



What You Need to Know About
**Field-Based Material Identification and
Authentication for Pharmaceuticals**

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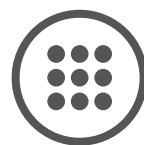
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overview

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Overview

By law, pharmaceutical manufacturers must identify and verify all incoming materials. Current Good Manufacturing Processes (cGMP) require that not only incoming raw materials but all in-process materials be tested for identity, strength, quality, and purity throughout the manufacturing process.

Falsified pharmaceuticals are increasingly entering the supply chain, representing a deadly and growing worldwide health risk for patients and a costly violation of intellectual property rights for pharmaceutical manufacturers. These drugs at best will not deliver the therapy they promise and at worst can endanger patients' lives.



Field-based Material Identification and Authentication for Pharmaceuticals

For Manufacturers: Verify the identity of Raw Materials

Handheld analytical instruments generate crucial, actionable information where needed so pharmaceutical manufacturers can make quick decisions in critical situations.



Why?

- Sustain product quality
- Improve raw material release time to production

Where?

- Anywhere in the plant
 - Loading dock
 - Dispensing booth where APIs are being manufactured
 - Final product inspection

Benefits

- Regulatory compliance
- Reduce risks and cost
 - Quality Assurance/Quality Control: replace laboratory testing and identify raw materials in their packaging without having to open or sample
 - Improve processes: yield efficiencies and cost reductions by lowering lab costs, faster release of materials, reduced risk of cross contamination, and more stable quality of materials



Field-based Material Identification and Authentication for Pharmaceuticals

For Health Agencies/Public/Brand Security Teams: Authenticate Medicines

Handheld analytical instruments generate crucial, actionable information where needed so customers can make quick decisions in critical situations.



Why?

- Prevent falsified and substandard medicines from entering the supply chain
- Handheld analyzers allow users without chemistry training to authenticate medicines in the field
- Brand protection of medication

Where?

- Wherever pharmaceuticals are distributed
- Authenticate directly through sealed packaging

Benefits

- Reduce risks and costs
 - Ensure customer safety and decrease worldwide health risk for patients
 - Reduction in backlogs and time delays associated with lab testing
 - Brand security: Avoid costly violation of intellectual property rights for pharmaceutical manufacturers



Falsified Medicines & Ensuring Consumer Safety



Patients and consumers expect reliable access to safe, efficacious, stable, and affordable high quality medicines.



Substandard and falsified medicines are dangerous to public health. They may cause death due to the absence of an active drug, as has happened with some vaccines and antibiotics, or because of a toxic material or contaminant.



Differences between real and counterfeit medicines can involve different active pharmaceutical ingredients (API) and excipients, and different concentrations.



Medicines may be considered substandard due to improper storage, climate, expiry dates, and traceability issues.



Outside of the traditional lab, handheld analyzers can be used to quickly screen for falsified and substandard medicines to help protect patient safety and the efficacy of pharmaceutical products. Handheld analyzers allow for quick screening in warehouses, ports, borders, and local shops without the inherent time delays with laboratory sampling analysis workflows.





QA/QC - On-site Analysis and Verification

A traditional workflow requires sending samples to a centralized laboratory for analysis at each step of the manufacturing process.

With handheld analyzers, non-technical operators can analyze materials on the warehouse floor and at any inspection point throughout the manufacturing process to increase inspection intervals, improve inventory management, and reduce global supply chain risk.



QA/QC - Improve On-site Processes



Handheld analyzers provide nondestructive measurements that yield information regarding biological, physical, and chemical attributes of materials. They can be employed by non-expert users anywhere in the plant.

Using handheld analyzers to move raw material authentication from the laboratory to the warehouse means fewer costly lab sample tests, faster release of raw materials, improved inventory management, and no risk of cross contamination by measuring through original packaging.



Protect Your Brand

- Pharmaceutical formulations are complex, multicomponent mixtures. There is a need to identify and verify components, and also to evaluate the distribution of these components.
- The distribution of components within a product can affect the stability and functionality of the final product.
- With the wide variety of active pharmaceutical ingredients (API) that can be combined with numerous excipients, it is important to be able to analyze and provide accurate data on a variety of formulations.
- Ensuring that patients are not using falsified medicines keeps the consumer safe, and also protects pharmaceutical companies' brand.
- Some handheld Raman analyzers are capable of multiple content discrimination and API content quantification and are therefore helpful in identifying substandard or falsified medicines.



