Operating Instructions

Raman flow assembly

KRFB, KRFC

Endress+Hauser
People for Process Automation

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1 About this document

This manual provides information about the flow cell apparatus used in conjunction with the Endress+Hauser Rxn-10 Raman spectroscopic probe. This includes the wetted flow cell and the flow bench optical interface.

Refer to the *Rxn-10 Raman spectroscopic probe Operating Instructions* for specific probe-related information.

1.1 Warnings

Structure of Information	Meaning
⚠ WARNING Causes (/consequences) Consequences of non-compliance (if applicable) ▸ Corrective action	This symbol alerts you to a dangerous situation. Failure to avoid the dangerous situation can result in a fatal or serious injury.
⚠ CAUTION Causes (/consequences) Consequences of non-compliance (if applicable) ▸ Corrective action	This symbol alerts you to a dangerous situation. Failure to avoid this situation can result in minor or more serious injuries.
NOTICE Cause/situation Consequences of non-compliance (if applicable) ▸ Action/note	This symbol alerts you to situations which may result in damage to property.

Table 1. Warnings

1.2 Symbols on the device

Symbol	Description
	The Laser Radiation symbol is used to alert the user to the danger of exposure to hazardous visible laser radiation when using the system.
	The High Voltage symbol that alerts people to the presence of electric potential large enough to cause injury or damage. In certain industries, high voltage refers to voltage above a certain threshold. Equipment and conductors that carry high voltage warrant special safety requirements and procedures.
	The WEEE symbol indicates that the product should not be discarded as unsorted waste but must be sent to separate collection facilities for recovery and recycling.

Table 2. Symbols

1.3 U.S. export compliance

The policy of Endress+Hauser is strict compliance with U.S. export control laws as detailed in the website of the Bureau of Industry and Security at the U.S. Department of Commerce.

1.4 Glossary

Term	Description
ANSI	American National Standards Institute
API	active pharmaceutical ingredient
ATEX	atmosphére explosible
°C	Celsius
cm	centimeter
°F	Fahrenheit
CRS	calibration reference standard
in.	inches
IO	immersion optic
kg	kilogram
LED	light emitting diode
m	meter
µin	microinches
µm	micrometer
mm	millimeter
mW	milliwatt
NCO	non-contact optic
nm	nanometer
oct/min	octaves per minute
PD	process development
psi	pounds per square inch
WEEE	Waste Electrical and Electronic Equipment

Table 3. Glossary

2 Basic safety instructions

The safety information in this section is specific to the flow cell that is compatible with the Raman Rxn-10 spectroscopic probe from Endress+Hauser. Refer to the *Rxn-10 Raman spectroscopic probe Operating Instructions* for additional information related to probe and laser safety.

2.1 Personnel requirements

- Installation, commissioning, operation, and maintenance of the probe/optics may be carried out only by specially trained technical personnel.
- Technical personnel must be authorized by the plant operator to carry out the specified activities.
- Technical personnel must have read and understood these Operating Instructions and must follow the instructions contained herein.
- The facility must designate a laser safety officer who ensures staff are trained on all Class 3B laser operating and safety procedures.
- Faults at the measuring point may only be rectified by authorized trained personnel. Repairs not described in this document must be carried out only directly at the manufacturer's site or by the service organization.

2.2 Designated use

The Raman micro flow cell and flow bench are designed for flow rates which are most applicable to product and process development and are optimized for biological samples. The micro flow cell is designed to connect to a flow path creating an enclosed, wetted interface which is separate from the flow bench. The flow bench, which is compatible with the Rxn-10, allows for the secure laser-sample interface as well as calibration and verification of the apparatus. The flow bench is required for use of the micro flow cell.

Recommended applications for the optics include:

Apparatus	Fields of application
Flow cell	▪ Perfusion stream ▪ Material recirculation loop ▪ Tangential flow filtration ▪ Eluate monitoring ▪ Monomer-aggregate differentiation

Table 4. Fields of application

The above table lists common applications for the flow cell apparatus. There are other possible fields of application, however, use of the device for any purpose outside of the fields of application described here poses a threat to the safety of people and of the entire measuring system, and invalidates any warranty.

