—It's Official—

REVISED CHANGES TO USP <781> Optical Rotation

What Pharmaceutical Polarimeter Users Need to Know About the November 22, 2023 Revision and what has now become standard.

Executive Summary

USP Chapter <781> Optical Rotation was officially revised on November 22, 2023. The new requirements introduce significantly more detailed guidance for the qualification, calibration, and ongoing verification of polarimeters used in pharmaceutical laboratories.

The changes affect:

- Polarimeter qualification (IQ/OQ/PQ)
- Accuracy verification
- Repeatability testing
- Linearity verification / Sample Bracketing
- Temperature validation
- Quartz Control Plate (QCP) calibration and traceability
- Multi-point calibration requirements across the user's operational testing range

For pharmaceutical manufacturers, contract laboratories, and quality control groups, compliance now requires a more structured approach to polarimeter qualification than previously described in USP <781>

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USP <781> - Key Updates

Revisions officially effective November 22, 2023

1

Qualification of Polarimeters Added

New section establishes IQ,OQ, and PQ requirements for polarimeters

Ensures instruments are installed correctly and perform as intended.

2

Temperature Validation Required

Temperature control must be verified and maintained

OQ must demonstrate temperature accuracy within ±0.5˚C and be traceable to NIST.

3

Accuracy across operational range

Accuracy of optical rotation must be verified at three or more values

Covers the user's operational range, not just a single point

4

Repeatability Requirements Clarified

At least five replicate measurements with % RSD calculated.

Results must meet manufacturer repeatability

5

Linearity Verification

Linearity must be verified at three or more values representing the operational range.

Ensures reliable quantitative results

6

Certified Reference Materials

QCPs must be calibrated by an NMI or ISO/IEC 17025 accredited laboratory.

Strengthens traceability and measurement confidence.

REVISED POLARIMETER QUALIFICATION

The 2023 revision to USP <781> moves polarimeter verification to a comprehensive, traceable process that supports measurement integrity across testing range.

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What Changed in USP <781>?

The most significant addition is an entirely new performance Qualification for Polarimeters.

IQ-OQ-PQ Polarimeter Qualification Flow

A complete lifecycle approach to polarimeter qualification per USP <781>

IQ
INSTALLATION QUALIFICATION

Verify hardware and software are properly installed.

Confirm environmental conditions (temperature and humidity)

Review installation checklist and documentation.

Outcome: Instrument is ready for operational testing.

OQ
OPERATIONAL QUALIFICATION

Verify temperature control (Accuracy within ± 0.5°C)

Verify wavelength accuracy and bandwidth

Verify optical rotation accuracy at three or more values (bracketing)

Verify repeatability (at least five replicates, %RSD).

Outcome: Instrument performs correctly under defined conditions

PQ
PERFORMANCE QUALIFICATION

Periodically verify optical rotation accuracy and linearity

Verify repeatability (at least five replicates)

Verify temperature control performance

Establish and follow ongoing verification frequency

Outcome: Ongoing assurance of performance in routine use.

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DOCUMENT - VERIFY - MAINTAIN

Proper documentation of IQ, OQ, and PQ activities ensures compliance, data integrity and audit readiness

USP redefines OQ and PQ qualification requirements:

Installation Qualification (IQ) - Unchanged

Verification that the instrument hardware and software are properly installed and environmental conditions are acceptable.

Operational Qualification (OQ) - Adjusted

Verification that the instrument performs correctly and includes:

- Optical rotation accuracy verification
- Repeatability verification
- Wavelength accuracy verification
- Temperature control verification

Performance Qualification (PQ) - Significant

Periodic verification of:

Suitability of use, utilizing customer samples and analysis. Cell must be filled, temperature control enabled, sample measured successfully.

Change #1: Who Can Supply and Calibrate Quartz Control Plates?

The revised USP language specifically states that Certified Quartz Control Plate Polarization Reference Standard should be used for Polarimeter Validation and Calibration and that both Calibration and Re-Calibration of these Quartz Control Plate Reference Materials must be performed by:

- A National Metrology Institute (NMI), or
- A laboratory accredited to ISO/IEC 17025 through an ILAC-MRA recognized accreditation body.

The USP Says:

"Qualification may be performed using a polarization reference standard, which consists of a plate of quartz mounted in a holder perpendicular to the light path. Acceptable periodic calibrations may be made by a National Metrology Institute (NMI) that is signatory to the International Committee for Weights and Measures Mutual Recognition Arrangement (CIPM MRA) or an ISO/IEC 17025 accredited laboratory for calibration where the accreditation body is a signatory to the International Laboratory Accreditation Cooperation Mutual Recognition Arrangement (ILAC MRA)."

