World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

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Verification of analytical performance of intact parathyroid hormone assay on the Abbott Alinity ci®: Experience of the central laboratory of Mohammed VI University Hospital of Oujda

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World Journal of Biology Pharmacy and Health Sciences, 2024, 19(03), 582–588

Publication history: Received on 16 August 2024; revised on 25 September 2024; accepted on 27 September 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.19.3.0691

Abstract

The primary goal of our study was to verify the analytical performance of intact parathyroid hormone measurements conducted on the Abbott CI analyzer using the immuno-chemiluminescence method. This verification took place in the biochemistry laboratory at Mohammed VI University Hospital in Oujda.

Our methodology was aligned with the recommendations outlined in the French accreditation committee (COFRAC) technical guide (GTA) 04, emphasizing the assessment of reproducibility and repeatability.

Overall, the results of this evaluation were satisfactory and met the standards set by both the supplier and the French Society of Clinical Biology. This study illustrates that the biochemistry laboratory at Mohammed VI University Hospital of Oujda is equipped to provide accurate and precise results, which are crucial for effective clinical diagnosis and decision-making.

Keywords: Intact parathyroid hormone assay; Analytical performance; Repeatability; Reproducibility; Alinity CI analyzer; Immuno-chemiluminescence

1. Introduction

Quality is an ongoing commitment to consistently achieving accurate test results. A quality assurance system encompasses all laboratory operations, both internal and external, integrating effective practices and improved management skills. This framework ensures that tests are conducted accurately on appropriate samples from the correct subjects in well-equipped facilities, leading to reliable interpretations based on accurate reference data. To embed quality principles within medical laboratories, it is essential to establish a targeted quality management program that upholds the integrity of laboratory results.

In recent years, significant advancements have been made to enhance quality in clinical laboratories, particularly through the implementation of accreditation based on ISO 15189 standards, which assess both technical and managerial capabilities. This accreditation process includes the validation, verification, and quality assurance of testing methods.

Accredited laboratories are required to evaluate and document the analytical performance of all methods not only prior to their implementation but also throughout their operational lifecycle. Clear, standardized, and practical guidelines are critical in this regard [1, 2].

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The verification of analytical methods in medical laboratories is vital to ensure that results accurately reflect the true reference values of samples, thereby guaranteeing the accuracy and reliability of measurements. This process involves a series of steps designed to meet the quality standards outlined in ISO 15189, including assessing the effectiveness of analytical procedures, measuring performance through standardized approaches, and comparing results against predefined benchmarks [3].

Improper implementation of these methods can lead to inaccurate assessments of method performance, potentially compromising patient safety and leading to incorrect diagnoses.

The central laboratory at Mohammed VI University Hospital in Oujda has developed a comprehensive quality strategy that includes a method verification protocol, which is integral to our study. Our research will focus on evaluating the analytical performance of intact parathyroid hormone measurements, using the criteria specified in Scope A of the detailed medical biology method verification and validation guide.

1.1. Interest of intact parathyroid hormone determination

PTH is a single chain polypeptide of 84 amino acids produced by the parathyroid gland. Intact PTH1-84 is secreted into the blood stream and undergoes extensive proteolytic modifications. In contrast to its degradation products, the concentration of intact PTH is relatively independent of glomerular filtration rate and reflects the biologically active portion of the hormone. The primary role of PTH is to regulate the blood calcium level. PTH synthesis and secretion are stimulated within a few minutes by low concentrations of ionized calcium (Ca). The biological activity of PTH is to increase absorption of dietary calcium, decrease renal clearance and mobilize skeletal calcium stores. Abnormally high Ca concentrations suppress secretion of PTH. In conjunction with serum calcium levels, the Alinity i® Intact PTH assay may be used as an aid in the differential diagnosis of hypercalcemia, hypocalcemia and parathyroid disorders. PTH determination is important in monitoring dialysis patients to manage renal osteodystrophy [4, 5].