2.3 Workplace safety

As the user, you are responsible for complying with the following safety conditions:

- Installation guidelines
- Local standards and regulations for electromagnetic compatibility

2.4 Operational safety

Before commissioning the entire measuring point:

- Verify that all connections are correct.
- Ensure that electro-optical cables are undamaged.
- Ensure fluid level and flow parameters are compatible with configured micro flow cell.
- Do not operate damaged products, and protect them against unintentional operation.
- Label damaged products as defective.

During operation:

- If faults cannot be rectified, products must be taken out of service and protected against unintentional operation.
- When working with laser devices, always follow all local laser safety protocols which may include the use of personal protective equipment and limiting device access to authorized users.

2.5 Service safety

Follow your company's safety instructions when removing a process probe or optic from the process interface for service. Always wear proper protective equipment when servicing the equipment.

2.6 Important safeguards

- Do not use the system for anything other than its intended use.
- Do not disconnect the Rxn-10 probe while the system is collecting Raman data.
- Do not remove the flow cell from the flow bench while the system is in use.
- Do not look directly into the laser beam.
- Do not point the laser at a mirrored or shiny surface, or a surface that can cause diffuse reflections. The reflected beam is as harmful as the direct beam.
- When not in use, close the shutter on the Rxn-10 probe. If an optic cap is available, place it on the unused optic.
- Always use a laser beam block to avoid inadvertent scatter of laser radiation.

2.7 Product safety

The product is designed to meet all current safety requirements, and has been tested and shipped from the factory in a safe operating condition. The relevant regulations and international standards have been observed. Devices connected to an analyzer must comply with the applicable analyzer safety standards.

3 Product description

The Raman flow cell and associated flow bench, powered by Kaiser Raman technology, enable enhanced signal generation while monitoring material in a flow path. The system is an optimized non-contact apparatus that leverages the internal design characteristics of the flow cell to enhance the total signal-to-noise ratio for faster sampling times and lower limits of detection. Refer to the sections below for descriptions of the parts and their functions.

3.1 Micro flow bench

The micro flow bench is configured and factory-tuned for the unique flow cell and application space needs, where the fluid-path thickness and the refractive index of the sample are known or well approximated. For optimal performance, it is recommended that the sample refractive index at the laser-wavelength be characterized so that proper factory-setting can be achieved. The fluid-path thickness is defined by the flow cell configuration. It is recommended that the micro flow bench and micro flow cell be configured together to ensure optimal performance in the field. The micro flow bench has been optimized for use in the near infrared (NIR) region (785 nm).

The micro flow bench comes standard with a light shield to safely acquire the Raman spectra while eliminating noise from the environment. In addition, a beam dump is available which safely blocks the amplifier to collect spectra in back-scatter mode only. This is useful for running experiments that do not require the signal enhancement.

The micro flow bench comes standard with an amplifier to enhance the Raman signal per unit-time.

3.1.1 Micro flow bench options

The micro flow bench provides application flexibility, and can be configured to the unique and demanding needs of a variety of flowed-sample conditions. The micro flow bench is currently available in an Rxn-10 compatible configuration which is factory tuned for the specific application needs. In most cases aqueous environments are an acceptable approximation; however, extension beyond these spaces is available.

If a unique mounting solution is required, the micro flow bench can be configured with OEM-specific hardware to directly integrate into the unique environment.

3.2 Micro flow cell

The micro flow cell has been designed to produce laminar flow within a wide range of volumetric flowrates, pressures, tubing diameters, and fitting options. Micro flow cells are ASME BPE SF4 Bio-Compatible and can be cleaned and sterilized for re-use, or can be discarded after each use similar to sleeved immersion optics from Endress+Hauser. Additionally, micro flow cells are configurable with a variety of fluid path thicknesses if the standard 2.5 mm option is not sufficient.

3.2.1 Micro flow cell options

The micro flow bench and micro flow cell system has been designed to ensure maximum transferability between cells and benches, allowing micro flow cells to be replaced on the flow bench with minimal impact to the resulting spectrum.

