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ORIGINAL ARTICLE

Performance Verification of Four Liver-Related Enzyme Assays on a Dry-Chemistry Biochemistry Analyzer

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ABSTRACT

Background: **This study aimed to verify the performance indices of aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (GGT), and lipase (LPS) and to comprehensively evaluate the performance of the newly commissioned QuidelOrtho VITROS 450 automatic biochemical analyzer in our laboratory, thereby enhancing laboratory work quality.**
Methods: **The analytical performance of the four items was evaluated via precision, trueness, linearity, and inter-instrument comparison. No unacceptable performance deviations were identified during the evaluation, confirming that the analytical performance of the detection method satisfied the clinical requirements for sample testing. The entire verification process adhered to the referenced standards, including CLSI EP15-A3 and EP09c-Ed3, WS/T 492-2016, WS/T 408-2024 and WS/T 403-2024.**
Results: **The within-run coefficient of variation (CV) of precision verification was less than 1/4 TEa, and the total CV was less than 1/3 TEa. The relative bias of the four items was less than 1/2 total allowable error (TEa). Linearity was verified, and the coefficient of determination (R^2) of the four items was ≥ 0.995, which could preliminarily judge that the linear range met the requirements. The comparison between instruments showed that there was no statistically significant difference in the four items between the QuidelOrtho VITROS 450 dry chemical analysis system and the imported VITROS 4600 dry chemical analysis system.**
Conclusions: **The verified precision, trueness, linear range, and inter-instrument comparison results for the four analytes fully met the established quality objectives, confirming that the QuidelOrtho VITROS 450 automatic biochemical analyzer is clinically applicable for the detection of these four analytes, thereby ensuring reliable results for routine laboratory testing.**
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KEYWORDS

QuidelOrtho VITROS 450, dry chemistry, performance verification, liver-function tests

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LIST OF ABBREVIATIONS

ALT - Alanine aminotransferase
AST - Aspartate aminotransferase
AUC - Area under the (ROC) curve
CI - Confidence interval
CLSI - Clinical and Laboratory Standards Institute
CNAS - China National Accreditation Service for Conformity Assessment
CRediT - Contributor Roles Taxonomy
CV - Coefficient of variation
DOI - Digital Object Identifier
EP06 - CLSI Evaluation of Linearity of Quantitative Measurement Procedures
EP07 - CLSI Interference Testing in Clinical Chemistry
EP09c - CLSI Measurement Procedure Comparison and Bias Estimation Using Patient Samples
EP10 - CLSI Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures (incl. Carryover)
EP15-A3 - CLSI User Verification of Precision and Estimation of Bias
EP17 - CLSI Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
EQA - External Quality Assessment
GGT - γ-Glutamyl transferase (Gamma-glutamyl transpeptidase)
IFCC - International Federation of Clinical Chemistry and Laboratory Medicine
ISO - International Organization for Standardization
IQR - Interquartile range
LoA - Limits of Agreement (Bland-Altman)
LoB/LoD/LoQ - Limit of Blank/Detection/Quantitation
LPS - Lipase

INTRODUCTION

Before the new detection system can be deployed for clinical sample testing and report issuance, laboratories must conduct a comprehensive verification of its analytical performance in accordance with industry standards. This process encompasses key performance indicators, including precision, trueness, linear range, and methodological comparisons. The reliability of the detection system can be affirmed for clinical testing purposes only when the verification results align with the manufacturer's declared performance criteria.

The QuidelOrtho VITROS 450 automatic dry biochemical analysis system represents China's first domestically designed and manufactured automatic dry biochemical analyzer with a localization rate exceeding 90% [1,2]. Tailored to the specific operational context of our laboratory, this study aimed to evaluate the methodological performance of the VITROS 450 system for detecting AST, ALT, GGT, and LPS and compare its performance against the VITROS 4600 biochemical analysis system. Detailed validation results are presented below.

MATERIALS AND METHODS

Experimental samples

The samples used in this validation evaluation were residual specimens from the VITROS 4600 analyzer collected in November 2024. All the samples were free of hemolysis, lipemia, or jaundice. External quality assessment (EQA) samples provided by the National Center for Clinical Laboratories (NCCL) of the National Health Commission of China were also included in the evaluation.

