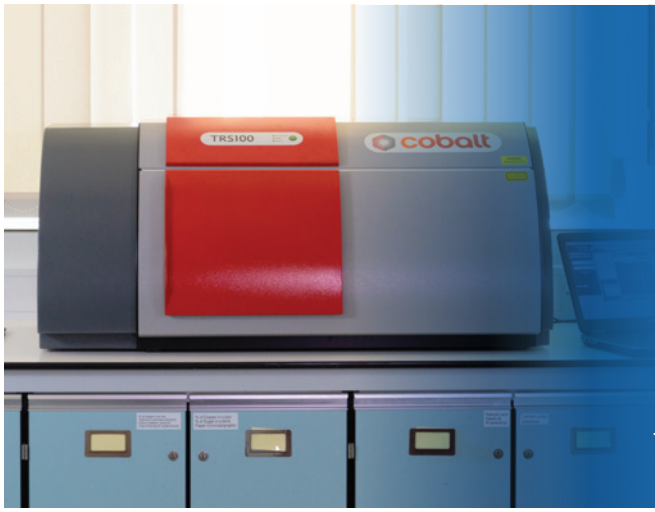
TRS100 - Quantitative Pharmaceutical Analysis System

cobalt
Insight from Light

Streamlined Quality Control



TEST HUNDREDS *of intact tablets or capsules in minutes*

QUANTIFY APIs *and excipients in a single measurement*

REDUCE COSTS *- No sample preparation, consumables or skilled testing resource*

REGULATORY-APPROVED METHODS *for Content Uniformity, Assay and ID*

TRS100 for Quality Control and Development

The TRS100™ is ideal for fast assay of tablets, capsules and other dosage forms. Cobalt's transmission Raman technology enables simple method-development and deployment in QC applications. It is easy to implement in analytical laboratories and production areas, and has regulatory approval for Content Uniformity (CU), Assay and ID applications.

- **HIGH-THROUGHPUT**
- **NON-DESTRUCTIVE**
- **NON-INVASIVE**
- **NO SAMPLE PREPARATION**

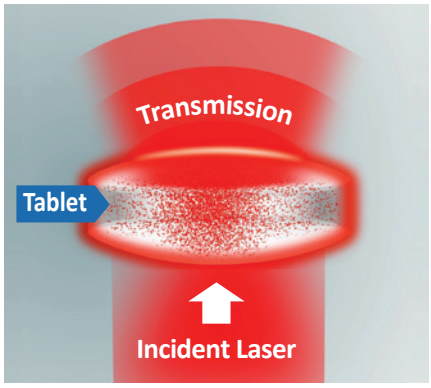
TRS100 measurements take seconds per sample and produce rich information for accurate quantitative analysis of intact samples in seconds. Routine applications include release testing, formulation development and high-throughput analysis. TRS is highly chemically-specific and sensitive to low concentrations of APIs and excipients but largely insensitive to interference from water/moisture, tablet density, tablet coatings or capsule shells.

Replacing Wet Chemistry

Using a single TRS100 an operator can complete CU, assay and ID analyses, to pharmacopoeial standards, in minutes. Unlike HPLC, there are no sample or standards preparation steps, no solvents or consumables, and batch tests can be finished as part of a normal working day, not overnight. The TRS100's tray system can hold up to 300 coated tablets or intact capsules, glass vials, powders and more. Replacing HPLC with TRS methods for CU, assay and ID allows significant cost savings per batch. A TRS100 can easily be deployed next to the tablet press for immediate QC results and release testing. Additionally, formulations with multiple APIs can be assayed in a single measurement for an even greater reduction in cost and analyst time.

What is TRS?

Transmission Raman Spectroscopy, unlike near-infrared spectroscopy, is not an absorption technique. This means TRS can measure through coated or uncoated tablets and coloured gel capsules ≥10mm thick. Raman spectroscopy produces a feature-rich spectrum that can be used to separately quantify API, polymorph and excipient components in one fast scan.