3.2.2 Micro flow bench and flow cell data collection zone

The micro flow bench and flow cell are configured together to maximize the performance of the system. The amplifier enhances the signal by collecting both forward and backward propagating scatter. The data collection zone has been designed for optimal use in clear samples. If collection in opaque samples is required, contact Service (*Repairing the Raman flow assembly)* → 🖹.

4 Incoming product acceptance and product identification

4.1 Incoming acceptance

- Verify that the packaging is undamaged. Notify the supplier of any damage to the packaging. Keep the damaged packaging until the issue has been resolved.
- Verify that the contents are undamaged. Notify the supplier of any damage to the delivery contents. Keep the damaged goods until the issue has been resolved.
- Check that the delivery is complete and nothing is missing. Compare the shipping documents with your order.
- Pack the product for storage and transportation in such a way that it is protected against impact and moisture. The original packaging offers the best protection. Make sure to comply with the permitted ambient conditions.
- If you have any questions, please contact your supplier or your local sales center.

NOTICE

Incorrect transportation can damage the micro flow cell and micro flow bench.

4.2 Product identification

4.2.1 Label

At a minimum, the optics are labeled with the following information:

- Manufacturer information
- Part number
- Serial number
- Wavelength
- KMAT (product configuration code)

Compare the information on the label/tag with the order.

4.2.2 Manufacturer address

Endress+Hauser
371 Parkland Plaza
Ann Arbor, MI 48103 USA

4.3 Scope of delivery

The scope of delivery comprises:

- Raman micro flow bench
- Raman micro flow cell
- *Raman flow assembly Operating Instructions*
- Local declarations of conformity, if applicable
- Material certificates, if applicable

If you have any questions, please contact your supplier or local sales center.

5 Installation

5.1 Installing the micro flow bench

The Endress+Hauser micro flow bench slips onto the Rxn-10 probe and is secured by a torque limiting thumb screw clamp. The thumb screw on the Rxn-10 probe should never be fully removed.

WARNING

When installing or removing optics, ensure the laser and emission shutter are in the closed position.

To install the Rxn-10 probe onto the micro flow bench:

1. Loosen the metal screw on the Rxn-10 probe by turning the screw counter-clockwise approximately one turn (do not remove).
2. Insert the end optic clamp of the probe onto the Rxn-10 adapter of the micro flow bench.

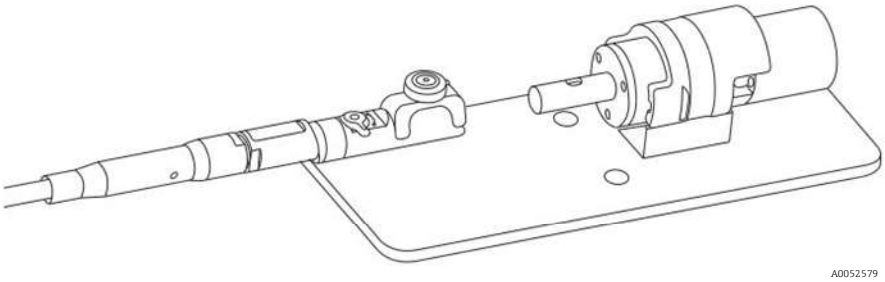

Figure 1. Inserting the Rxn-10 probe onto the Rxn-10 adapter of the micro flow bench