Instruments and reagents

The QuidelOrtho V450 automatic biochemical analyzer, reagents, calibrators, and quality control products used in the entire detection process were all within the validity period, using the original reagent calibrators and quality control products of QuidelOrtho.

Methods

Precision verification

According to the document analytical performance standard for routine analytes in clinical chemistry (WS/T 403-2024) Guidelines for Analytical Performance Verification of Quantitative Examination Procedures (WS/T 408-2024), and CLSI EP15-A3 [2], one batch and two concentrations of the original quality control products of QuidelOrtho were analyzed every day; each concentration was repeated three times, and 24 test items were detected for five consecutive days. The data were calculated to obtain the intra-assay coefficient of variation (CV) and the total CV of precision. The intra-assay CV was less than 1/4 of the total allowable error (TEa) and the total CV was less than 1/3 TEa. WS/T 403-2024 standard was used to allow imprecision.

Trueness verification

According to document WS/T 492-2016, Guidelines for Analytical Performance Verification of Quantitative Examination Procedures (WS/T 408-2024) and CLSI EP15-A3 [2,3], the results of external quality assessment (EQA) organized by the National Center for Clinical Laboratories of the National Health Commission were collected as a reference. Five levels of EQA samples were selected and detected using a QuidelOrtho VITROS 450 automatic biochemical analyzer, one batch per day, and each batch was repeated twice. Five days after the operation, 10 results were obtained for each level, and the mean value was calculated. The bias was calculated by comparing the results with the reference results. The evaluation criteria were as follows: the bias was less than 1/2 TEA and the trueness of the equipment was considered to meet the requirements. WS/T 403-2024 criteria were used to allow bias.

Linear verification

Referring to document WS/T 403-2024 and guidelines for Analytical Performance Verification of Quantitative Examination Procedures (WS/T 408-2024), two samples with high and low concentrations close to the upper and lower limits of the linear interval were selected, and

six concentrations were prepared according to the equal spacing method. All the samples were tested simultaneously within a run batch, and each sample was tested three times. The regression equation was obtained by line fitting using the known theoretical value on the X-axis and the measured mean value on the Y-axis. WS/T 403-2024 standard was used to calculate the total allowable error.

Sample comparison between instruments

Following the guidelines for Analytical Performance Verification of Quantitative Examination Procedures (WS/T 408-2024) and the CLSI EP09c-Ed3 guidelines [1], a comparative analysis between the QuidelOrtho VITROS 450 and the laboratory reference instrument (imported VITROS 4600, which participates in proficiency testing/external quality assessment) was conducted using patient samples. A minimum of 40 patient specimens were analyzed by both the experimental and reference instruments in a random order, with each measurement repeated once. Data analysis was performed to calculate bias at the medical decision level based on the fitted slope and intercept. The allowable total error (TEA) was determined according to WS/T 403-2024, requiring a bias of < 1/2 TEA.

RESULTS

Precision verification results

The within-run CV and total CV of the four test items verified by the QuidelOrtho VITROS 450 automatic biochemical analyzer were within the required range, and the specific results are shown in Table 1.

Trueness verification results

The relative bias of the four items verified was less than 1/2 TEA, indicating that the truthfulness verification of the four items of the QuidelOrtho VITROS 450 automatic biochemical analyzer met the requirements Table 2.

Linear verification

The verification results of the linear range and reportable range measured according to the requirements are shown in Table 3. The linear coordinates of AST, ALT, GGT, and LPS levels are shown in Figure 1. Scatter plots (upper panel) show a high linear correlation between measured mean values and theoretical concentrations across the entire validation range, with points closely aligned to the fitted line and its 95% confidence intervals. Residual plots (lower panel) demonstrate that residuals were randomly and evenly distributed around zero, with no systematic trends, indicating that the first-order linear model adequately described the relationship without significant non-linear effects. These results confirm that the method meets the required linearity performance.

