1.08%	-0.53%	2.31%	16.27

in potassium measurement quality control.

Discussion

This research illustrates the sensitivity of sigma metrics to the selected Allowable Performance Specifications (APS) even when the analytical CV and bias are held constant. As shown in the potassium, glucose, and phosphorus data, increasing APS tends to overshoot the targeted sigma metric, yielding an increase indicating an "improvement" in performance despite being non-analytically empirically verified. For instance, the sigma metric for potassium increased excessively from 1.73 at 2.40% APS to 16.27 at 18.10% APS under the same analytical conditions. This behavior complicates how tighter APS contours can improve the expressed sigma metrics and exposes the troublesome APS as an evaluation criterion used to determine laboratory methods' "satisfactory" quality (Jones, 2024).

In corroboration of these findings, (Levin *et al.,* 2024) defend that sigma metrics can effectively track laboratory performance, with the caveat that they are sensitive to the applied APS. Suppose APS values are set too comfortably, particularly those lacking biological relevance or clinical importance. In that case, the sigma values will be overstated, and the tests' accuracy, precision, and reliability will be grossly overestimated. For the same reason, (Li & Huddleston, 2025) pointed out that applying quality goals grounded on biology is a more comprehensive approach

as it helps mitigate clinical risk while still addressing the patient's perspective. Hence, while sigma metrics allow uniform comparability in assessing performance, their evaluation is placed within evidence-based APS set normative criteria.

The study (Li *et al.,* 2024) argues that setting performance specifications without considering clinical intent from regulations or manufacturer resources places patients at risk; adopting such spec fosters hollow patient-centric care. As these authors highlight, laboratory quality indicators must always be underpinned by biological and clinical essentials to inform relevant decisions rather than exploiting statistical convenience. As per their discussion, clinical laboratories must adopt an active strategy for APS for sigma computations. APS that underachieve clinical thresholds must be avoided because such practices compromise minimum acceptable clinical benchmarks (Oosterhuis, 2017). Such a framework provides appropriate control over the quality of service diagnostics to provide improved patient safety.

CONCLUSION

This study highlights the importance of APS value(s) selection in calculating sigma metrics and evaluating laboratory performance. The analysis showed that at a particular level, APS values negotiated with the system substantially affect the results of APS calculations, which in turn impact the reliability of the laboratory results. Laboratories need to evaluate the effect of these values on these metrics and ensure that their APS values are relevant to the test in question or clinically more appropriate. The accuracy of laboratory quality control measures has been neglected, as in the case of sigma metrics, APS values, which should be for precision laboratory tests, were found to be in accord. There is also the need to adopt more realistic and precise metrics, which aid the overall performance and healthcare delivery. Moreover, the use of optimized APS values helps reduce analytical errors, which enhances the safety of patients. Thus, laboratories must revise their APS choices frequently and continually due to shifting standards and positions of best practice.

RECOMMENDATIONS

As discussed in this study, it is suggested that the laboratories target the APS values as close as possible to the clinically pertinent target values since this will result in the sigma metric reflecting laboratory performance with greater accuracy and subsequently improving these diagnostic tests and quality control. Laboratories must follow strict processes for setting these APS value protocols, which should be based on specific characteristics of each test, such as its bias, variability, and range. Additionally, laboratories must periodically verify whether these selections are effective and adjust them if necessary (Rojas-Rivera *et al.,* 2023). By setting diagnostic processes that continuously review the quality of the sigma metric, the labs can better manage their analytical errors, decreasing the chance of misdiagnoses. Because it is vital for laboratories to uphold accurate and dependable standards, there should be a commitment to acquiring sophisticated equipment and education that deepen understanding of how the selection of APS values impacts test performance.

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