1.2. Principle of intact parathyroid hormone assay method

This assay is a two-step immunoassay for the quantitative determination of intact PTH in human serum and plasma using chemiluminescent microparticle immunoassay (CMIA) technology. Sample, anti-PTH coated paramagnetic microparticles, and assay diluent are combined and incubated. The intact PTH present in the sample binds to the anti-PTH coated microparticles. The mixture is washed. Anti-PTH acridinium-labeled conjugate is added to create a reaction mixture and incubated. Following a wash cycle, Pre-Trigger and Trigger Solutions are added. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of intact PTH in the sample and the RLUs detected by the system optics [6].

2. Material and methods

This prospective study was conducted over a 30-day period in the biochemistry laboratory at Mohammed VI University Hospital.

Our research consisted of two phases. The first phase focused on evaluating reproducibility, also known as intermediate fidelity, by performing daily internal controls across three measurement levels: low, medium, and high. This was done to assess consistency over the 30 days. For this phase, we selected a range of serum samples with intact parathyroid hormone values that were evenly distributed across the measurement spectrum. These samples were categorized into three groups: low, medium, and high based on their intact parathyroid hormone levels.

In the second phase, we assessed repeatability by running thirty repetitions of each sample. The analytical procedure utilized the Alinity i® intact parathyroid hormone reagent kit on the immunoassay system.

Our operational approach was guided by the recommendations outlined in the COFRAC GTA 04 accreditation technical guide. Statistical analysis of the data was performed using the EVM intermediate module from BYG Informatics.

3. Results

3.1. Reproducibility results

Intra-laboratory reproducibility, also known as intermediate fidelity, is assessed by repeatedly measuring samples under various operational conditions (such as time, reagent batches, calibrations, operators, and equipment) to evaluate how these factors affect the results.

The collected data is used to calculate the mean, standard deviation, and coefficient of variation (CV) for each series, as well as within-series and between-series comparisons, and for the overall data set [7].

The intermediate fidelity results were found to be acceptable at all three levels: low, medium, and high, with coefficients of variation of 12.08%, 5.97%, and 4.44%, respectively. The reproducibility CV for each level is satisfactory, remaining below the thresholds established by both the SFBC (quality control system) and the RICOS (global quality control network).

To visually represent these results, Levey-Jennings plots (Fig. 1, Fig. 2, and Fig. 3) have been created, enhancing the clarity of the findings.

Table 1 Reproducibility results of blood assay by level with comparison to FSBC and RICOS data

Level of IQC	Number of values	Mean (g/l)	Standard Deviation	Coefficient of Variation CV (%)	CV SFBC 1999 (%)	CV RICOS S. (2014) (%)
Low	30	7.50 pg/ml	0.906 pg/ml	12.08 %	15.00 %	12.95 %
Medium	30	60.34 pg/ml	3.601 pg/ml	5.97 %	8.00 %	12.95 %
High	30	227.71 pg/ml	10.116 pg/ml	4.44 %	8.00 %	12.95 %