Sample comparison between instruments

The comparison results between the detection system and the laboratory target machine 4600 showed that the detection system had good comparability of results. The qualified rate of sample comparison between the QuidelOrtho VITROS 450 automatic biochemical analyzer and the target VITROS 4600 automatic biochemical analyzer was ≥ 90%. The comparison met the requirements (≥ 80%). The systematic error (% bias) at the medical decision level, calculated according to the relevant formula, met the requirements, as shown in Table 4.

Method comparison between the test system (VITROS 450) and the reference instrument (VITROS 4600) was performed using Bland-Altman analysis for agreement assessment and Passing-Bablok regression for proportional and systematic bias evaluation (Figure 2). For AST, the mean bias was 0.05 U/L (SD = 4.652 U/L), with 95% limits of agreement (LoA) of -9.067 to 9.167 U/L, indicating excellent concordance. For ALT, the mean bias was 0.35 U/L (SD = 2.788 U/L, 95% LoA: -5.114 to 5.814 U/L). For GGT, the mean bias was -0.075 U/L (SD = 7.155 U/L, 95% LoA: -14.10 to 13.95 U/L). For LPS, the mean bias was -1.125 U/L (SD = 9.504 U/L, 95% LoA: -19.75 to 17.50 U/L). All parameters showed clinically acceptable bias and narrow 95% LoA, supporting interchangeability between the two systems.

DISCUSSION

LPS is a lipolytic enzyme that is primarily secreted by the pancreas and serves as the main source of LPS in the human body. Elevated serum LPS levels are commonly observed in acute pancreatitis (AP) and pancreatic cancer, making it a key serological marker for AP diagnosis [4,5]. Transaminases, including AST and ALT, are active substances in hepatocytes and other organ cells [6]. They participate in intracellular biochemical reactions, such as substance transformation, and serve as essential mediators of physiological metabolism. AST localizes to the hepatic mitochondrial matrices, whereas ALT resides in the hepatocyte cytoplasm [6]. Liver dysfunction triggers altered AST and ALT levels, with ALT being particularly sensitive to hepatocellular damage [7,8]. GGT, which is widely distributed in the liver, kidneys, and pancreas, is intricately linked to glucose and lipid metabolism. Blood GGT levels rise acutely in response to biliary excretion disorders or hepatic steatosis [9,10]. The clinical monitoring of these biomarkers is essential for disease staging and prognosis.

While dry chemistry technology has seen widespread clinical adoption, our laboratory recently introduced the QuidelOrtho VITROS 450 automatic biochemical analyzer. Although China has established national metrological verification regulations for newly purchased or

Table 1. Precision verification results of four test items of QuidelOrtho V450 automatic biochemical analyzer.

Item	Within-run CV (%)		Range of tolerance 1/4 Tea (%)	Total CV (%)		Range of tolerance 1/3 Tea (%)	Conclusion
	Low concentration	High concentration		Low concentration	High concentration		
AST	1.3	0.8	3.75	2.5	1.6	5	success
ALT	1	1.6	4	1.8	1.6	5.33	success
GGT	0.7	0.6	2.75	0.7	0.6	3.66	success
LPS	1.2	0.9	5	1.6	0.9	6.67	success

Table 2. Trueness verification results of 4 test items of QuidelOrtho VITROS 450 automatic biochemical analyzer.

Item	Relative bias (%)					Allowance for bias 1/2 Tea (%)	Conclusion
	Level 1	Level 2	Level 3	Level 4	Level 5		
AST	-6.59	-6.24	-5.6	-4.6	-5.36	7.5	success
ALT	-7.27	-1.84	-0.18	0.48	-5.22	8	success
GGT	-3.82	-2.61	-0.71	-1.2	-2.55	5.5	success
LPS	-1.65	-2.66	-1.45	-5.62	0.43	10	success

Relative bias = (measured values - target value)/target value x 100%.

Table 3. Linear range and regression equation of this detection system.