3. Slide the probe over the Rxn-10 adapter of the micro flow bench until it stops.

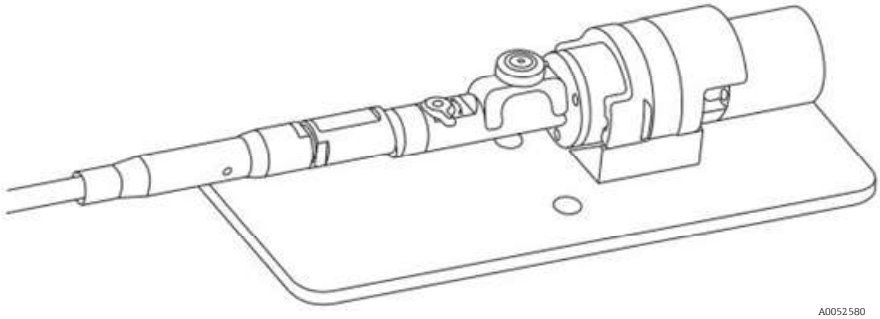

Figure 2. Final position of the Rxn-10 probe with the micro flow bench

4. Tighten the thumb screw by gently turning it clockwise until there is an audible “click” sound. This indicates the thumb screw has reached the desired torque. Failure to tighten the screw will result in the optic coming loose, potentially damaging the optic.
5. After installing the micro flow bench, use the micro flow bench calibration kit to perform an intensity calibration for the probe with the new optic.

To remove the Rxn-10 probe from the micro flow bench:

1. Loosen the torque limiting thumb screw by turning it counter-clockwise approximately one turn so that the Rxn-10 adapter is released from the clamp. Do not remove the screw.
2. Slide the probe off of the adapter.

5.2 Inspecting the micro flow cell

It is important to inspect the exterior window surfaces of the micro flow cell before installation of any tubes. See inspection and cleaning procedures in *Maintenance* → .

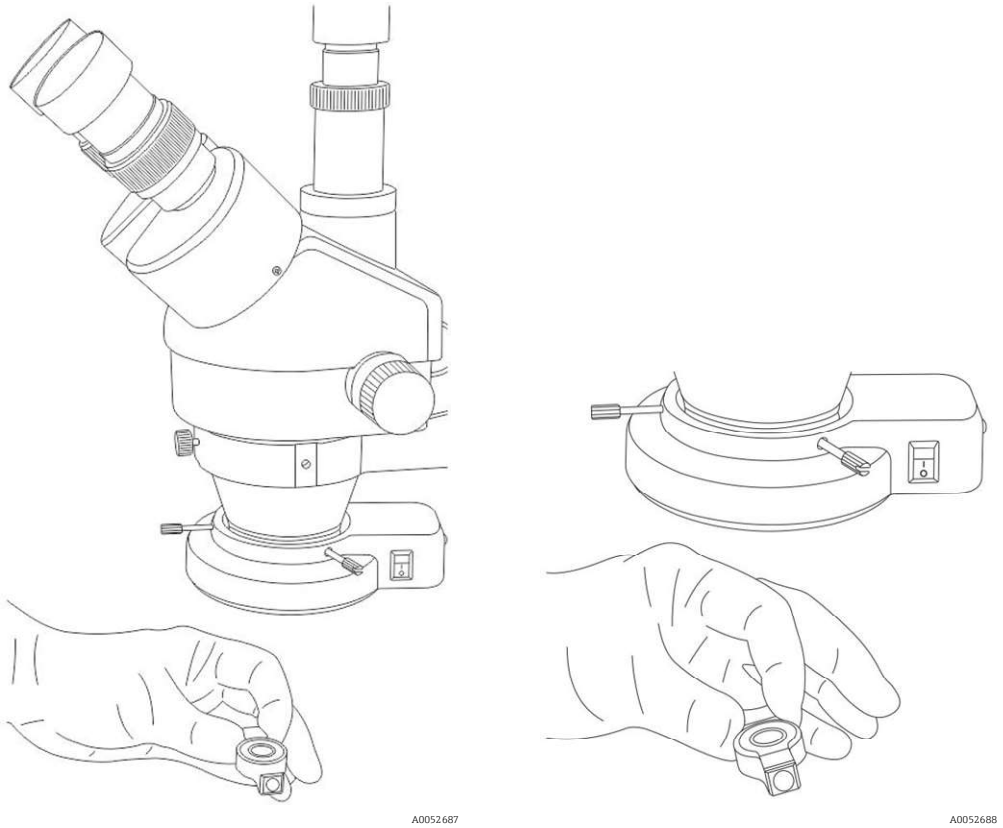

Figure 3. Normal (left) and off-axis (right) inspection of a cell under a microscope

5.3 Installing tubing sets to the micro flow cell

The micro flow cell comes standard with 5/16-24 flat-bottom threaded ports for adapting to the flexible tubing ferrules commonly used in bioprocessing and HPLC streams. However, the micro flow cell can be configured with OEM-specific ports to enable unique applications. Tubing must be installed by trained and qualified personnel according to standard operating procedures (SOP).