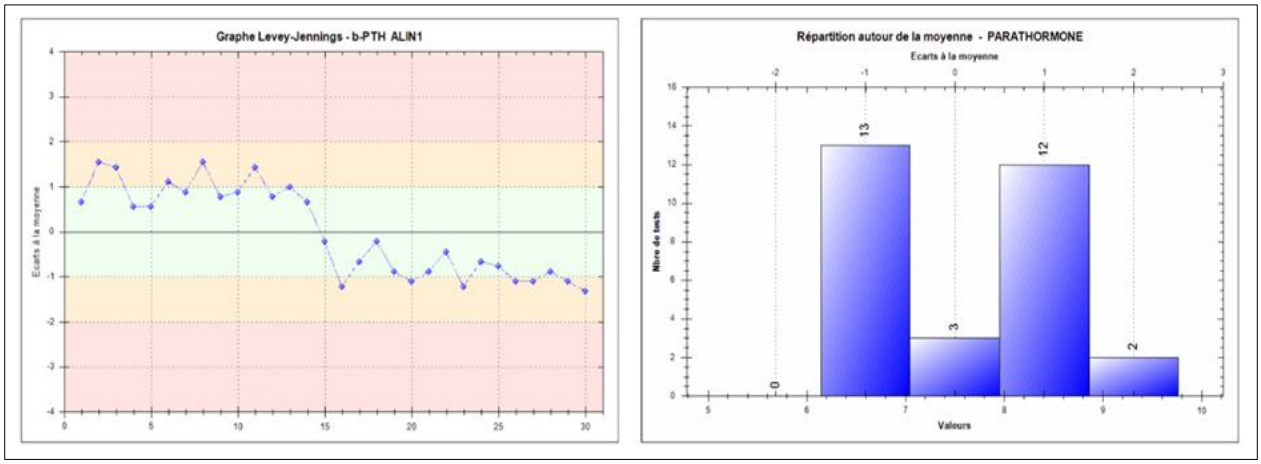

Figure 1 Low Level of Reproducibility: Levey Jennings graph and the distribution around the mean - Intact Parathyroid Hormone

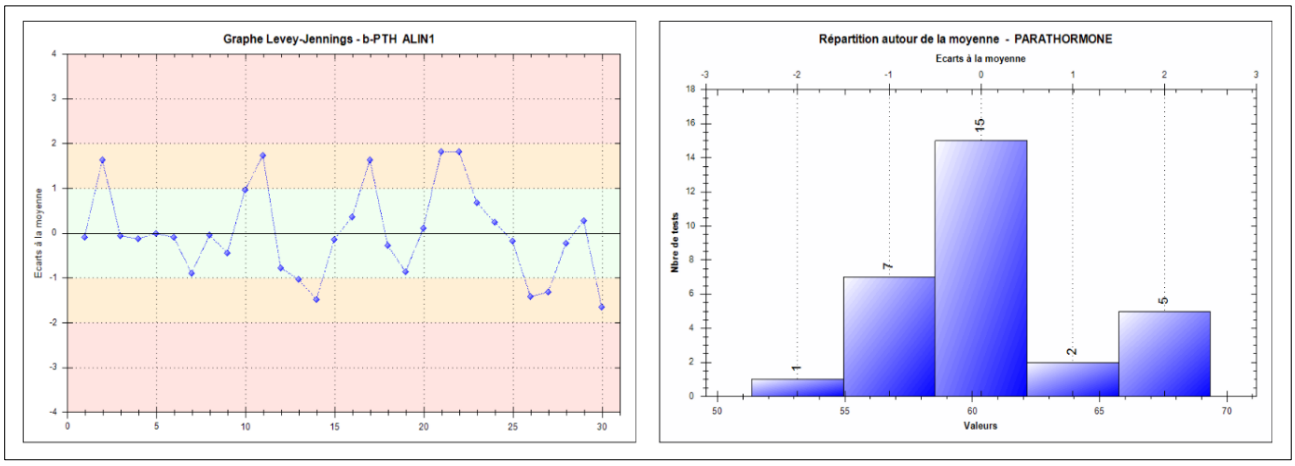

Figure 2 Medium Level of Reproducibility: Levey Jennings graph and the distribution around the mean - Intact Parathyroid Hormone