How Rudolph Meets These New Manufacture Calibration Requirements Polarimeter manufacturers providing Quartz Control Plates operate under ISO 17025 and manufacture Quartz Reference Material to comply with ISO 17034

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Example Quartz Control Plate (QCP) Certificate

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ilac-MRA

A2LA ACCREDITED

CERT #7528.01
CERT #7528.02

Quartz Control Plate (QCP)
Certified Reference Material - Calibration Certificate

QCP Calibration Certificate	Serial Number	Calibration Date
	19176	11-May-2026

This document certifies the calibration and certification of the above stated Quartz Control Plate has been calibrated and tested in accordance with Rudolph Research Analytical factory procedure CD00008. The flatness, parallelism, axis, optical homogeneity and mounting of the quartz were found to be within required specifications and quality.

QCP Calibration Results: α546.2271 = 13.6287° +/- 0.0020°

Calibration uncertainty: 0.0020° with a coverage factor of k=2

Optical Rotation and Sugar Values at 20.0°C
Plate No.19176

Wavelength,nm	Rotation, deg	Wavelength,nm	ISS,°Z
325	43.095	587	33.483
365	32.954	589	33.486
405	25.989	880	33.545
436	22.169	882	33.544
546	13.6329		
589.3 Air	11.595		
589.44 Vac	11.595		
633	9.975		

(Shaded value in the table does not appear on the label affixed to the assembly)

All wavelengths shown are with reference to Vacuum, except for 589.3 which is with reference to air and is included to satisfy various Pharmacopoeias.

Operator (Print)	John Smith	**Operator (Signature)**	*John Smith*	**Date**	11-May-2026
Authorized Signatory (Print)	Bill Jones	**Authorized Signatory (Signature)**	*Bill Jones*	**Date**	11-May-2026

Calibration activities are performed under ISO/IEC 17025 accreditation by A2LA, Certificate No. 7528.01. CRM production and certification activities are performed under ISO 17034 accreditation by A2LA, Certification No. 7528.02.

All measurements were performed at
Rudolph Research Analytical
55 Newburgh Road, Hackettstown, NJ 07840

Phone: 973-584-1558
Fax: 973-584-5440

Email: standards@rudolphresearch.com
Website: www.rudolphresearch.com

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Change #2: Linearity / Sample Bracketing Calibration Is Now Required

The USP Says: *"Linearity is verified if three or more optical rotation values representing the operational range meet the criteria for accuracy."*

Bracketing Calibration- Three Verification Points

USP <781> now requires verification across the operational range using three calibration points.

Negative QCP (-)

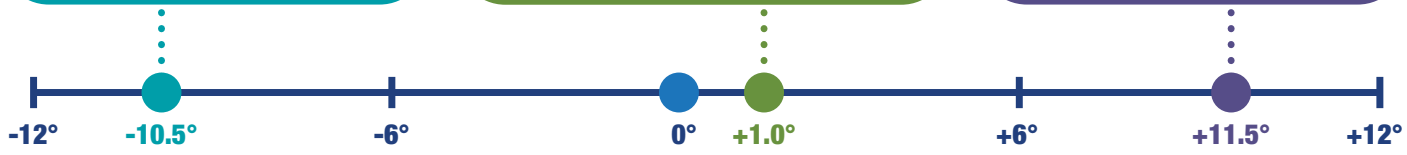
Example: -10.5° QCP
Verifies performance at the negative end of the range

Combined QCP (≈ Zero Point)

Example: (+11.5°) + (-10.5°) ≈ + 1.0°
Verifies performance near zero (midpoint)

Positive (+)

Example: +11.5° QCP
Verifies performance at the positive end of the range



Why bracketing matters

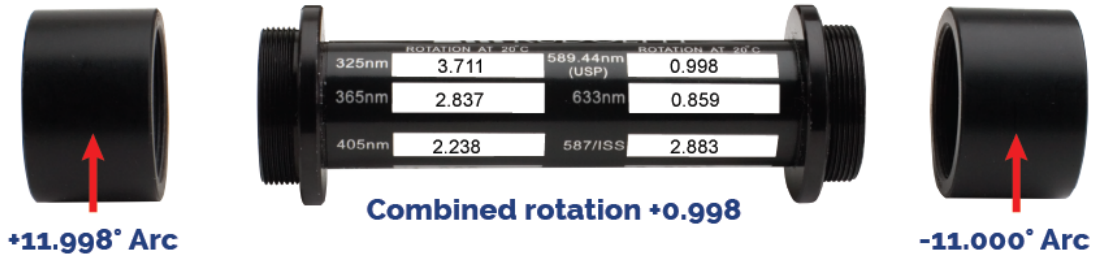
Using negative, positive, and combined quartz control plates verifies instrument performance across the full measurement range - not just at a single point.

Benefit

Greater confidence in accuracy, linearity, and overall measurement reliability.

