**World Journal of Pharmaceutical Sciences**
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: https://wjpsonline.com/
**Research Article**

# STABILITY INDICATING RP-HPLC METHOD FOR THE DEVELOPMENT AND VALIDATION OF FINERENONE IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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***Received: 08-10-2025 / Revised Accepted: 11-10-2025 / Published: 14-10-2025***

## ABSTRACT
Finerenone in pharmaceutical formulation. The chromatogram was analysed using a Sunfire C18 column (4.6 mm x 250 mm, 5 µm). Mobile phase including 0.1% OPA: Methanol, in a 60:40 ratio, was pumped through the column at a flow rate of 1.0 ml/min. The temperature was sustained at 30°C. The chosen optimised wavelength was 219.0 nm. The retention time of Finerenone was determined to be 2.262 minutes. The %RSD of Finerenone was determined to be 0.3%. The relative standard deviation (RSD) of the method precision for Finerenone was determined to be 0.3%. %The recovery for Finerenone was determined to be 100.03%. The limits of detection (LOD) and quantification (LOQ) values derived from the regression equation for Finerenone are 0.08 and 0.24, respectively. The regression equation for Finerenone is expressed as y = 23931x + 2701.6. The retention periods and run times were reduced, indicating that the suggested approach is straightforward and cost-effective, suitable for frequent quality control testing in industries.

**Key Words:** Finerenone, Method development, Validation, RP-HPLC.

## INTRODUCTION[1-10]
Finerenone is a non-steroidal, selective mineralocorticoid receptor antagonist (MRA) that has gained attention for its role in the treatment of chronic kidney disease (CKD) associated with type 2 diabetes (T2D). Finerenone distinguishes itself from other MRAs, such as spironolactone and eplerenone, due to its higher receptor selectivity and a lower risk of adverse effects like hyperkalemia and gynecomastia, which are commonly observed with steroidal MRAs.

Mineralocorticoid receptors (MRs) are primarily found in the kidneys, heart, and vasculature, and are activated by the hormone aldosterone. Excessive activation of these receptors leads to inflammation and fibrosis in the heart and kidneys, which are central to the pathogenesis of diseases like heart failure and CKD. Finerenone blocks these receptors, reducing aldosterone-related organ damage, particularly in the kidneys. In patients with CKD and T2D, finerenone has demonstrated significant benefits in slowing the progression of kidney disease and reducing cardiovascular risks.

The development of finerenone comes at a critical time when the prevalence of CKD among individuals with diabetes continues to rise globally. Traditional therapies, including angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), have been foundational in the management of CKD in these patients. However, despite these therapies, many patients continue to experience disease progression, underscoring the need for novel treatments like finerenone that address additional pathways involved in kidney and cardiovascular protection.

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**How to Cite this Article:** Ruhi Rukhsar, STABILITY INDICATING RP-HPLC METHOD FOR THE DEVELOPMENT AND VALIDATION OF FINERENONE IN BULK AND PHARMACEUTICAL DOSAGE FORMS, World J Pharm Sci 2025; 13(03): 225-232; https://doi.org/10.54037/WJPS.2022.100905

Finerenone was approved by the U.S. Food and Drug Administration (FDA) in July 2021 under the brand name Kerendia for the treatment of CKD in patients with T2D, based on data from large-scale clinical trials such as the FIDELIO-DKD and FIGARO-DKD studies. These trials demonstrated finerenone's ability to significantly reduce the risk of CKD progression and cardiovascular events in patients with T2D and CKD. Importantly, its safety profile, with a lower incidence of hyperkalemia compared to traditional MRAs, has made finerenone a viable treatment option in this high-risk population.

Finerenone works by selectively blocking the mineralocorticoid receptor (MR) in key organs like the kidney and heart, preventing aldosterone-mediated damage such as inflammation and fibrosis. This effect is particularly beneficial in patients with CKD and T2D, as the reduction in aldosterone activity helps protect kidney function and reduce cardiovascular risks.