Endress+Hauser recommends that all tubing ports be inspected before installing tubing or sealing ferrules. All tubes should be cut square with approved cutting tools and techniques to ensure leak-free connections. When installing tubing and ferrules into the ports, ensure the tubing and ferrules are flush for the best performance.

NOTICE

Wear appropriate gloves when attaching tubing to avoid possible contamination of micro flow cell window surfaces.

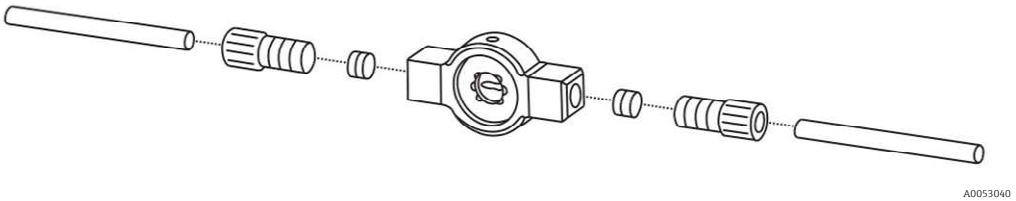

Figure 4. Placement of tubing sets to the micro flow cell

5.4 Installing the micro flow cell

Before installing the micro flow bench, ensure the Rxn-10 laser shutter is closed and confirm that no data collection is occurring. Ensure all flow connections are correctly affixed and are functioning as intended.

To install the micro flow cell:

1. Pull back on the light shield. The light shield stroke path is embossed on the top of the light shield.
2. Install the flow cell with the probe-indicating arrows pointing toward the Rxn-10 probe.
3. Adjust the light shield forward until the plunger contacts and fixes the micro flow cell in place.
4. Confirm the beam dump is open or closed, according to the application requirements.
5. Close the light shield completely.

Before collecting data, open the Rxn-10 shutter.

6 Commissioning

The micro flow bench is delivered ready to connect to the Rxn-10 probe. Follow the instructions below to commission the micro flow bench for use in conjunction with the probe.

⚠ WARNING

No additional alignment or adjustment to the system is required and we strongly recommend that customers not attempt adjustments.

6.1 Receipt of product

Perform the steps for incoming product acceptance described in *Incoming acceptance* → 🖹.

6.2 Calibration and verification

The probe and the analyzer must be calibrated before use.

6.2.1 Raman flow assembly calibration and verification kit

After installing the Rxn-10 probe onto the micro flow bench, use the Raman flow assembly calibration and verification kit to perform an intensity calibration and verification for the probe head with the new micro flow bench.

Refer to the *Raman flow assembly calibration and verification kit Operating Instructions* for additional information about the Raman flow assembly calibration and verification kit.

6.2.2 Performing calibration and verification of the probe

Refer to the *Raman flow assembly calibration and verification kit Operating Instructions* for steps to:

- Perform internal analyzer calibration which may include alignment calibration, full wavelength calibration and/or full laser wavelength calibration depending on status of analyzer
- Perform probe calibration: requires Raman flow assembly calibration and verification kit
- Perform probe verification: verifies the calibration results using a standard reference sample; verification cell
- View calibration and verification reports

NOTICE

Do NOT immerse any components of the micro flow bench or Rxn-10 directly into a sample.

▶ The verification cell accessory should be used for verification of the micro flow bench.

The Raman RunTime software will not allow spectra to be collected without passing internal and probe calibrations. Passing the probe verification step is not required but is highly recommended.

Raman Rxn analyzer operating instructions are available by searching the Downloads area of the Endress+Hauser website: https://endress.com/downloads.

7 Operation

7.1 Micro flow cell

⚠ WARNING

Hydrocarbon solvents can degrade hardware performance and invalidate the warranty.

- Do not use the micro flow cell with hydrocarbon solvents (including ketones and aromatics).
- The micro flow bench and micro flow cell are NOT intended to be submerged into any liquid.

