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RESEARCH ARTICLE

VERIFICATION OF ANALYTICAL PERFORMANCE OF FSH ASSAY ON THE ABBOTT ARCHITECT CI®: EXPERIENCE OF THE CENTRAL LABORATORY OF MOHAMMED VI UNIVERSITY HOSPITAL OF OUJDA

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ABSTRACT: Verification of analytical methods is a fundamental requirement for ensuring the accuracy, precision, and reliability of laboratory results, particularly for clinically important biomarkers such as follicle-stimulating hormone (FSH). This study evaluates the analytical performance of the FSH assay performed using chemiluminescent microparticle immunoassay (CMIA) on the ABBOTT ARCHITECT Ci analyzer in the central laboratory of Mohammed VI University Hospital. The verification process included two phases: assessment of intermediate precision over a 30-day period using three levels of internal quality control, and evaluation of repeatability based on 30 consecutive measurements for three concentration levels. Intermediate precision showed coefficients of variation (CVs) of 5.55%, 6.27%, and 9.08%, while repeatability demonstrated excellent performance with CVs of 3.96%, 3.19%, and 2.22% across low, medium, and high levels, respectively. All results met the acceptance criteria defined by RICOS and FSCB. These findings confirm that the CMIA FSH assay provides reliable, reproducible, and clinically robust measurements. Incorporating this verification into routine practice strengthens the laboratory's quality management system and ensures that FSH results are accurate, reproducible, and directly supportive of clinical decision-making.

Keywords: FSH; Analytical performance; Repeatability; Reproducibility; Architect ABOTT Ci Analyzer; CMIA.Alinity**i®**

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INTRODUCTION:

Ensuring the quality of medical laboratory testing is essential for generating accurate, reliable, and clinically interpretable results. Analytical method verification constitutes a fundamental step in this process, allowing laboratories to evaluate the performance of each method under routine conditions before implementation. Performance metrics are then compared with predefined acceptability criteria established by recognized professional organizations, such as RICOS and the French Society of Clinical Biology (FSCB), to ensure clinical fitness.

A comprehensive laboratory quality assurance system integrates both internal analytical workflows and external regulatory requirements. Structured quality management supports continuous monitoring of analytical performance and maintains consistency over time. International standards, including ISO 15189, have significantly contributed to improving laboratory quality by defining requirements for technical competence, method verification, and ongoing performance evaluation throughout a method's operational lifecycle. Clear, standardized, and practical guidelines are therefore essential for maintaining reliability and clinical relevance [1-2].

Follicle-stimulating hormone (FSH) is a critical endocrine biomarker routinely measured to assess reproductive function and related disorders in both women and men. In our laboratory, FSH determination is performed using a chemiluminescent microparticle immunoassay (CMIA) on the ABBOTT ARCHITECT Ci automated system. Given the clinical importance of FSH and potential variability introduced by local pre-analytical and analytical conditions, laboratory-specific verification of analytical performance is indispensable.

Independent verification studies of FSH assays under routine clinical conditions remain scarce, particularly those combining COFRAC GTA-04 recommendations with analytical performance specifications from RICOS and FSCB. This study addresses this gap by providing original, real-world verification data for the FSH CMIA assay on the ARCHITECT Ci Analyzer. By applying a structured verification approach integrating these frameworks, the study evaluates both repeatability and intermediate precision, providing critical methodological and analytical insights. These findings reinforce confidence in the reliability, reproducibility, and clinical suitability of the FSH assay, supporting its routine use in the central laboratory of Mohammed VI University Hospital.

About FSH

FSH (follicle-stimulating hormone) is the key hormone involved in reproduction in mammals. It is essential for the development and maturation of the gonads during puberty, as well as for the production of gametes during the fertile phase of life. In association with LH, this gonadotropin is produced and secreted by the pituitary gland in the form of a highly heterogeneous glycoprotein [3-4].

