BIOSPECTRA

100 Majestic Way, Bangor, PA 18013 / www.biospectra.us

SPECTRUM TWO UATR SOP

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1. PURPOSE:

1.1. To provide Laboratory personnel with operation and calibration instructions for the PerkinElmer Spectrum Two FT-IR Spectrometer and UATR attachment.
1.2. To provide Laboratory personnel with a procedure to verify the identity of a specified material by examining absorption in the Infrared region of the electromagnetic spectrum.

2. SCOPE:

2.1. Applies to the operation and calibration of the Perkin Elmer Spectrum Two Spectrometers located at both the Stroudsburg and Bangor facilities.
2.2. The user settings set forth in this SOP are recommended for optimal performance of the ES software.

3. RESPONSIBILITIES:

3.1. The Director of Laboratory Testing, or other qualified designated individual, is responsible for the implementation, control, training, and maintenance of this procedure.
3.2. The Director of Laboratory Testing, or other qualified designated individual, is responsible for the visual inspection of spectra with a correlation below 0.95.
3.3. All laboratory personnel are responsible for complying with the requirements of this procedure.
3.4. If any abnormalities are determined during routine use of the spectrometer or during calibration, the Director of Laboratory Testing shall be promptly notified. If necessary, the spectrometer will be serviced and recalibrated by Perkin Elmer before being approved for use.
3.5. PerkinElmer Spectrum Two User's Guide

4. EQUIPMENT:

4.1. PerkinElmer Spectrum Two Spectrometer
4.2. PerkinElmer UATR Two Attachment

5. MAINTENANCE:

5.1. To protect UATR crystal from moisture or damage, place the plastic cover over the UATR attachment when not in use.
5.2. Clean the UATR crystal and swinging arm with a KimWipe and methanol.
5.2.1. Methanol is to be sprayed onto a KimWipe, not directly on the instrument.
5.3. Immediately clean any spilled materials on or around the instrument.
5.4. For optimal performance, the instrument should remain on at all times and be connected to a battery back-up source.
5.4.1. In the case of a power outage, the battery backup will allow enough time to properly shut down the instrument.
5.4.1.1. In order to shut the instrument down, press the standby button located on the front right side of the instrument. Once the light turns orange, the power plug can be disconnected from the back of the instrument.

6. PREPARATION OF REFERENCE STANDARDS:

6.1. Each product must have a USP, NIST, or in-house prepared Reference Standard.
6.2. USP and NIST standards should be prepared according to that product's UATR/Loss on Drying procedure.
6.3. If a USP or NIST standard is not available for a product, an in-house Reference Standard will be prepared as follows:
6.3.1. Solid Materials:
6.3.1.1. Prepare by placing a suitable amount of material from an outside source and dry (if applicable) according to that product's UATR/Loss on Drying procedure.