Item	Equation of regression	R^2	The linear range given by the manufacturer
AST	y = 1.004 x - 18.93	0.9958	3 - 750 U/L
ALT	y = 1.002 x - 1.970	0.9973	4 - 750 U/L
GGT	y = 0.9899 x - 12.30	0.9967	10 - 1,400 U/L
LPS	y = 0.9997 x + 28.73	0.999	10 - 2,000 U/L

Table 4. The systematic error (% bias) at the medical decision level.

Item	Range of comparison	Equation (GS)	Systematic errors at the level of medical determinacy
AST	15 - 576 U/L	y = -0.317 + 0.987 x	success
ALT	13 - 299 U/L	y = 2.006 + 0.969 x	success
GGT	11 - 1,142 U/L	y = -0.161 + 0.984 x	success
LPS	21 - 1,713 U/L	y = -0.760 + 1.032 x	success

in-use instruments, clinical validation data for certain devices, including dry chemistry analyzers, remain insufficient in real-world practice.

Some studies [11,12] have pointed out that the analytical performance verification content of quantitative test procedures should at least include the reportable range, trueness, and precision. Precision is the most important index for evaluating the analytical performance of instruments, detection methods, or kits to evaluate the stability of the precision evaluation process [13]. To verify the reliability of the basic performance of the VITROS 450 automatic biochemical analyzer, clinical perfor-

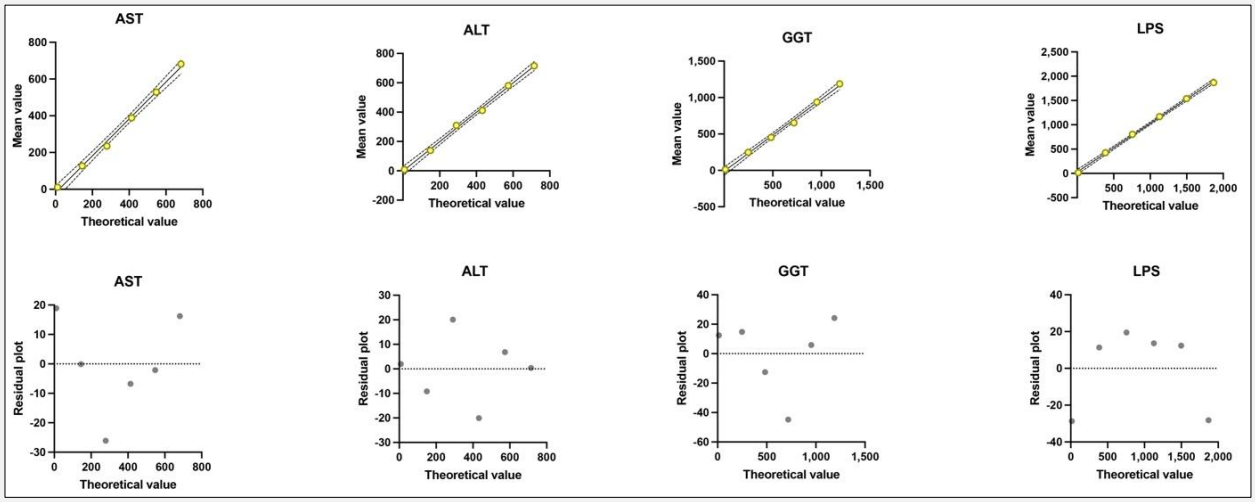

Figure 1. Linear coordinate plots of AST, ALT, GGT, and LPS.