Analytical Background11

Finerenone is approximately 90% metabolized by CYP3A4, and 10% metabolized by CYP2C8. There is a minor contribution to metabolism by CYP1A1. Finerenone has no active metabolites. It is chemically known as (4S)-4-(4-cyano-2-methoxyphenyl)-5-ethoxy-2,8-dimethyl-1,4-dihydro-1,6-naphthyridine-3-carboxamide

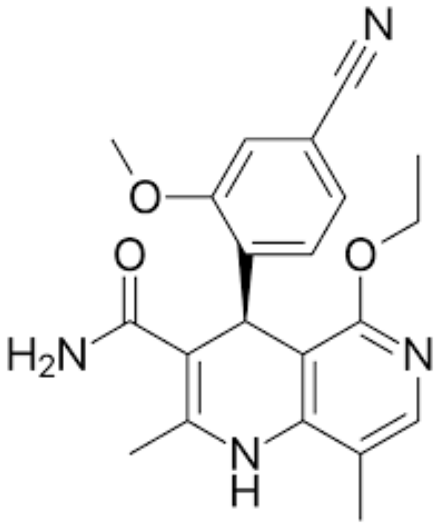


**Figure 1 structure of Finerenone**

High Performance Liquid Chromatography (HPLC) plays a crucial role in the validation of Finerenone, In the review of literature, more economical methods were observed [12-16], hence a simple, cost-effective stability-indicating simultaneous estimation of Finerenone by RP-HPLC in pharmaceutical dosage form must be developed and validated as per the guidelines of ICH (Q2 specification).

**MATERIALS:**

Finerenone pure drug (API), Finerenone formulation (Kerendia), Distilled water, Acetonitrile, Phosphate buffer, Methanol, Potassium dihydrogen ortho phosphate buffer, Ortho-phosphoric acid. All the above chemicals and solvents are from Rankem.

**INSTRUMENTATION**

The development and method validation were conducted using a WATERS HPLC, specifically the model 2695 SYSTEM, equipped with a Photo diode array detector. The system also included an automated sample injector and the Empower 2 software.

**Table 1: Chromatographic Conditions:**

| | |
|---|---|
| **Mobile phase** | 0.1% OPA: Acetonitrile (60:40 v/v) |
| **Flow rate** | 1.0 ml/min |
| **Column** | Sunfire C18 (4.6 x 150mm, 5µm) |
| **wave length** | 219 nm |
| **Column temperature** | 30°C |
| **Injection volume** | 10µL |
| **Run time** | 10.0 min |
| **Buffer** | OPA |

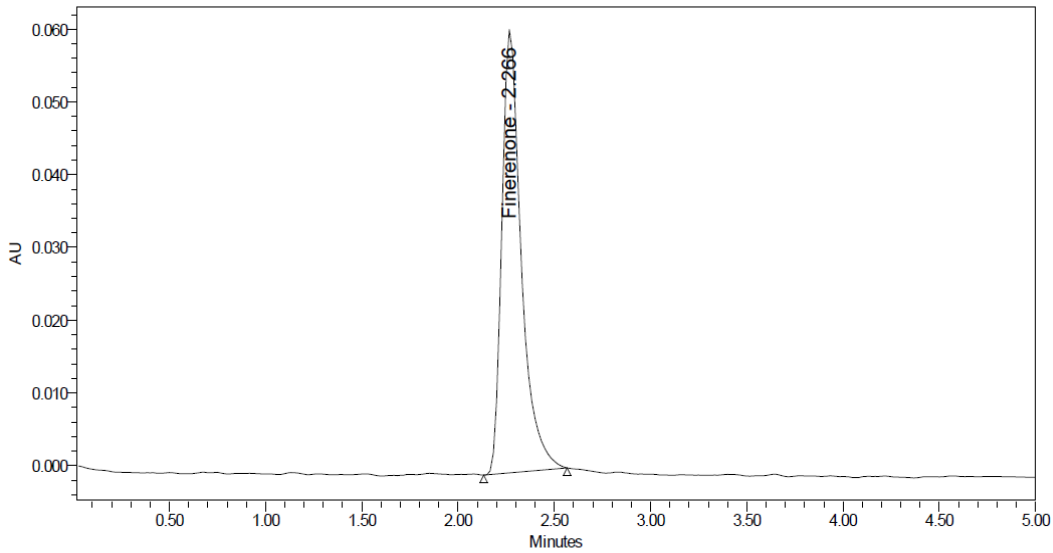


**Figure 2: Optimized Chromatogram**

**Methods:**

**Preparation of Standard stock solutions:** Accurately weighed 10mg of Finerenone transferred 50ml and volumetric flasks ,3/4 th of diluents was added and sonicated for 10 minutes. Flasks were made up with diluents and labeled as Standard stock solution (200µg/ml of Finerenone)