TRS quantification has:

- ✓ Low or no sensitivity to moisture, particle size and thickness variation
- ✓ Easy-to-interpret sharp spectral features
- ✓ Low LOQ: <1% is often possible
- ✓ Sensitivity to the sample bulk

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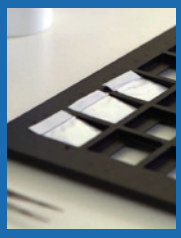
Content Uniformity • Assay • ID • Polymorph Quantification • Formulation Development

Tablets

Coated Tablets

Capsules

Powders



Liquids and Gels

Well Plates

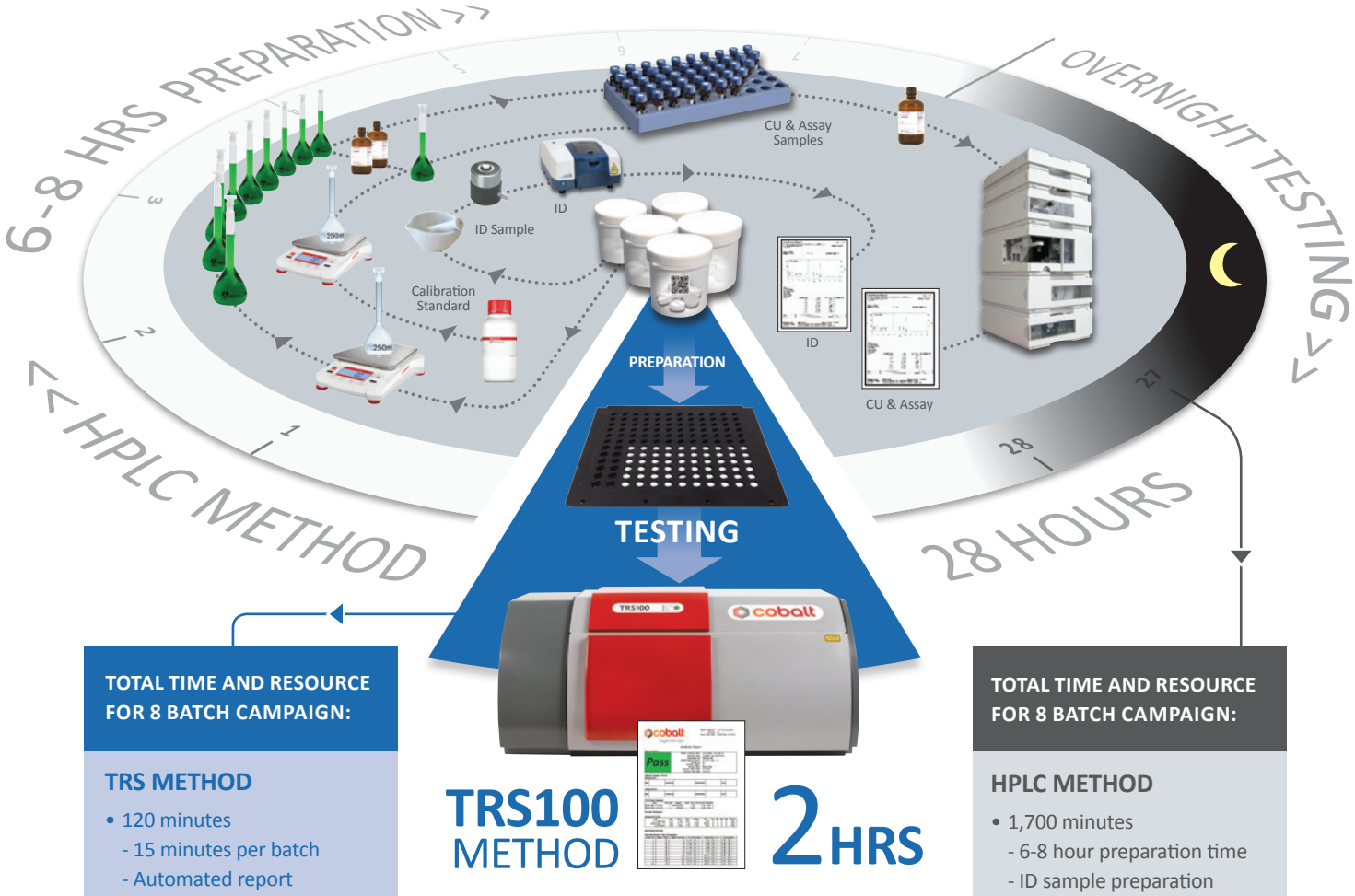
Analyse up to 300 samples on a single tray • Flexible sample presentation