Process Improvement

As part of **cGMP** many pharmaceutical manufacturers are adopting Process Analytical Technologies (**PAT**), Quality by Design (**QbD**), or Process Validation (**PV**).

cGMP and associated process monitoring necessitates continuous process verification and analysis. **Analytical instruments such as near-infrared and Raman spectroscopy and chemometric modeling software may be used to measure quality throughout the process.**



COMPLIANCE

Law

Requirements

Rules

Standards

Governance

Regulations

Transparency

compliance



Regional Compliance Regulations

Pharmaceutical manufacturers are required to follow regional compliance regulations to verify the quality of their materials throughout the manufacturing process

Federal Food, Drug and Cosmetic Act (FD&C Act) – requires conformity with Current Good Manufacturing Practice (cGMP)

- 21 CFR (Code of Federal Regulation) 210 & 211 – regulations which implement FD&C Act
 - Minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product. These regulations make sure that a product is safe for use, and that it has the ingredients and strength it claims to have.

Pharmaceutical Inspection Co-operation Scheme (PIC/S), Annex 8

- PIC/S is a non-binding, informal co-operative arrangement between Regulatory Authorities in the field of Good Manufacturing Practice (GMP) of medicinal products for humans or veterinary use. It is open to any Authority having a comparable GMP inspection system. PIC/S seeks to harmonize inspection procedures worldwide by developing common standards for GMP and providing training to inspectors.
- Requires that individual samples be taken from **all incoming containers** and an identity test be performed on each sample.
- This is a change from the traditional practice of allowing composite sampling of a statistical subset of the batch and identity testing of the single composited sample, in order to release the batch to manufacturing.



Regional Compliance Regulations

Pharmaceutical manufacturers look to improve efficiency and reduce costs while maintaining quality and regulatory compliance.

The Food and Drug Administration's (FDA) FD&C Act **requires conformity with cGMP** for manufacture of drugs and **makes no distinctions between API, excipients, and finished pharmaceuticals.**



Mandates:

- Testing of in-process materials for identity, strength, quality, and purity
- Developing a well controlled, validated, and vigorous pharmaceutical manufacturing process, able to **reliably deliver** intended quality of product



Electronic Signature and Traceability

21 CFR Part 11 – Electronic Records, Electronic Signatures:

Electronic Signature and Traceability

- Protect the stored electronic data related to quality assurance within manufacturer's computer systems
- Put controls in place to keep records authentic, incorruptible, and confidential
- Electronic signatures signify that the user is taking responsibility for the electronic data in the system
- Required in the data record: date and time of scan, name of the unique signer, and technological controls to ensure security (e.g. passwords)





technology 

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Portable/Handheld Technology

Pharmaceutical manufacturers **must not only verify the identity of incoming raw materials, but also test the identity, strength, quality, and purity of materials during all phases of manufacturing.**

Traditionally a centralized laboratory in the facility receives samples from all over the plant and at every stage of manufacturing and performs identification and verification tests. This is time consuming, requires lots of sample handling, and is costly in time and expert personnel.

Handheld analyzers allow process and plant engineers to identify and quantify raw materials, intermediates, and finished products on site in seconds.

Handheld analyzers can identify raw materials:

- Non-contact analysis through plastic bags, glass containers, blister packs and clear gel caps
- Non-destructive
- Point-and-shoot sampling principle
- Rapid verification of a broad range of chemical compounds, including cellulose-based products
- No need to send samples out to the lab
- Analyze at the line and point of need



Analytical Techniques

Spectroscopy = study of the interaction between matter and electromagnetic radiation

Vibrational Spectroscopy = characterizes materials by the frequencies of their molecular vibrations

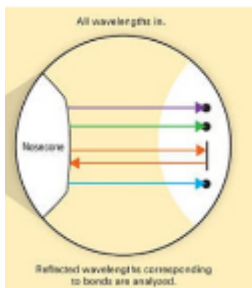


[Learn about Raman spectroscopy](#)

Raman spectroscopy

A spectroscopic technique that relies on light, usually from a laser, to observe vibrational, rotational, and other low-frequency modes in a system. **Raman spectroscopy** is commonly used in chemistry to provide a fingerprint by which molecules can be identified.*

Named after Sir C. V. **Raman, an Indian physicist who carried out ground-breaking work in the field of light scattering (https://en.wikipedia.org/wiki/Raman_spectroscopy)*



[Learn about NIR spectroscopy](#)

Near-Infrared (NIR) spectroscopy

A spectroscopic method that uses the near-infrared region of the electromagnetic spectrum, and is based on overtones and combinations of bond vibrations in molecules.