**Preparation of Standard working solutions (100% solution):** 1ml of Finerenone from each stock solution was pipetted out and taken into a 10ml volumetric flask and made up with diluent. (20µg/ml of Finerenone)

**Preparation of Sample stock solutions:** 5 tablets were weighed and the average weight of each tablet was calculated, then the weight equivalent to 1 tablet was transferred into a 100 ml volumetric flask, 50ml of diluents was added and sonicated for 25 min, further the volume was made up with diluent and filtered by HPLC filters.(200 µg/ml of Finerenone)

**Preparation of Sample working solutions (100% solution):** 1ml of filtered sample stock solution was transferred to 10ml volumetric flask and made up with diluent. (20µg/ml of Finerenone)

**Validation:**

**System suitability parameters:**

The system suitability parameters were determined by preparing standard solution of Finerenone (20 ppm) and the solution were injected six times and the parameters like peak tailing, resolution and USP plate count were determined.

The % RSD for the area of six standard injections results should not be more than 2%.

**Specificity (Selectivity):** Checking of the interference in the optimized method. We should not find interfering peaks in blank and placebo at retention times of these drugs in this method. So, this method was said to be specific. Representative chromatogram is shown in Figure 3 and experimental data is given in Table 2.

**Table: 2 System suitability parameters for Finerenone**

| S no | Finerenone | | |
|---|---|---|---|
| **Inj** | **RT(min)** | **USP Plate Count** | **Tailing** |
| 1 | 2.252 | 2283 | 1.38 |
| 2 | 2.254 | 2262 | 1.39 |
| 3 | 2.255 | 2241 | 1.40 |
| 4 | 2.256 | 2254 | 1.42 |
| 5 | 2.261 | 2281 | 1.41 |
| 6 | 2.269 | 2287 | 1.40 |

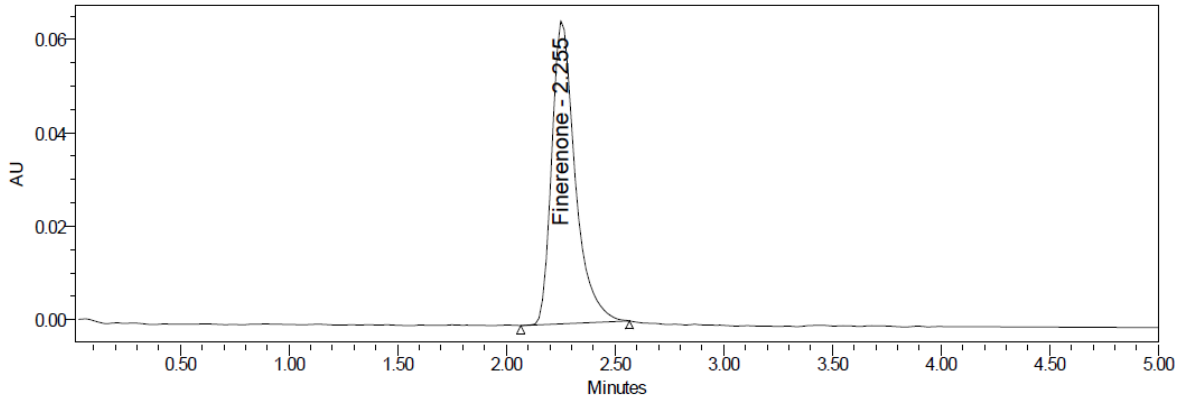


**Figure 3: System Suitability Chromatogram of Finerenone**

**Table 3: Specificity Data**

| Peak name | Rt | Area | USP plate count | Tailing |
|---|---|---|---|---|
| **Finerenone** | 2.262 | 481629 | 2821.1 | 1.5 |