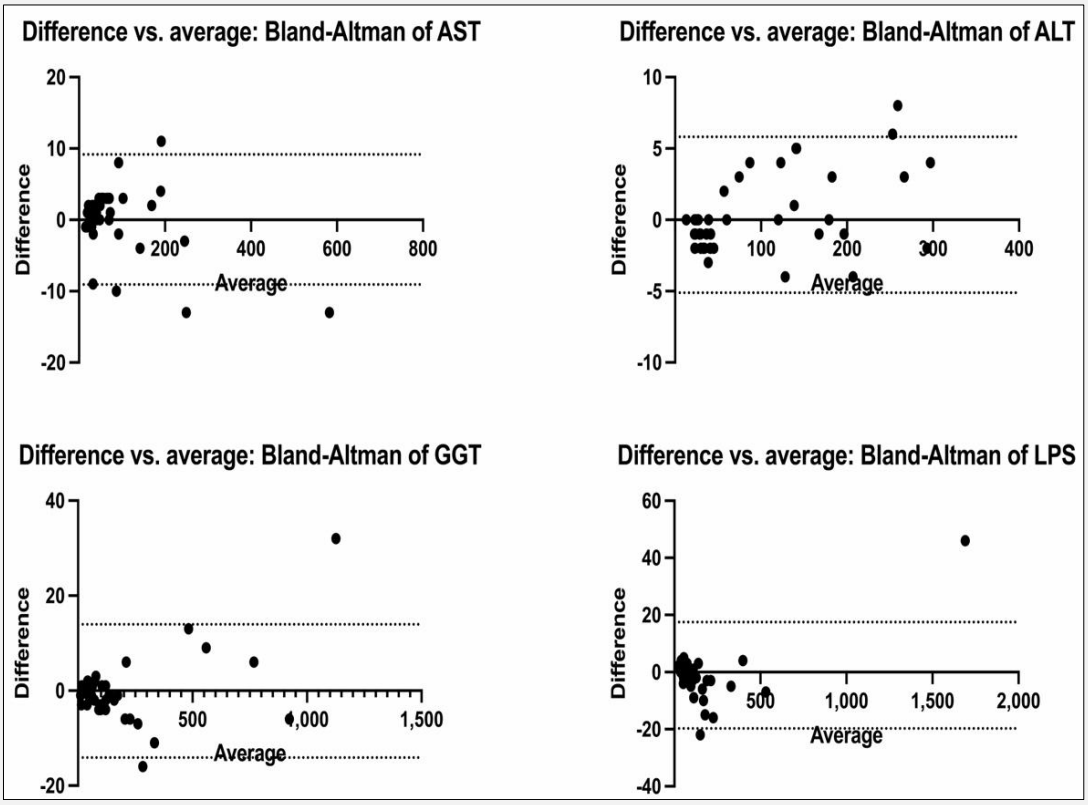

Figure 2. Comparison results of 40 samples between the two instruments using Bland-Altman analysis.

formance verification and evaluation of this instrument were performed by referring to CLSI documents and related materials [1,2]. The results showed that the intra-batch precisions of AST, ALT, GGT, and LPS were 0.8% - 1.3%, 1% - 1.6%, 0.6% - 0.7% and 0.9% - 1.2% respectively, while the inter-batch precision was 1.6% - 2.5%, 1.6% - 1.8%, 0.6% - 0.7% and 0.9% - 1.6%, respectively, which were less than the allowable range. The results showed that the repeatability of AST, ALT, GGT, and LPS in the VITROS 450 automatic biochemical analyzer met these requirements. According to WS/T 403-2024, trueness refers to the closeness between measured and true values, reflecting the systematic error of the detection system. According to the CNAS-CL02-A003 Guidance [14] on the Application of Accreditation Criteria for the Medical Laboratory Quality and Competence in the Field of Clinical Chemistry, when the trueness verification can be performed using non-matching analysis system, the participant should participate in the appropriate proficiency testing/EQA and pass the test in the last complete cycle. In this study, AST, ALT, GGT, and LPS EQA samples with five levels each were selected for detection using a QuidelOrtho VITROS 450 automatic biochemical analyzer. As shown in Table 2, the relative bias of the three items was less than 1/2 TEA, indicating that the detection results of this instrument were accurate and reliable. Linearity verification is a process used to evaluate whether a measurement system or an experimental method has linear characteristics within a certain range. Referring to the method in CNAS-GL037 [2], AST, ALT, GGT, and LPS were tested simultaneously with six patient samples at different concentrations in one run batch, and each sample was repeated three times. Figure 1 shows that in the regression equation of AST, ALT, GGT, and LPS, the correlation coefficients were 0.9958, 0.9973, 0.9967, and 0.999, respectively; that is, $R^2 > 0.995$, and the linearity was good, which met the needs of clinical results reporting [2]. Inter-sample comparison: It is an important component of laboratory quality management to achieve comparability of test results of the same item by different detection systems. The comparability of the test results guarantees the mutual recognition of test results between different reagents. The laboratory accreditation standard ISO 15189 requires the traceability and comparability of test results and emphasizes that the methodological comparison test is an important way to achieve accuracy traceability and comparability of test results of patient samples. This experiment was performed using the CLSI EP09c-Ed3 file [1], using a VITROS 4600 automatic biochemical analyzer as the experimental system, and a comparative study of AST, ALT, GGT, and LPS samples from 40 patients was performed using Quidel Ortho VITROS 450. The expected deviation or relative deviation of the test results at the level of medical decision was calculated according to the linear regression equation of each test, and clinical acceptability was evaluated. Table 4 shows that all four items had acceptable offsets at the medical decision level.