TRS100

Transform your End-Product Testing

Content Uniformity, Assay and ID – Faster, Leaner, Lower Cost

TRS is a proven alternative to wet-chemistry analytical methods, needs no consumables or solvents and no preparative chemical skills. A single TRS100 CU test can often be completed in around 15 minutes, which enables a high throughput for QC testing and low resource usage compared to traditional HPLC methods.



TOTAL TIME AND RESOURCE FOR 8 BATCH CAMPAIGN:

TRS METHOD

- 120 minutes
  - 15 minutes per batch
  - Automated report
- No consumables

TRS100 METHOD **2 HRS**

TOTAL TIME AND RESOURCE FOR 8 BATCH CAMPAIGN:

HPLC METHOD

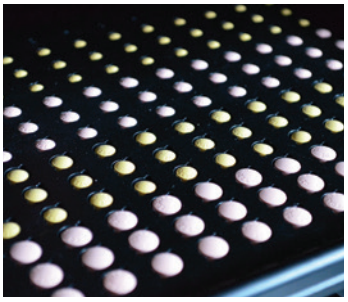
- 1,700 minutes
  - 6-8 hour preparation time
  - ID sample preparation
  - Overnight HPLC
  - Consolidate data and write-up
- 5.8l solvent, column and UV lamp life, KBr
- 96 volumetric flasks

High Throughput Testing - QC During Manufacturing

- **LARGE 'N' TESTING***
- **IPC MONITORING**
- **PROCESS VALIDATION**
- **REAL-TIME RELEASE TESTING**

The TRS100's sample-handling trays can hold up to 300 tablets at once, enabling high-throughput automated quantitative testing right at the point of manufacture, whether effective in-process control monitoring or real-time release testing (RtRT).

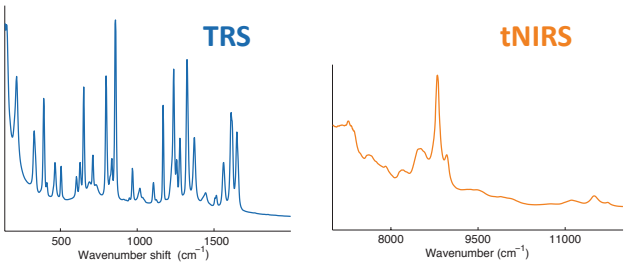
*Large 'n' testing extends CU testing to ≥100 tablets or capsules. See, for example, Ph.Eur Chapter 2.9.47, Demonstration of Uniformity of Dosage Units using large Sample Sizes.



Method Development

Spectroscopic techniques, such as near infrared spectroscopy, can be challenging for quantitative method development. TRS has several advantages over other techniques:

- Rich spectral features with high chemical specificity
- Fast method development to ICH and pharmacopoeial standards
- Development typically uses a lean calibration design of experiments (DoE)



TRS spectrum with discrete API and excipient features, compared with transmission NIR for the same 3-API product

Regulatory Approvals

CU, assay and ID methods are approved for releasing commercial batches of products using the TRS100.

- Regulatory approvals achieved following International Committee on Harmonization (ICH)* and spectroscopy guidance†
- Equivalency demonstrated with primary reference methods

For methods other than CU, assay and ID other regulatory guidance may apply.

*ICH Q2 (R1), Q8, Q9 and Q10.

†FDA's Development and Submission of Near Infrared Analytical Procedures Guidance for Industry.

EMA's Guidance on the Use of Near Infrared Spectroscopy by the Pharmaceutical Industry and the Data Requirements for New Submissions and Variations.

Measuring Low Dose APIs and Polymorph Content

TRS is highly sensitive to APIs, which is ideal for quantification of low-dose drug products. Limits of detection (LOD) can be 0.1-1% w/w with limits of quantification (LOQ) in a similar range. TRS works well with low-dose API, polymorph and salt form analysis and stability studies.