**Specificity:**

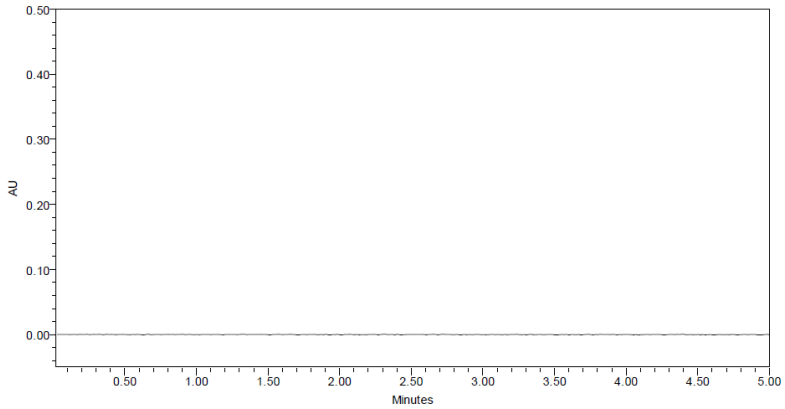


**Figure 4 Chromatogram of blank.**

The forced degradation conditions are mentioned in Table 4 and the results are mentioned in Table 5

**Table 4: Forced degradation conditions for Finerenone**

| Stress condition | Solvent | Temp($^0$C) | Exposed time |
|---|---|---|---|
| **Acid** | 2N HCL | 60$^0$c | 30 mins |
| **Base** | 2N NAOH | 60$^0$c | 30 mins |
| **Oxdation** | 20% $H_2O_2$ | 60$^0$c | 30 mins |
| **Thermal** | Diluent | 105$^0$c | 6 hours |
| **Photolytic** | Diluent | - | - |
| **Hydrolytic** | Water | 60$^0$c | |

From the results, degradation peaks were observed when the samples were exposed to acid. According to the stress study, none of the degradant co-eluted with the active drug peaks formed.

**Table 5: Degradation profile results**

| Degradation Condition | % Drug Un Degraded | % Drug Degraded |
|---|---|---|
| **Acid** | 93.55 | 6.45 |
| **Base** | 96.75 | 3.25 |
| **Oxidation** | 94.46 | 5.54 |
| **Thermal** | 97.64 | 2.36 |
| **Photolytic** | 97.90 | 2.10 |
| **Hydrolytic** | 99.29 | 0.71 |

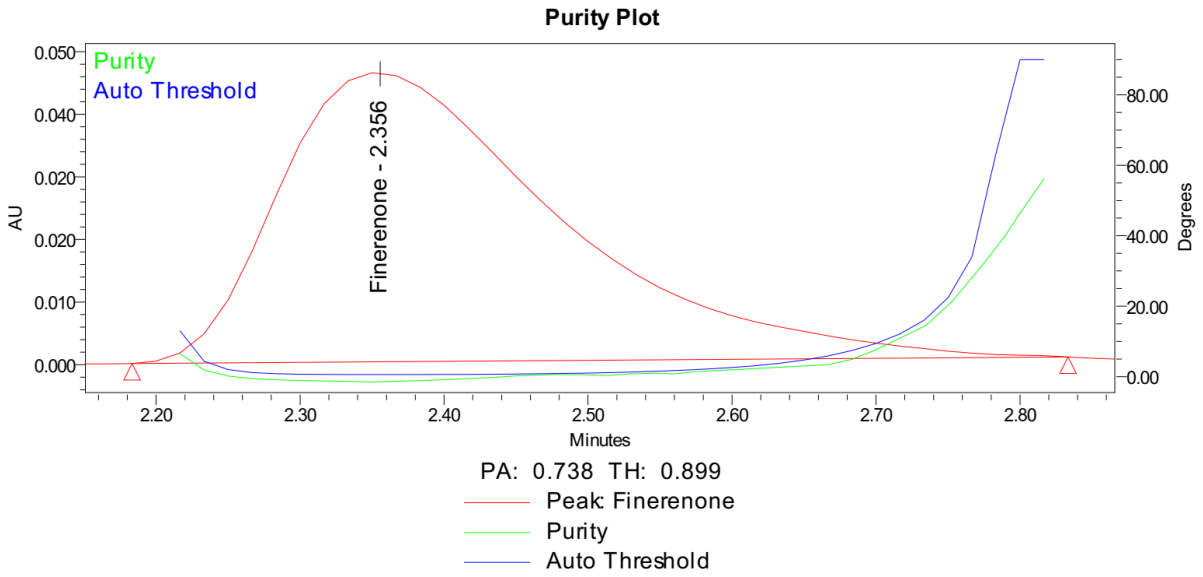


**Figure 5: Purity Plot of Acid**

**Limit of detection (LOD)** The detection limit is considered as very low level of concentration of an analyte in a sample that can be detected, but not necessarily quantitated.