3 Rotation Standard Quartz Plate

Standard Quartz Control Plate Version A700-2 with 3 Rotations



How it Works

The plate consists of three quartz elements. The left element is +11.998° Arc, the center element is +0.998° Arc, and the right element is -11.000° Arc

Combined rotation = +11.998° + 0.998° – 11.000° = +0.998° Arc

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Understanding Optical Rotation vs. Specific Rotation

One of the most common misconceptions in polarimetry is the difference between Optical Rotation and Specific Rotation. While USP monographs almost always specify acceptance limits in Specific Rotation, the polarimeter itself directly measures only Optical Rotation.

Optical Rotation (α) is the actual angular rotation of polarized light caused by a sample. This measured value depends on several factors, including the concentration of the sample, the optical path length of the measurement cell, the wavelength of light used, and the sample temperature. The polarimeter measures this optical rotation directly and reports it in degrees Arc.

Specific Rotation, however, is a normalized value that removes the effects of concentration and path length so that results can be compared consistently between laboratories. USP monographs specify acceptance criteria in Specific Rotation because it represents an intrinsic property of the material rather than a measurement that depends on how the sample was prepared. USP <781> defines the relationship between Optical Rotation and Specific Rotation as:

Measurement of optical rotation is performed using a polarimeter. For a neat, undiluted liquid, the **specific rotation** is a function of the density of the liquid at the temperature of interest:

$$[\alpha]_{\lambda}^{t} = \frac{\alpha}{l\rho}$$

When measuring the specific rotation of an analyte in solution, it may be convenient to prepare the **Sample solution** in a volume containing a mass of the analyte, with a concentration of the analyte per unit of volume (**g analyte/mL solution**), c_v, or per unit of mass (**g analyte/g solution**), c_w. The equations for determining the specific rotation of a **Sample solution** are:

For Sample solution (g/mL):

$$[\alpha]_{\lambda}^{t} = \frac{\alpha}{lc_v}$$

For Sample solution (g/g):

$$[\alpha]_{\lambda}^{t} = \frac{\alpha}{l\rho c_w}$$

- $[\alpha]_{\lambda}^{t}$ = specific rotation at wavelength **λ** and temperature **t (°C)**. The units of specific rotation are **(° · mL · dm⁻¹ · g⁻¹)**, which is typically expressed simply as **degrees (°)**.
- **α** = observed rotation in degrees (°)
- **l** = path length (dm)
- **ρ** = density of the solution or liquid at temperature **t** (g/mL)
- $\mathbf{c_v}$ = concentration of the analyte per unit of volume (g analyte/mL solution)
- **c*w*** = concentration of the analyte per unit of mass (g analyte/g solution)

For some pharmaceutical substances, especially liquids such as essential oils, the optical rotation requirement is expressed in terms of the **observed angle of optical rotation, α**, measured under conditions defined in the monograph.

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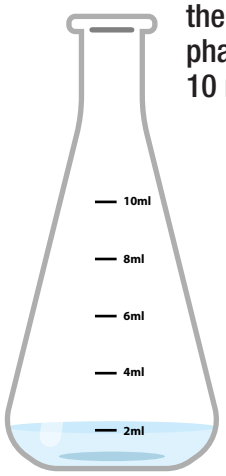
From Optical Rotation to Specific Rotation: How your Polarimeter Delivers USP Monograph Results

1 Sample Preparation

Prepare sample as required by the USP monograph. Typical pharmaceutical concentration : 10 mg/mL (1g /100mL).



Typical Concentration

10mg/mL

=

1 g/100mL

2 Polarimeter Measures Optical Rotation

The instrument measures the actual rotation (α) of plane polarized light caused by the chirality and concentration of the sample.

3 USP Formula Applied

The polarimeter automatically applies the USP equation to convert the measured optical rotation to specific rotation.

USP Equation

$$[\alpha]^{T}_{\lambda} = \frac{100\alpha}{lc}$$

$[\alpha]^{T}_{\lambda}$ = Specific Rotation
α = Optical Rotation (degrees)
l = Path length (dm)
c = Concentration (g/100 mL)
λ = Wavelength (nm)
T = Temperature (°C)

Typical Lab Conditions

- Path length (l) = 1dm
- Concentration (c) = 1 g/100 mL (10mg/mL)

4 Specific Rotation Reported

The result is reported as Specific Rotation, which is what USP monographs specify.

Specific Rotation

+15.00°

$[\alpha]^{20}_{D}$

Reported in accordance with USP Monograph Acceptance Limits

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Why This Matters

Optical Rotation depends on concentration and path length. Specific Rotation is an intrinsic property of the substance and allows consistant compaison between laboratories.