7.2 Storing the micro flow cell

Store the micro flow cell in the original factory packaging until its intended use and installation into a flow-system. If re-use is intended after flowing sample through the micro flow cell, it is recommended that the flow cell be purged by standard operating procedures (SOP) and dried with clean and filtered air. Refer to flow cell inspection and cleaning section on air cleanliness in *Cleaning the micro flow cell window* → 🖹.

Remove all residual moisture from the cell through a clean drying process such as bake-out. Endress+Hauser does not recommend a specific cleaning procedure as application SOPs may necessitate different parameters. Any bake-out procedure should be done within the qualified storage temperature limits found in *Micro flow cell* → 🖹. Exceeding these can damage the flow cell.

7.3 Storing the micro flow bench

When storing the micro flow bench, keep the system closed to minimize contamination. To do this, adjust the beam dump to closed position, close the light shield fully, and place the cap over the Rxn-10 adapter as shown in figures 5 and 6 below. Store the micro flow bench in the original shipping box and materials. If these are not available, storing the device in a clean bag within the specified environmental conditions will provide sufficient protection.

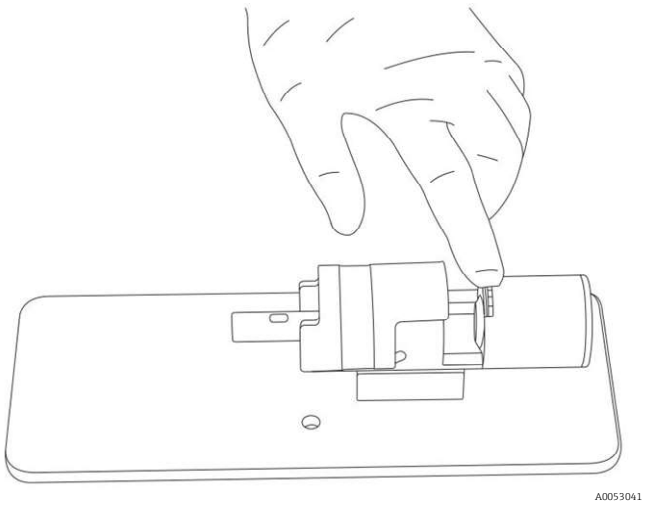

Figure 5. Shutter closure open, close beam dump

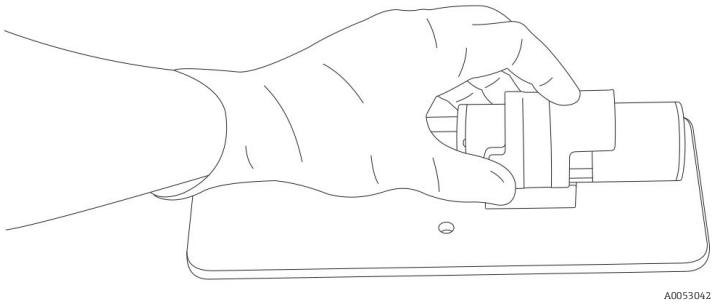

Figure 6. Shutter closure closed

8 Diagnostics and troubleshooting

Endress+Hauser Raman flow assemblies provide consistent and reliable long-term and repeated operation. Refer to the *Rxn-10 Raman spectroscopic probe Operating Instructions* (BA02160C) to troubleshoot issues with the Rxn-10 probe and accessory optics.