**Limit of quantitation (LOQ):** The limit of quantitation is considered as the lowest concentration of an analyte in a sample that can be determined with acceptable precision and accuracy of the method.

The LOD values obtained for Finerenone are listed in Table 6.

**Table 6: Summary of limit of detection**

| Sample | Conc (µg/ml) |
|---|---|
| LOD | 0.08 |
| LOQ | 0.24 |

**Linearity:** The linearity of the method was demonstrated for Finerenone by analyzing the solutions ranging from 25% to 150% of the specification limit (Table 7). The correlation coefficient for Finerenone was 0.999. This indicates good linearity

**Linearity:**

Calibration data is given in table 7 and regression data in table 8 and calibration curve in figure 6

**Table 7: Calibration data of Finerenone**

| Finerenone | |
|---|---|
| **Conc (µg/mL)** | **Peak area** |
| 0 | 0 |
| 5 | 121290 |
| 10 | 246559 |
| 15 | 361776 |
| 20 | 482606 |
| 25 | 601515 |
| 30 | 717968 |

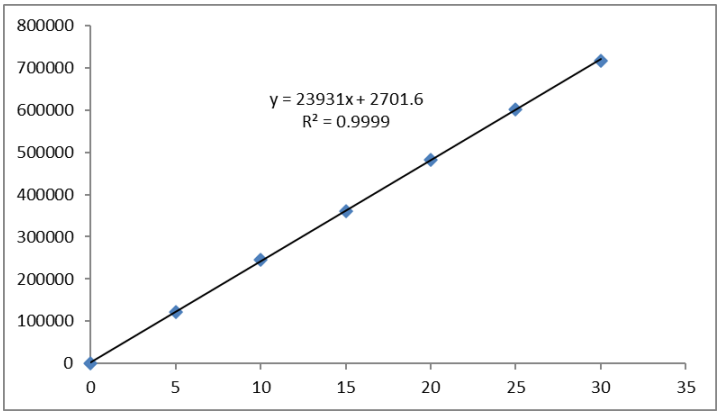


**Figure 6: Calibration curve of Finerenone**

**Table 8: regression data**

| Parameter | Finerenone |
|---|---|
| Conc range (µg/mL) | 5-30µg/ml |
| Regression Equation | y = 23931x + 2701.6 |
| Co-relation | 0.999 |

**Accuracy:** The accuracy of the method was determined by using solutions containing spiked samples of Finerenone at 50%, 100% and 150% of the working strength. All the solutions were prepared in triplicate and analysed. The percentage recovery results obtained for each impurity was listed in Table 9

**Table 9 Accuracy table of Finerenone**

| % Level | Amount Spiked (µg/mL) | Amount recovered (µg/mL) | % recovery |
|---|---|---|---|
| 50% | 10 | 9.98 | 99.84 |
| | 10 | 10.05 | 100.48 |
| | 10 | 10.01 | 100.12 |
| 100% | 20 | 20.07 | 100.33 |
| | 20 | 20.05 | 100.23 |
| | 20 | 20.07 | 100.37 |
| 150% | 30 | 30.17 | 100.56 |
| | 30 | 29.67 | 98.89 |
| | 30 | 29.83 | 99.42 |
| Mean % recovery | | | 100.03 |

**System Precision:** The system precision was performed by analyzing six replicate injections of standard solution at 100% of the specified limit with respect to the working strength of Finerenone. Results of peak area are summarized in Table 10

**Table 10 System precision table of Finerenone**

| S. No | Area of Finerenone |
|---|---|
| 1. | 484249 |
| 2. | 481467 |
| 3. | 485610 |
| 4. | 482878 |
| 5. | 479930 |
| 6. | 475207 |
| **Mean** | **481557** |
| **S.D** | **3698.6** |
| **%RSD** | **0.8** |