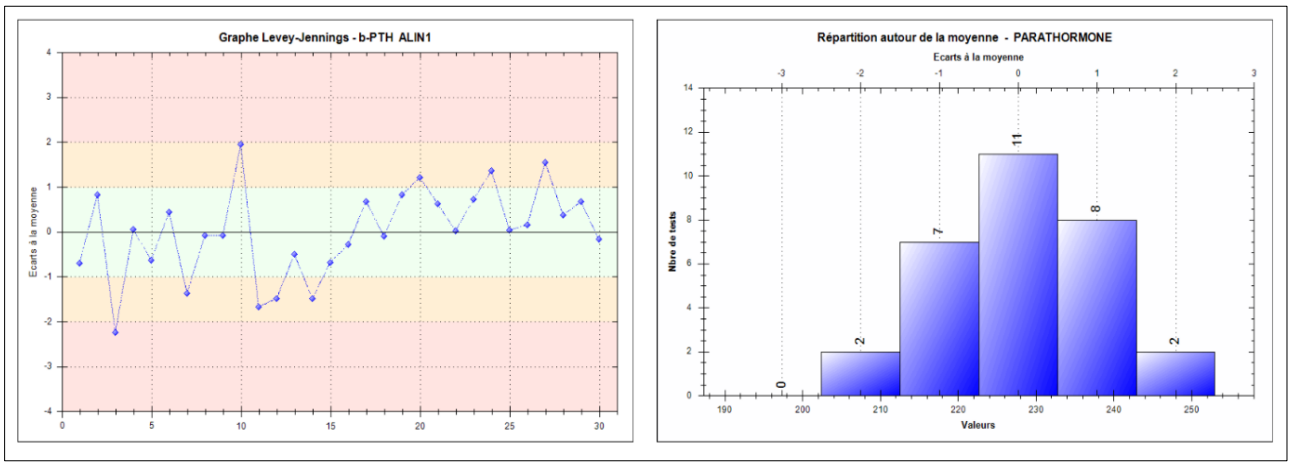

Figure 3 High Level of Reproducibility: Levey Jennings graph and the distribution around the mean - Intact Parathyroid Hormone

3.2. Repeatability Results

Repeatability is evaluated by conducting multiple assays of the same samples by the same operator under consistent conditions, which include factors such as reagent, calibration, instrument, and operator, all within the shortest possible timeframe.

This repeatability assessment allows for the determination of initial performance and verifies the proper functioning of the system (instrument and reagent) for the specific analyte. Variability is again measured using coefficient of variation (CV) values [7].

As shown in Table 2, the results for the various verification criteria of the intact parathyroid hormone assay indicate satisfactory repeatability across all three levels: low, medium, and high, with coefficients of variation of 3.93%, 2.77%, and 2.56%, respectively, based on 30 samples.

Table 2 Repeatability results for intact parathyroid hormone on the Alinity i® automated system by level with comparison to SFBC and RICOS data

Level of IQC	Number of values	Mean (g/l)	Standard Deviation	Coefficient of Variation CV (%)	CV SFBC 1999 (%)	CV RICOS S. (2014) (%)
Low	30	5.67 pg/ml	0.223 pg/ml	3.93 %	11.25 %	9.71 %
Medium	30	53.23 pg/ml	1.448 pg/ml	2.77 %	6.00 %	9.71 %
High	30	210.43 pg/ml	5.383 pg/ml	2.56 %	6.00 %	9.71 %

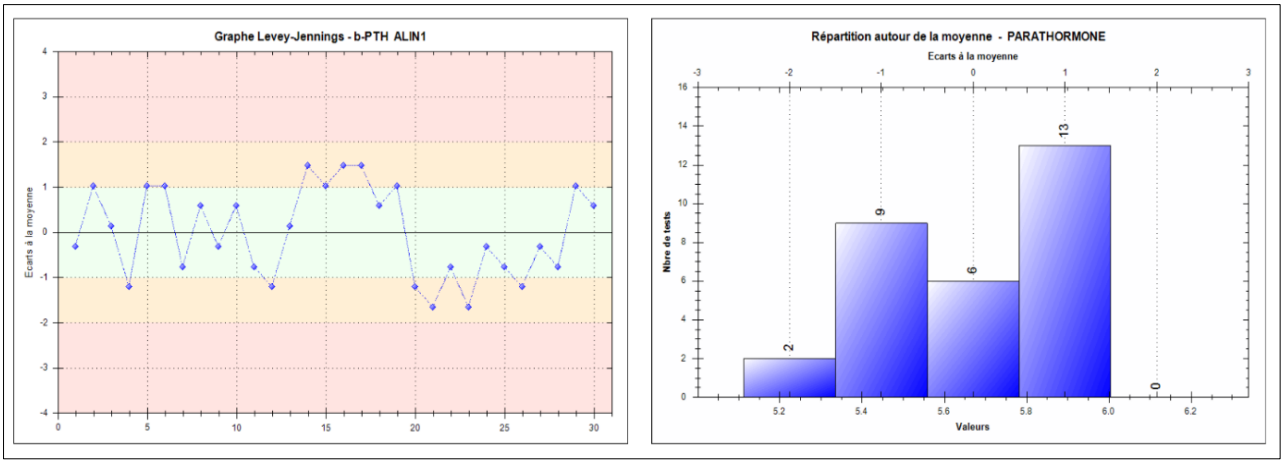

Figure 4 Low Level of Repeatability: Levey Jennings graph and the distribution around the mean - Intact Parathyroid Hormone