Symptom		Possible cause	Action
1	Substantial reduction in signal	External surfaces of windows are dirty	1. Carefully remove the cell from the flow bench and inspect both optical windows for residue, fingerprints, etc. 2. If necessary, clean the windows with isopropyl alcohol and a lint free wipe or swab before returning to the flow bench.
		Beam dump is in the closed position	Verify the position of the beam dump using the control wheel and correct if necessary.
		Cell is not correctly installed into bench	Open light shield and verify that the flow cell is properly installed in the bench, and that the plunger is fully contacting the cell without any gaps. Cell should rotate slightly relative to the probe axis but should not wiggle free or move around easily.
2	Complete loss of signal while laser is powered and laser emission indicator is lit	Material is not flowing through the cell or beam path is obstructed by bubble	Ensure the cell is charged with liquid and free of bubbles. If bubbles are a consistent problem, consider mounting the bench such that the flow path is vertical with material moving from the bottom up.
		Rxn-10 is not properly connected or Rxn-10 shutter is closed	Ensure the Rxn-10 is properly attached, and the laser beam shutter is in the open (I) position.
3	Flow bench not calibrating	Beam dump is not in the “open” position	Verify the position of the beam dump using the control wheel and correct if necessary.
		Calibration cell is not installed correctly	Ensure that the calibration cell is installed in the correct direction with probe-indication arrows pointing correctly towards the Rxn-10 Probe.
		Light shield is still in the retracted position	Fully close the light shield to ensure the optic is properly engaged with the cell.
		Rxn-10 Probe is not properly connected or Rxn-10 shutter is closed	Ensure the Rxn-10 is properly attached, and the laser beam shutter is in the open (I) position.
4	Flow bench not passing verification	Bubbles in the verification cell	Carefully open the cell and use the supplied blunt tip syringe to fill the cell with 70 % IPA.
		70 % IPA is contaminated	Ensure clean and un-contaminated 70 % IPA is used in the cell. Flush the cell and replace the volume.
		Calibration cell or verification cell have contamination in the clear aperture.	Remove the cell and inspect visually for contamination. Follow proper cleaning procedures to clean any contamination from the optical surfaces.

Symptom		Possible cause	Action
		Beam dump is not in the “open” position	Verify the position of the beam dump using the control wheel and correct if necessary.
		Light shield is still in the retracted position	Fully close the light shield to ensure the optic is properly engaged with the cell.
		The incorrect source spectral file (SSF) was used during calibration of the instrument	Confirm the correct source spectral file (SSF) and calibration date of the Calibration Cell.
		Rxn-10 probe is not properly connected or Rxn-10 shutter is closed	Ensure the Rxn-10 is properly attached, and the laser beam shutter is in the open (I) position.
		Calibration cell is not installed correctly	Ensure that the calibration cell is installed in the correct direction with probe-indication arrows pointing towards the Rxn-10 probe.
		Calibration temperature was incorrectly input into RunTime software	Ensure that the proper units (°F or °C) correspond on the temperature meter and in RunTime.
		Calibration cell temperature was not stable during calibration	Ensure that the calibration cell has reached thermal stability* before calibrating the instrument. Ensure that the system is not subject to excessive heat sources such as exhaust fans, hot plates, or handling. * Refer to the *Raman flow assembly calibration and verification kit Operating Instructions* (BA02294C) for instructions on measuring the temperature of the micro flow bench calibration cell.
5	Flow cell tubing ports are leaking	Tubing was not cut square or was crushed during cutting	Use only approved tubing cutting tools designed for the tubing material. Use only tubing sizes intended for the flow cell. Re-cut ends if necessary.
		Fittings incorrectly installed	Confirm that fittings are for the correct tubing size and are compatible with the flow cell threads. Replace if necessary.

Table 5. Diagnostics and troubleshooting

9 Maintenance

If the micro flow cell windows have come in contact with a sample, dust or fingerprints, etc., they may need to be cleaned.

For all other maintenance, it is recommended that the optics are serviced at the manufacturer's site.

9.1 Cleaning the micro flow cell window

The optical surfaces of the micro flow cell must be clean before use. If cleaning is required, Endress+Hauser recommends the process below. Clean gloves are recommended whenever handling the micro flow bench and micro flow cell to minimize the transmission of oils or other film-type contamination to the exterior optical window surfaces.

Contaminant	Cleaning process
Large particles and dust	▪ Blow off the surface with clean, dry air. **NOTICE** **Oil contamination in the air lines can result in film on the optical surface.** ▶ Ensure only clean air is used. ▪ Inspect the surface. Repeat the cleaning process if large particles or dust remain.
Small particles	▪ Gently clean with the lens wipes provided with the Raman micro flow cell. o Do not damage the optical surface with excessive or aggressive cleaning. o Use a fresh cleaning wipe to avoid scratching the surface with trapped debris. o Minimize liquid buildup on the window surface to avoid leaving film contamination on the surface. ▪ Inspect the surface. Repeat the cleaning process if contaminants remain.
Film-type contamination	▪ Gently clean with the lens wipes provided with the Raman micro flow cell. o Do not damage the optical surface with excessive or aggressive cleaning. o Use a fresh cleaning wipe to avoid scratching the surface with trapped debris. o Minimize liquid buildup on the window surface to avoid leaving film contamination on the surface. ▪ Inspect the surface. Repeat the cleaning process if contaminants remain.

