PURIFICATION, PURITY ANALYSIS, AND IMPURITY ANALYSIS SOLUTIONS FOR PHARMACEUTICAL RESEARCH AND DEVELOPMENT

The Measure of Confidence

Agilent Technologies
The current environment within the pharmaceutical industry—an environment shaped by patent expirations, high failure rates for new chemical entity (NCE) development, and high-profile drug recalls—provides constant pressure to increase productivity. The regulatory environment is also challenging the industry to improve its processes, requiring greater sensitivity, accuracy, and precision in quality measurements. Because of substantial overlap in the practices and technologies used, contract research and manufacturing organizations (CROs and CMOs), as well as the generic pharmaceutical industry, are faced with similar challenges.

Three key areas—purity analysis, purity analysis, and impurity analysis—are vital to the future success of these industries, as they offer the potential both to increase productivity and to facilitate regulatory compliance.
Purification, Purity analysis, and Impurity analysis

Target Selection

Target Validation

Purification solutions: Flash & Preparative HPLC

Flash 971-FP Chromatography system

Analytical solutions for Purity determination: LC, GC, LC/MS, CE, & SFC

1200 Infinity Multi-Method Solution
**Lead Identification**

**Lead Optimization**

**Pre-Clinical Development**

**Solutions for Purity Determination:** LC, GC, LC/MS, CE, & SFC

- 6100 Series Single Quadrupole (SQ) LC/MS systems
- OpenLAB ELN software
- PrepStar SD-2 System with Load & Lock columns

**Organic Impurity Profiling Solutions:**

- 1200 Infinity Series LC
- 6100 Series Single Quadrupole LC/MS systems

**Heavy Metal Impurity Analysis:** ICP-MS,

- 7700 Series ICP-MS
- 720/730 Series ICP-DES
### Development

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### Commercialization

**OpenLAB ECM software**

**J&W Ultra Inert GC columns**

**7890A GC system with 7697A Headspace Sampler and 5975C Series GC/MSD system**

**6500 Series Accurate-Mass Q-TOF LC/MS systems**

**6400 Series Triple Quadrupole LC/MS systems**

**Poroshell 120 LC columns**

**400-MR DD2 NMR system**

**Cary 600 Series FTIR**

**Residual Solvent Analysis: GC & GC/MS**

**J&W Ultra Inert GC columns**

**Poroshell 120 LC columns**

**OpenLAB ECM software**

### LC, LC/MS, CE, SFC, NMR, & FTIR

**6500 Series Accurate-Mass Q-TOF LC/MS systems**

**6400 Series Triple Quadrupole LC/MS systems**

**Poroshell 120 LC columns**

**400-MR DD2 NMR system**

**Cary 600 Series FTIR**

**OpenLAB ECM software**

**OpenLAB ECM software**
Agilent offers a wide range of advanced technologies and innovative solutions for purification, purity analysis, and impurity analysis throughout drug discovery and development. Trust Agilent to provide a suite of tools specifically designed to meet the unique challenges of your process.
The purification of synthesized compounds is one of the most recognized and challenging bottlenecks in drug discovery. Target compound purity has a profound impact on the ability to progress from hit to viable drug candidate with minimum rework.

There has been a steady increase in the number of new chemical entities undergoing purification before any biological assays are undertaken, due primarily to the fact that valuable resources are often wasted screening impure compounds. This has led to a rise in false positives.

From the high-throughput, lower-scale (milligram) purification requirements of the medicinal chemist to the process chemist’s larger-scale (grams to hundreds of grams) purification of a limited number of compounds, Agilent sets the standard in preparative liquid chromatography (LC). A broad portfolio of flexible solutions offers the performance required to meet all purification needs, from discovery to development.

**Purification Solutions**

- Purification of routine synthetic mixtures by flash chromatography
- Small-scale purification solutions for medicinal chemists
- Large-scale purification solutions for process chemists

- 971-FP Flash Purification System
- 1260 Infinity Preparative-Scale LC/MS Purification System
- PrepStar SD-2 System for High-Throughput Purification
Although the specific purity needs vary for drug discovery, development, and manufacturing, establishing the purity of compounds is an essential consideration across the process.

Medicinal chemists screen compound libraries in a high-throughput manner that requires rapid, generic methods. Analytical chemists in process chemistry and formulation focus on method development of reproducible and regulatory-compliant analysis methods appropriate for a limited number of target compounds. In the manufacturing phase, analytical chemists work in a fast-turnaround and highly regulated environment that requires appropriate and robust QA/QC analytical methods for a single fully characterized compound.

Agilent provides a range of liquid and gas chromatography solutions coupled with mass spectrometry (MS) systems to provide the right technology for purity analysis at each stage of the process.
A relatively new and pressing challenge for pharmaceutical scientists is the increased regulatory focus on impurities in active pharmaceutical ingredients and/or finished dosage forms. These regulations cover three main areas: organic impurities, heavy metal impurities, and residual solvents.

New regulations require disclosure of each identified degradation product, each unidentified degradation product, and total degradation products; impurities must be identified and profiled (qualified) even when present in very minor quantities.¹ There has been recent emphasis on heavy metal impurities as well, requiring much more specific instrumental methods.² The USP guidelines for residual solvents have also been updated with more comprehensive test requirements.³

Agilent is uniquely positioned to offer comprehensive solutions across all three of these impurity analysis areas, ranging from HPLC, LC/MS, CE, and SFC for organic impurities, to ICP-MS and ICP-OES for heavy metals, and GC/GC-MS for residual solvents.

¹ ICH Guidance for Industry: Q3B(R2) Impurities in New Drug Products
² USP <232> - Elemental impurities (limits) and USP <233> - Elemental impurities (procedures).
³ General Chapter <467> Residual Solvents/Organic Volatile Impurities

Visit www.agilent.com/lifesciences/realizepharma to see a detailed overview of the various technologies available to address the challenges faced by the pharmaceutical industry in purification, purity analysis and impurity analysis.
For more information

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