6.3.1.1.1. Allow the standard to cool and store in a desiccator. Cap the LOD vial once it has cooled.
6.3.1.1.2. Record the preparation in the laboratory's IR Reference Standard Preparation notebook and assign a one-year expiration date.
6.3.1.1.3. Label the LOD vial with the IR Reference Standard Preparation Lot Number, expiration date, preparers initials, and the date of preparation, using the following lot numbering convention:
6.3.1.1.3.1. Notebook number (which begins with BIR for reference standards qualified by the Bangor Lab or SIR for reference standards qualified by the Stroudsburg Lab), the letter P, and the page number, with no spaces between.
6.3.1.1.3.2. Example: BIR03P74 would be the third logbook of qualified reference standards by the Bangor Lab with the preparation documented on page 74.
6.3.1.1.4. Crush the Reference Standard with a mortar and pestle.
6.3.1.1.5. Proceed to Step 7.4.
6.3.1.2. Run the reference standard once, save, and compare it to a previously approved reference scan.
6.3.1.2.1. Enter the following information in the Sample ID field in the software:
6.3.1.2.1.1. Material Name Reference Standard
6.3.1.2.1.2. Lot Number
6.3.1.2.1.3. Expiration Date (If Applicable) or Current Lot
6.3.1.3. Save the scan to the Reference Standard folder, QC (R:)/QC files/Spectrum 2/_Solid Reference Standards
6.3.1.4. The Correlation must be greater than 0.95 between each scan.
6.3.1.5. If the correlation does not align, contact Laboratory Management immediately.
6.3.2. Liquid Samples:
6.3.2.1. Prepare liquid reference utilizing respective product Analytical Testing Methods procedure.
6.3.2.2. Proceed to Step 7.5.
6.3.2.3. Run the reference standard once, save, and compare it to a previously approved reference scan.
6.3.2.3.1. Enter the following information in the Sample ID field in the software:
6.3.2.3.1.1. Material Name Reference Standard
6.3.2.3.1.2. Lot Number
6.3.2.3.1.3. Expiration Date (unless standard is single use)
6.3.2.4. Save the scan to the Reference Standard folder, QC (R:)/QC files/Spectrum 2/_Liquid Reference Standards
6.3.2.4.1. Standards prepared at time of use will be saved in the following location: QC (R:)/QC files/Spectrum 2 and compared to the most recent previous standard preparation.
6.3.2.5. The Correlation must be greater than 0.95 between each scan.
6.3.2.6. If the correlation does not align, contact Laboratory Management immediately.
6.3.3. When a reference standard expires, IT will be contacted to move the reference scan to an archive folder.

6.4. **NOTE: All new reference standard spectra must be approved by Laboratory Systems, prior to comparison with a sample spectrum.**

6.5. **NOTE: In cases where a reference standard is not commercially available to establish a reference spectrum, the spectrum of a previously approved lot may be utilized.**

6.6. **NOTE: In cases where a spectrum has not yet been established for a reference standard, or as directed by laboratory management, a spectrum may be generated at the time of comparison with the sample.**

7. OPERATION:

7.1. Log in to the computer using the Individual Windows login for the computer.

7.2. Open the Spectrum software and log in.

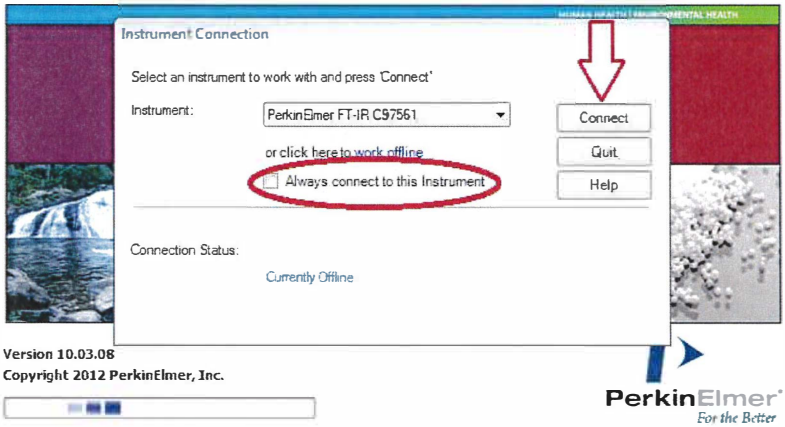
7.2.1. Each analyst/specialist has a unique login. The username is the first initial and last name of the analyst performing the analysis and the password is known only to that analyst.

7.2.1.1. Each analyst/specialist is responsible for logging out of the Spectrum software every time they are finished with each analysis.

7.2.1.2. **NOTE: Failure to log out of the spectrum software will result in a discrepancy investigation.**