Raman Advantages & Disadvantages

ADVANTAGES

- High specificity
- No sample preparation required
- Scan through clear and amber glass, plastic, packaging
- Eliminates contamination of samples, operator exposure, won't effect expiration date of sample
- No interference from water
- Scan liquids or solids
- Sensitive only to chemical make up of material

DISADVANTAGES

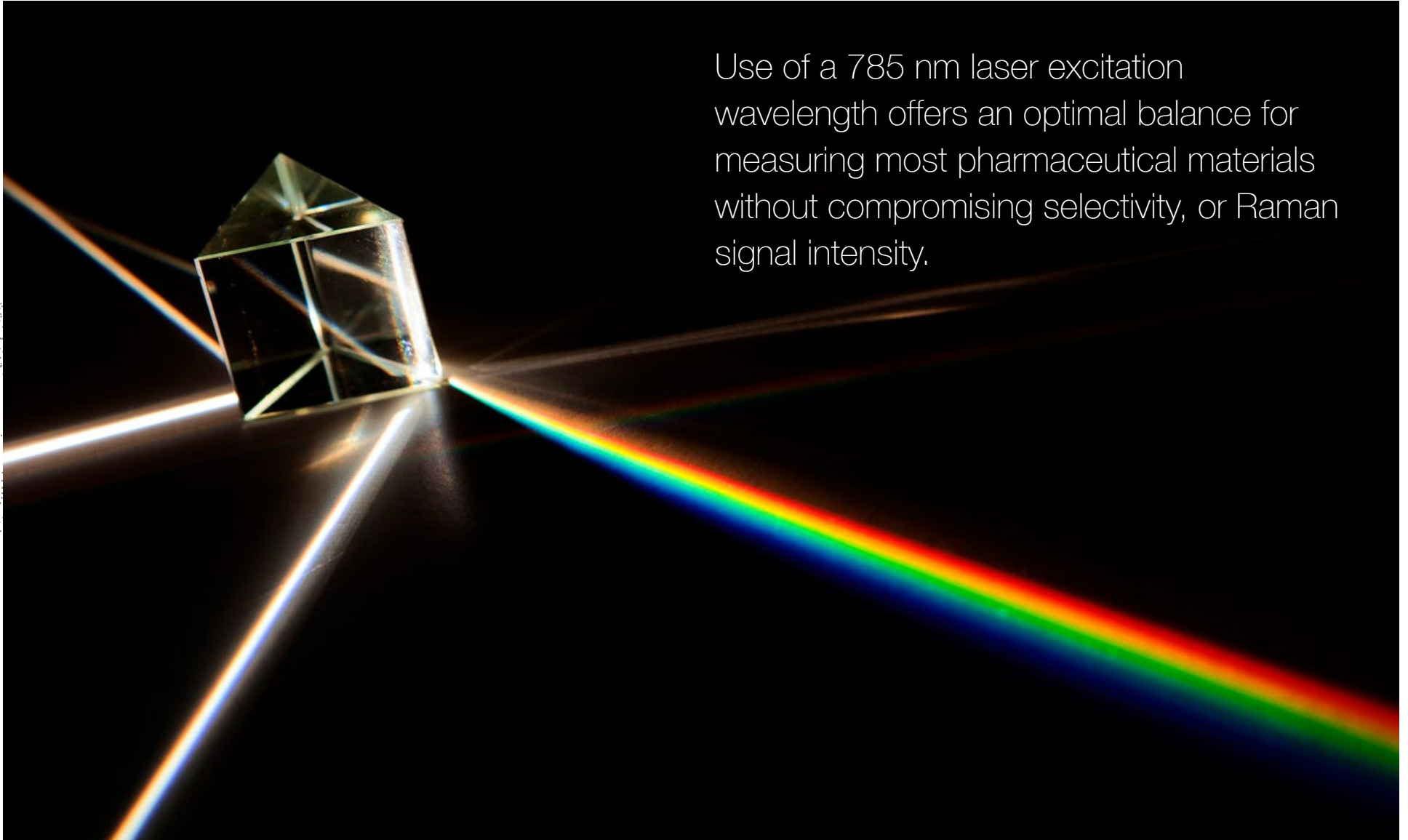
- Opaque and colored tubs and bottles may be a challenge
- Can't scan metals or alloys
- Fluorescence can prevent scan
- Analysis speed slower than IN/NIR



Wavelengths

Handheld Raman Analyzers Utilize Lasers

Use of a 785 nm laser excitation wavelength offers an optimal balance for measuring most pharmaceutical materials without compromising selectivity, or Raman signal intensity.