FSH acts by binding to specific receptors located exclusively in the gonads. The FSH receptor belongs to the family of G protein-coupled receptors (GPCRs), complex transmembrane proteins characterized by seven hydrophobic helices anchored in the plasma membrane, as well as intracellular and extracellular domains whose dimensions vary depending on the type of ligand [5]. The intracellular portion of the FSH receptor is coupled to a Gs protein. When the hormone interacts with the extracellular domain of the receptor, the receptor is activated, triggering a cascade of intracellular signals that cause the specific biological effects of this gonadotropin.

Measuring follicle-stimulating hormone (FSH) levels plays a pivotal role in assessing reproductive function in both women and men.

In women, FSH testing is an effective tool for diagnosing premature ovarian failure, confirming the onset of menopause, and guiding the management of ovulation disorders in the context of infertility. As highlighted by Berger (1994), FSH is a sensitive marker of hormonal changes during the menopausal transition, showing a significant increase with a decrease in ovarian reserve [6].

In men, FSH is also a key indicator of testicular function. It helps to distinguish between primary hypogonadism, which is characterised by high FSH levels due to testicular failure, and secondary (central) hypogonadism, where FSH levels are typically low or within normal range due to a defect in the function of the hypothalamus or pituitary gland. Multiple studies have demonstrated a strong correlation between serum FSH levels and testicular tissue, particularly in cases of azoospermia or significantly impaired spermatogenesis [7]. Elevated FSH levels often indicate untreatable damage to the testes, such as tubular sclerosis, while low or normal levels may indicate a central origin [7].

From a physiological perspective, FSH is secreted from the anterior pituitary gland under the control of gonadotropin-releasing hormone (GnRH) and acts in coordination with

Biological Principles of the Method

The ARCHITECT FSH assay is a two-step immunoassay designed to quantitatively determine FSH in human serum and plasma using CMIA technology, employing flexible Chemiflex protocols. First, the specimen is incubated with paramagnetic micro particles coated with antiβ FSH antibodies, allowing any FSH present to bind. After washing, an acridiniumlabeled antiα FSH antibody conjugate is added to form a reaction mixture. A second wash is performed, followed by the addition of preactivation and activation solutions. The resulting chemiluminescent reaction is measured in Relative Light Units (RLU), with a direct proportional relationship between the amount of FSH in the sample and the RLUs detected by the ARCHITECT iSystem optics.

MATERIAL AND METHODS:

This prospective study was conducted in the biochemistry laboratory of Mohammed VI University Hospital over a 30-day period. The study was designed in accordance with ISO 15189 principles and consisted of two analytical verification phases.

The first phase assessed intermediate precision (reproducibility) by performing daily internal quality control measurements at three concentration levels (low, medium, and high) throughout the study period. This approach enabled evaluation of analytical stability over time. Serum samples with follicle-stimulating hormone (FSH) concentrations evenly distributed across the analytical measurement range were selected and classified into three groups based on their FSH levels. All serum samples were stored at 8 °C under controlled pre-analytical conditions, and no freeze–thaw cycles were applied prior to analysis.

The second phase evaluated repeatability (within-run precision). For each concentration level, thirty consecutive measurements were performed during a single analytical run under identical operating conditions.

FSH concentrations were measured using the ARCHITECT FSH 7K75 reagent kit on the ABBOTT ARCHITECT iSystem. Calibration was performed using the manufacturer-provided FSH calibrator in accordance with the manufacturer's recommendations. Internal quality control materials supplied by the manufacturer were analyzed at three concentration levels and were independent of the calibrators. Quality control lot numbers were recorded and monitored according to routine laboratory quality assurance procedures.

The analytical verification protocol followed the operational recommendations of the COFRAC GTA-04 accreditation technical guide. Statistical analysis was conducted using the EVM Intermediate module of BYG Informatique software. Data distribution normality was assessed prior to analysis, and potential outliers were evaluated according to predefined statistical criteria. Precision results were compared with acceptable analytical performance specifications derived from RICOS and/or FSCB recommendations, using allowable imprecision and total allowable error as acceptance criteria. The BYG Informatique software functioned as an intermediary platform between the ABBOTT analytical system and the iLab laboratory information system.