7.2.2. After logging in, the following screen will appear:

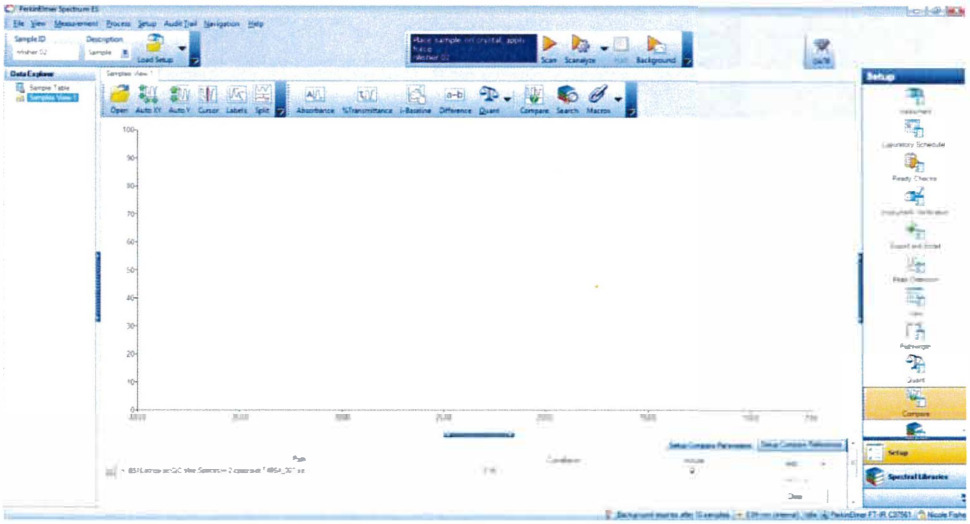
PerkinElmer Spectrum ES



7.2.3. Make sure the Instrument being used is selected and then click "Connect".

7.2.3.1. **NEVER check the box for the "Always Connect to this Instrument"option. If this happens, contact your supervisor to correct your user settings.**

7.2.4. Once the software is loaded, the home screen will open, as follows:



7.2.5. Prior to performing any sample scans, in the Sample Table window, make sure the "Preview" box is checked, as follows:

7.3. Perform a background scan prior to use each day and after every ten samples.
- 7.3.1. Remove the plastic cover and clean the UATR crystal using methanol and a KimWipe.
- 7.3.2. With the swinging arm to the side, click Background at the top of the screen.

7.4. Solid Sample Analysis:
- 7.4.1. Enter the following information in the Sample ID field in the software:
  - 7.4.1.1. Lot Number
  - 7.4.1.2. Stability Time Pull and Packaging (if applicable)
  - 7.4.1.3. Analyst Initials
  - 7.4.1.4. Date of Analysis
- 7.4.2. Solid Sample Types:
  - 7.4.2.1. Finished Goods and Stability Samples, are prepared from the dried, LOD sample, unless the product does not require LOD analysis or it is otherwise stated in the respective Analytical Test Method (ATM), Analytical Procedure, or Product Specification. After the LOD analysis has been completed, crush the sample to a fine powder in a mortar and pestle prior to performing IR.
  - 7.4.2.2. Repack Samples are run as-is. Crush the sample to a fine powder in a mortar and pestle prior to performing IR.
    - 7.4.2.2.1. For repacks of Bio Ultra Grade or Bio Buffer Solution Grade material, the sample can be run utilizing the following preparation when applicable:
      - 7.4.2.2.1.1. Run sample as-is. Crush the sample to a fine powder in a mortar and pestle prior to performing IR.
      - 7.4.2.2.1.2. Dry the sample in accordance with the applicable Loss on Drying procedure and analyze.
      - 7.4.2.2.1.3. Re-crystallize both the standard and sample under identical conditions to produce the same solid-state form and compare.
  - 7.4.2.3. Unless otherwise stated in the respective Analytical Test Method (ATM), Analytical Procedure, or Product Specification, the following samples are run as-is, crushing the sample with a mortar and pestle into a fine powder prior to performing the IR.
    - 7.4.2.3.1. Raw Material samples
    - 7.4.2.3.2. Dry Crystal samples
    - 7.4.2.3.3. Wet Crystal samples
      - 7.4.2.3.3.1. If the required correlation is not met due to water interference, the sample may be dried according to the LOD procedure for that product, and analyzed.
  - 7.4.2.4. For Validation samples with a report/monitor specification, the initial correlation can be accepted even if it is below the required correlation
- 7.4.3. Place the prepared solid sample on the UATR crystal using a static free scoop.
- 7.4.4. Align the swinging arm with the crystal and apply force by turning the green arm clockwise.