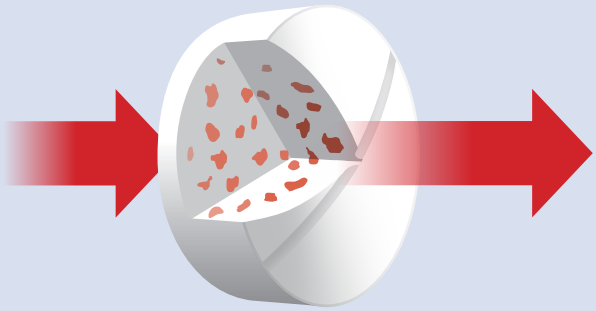
Residual Polymorphs in Intact Tablets

Most means of residual polymorph analysis quantification are invasive, destructive, slow and expensive.

- TRS has high sensitivity to polymorphs down to 0.1-1% - comparable with solid state NMR in a fraction of the time
- Low-energy "phonon mode" region measures crystalline vibrational modes directly
- Recrystallisation may occur in hotspots throughout the tablet - TRS quantifies the intact dosage form, sampling the entire tablet volume, including any hotspots
- No sample preparation or risk of form conversion
- Low cost per test

*Data from Kumar et al, American Pharmaceutical Review, 19(1), February 2016.

Method*	LOQ (w/w)	Time per sample
pXRD	2.5-10%	≈1 hour
ssNMR	<1%	24+ hours
TRS100	**<1%**	**≈10 seconds**

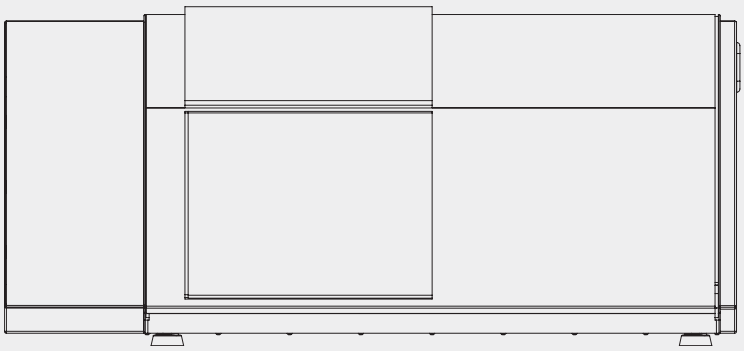


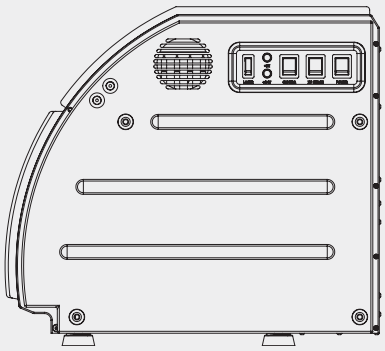
Polymorph HOTSPOTS of recrystallised API in a tablet – why TRS bulk-averaging works

Quantitative Pharmaceutical Analysis

TRS100 Compliance

Designed exclusively for quality control, analysis and testing in pharmaceutical manufacturing, working to the industry's strict regulatory requirements. Integrated sample-handling for minimal operator interaction. Automatic calibration using NIST and ASTM-approved standards. Meets relevant USP, EP and 21 CFR part 11 requirements.





Dimensions: 1124mm (44.3") wide / 521mm (20.5") high / 575mm (22.6") deep

Regulatory
- 21 CFR Part 11 compliant
- Meets relevant USP and EP guidance

Laser
- Class 1 laser
- 830 nm

Power
- 90-264VAC 50-60Hz

Software
- Requires minimum of Windows 7 Pro OS
- Supplied with Cobalt's ContentQC™ analysis and management software
- Integrated Eigenvector Solo chemometrics engine

Sample Trays
- Standard trays for common capsule and tablet sizes
- Customisable tray designs accommodate any sample
- Optional Beam Enhancer™ technology available for increased speed and sensitivity

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