RESULTS:

Intermediate precision results

The intermediate precision test (intra-laboratory reproducibility) consists of assaying the same sample under different conditions by varying at least one of the following factors: operator, time, reagent batches, calibrations, etc. It allows the acceptance criteria to be set in combination with biological variations, particularly in the case of decision support systems. [8] The intermediate precision results were satisfactory for all three levels: low, medium and high, with: CV1 = 5,55 %, CV2 = 6,27 % and CV3 = 9,08 respectively. These results are illustrated in the Levey-Jennings graphs (Fig. 1, Fig. 2, Fig. 3).

Table 1 Reproducibility results of blood assay by level

Level of Internal quality control (IQC)	Number of values	Mean (mUi/ml)	Standard Deviation (mUi/ml)	Coefficient of Variation CV (%)	Reference CV: FSBC 1999
Low	45	8,34	0.463	5,55	10
Medium	47	16,42	1,030	6,27	8
High	44	36,62	3,327	9,08	9.39

with comparison to FSBC

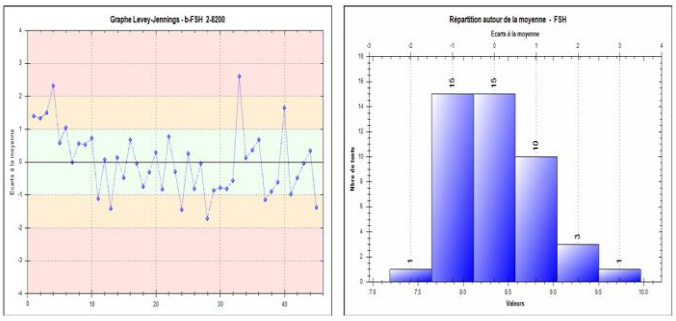

Figure 1 Low level of reproducibility: Levey Jennings graph and the distribution around the mean

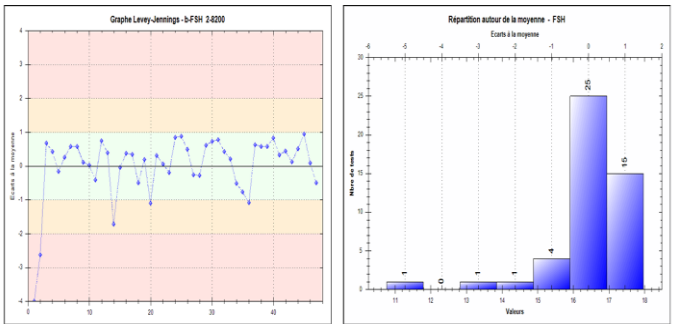

Figure 2 Medium level of reproducibility: Levey Jennings graph and the distribution around the mean

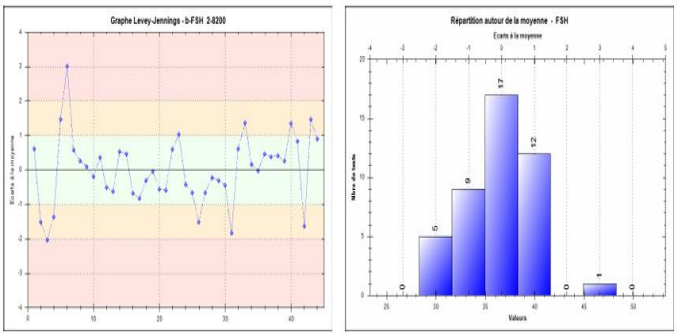

Figure 3 High level of reproducibility: Levey Jennings graph and the distribution around the mean

Repeatability results

The repeatability test consists of analyzing the same sample under the following conditions.

Same operator, same batch of reagents, same instrument, same calibration in the shortest possible time. The objective is to determine the best possible performance under optimal conditions and to verify the proper functioning of the system (instrument/reagent) for the analyte concerned. [8,9].

