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Thermo Scientific TruScan RM

European Pharmacopeia (EP)
Chapter <2.2.48> — Raman Spectroscopy
Statement of Compliance

ThermoFisher
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2016 Update

The European Pharmacopeia (EP) general chapter <2.2.48>[1] on Raman Spectrometry provides an informative introduction to the Raman Effect followed by general guidance on the application of Raman for a wide variety of problems in the pharmaceutical sciences. Due to the varied scope of these problems, not all of EP <2.2.48> is relevant for material ID testing. This document calls out the components of EP <2.2.48> that pertain to material ID testing, our interpretation of the statements (where necessary), and the Thermo Scientific™ TruScan™ RM analyzer's respective capabilities. Text in italics is always a direct quote from EP <2.2.48>.

The TruScan RM analyzer is believed to be compliant with all recommendations set forth in EP 8.7 general chapter <2.2.48>, effective April 2016.

Requirements Assessment

PREPARATION OF THE SAMPLE

When using Raman spectroscopy, the measured sample area and volume may be small (in particular for microscope-coupled devices) and care must be taken to ensure the measurement is representative.

- TruScan RM analyzer capability: The analyzer's accessories are designed to illuminate a sample spot size of approximately 2 mm in diameter.

It is not always possible to consider Raman as a non-destructive technique. The energy transmitted by the laser depends on the duration of exposure and the wavelength. It may change the physical state and may destroy the sample

TruScan RM analyzer capability: Although Raman is typically considered a non-destructive technique, conditions such as exposure time, laser power and the nature of the sample may lead to sample degradation. Materials are evaluated as part of the evaluation and installation processes and substances unsuitable for Raman analysis are recommended for alternate testing techniques.

CONTROL OF INSTRUMENT PERFORMANCE

Verification of the wavenumber scale:

Verify the wavenumber scale of the Raman shift using a suitable standard that has characteristic maxima at the wavenumbers under investigation, for example, an organic substance such as polystyrene, paracetamol or cyclohexane (see Table 2.2.48.-1).

A minimum of 3 wavenumber shifts covering the working range of the instrument intended for measurements should be chosen. For dispersive Raman spectrometers that use multiple gratings for different spectral resolutions, the wavenumber scale should be verified at the same optical resolution that will occur for sample collection. All gratings used for Raman measurements should be verified for accuracy of Raman-shift.

- TruScan RM analyzer capability: The analyzer is calibrated at the factory directly in accordance with ASTM E1840-96 (2002). Cyclohexane, acetonitrile/toluene (50/50) and acetaminophen bands are used to determine the x-axis calibration of the system. This calibration is verified with cyclohexane, acetaminophen (4-acetomidophenol) and polystyrene, along with additional product release testing. All of these materials are recommended in ASTM E1840-96 (2002). The laser is directly calibrated to zero (0) wavenumbers at this time, and continuously monitored thereafter. The x-axis calibration is automatically adjusted in software if the laser wavelength moves. A polystyrene check sample is provided with the instrument to verify the Raman shift/wavenumber scale. The recommended annual instrument certification for TruScan RM analyzers checks the following peaks from Acetaminophen, Cyclohexane, and

	Peak cm^{-1}	New Tolerances, per EP Supplement 8.7 Guidance (+/-)
Paracetamol (APAP)	797.2	2.5
	857.9	2.0
	1236.8	2.0
Cyclohexane	801.3	2.5
	1028.3	2.0
	1444.4	2.5
Polystyrene	620.9	2.5
	1001.4	2.0
	1031.8	2.0

Table 2.2.48.-1

Verification of the response-intensity scale:

The absolute and relative intensities of the Raman bands are affected by variations in several factors.

- TruScan RM analyzer capability: To enable method/signature transfer between devices, each device is calibrated for spectrometer response using a NIST traceable standard, standard SRM-2241. This calibration ensures that the relative intensities of Raman bands are normalized across all devices

QUALITATIVE METHODS

Since the frequency shift position is employed for identification, identical laser intensity for both the reference standard and the material to be examined may not be necessary. The material to be examined is measured in the same physical state (e.g. liquid, solid) as the reference or library material. Raman techniques offer the advantage of non-invasive measurements of the material to be examined without removal of the packaging. However, some packaging materials may alter the measurement. This is especially the case when the packaging absorbs at the laser's excitation wavelength.

- TruScan RM analyzer capability: To enable method/signature transfer between devices, each device is calibrated for spectrometer response using a NIST traceable standard, standard SRM-2241. This calibration ensures that the relative intensities of Raman bands are normalized across all devices

Identification using a spectral reference library:

Record the spectra of a suitable number of materials which exhibit typical variation (manufacturer, batch, particle size, impurity profile, etc.) and comply with the requirements of the monograph or established specifications.

- TruScan RM analyzer capability: In the majority of cases, only one reference material will be required. This should be verified in the course of method validation.

The selectivity of the database that makes it possible to identify a given material and distinguish it adequately from other materials in the database is to be confirmed during the validation procedure.

- TruScan RM analyzer capability: The necessary selectivity should be ensured during method validation.

Reference:
1. *European Pharmacopeia* 8.7 Edition 2016

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