AST showed a consistent negative bias (-4.60% to -6.59%, mean -5.7%) across all five EQA levels, representing a systematic underestimation rather than random error. This may result from calibration shifts on the dry-slide platform, matrix effects in EQA materials, or minor differences in analytical conditions between instruments. The bias remained within the total allowable error (TEa) for AST, with minimal clinical impact on patient classification. Our linearity verification was performed according to the WS/T 408-2024 (equivalent to EP6-A) standard, which assesses the linear trend between measured sample concentrations (x) and instrument response values (y) using polynomial regression, focusing on the observed data range rather than mathematical extrapolation. The negative predicted concentrations derived from the regression equation do not indicate linearity failure; they merely reflect minor systematic bias near the low-concentration points, possibly related to background noise or matrix effects, while the linearity test (first-order model significantly superior to higher-order models, with acceptable deviation) was fully passed within the manufacturer's claimed range. This study has several limitations that should be acknowledged. First, this was a single-center study with only one comparative instrument used as the reference method, which may limit the generalizability of the findings. Second, performance verification was conducted for only four analytes, whereas the biochemical platform supports more than 20 parameters. Third, precision evaluation included only two concentration levels of quality control materials, which may not fully represent the analytical performance across the entire measuring range. Fourth, this performance verification was conducted in accordance with YY/T 0655-2024 (Medical device industry standard of the People's Republic of China: Dry chemical analyzers). Given the design of the dry-slide-based system (with disposable single-use slides eliminating carryover risk) and the scope of this study, we focused on the core analytical performance indicators specified in the standard, including precision, accuracy, linearity, and method comparison. Tests for carryover, interference, and other extended performance characteristics were not performed, as they are not required by the standard for this type of platform. Fifth, measurement uncertainty was not estimated in accordance with ISO standards. Sixth, total precision was evaluated over only 5 days, which is insufficient to reflect long-term analytical stability. Seventh, reagent lot-to-lot variation and operator-to-operator variation were not investigated. Eighth, method comparison was performed using only 40 patient samples with single measurements per sample, which limits the robustness of bias estimation. Ninth, no formal equivalence testing (e.g., TOST) was applied to confirm analytical interchangeability. Finally, potential matrix effects of EQA materials on the dry-slide chemistry system were not explored or discussed. Through this experiment, combined with the actual application, the main analytical

performance of the four biochemical indicators of the VITROS 450 automatic biochemical analyzer meets the quality target requirements and can be used for clinical laboratory testing.

Ethical Approval:
This study was approved by the Ethics Committee of Shanghai East Hospital (Approval No.: 2024YS-136). It used residual, de-identified specimens obtained from routine clinical laboratory testing. No additional patient specimens were collected, and all personal identifiers were permanently removed to protect patient privacy. Given the non-interventional nature of the study, the lack of additional patient risk, and the use of leftover, anonymized materials, formal ethical review was waived, and the research was exempted from the requirement for informed consent.

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Availability of Data and Materials Statements:
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Disclaimers:
The authors declare that they have no conflict of interest related to this search or the publication of this manuscript.

Declaration of Generative AI in Scientific Writing:
We confirm that the work complies with the ethical and academic standards of scientific writing, and no unauthorized use of generative AI has been made in the preparation of this manuscript.

Declaration of Interest:
The authors declare that they have no competing interests.

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