For a given analyzer, this calculation must be performed for each analyte/matrix to be measured and at several concentration levels. The levels are chosen according to the medical decision-making domains. The calculated CV is compared to the acceptable CV limit chosen in advance. The results obtained showed good repeatability for the three

levels: low, medium and high, with: CV1 = 3,96 %, CV2 = 3,19 %, CV3 = 2,22 %, respectively. The Levey Jennings graphs illustrate these results. (Fig. 4, Fig. 5, Fig. 6)

Table 2 Repeatability results of blood assay by level with comparison to FSBC

Level of Internal quality control (IQC)	Number of values	Mean (mUi/ml)	Standard Deviation (mUi/ml)	Coefficient of Variation CV (%)	Reference CV: FSBC 1999
Low	30	5,14	0.203	3,96	7,50
Medium	30	20,30	0.648	3,19	6,00
High	30	37,92	0.842	2,22	6,00

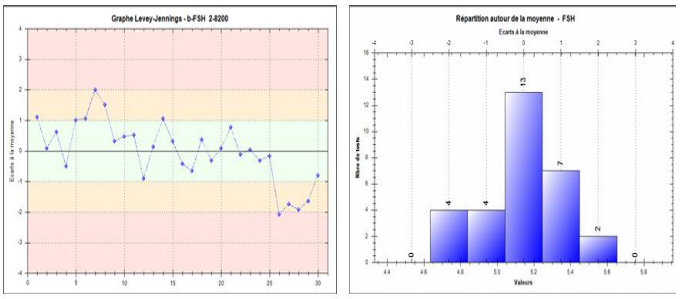

Figure 4 Low level of repeatability: Levey Jennings graph and the distribution around the mean

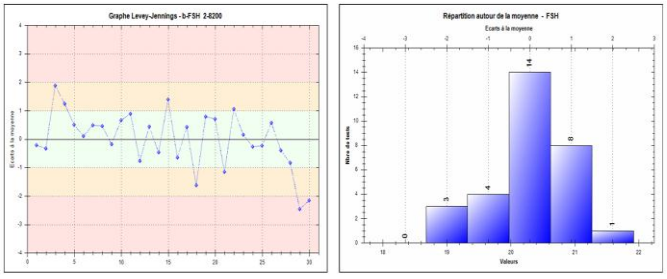

Figure 5 Medium level of repeatability Levey Jennings graph and the distribution around the mean

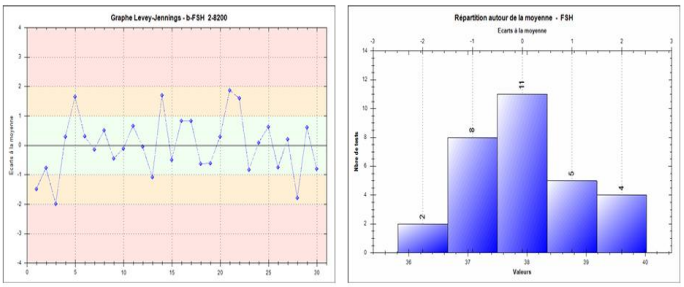

Figure 6 High level of repeatability Levey Jennings graph and the distribution around the mean

DISCUSSION:

Medical biology testing occupies a central role in preventive, diagnostic, prognostic, and therapeutic decision-making. The clinical laboratory is responsible for generating reliable results that guide medical practice, and this responsibility extends across the entire analytical workflow—from pre-analytical handling to analytical processing and post-analytical interpretation [1]. Such responsibilities are emphasized in international standards such as NF EN ISO 15189 and NF EN ISO/IEC 17025, which define the general requirements for quality and competence in medical testing laboratories [11]. These standards highlight that quality is not an option but an ongoing commitment shared by all laboratory professionals [2].

In this context, method verification represents a crucial component of quality assurance. Unlike full validation, which applies mainly to newly developed or modified methods, verification confirms that a commercial method performs according to the specifications claimed by the manufacturer when implemented under local laboratory conditions [3-5]. In this study, we applied the requirements outlined in ISO 15189 and followed the COFRAC SH-GTA-04 guidance document to verify the precision of the FSH assay performed using CMIA technology on the Abbott Architect Ci system [8]. This assay is already used in our laboratory and therefore requires verification rather than initial validation. Verification ensures that performance meets clinical needs and complies with accreditation expectations [11-12].