USP requires results in Specific Rotation

Example Calculation

(Typical Conditions)

- Measured Optical Rotation (α) = +0.150°
- Path Length (l) = 1dm
- Concentrations (c) = 1g/100mL

$$[\alpha]_D^{20} = \frac{100 \times 0.150}{1x1} = +15.00°$$

Specific Rotation Reported: +15.00°

Measure Optical Rotation. Apply the USP Formula. Report Specific Rotation.

Change #3: Verification Must Cover the User's Operational Range

USP now specifically states: *"Linearity should be verified at three or more values representing the operational range."*
USP requires verification at multiple optical rotation values representing the instrument's operating range.
This means calibration can no longer rely on a single quartz standard. A compliant qualification should include:

What Is Operational Range?

The operational range is the range of optical rotation values the samples under test that are measured in the laboratory.

Examples:

User A

Measures products between: +0.5° and +3°
Their qualification must verify this region.

User B

Measures products between: -10° and +12°
Their qualification must verify this broader range.

Why This Matters

Many laboratories currently verify performance at only one quartz value.
The revised USP guidance now expects verification at multiple points spanning actual use conditions.

Change #4: Temperature Validation Is Now Explicitly Required

The new USP section identifies temperature control as a critical component of polarimeter qualification.

USP states that:

- Optical rotation is affected by sample temperature.
- Temperature must be controlled and monitored.
- OQ should demonstrate temperature accuracy within ±0.5°C.
- Verification should be traceable to NIST standards.

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Why Temperature Matters

Small temperature deviations can create measurable optical rotation errors.

How Rudolph Addresses Temperature Validation

Rudolph offers:

- TempTrol™ temperature validation cells
- Traceable temperature verification systems
- Automated temperature reporting

The system allows users to validate:

- Polarimeter temperature control
- Cell temperature performance
- Compliance with USP temperature requirements at ±0.2°C

TempTrol™ Validation Cell

Polarimeter must control temperature to either

20°C ±0.5°C for the EP or
25°C ±0.5°C for the USP.

For customer who prefer not to use a standard thermometer, Rudolph now offers a **NIST traceable thermoprobe.**

In Conclusion

USP now requires:

- At least five replicate measurements
- Calculation of %RSD
- Results meeting manufacturer repeatability specifications.

Rudolph documentation explains that %RSD varies with optical rotation value and demonstrates repeatability calculations at multiple optical rotation levels.

REPEATABILITY

Perform at least five replicate measurements of a reference material at the operating wavelength. Calculate the relative standard deviation (% RSD) of the replicates. The result should be equal to or less than the stated repeatability performance specification of the instrument (as provided by the manufacturer)

Rudolph calculates %RSD according to the following formula:

$$\%RSD = \frac{S \times 100}{x \text{ or } n}$$

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Change #6: Recalibration of Quartz Control Plates

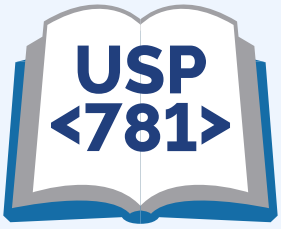
USP's increased emphasis on certified reference materials means laboratories should establish documented recalibration intervals for their Quartz Control Plates.

In addition it is advisable to use a Polarimeter from a manufacturer who can also supply and recertify Quartz Plates and is accredited to by ISO/IEC 17025 and 17034

From USP <781> Requirement to Compliant Polarimeter Calibration

A Traceable Path to Accuracy and Compliance

1



USP <781>

Pharmaceutical standard for Optical Rotation

- Establishes requirments for qualification, accuracy, repeatability, linearity, and traceability

2

ISO/IEC 17025 & ISO 17034 Accredited Laboratory

Calibration must be performed by a laboratory accredited to ISO/IEC 17025 and accredited to ISO 17034.

- ILAC-MRA recognized accreditation
- Traceable to NIST and international standards

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3

Certified Quartz Control Plate

Certified reference material with assigned optical rotation value(s).

Must be certified by an entity with ISO 17034 certification

- Calibrated across multiple wavelengths
- Measurement uncertainty reported
- Certified values traceable to NIST

ISO 17034
CERTIFIED REFERENCE MATERIAL PRODUCER

ISO 17034 specifies the general requirements for the competence of reference material producers and ensures the highest level of confidence in certified reference materials such as Quartz Control Plates.

4

Compliant Polarimeter Calibration

Polarimeter calibrated and verified in accordance with USP <781>

- Meets accuracy, repeatability, linearity, and temperature
- Supports IQ / OQ / PQ and audit readiness

Conclusion

The November 22, 2023 revision to USP <781> establishes a new standard for polarimeter qualification. Laboratories are now expected to verify performance using certified reference materials, validate temperature control, perform repeatability studies, and demonstrate accuracy across their actual operating range.

Rudolph Research Analytical's ISO 17025 accredited calibration services, certified Quartz Control Plates, IQ/OQ/PQ documentation, and temperature validation solutions provide a complete pathway to USP <781> compliance.