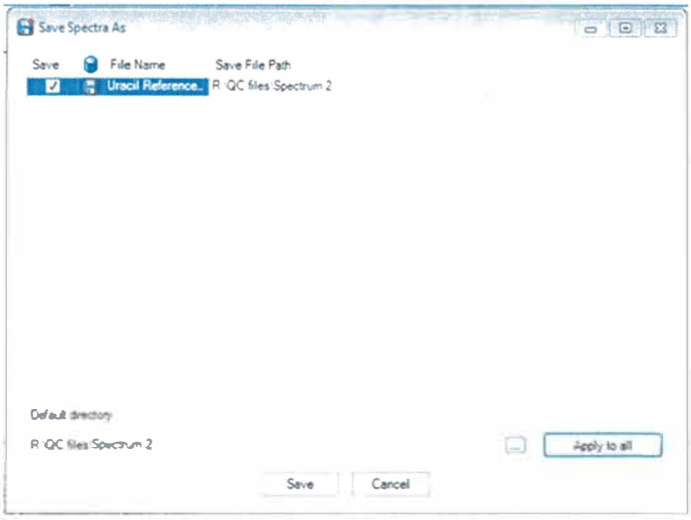
7.4.5. Press "Scan" on the top Toolbar. The program will preview the sample. Turn the green arm until the Force Gauge is approximately 125, or until the noise has subsided.
7.4.6. Once the Force Gauge is adjusted, press "Scan".
7.4.7. Once the scan is complete, release the swinging arm by turning it counterclockwise.
7.4.8. Clean the UATR crystal and the swinging arm with methanol and a KimWipe.

7.5. Liquid Sample Analysis:

7.5.1. Enter the following information in the Sample ID field in the software:
7.5.1.1. Lot Number
7.5.1.2. Stability Time Pull and Packaging (if applicable)
7.5.1.3. Analyst Initials
7.5.1.4. Date of Analysis
7.5.2. All sample types will be run as-is
7.5.2.1. For Validation samples with a report/monitor specification, the initial correlation can be accepted even if it is below the required correlation
7.5.3. Using a disposable transfer pipette, place sufficient sample to cover the UATR crystal.
7.5.4. Press "Scan" on the top Toolbar. The program will preview the sample. Then press "Scan".
7.5.5. Once the scan is complete, clean the UATR crystal with methanol and a KimWipe.

7.6. Saving Sample Scans:

7.6.1. Save all scans by choosing "File" then "Save As". The following screen will appear:

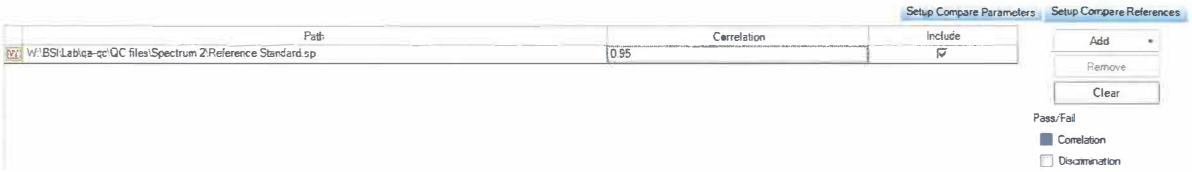


7.6.2. Select the file path by selecting the button with 3 dots and select the following file path: QC (R:)/QC files/Spectrum 2
7.6.3. Select "Apply to all" and "Save".