Intermediate precision (inter-laboratory reproducibility) is fundamental for evaluating the robustness of an analytical method in routine practice

[6]. It takes into account variations inherent to daily laboratory conditions, including changes in operators, reagent lots, calibrations, environmental conditions, and instrument maintenance cycles. [7-9] These sources of variability reflect real-world conditions far more accurately than controlled repeatability studies. According to Westgard et al., reproducibility evaluation is indispensable for determining whether analytical variability remains within clinically acceptable limits, particularly when clinical decision thresholds are narrow [13-21].

In our study, intermediate precision showed satisfactory performance across all concentration levels, with CVs of 5.55%, 6.27%, and 9.08%. These results are consistent with the literature reporting similar levels of imprecision for CMIA assays on the Architect system [15-17]. Hansen et al. [17] and Lyons et al. [16] demonstrated comparable reproducibility for gonadotropin assays, confirming the stability of the Architect platform across hormonal analyses. The CVs observed in our study fall within the limits recommended by FSCB and RICOS, [24-25] whose biological variation–based specifications are widely recognized as clinically meaningful criteria for analytical performance.

Repeatability represents the intrinsic precision of an assay under optimal conditions (same operator, same reagent lot, same calibration, minimal time variation) [4-14]. It is considered the "best achievable precision" and reflects the method's analytical capacity in the absence of external variability. In our evaluation, repeatability CVs were remarkably low 3.96%, 3.19%, and 2.22% indicating high measurement stability and minimal dispersion. These findings align with values described in earlier method verification studies for reproductive hormones using CMIA and similar immunoassay technologies [16-18-22].

Repeatability is especially important for hormones such as FSH, where small analytical differences may significantly impact clinical interpretation, particularly in the evaluation of ovarian reserve, menopausal transition, spermatogenic dysfunction, and pituitary disorders [18,19,20]. Our results confirm that the CMIA FSH method is capable of delivering highly reproducible results, a necessary condition for clinical confidence and diagnostic accuracy.

Combining intermediate precision and repeatability results provides an overall picture of method robustness under both optimal and routine conditions [23]. He complementary nature of these two evaluations is essential, as repeatability reflects the intrinsic technical performance of the analyzer, while intermediate precision reflects its stability during real-life laboratory conditions over time. When both parameters show acceptable CV as observed in our study it confirms that the method can reliably support patient care and clinical decision-making.

Several authors emphasize the key role of biological variation–based specifications in determining whether analytical imprecision remains acceptable [24-25]. Compliance with these specifications is crucial, especially for hormones involved in reproductive endocrinology, where diagnostic cut-offs are often narrow and clinically sensitive[3-6, 18]. Our study shows that FSH measurement performance fully meets these international standards, ensuring that the assay can reliably distinguish between clinically relevant hormonal states such as menopausal transition, premature ovarian insufficiency, primary vs secondary hypogonadism, and various forms of azoospermia [6-7, 18-20].

At Mohammed VI University Hospital's central laboratory, the pursuit of ISO 15189 accreditation represents a strategic institutional objective. Method verification contributes significantly to meeting accreditation requirements by ensuring that each analytical method is fit for purpose, reproducible, and aligned with international standards [11-12, 26]. The excellent analytical performance demonstrated in this study reinforces confidence in our FSH assay results and contributes to strengthening our overall quality management system.

Beyond technical compliance, the demonstrated robustness of the method enhances clinical reliability and supports improved medical decision-making [27]. Given the essential role of FSH in evaluating ovarian and testicular function, hormonal disorders, and fertility issues, accurate measurement is fundamental

to patient management [18,19,20]. The strong performance of the CMIA FSH assay the reform provides reassurance that results delivered to clinicians are dependable, consistent, and clinically interpretable.

CONCLUSION:

The verification of the FSH assay on the Abbott Architect Ci® using the CMIA method shows that our testing system performs reliably and consistently. Both repeatability and intermediate precision remained well within the limits recommended by RICOS and FSCB, confirming the stability of the method across all tested levels.

These findings reassure us that the assay is fully suitable for routine use in daily clinical practice, providing accurate and clinically meaningful FSH measurements. By incorporating this verification into our quality management process and ISO 15189 accreditation efforts, the central laboratory of Mohammed VI University Hospital continues to demonstrate its commitment to maintaining high analytical standards and delivering trustworthy diagnostic results for optimal patient care.

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