Table 6. Cleaning the micro flow cell window

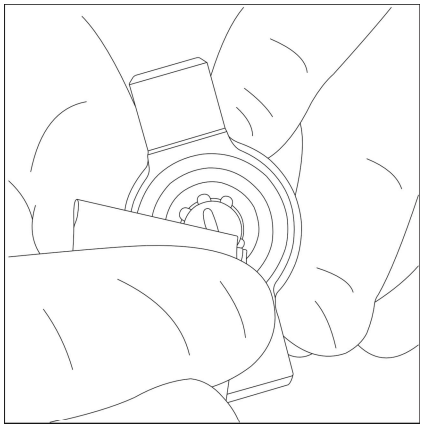

Figure 7. Cleaning the optical surface with a lens wipe

10 Repair

10.1 Repairing the Raman flow assembly

Repairs not described in this document must be carried out only at the manufacturer's site or by the service organization. For Technical Service, refer to our website (https://endress.com/contact) for the list of local sales channels.

If a product must be returned for repair or replacement, follow all decontamination procedures indicated by your service provider.

⚠ WARNING

Failure to properly decontaminate wetted parts before return can result in a fatal or serious injury.

To ensure swift, safe and professional product returns, please contact your service organization.

For additional product return information, refer to the following site and select the applicable market/region: https://www.endress.com/en/instrumentation-services/instrumentation-repair.

10.2 User serviceable parts

There are no user serviceable parts for the Raman flow assembly.

11 Technical data

The specifications for the micro flow cell and micro flow bench are listed in the tables below.

11.1 Micro flow bench

Item		Descript
Laser wavelength		785 nm
Spectral coverage		limited by the coverage of the analyzer being used
Maximum laser power into probe head		< 499 mW
Shipping and storage	Temperature	−10 ˚C to 50 ˚C (−22 ˚F to 302 ˚F) per IEC 60068-2-14
	Shock and vibe	Vibe: 5-500 Hz @ 2 g 1 octave/min ± 3 axes Shock: 50 g, 10 ms ± 3 axes
Performance	Amplification factor	> 3.0 (typical), > 2.5 (minimum)
	Temperature range	0 ˚C to 40 ˚C
Integration		Raman Rxn-10 probe
Calibration method	785 nm	Calibration cell with calibration reference standard* * See Raman flow assembly calibration and verification kit manual for details
Verification method	785 nm	Verification cell with 70 % IPA

Table 7. Micro flow bench specifications

11.2 Micro flow cell

Item	Description
Laser wavelength	785 nm
Wetted materials	Housing: 316 stainless steel Surface finish: Ra 0.38 µm (Ra 15 µin) with electropolish, ASME BPE SF4 Adhesive: USP Class VI and ISO 10993 compliant Window: proprietary material optimized for bioprocesses Connection: 1/16 through 3/16 in (OD tubing compatible)
Sample interface and flow conditions	0 °C to 40 °C ≤ 70 psig 15 mL/min* maximum volumetric flow rate * Maximum volumetric flow rate to ensure laminar flow specified for micro flow cell with water.
Storage	−20 °C to 60 °C ≤ 90 % RH non-condensing
Sterilization	SIP, CIP

Table 8. Micro flow cell specifications

12 Supplementary documentation

All documentation is available:

- On the Endress+Hauser Operations App for smartphone/tablet
- In the Downloads area of the Endress+Hauser website: https://endress.com/downloads

Part number	Document type	Document title
BA02295C	Operating Instructions	Raman flow assembly calibration and verification kit
TI01635C	Technical Information	Raman flow assembly Technical Information

Table 9. Supplementary documentation

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