**Method Precision:** The precision of the method was determined by analyzing a sample of Finerenone). Data obtained is summarized in Table 11

**Table 11 Repeatability table of Finerenone**

| S. No | Area of Finerenone |
|---|---|
| 1. | 483638 |
| 2. | 482194 |
| 3. | 483343 |
| 4. | 481292 |
| 5. | 479262 |
| 6. | 481589 |
| **Mean** | **481886** |
| **S.D** | **1588.3** |
| **%RSD** | **0.3** |

**Intermediate precision:** It is differently from the repeatability, the precision obtained within a single laboratory over a longer period (generally at least several months) and considers more changes than repeatability. Data obtained is summarized in Table 12

**Table 12 Intermediate precision table of Finerenone**

| S. No | Area of Finerenone |
|---|---|
| 1. | 474459 |
| 2. | 471432 |
| 3. | 479902 |
| 4. | 479569 |
| 5. | 479609 |
| **Mean** | **476994** |
| **S.D** | **3849.9** |
| **%RSD** | **0.8** |

**Robustness:** The chromatographic conditions were deliberately changed to evaluate the robustness of the existing method. To determine the robustness of method, system suitability solution is prepared as per methodology and injected into HPLC at different altered conditions to check the method's ability like flow rate (± 10%), column oven temperature (± 5°C) and Mobile phase (± 10%) from actual method conditions. No significant change is observed by changing flow, temperature, Mobile phase, and system suitability also complied as per methodology. The robustness results are summarized in Table 13.

**Table 13 Robustness data for Finerenone**

| Condition | %RSD of Finerenone |
|---|---|
| **Flow rate (-) 0.9ml/min** | 0.6 |
| **Flow rate (+) 1.1ml/min** | 0.5 |
| **Mobile phase (-) 55B:45A** | 0.6 |
| **Mobile phase (+) 65B:35A** | 0.2 |
| **Temperature (-) 27°C** | 0.4 |
| **Temperature (+) 33°C** | 0.4 |

**Assay data: -**

Kerendia Tablet bearing the label claims Finerenone 300 mg. Assay was performed with the above formulation. Average % Assay for Finerenone obtained was 99.47% respectively. Assay data shown in table no 14.

**Formula to calculate assay:**

$$\%\ \text{Assay} = \frac{AT}{AS} \times \frac{WS}{100} \times \frac{1}{10} \times \frac{10}{1} \times \frac{P}{5} \times \frac{FV}{100} \times \frac{100}{L.C}$$

| | |
|---|---|
| AT | Average Peak area of Carboprost in test solution |
| AS | Mean peak area of Carboprost in standard solution |
| WS | Weight of Carboprost working standard taken in mg |
| P | Assay of Carboprost working standard in % on dried basis |
| L.C | Label Claim |
| FV | Filled volume(1ml of a vail) |

**Table 14: Assay Data of Finerenone**

| S.no | Standard Area | Sample area | % Assay |
|---|---|---|---|
| 1 | 484249 | 483638 | 100.23 |
| 2 | 481467 | 482194 | 99.93 |
| 3 | 485610 | 483343 | 100.17 |
| 4 | 482878 | 481292 | 99.75 |
| 5 | 479930 | 479262 | 99.32 |
| 6 | 475207 | 481589 | 99.81 |
| **Avg** | **481557** | **481886** | **99.87** |
| **Stdev** | **3698.6** | **1588.3** | **0.33** |
| **%RSD** | **0.8** | **0.3** | **0.33** |

**CONCLUSION**

The results of the Finerenone HPLC study demonstrate that this method can accurately quantify the concentration and purity of the drug. This technique is optimal for pharmacokinetic investigations and standard quality control owing to its ability for repeated application with precise peak resolutions and stable retention

durations. The efficacy and safety of Finerenone for medical application, as well as the verification of its chemical composition, depend on HPLC analysis.

**ACKNOWLEDGEMENT:**

The authors are thankful to, Department of Quality Assurnce, Sultan-ul-uloom, Affiliated to JNTUH India and Spectrum Pharma Research Solutions, Hyderabad, Telangana, India for providing with the gift sample of Finerenone Pure API.

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