NIR Advantages & Disadvantages

ADVANTAGES

- Non-destructive analysis
- Fast analysis speed
- Penetrates much further into sample
- Scan through plastic bag liners and glass containers
- Eliminates contamination of samples, operator exposure, won't effect expiration date of sample
- Not affected by fluorescence as much as other analytical techniques
- Very useful in probing bulk material with little or no sample preparation

DISADVANTAGES

- Not as chemically specific as Raman
- More complex to interpret spectra; it can be difficult to assign specific features to specific chemical components
- Careful development of a set of calibration samples and application of multivariate calibration techniques is essential for near-infrared analytical methods.



NIR and Raman: Complementary Technologies

NIR

- Grains
- Polymers, linked groups
- Light sensitive materials
- Fluorescent samples



- Light-colored materials (excipients, API)
- Solids, gel, pastes, syrups

RAMAN

- Polyatomic ionic salts
- Non-polar materials (no H bond)
- Aqueous solutions



Gases, ionic salts, and some biologics excluded



Analytical Methodologies

HQI (Hit Quality Index)

Assessment of similarity metrics calculated via peak table comparisons or more commonly from those generated by full spectrum comparison. Full spectrum approaches generate HQI between the unknown and each library spectrum.

Chemometrics

Users build custom qualitative and quantitative methods for complex material analysis problems. Some handheld analyzers have embedded chemometric software which enables non-expert users to run quantitative analysis anywhere onsite.

Probabilistic Approach (P-Value)*

Determines whether the measured spectrum of the unknown sample lies within the multivariate domain of a referenced spectrum of interest, based on uncertainty characteristics:

- Measurement settings
- Environmental properties
- Sample properties



*Thermo Fisher Scientific utilizes a patented P-value. See details on page 29.





products 

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Analytical Instruments

Handheld Raman and NIR analyzers can authenticate medications directly in the field, wherever pharmaceuticals are distributed. These easy-to-use tools enable a higher level of screening, reducing the backlogs associated with lab testing. Most analyzers can even confirm the authenticity of pharmaceuticals directly through sealed packaging.

Regulatory agencies and customs in North America, Europe, Asia, and Africa use handheld Raman and NIR analyzers:

- Canada – Health Canada
- China – CFDA
- Denmark – DMA
- France – ANSM
- Indonesia - NAFDC
- Netherlands – Dutch Medicines Authority
- Nigeria – NAFDAC
- Sierra Leone – Ministry of Health
- Switzerland - SwissMedic
- Thailand – FDA
- Uganda – National Medical Stores & NDA
- United Kingdom – MHRA
- United States – US FDA, US Customs



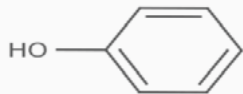
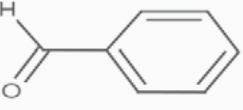
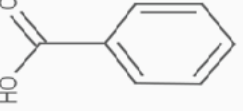
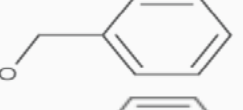
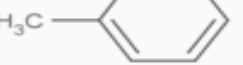
TruScan RM

The **Thermo Scientific™ TruScan™ RM** Raman Analyzer utilizes state-of-the-art optics paired with a patented multivariate residual analysis that offers an effective chemometric solution for material identification, with two spectral pre-processing options that are easy to operate in challenging environments and sampling conditions.

- Meets 21 CFR Part 11 and cGMP requirements with biometric login, complex password options, and audit trail features
- Compliant with United States Pharmacopeia (USP) Chapter <1120> and with European Pharmacopeia (EP) 8.7 general chapter <2.2.48> on Raman spectroscopy
- Intuitive interface allows non-expert field technicians to successfully use analyzer
- Rapid verification of a broad range of chemical compounds, including cellulose-based products



TruScan RM's Patented P-Value Algorithm

| | Patented P-value | HQI |
|---|--|--------|
|  | phenol 0.45 | 0.9981 |
|  | benzaldehyde 0.00000000000000000000000000000015 | 0.9902 |
|  | benzoic acid 0.00000000000000000000000000000011 | 0.9827 |
|  | benzyl alcohol 0.00000000000000000000000000000012 | 0.9714 |
|  | toluene 0.00000000000000000000000000000054 | 0.9890 |