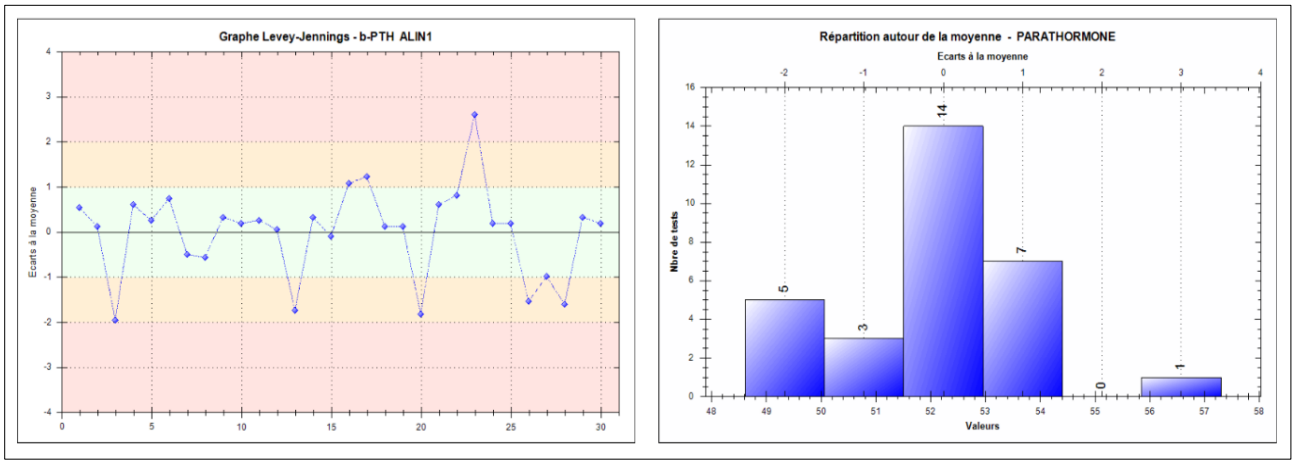

Figure 5 Medium Level of Repeatability: Levey Jennings graph and the distribution around the mean - Intact Parathyroid Hormone

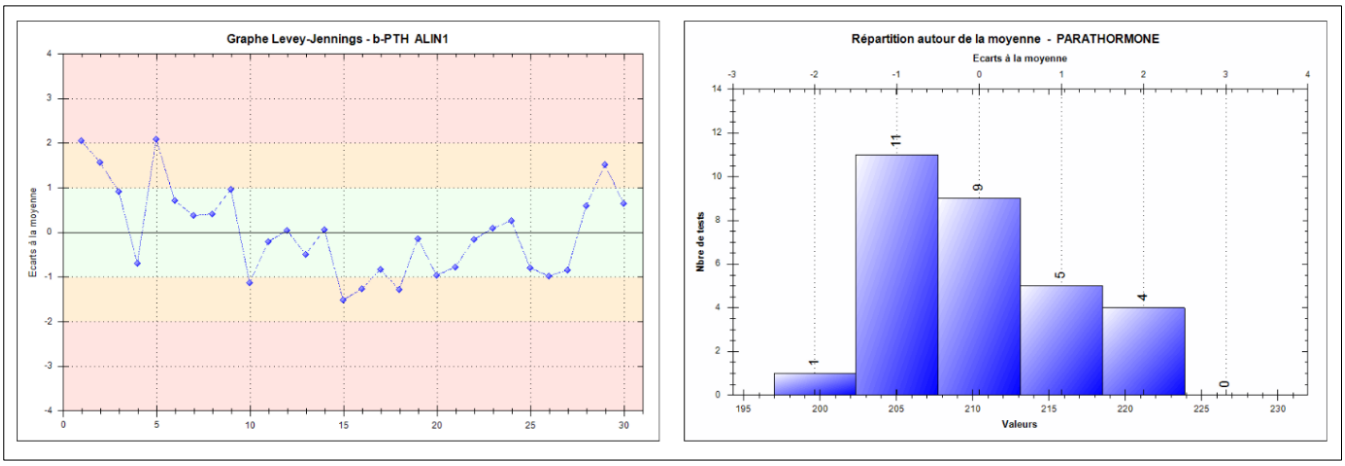

Figure 6 High Level of Repeatability: Levey Jennings graph and the distribution around the mean - Intact Parathyroid Hormone