7.7. Comparing Scans:

7.7.1. In the "Setup" pane on the right-hand side, choose "Compare".
7.7.2. On the bottom pane click the "Setup Compare References" tab.
7.7.3. Click "Clear" to remove any previous Reference Scans and then click "Add" and "Single Spectrum".
7.7.4. Select the desired Reference Standard from the Reference Standard folders of the Spectrum 2 network folder. QC (R:)/QC files/Spectrum 2/_Solid Reference Standards or QC (R:)/QC files/Spectrum 2/_Liquid Reference Standards.
7.7.4.1. Check to ensure that the reference has not expired:

7.7.4.1.1. Based on the given expiration date for in-house prepared reference standards.
7.7.4.1.2. Checking for an expiration date or current lot status with NIST and USP.
7.7.4.2. If a reference has expired refer to Section 6 to prepare a new standard.
7.7.4.3. **Note: Time of use standards will be located in the following folder: QC (R:)/QC files/Spectrum 2**
7.7.5. Change the Correlation to 0.95. The "Setup Compare References" tab should appear as follows:



7.7.6. In the left-hand pane, select the sample being analyzed.
7.7.7. In the toolbar select "Compare". The Reference Standard and sample will be overlaid on the same spectrum and compared with a Correlation coefficient.
7.7.8. If the correlation is above 0.95, the comparison will be reported with Pass as the result.
7.7.9. If the correlation is below 0.95, the comparison will be reported as Fails and are subject to visual inspection by the Laboratory Manager or qualified designee.

7.8. Printing Reports:
7.8.1. Click "File" and then "Print". Be sure to select a printer that can print in color.
7.8.2. When the report is printed, the analyst must initial and date at the top of the report page and reference the location of the testing. If the report is multiple pages, staple them together and initial and date and add a reference to all subsequent pages.
7.8.3. If the report is printed in grayscale, notify Laboratory Systems and Laboratory Management then reprint the report in color upon their acknowledgement.

8. INSTRUMENT VERIFICATIONS AND CALIBRATIONS:

8.1. All Instrument Calibration and Verification documentation will be stored in the Laboratory in the "UATR Two" binder.

8.2. Verifications:
8.2.1. NOTE: If the UATR attachment is removed, the functionality of the attachment must be verified by performing an Instrument Verification prior to its next use.
8.2.2. Instrument Verification is performed on a monthly basis to ensure that the instrument is within calibration.
8.2.3. Prior to running the required monthly Instrument Verification or instrument verification after UATR attachment has been removed, choose "Instrument Verification" in the Setup toolbar on the right-hand side of the screen.
8.2.3.1. Under the "Setup Instrument Verification" tab, ensure "Internal APV" is selected.
8.2.4. To run Instrument Verification, choose "Measurement", "Instrument Checks", then "Instrument Verification".
8.2.5. The following tests will be completed:
8.2.5.1. Abscissa Check
8.2.5.2. Noise Check
8.2.5.3. Ordinate Check

8.2.6. Once all tests are performed print the report by choosing "File" then "Print".
8.2.6.1. When the report is printed, sign and date at the top of the report page. The analyst must also reference the location of the testing at the top of the report. If the report is multiple pages, staple them together and initial and date the subsequent pages.
8.2.7. If any tests report "Fails", notify a supervisor immediately.

8.3. Calibrations:

8.3.1. Calibrations are performed on an annual basis, by a certified Perkin Elmer Service Technician.
8.3.2. Calibrations must be documented in the appropriate instrument notebook.
8.3.3. Upon completion of a calibration, the Perkin Elmer technician will place a calibration sticker on the instrument.
8.3.4. NOTE: If the Next Calibration due date assigned by the Perkin Elmer technician differs from the BioSpectra Calibration due date, the date that occurs soonest will be utilized as the official Next Calibration due date.

9. ANALYSIS OF UNKNOWN MATERIALS:

9.1. Ensure there is enough material for analysis.
9.1.1. If there is not enough material for analysis, contact the sample owner (the individual that submitted the sample) to increase the amount submitted.
9.2. Analysis of unknown materials will follow sections 7.4. and 7.5.
9.3. Since materials submitted to the Laboratory for investigation or research purposes may not have a formal lot number, a unique description must be entered into the Sample ID field. For example, this may be a physical description followed by the analysis date or time.
9.4. Select the appropriate project library and compare the spectra against appropriate internal and/or external databases.
9.5. Report the correlation and title of the best match.