- **HQI** and other correlative techniques only measure the similarity between test materials.
 - Relatively insensitive to minor differences and make the validation of structural analogs challenging
- **Patented p-value algorithm** –
 - Doesn't simply measure the similarity between library spectra & test material - looks at the **differences** which strengthens ability to discriminate between 2 materials
 - Highly sensitive to minor differences – allows strong **discrimination of structural analogs** through validation
 - Typically 1 single match result can be achieved
 - Doesn't require advanced validation as the threshold is fixed
- Multivariate analysis takes into account factors influencing the measurement know as **uncertainty characteristic** of a measurement:
 - Measurement settings – e.g. exposure time and number of scans or sweeps
 - Environmental properties – e.g. temperature, dark current
 - Properties of the sample itself – e.g. Raman cross section, absorbance, refractive index



TruScan RM and TruTools – Handheld Raman Analyzer with Embedded Chemometrics Software

The Thermo Scientific™ TruTools™ is embedded chemometric software that runs on the TruScan RM analyzer and allows users to build customized qualitative and quantitative methods for complex material analysis problems.

TruScan RM and TruTools methods can:

- Support quantification of up to 10 chemicals
- Discriminate between materials with similar chemical compounds such as calcium stearate, zinc stearate, and magnesium stearate, or ethanol vs. methylated spirits
- Replace slower lab testing and run qualitative and quantitative methods at line
- Expand TruScan RM's raw materials verification capabilities – allows for finer discrimination of materials

*Meets cGMP and
21 CFR Part 11 requirements*



A PCA TruTools method screen result



A PLS TruTools method screen result.



microPHAZIR RX

The Thermo Scientific™ microPHAZIR™ RX is a handheld near-infrared (NIR) instrument designed for rapid on-site pharmaceutical material identification and analysis.

- Handheld design allows operators to perform analysis right in the warehouse
- Non-invasive sampling permits 100% container inspection – measures directly through plastic drum liners and glass containers
- USP <1119> and EP 2.2.48 compliant; supports 21CFR Part 11 compliant processes
- USP 34 Chapter 1119, JP 15 Supplement 2, EP 2.2.49 Near Infrared compliant
- Enables manufacturers to meet global cGMP requirements

Applications Include:

- Incoming raw material identification
- Quality control and assurance
- Counterfeit product screening
- At-Line Process Analytical Technology (PAT)
- Process troubleshooting
- Quantitative analysis



Frequently Asked Questions

Are they delicate instruments?

They are rugged and sealed; impact-resistant screen helps guard against damage by accidental drop or daily use. The TruScan RM has a IP65 rating which means it is both water and dust tight.



Can they be cleaned of old material before analyzing new material?

They can be fully decontaminated with water, isopropyl alcohol, or a 5% solution of bleach (sodium hypochloride).

Is the software secure?

Software and decision engine is part of a closed system that cannot be altered.

Are laser systems safe?

Some lasers emit radiation in the form of light. Others emit radiation that is invisible to the eye, such as ultraviolet or infrared radiation. In general, laser radiation is not in itself harmful, and behaves much like ordinary light in its interaction with the body. Common sense operation of instruments dictates that you never point the instrument at yourself or others, and that you never start or end a scan without a sample in front of the laser aperture.

Is there any training or support on how to use the instruments?

Thermo Fisher Scientific subject matter experts provide training and technical consultation from method development and validation to general operator usage. Once up and running, we provide support anywhere in the world. Prepared templates and documentation include: IQ/OQ/PQ, SOP templates, and statements of compliance.



Thermo Fisher Scientific Field Safety Instruments for Pharmaceuticals



Thermo Scientific's Field and Safety Instruments (FSI) handheld Raman and NIR analyzers deliver lab-quality, actionable information to the pharmaceutical market. We supply instruments to the majority of top pharmaceutical manufacturers and regulatory agencies worldwide.

TruScan RM (Raman) and microPHAZIR RX (NIR) handheld analyzers enable rapid raw material testing and verification, identify and eliminate dangerous counterfeit and substandard products in the supply chain, and ensure the quality and strength of finished products at the point of need. The analyzers perform non-destructive analysis, operate through plastic or glass containers, support 21 CFR part 11 compliance, and meet cGMP requirements.





About Thermo Fisher Scientific

Thermo Fisher Scientific Inc. (NYSE: TMO) is the world leader in serving science, with revenues of more than \$20 billion and approximately 70,000 employees globally. Our mission is to enable our customers to make the world healthier, cleaner and safer. We help our customers accelerate life sciences research, solve complex analytical challenges, improve patient diagnostics, deliver medicines to market and increase laboratory productivity. Through our premier brands – Thermo Scientific, Applied Biosystems, Invitrogen, Fisher Scientific and Unity Lab Services – we offer an unmatched combination of innovative technologies, purchasing convenience and comprehensive services.

For additional information or to request a quote, please click below.