4. Discussion

Variations in parathyroid hormone (PTH) levels are expected throughout the diurnal cycle, influenced by factors such as sex, sun exposure (season, geography, clothing customs, skin pigmentation), diet (estimating daily intake of calcium and vitamin D), and level of physical activity. There are also variations related to medication use, including diuretics (thiazides), hormonal treatments (corticosteroids, sex steroids), and bone remodeling therapies (bisphosphonates, vitamin D, estrogens, and androgens). Additionally, PTH secretion is altered in various endocrine disorders (e.g., hyperthyroidism), as well as in gastrointestinal and renal diseases.

The Abbott Alinity ci® system is a comprehensive multiparametric platform that integrates clinical chemistry with immunoassay capabilities, facilitating the measurement of a wide array of standard biochemical parameters and specific proteins. For the intact parathyroid hormone assay, the CMIA (microparticle chemiluminescence immunoassay) method is employed, which eliminates the need for validation; instead, we focus on verification following the "scope A verification/validation" framework. This ensures that recognized methods are pre-validated within their intended applications, thus confirming the accuracy and reliability of the results obtained [8].

This verification process is essential for adherence to regulatory standards outlined in the Moroccan Guide for the Proper Execution of Medical Laboratory Analyses (GBEA) and complies with ISO 15189:2022 requirements. By setting clear analytical goals through this control, we can ensure the generation of accurate and trustworthy results.

A reproducibility test is conducted to evaluate the consistency of assay results when different variables are introduced. Our study confirmed the reliability of the intact parathyroid hormone assay for reproducibility assessment across three distinct levels: low, medium, and high. Each level involved the analysis of 30 values, resulting in means of m1 = 7.50 pg/ml, m2 = 60.34 pg/ml, and m3 = 227.71 pg/ml, with coefficients of variation (CV) of CV1 = 12.08%, CV2 = 5.97%, and CV3 = 4.44%. The low CV values indicate consistent results that remain close to the mean, even when various factors are adjusted. This reliability is crucial in medical testing, where consistent results are vital for clinical decision-making. The fact that the CV values align with established quality control limits indicates compliance with industry standards for reproducibility, thereby enhancing its suitability for accurate diagnostics.

The focus of the repeatability test is on the precision of the assay under controlled conditions. This evaluation is important as it measures the method's capability to yield consistent results when the same sample is analyzed repeatedly. In our assessment of repeatability at three levels (low, medium, and high), we analyzed 30 values for each, resulting in remarkably low coefficients of variation (CV): CV1 = 3.93%, CV2 = 2.77%, and CV3 = 2.56%. These low CV values reflect minimal variability, underscoring the assay's high precision.

The stability and predictability of the assay's outcomes under controlled conditions are critical, especially in clinical settings where minor variations can significantly affect patient care.

At the Mohammed VI University Hospital in Oujda, our laboratory has implemented a comprehensive quality strategy that includes a robust method verification protocol. This investigation is vital for establishing a credible accreditation

pathway for the analyses conducted. Serving as a primary reference center in Eastern Morocco, our laboratory not only addresses the needs of referred and hospitalized patients but also significantly contributes to understanding the overall health of the regional population through various scientific initiatives [9, 10].

5. Conclusion

The role of medical biology has become essential in the healthcare landscape, evolving the choice of analytical methods from random selections to a systematic approach driven by defined criteria based on the principles of the technique and its validation or verification processes. At the Mohammed VI University Hospital's central laboratory, there is a strong commitment to the accreditation process, with method validation and verification recognized as vital steps in this endeavor. The results for reproducibility and repeatability are exceptional, conforming to the standards established by RICOS and the guidelines in the Valtec protocol (FSCB). These results strongly indicate the robustness and reliability of the serum intact parathyroid hormone assay. This investigation underscores the rigorous quality control practices in medical laboratories, enriching the essential knowledge base necessary for accurate serum intact parathyroid hormone measurements and thereby improving the clinical relevance of this assay.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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