



Quality Management Systems and Advanced Analytical Technologies

Future of the IVD Industry



While conventional analytical methods remain valuable, advanced technologies such as RP-HPLC, SEC-HPLC, LC-MS/MS, ECLIA, RT-PCR, Nano DLS, Electron Microscopy, and Particle Size Analysis provide comprehensive characterization of critical quality attributes that are essential for today's complex diagnostic products.



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The *In Vitro* Diagnostics (IVD) industry is undergoing a rapid transformation driven by technological innovation, evolving regulatory expectations, and the growing demand for accurate, rapid, and reliable diagnostic solutions. The emergence of native proteins, recombinant proteins, monoclonal antibodies, recombinant antibodies, multiplex immunoassays and molecular diagnostics medicine has significantly increased the complexity of IVD products by enabling the detection of multiple and highly specific biomarkers with greater sensitivity and accuracy. Consequently, ensuring consistent product quality and analytical reliability has become more critical than ever. For trusted raw material developers like Yashraj Biotechnology Ltd., which manufactures a comprehensive suite of IVD raw materials - navigating this complexity requires moving far beyond basic compliance.

At the heart of this transformation is a robust Quality Management System (QMS), which provides a structured framework to ensure product quality throughout the entire product lifecycle - from design and development to manufacturing, validation, product release, post-market surveillance, and continual improvement. By integrating quality risk management, process validation, equipment qualification, analytical method validation, change control, CAPA, data integrity, and continuous monitoring, QMS ensures that every diagnostic product consistently meets the compliance for legal and regulatory requirements, and delivers reliable clinical performance.

Evolution of Advanced Analytical Technologies in IVD

Traditionally, analytical testing and release of IVD products relied primarily on conventional techniques such as Enzyme-Linked Immunosorbent Assay (ELISA), Turbidimetric / Turbidatex assays, SDS-PAGE, Western Blotting, protein estimation methods, conventional PCR and routine microbiological testing. Although these classical methods continue to play an important

role in quality control, they provide limited information regarding molecular integrity, structural stability, aggregation, purity, and other critical quality attributes of IVD raw materials.

With increasing regulatory expectations under ISO 13485, IVDR and other global regulatory frameworks, release testing has evolved from conventional quality control to comprehensive analytical characterization. Modern IVD raw material manufacturers increasingly utilize advanced analytical technologies such as Reverse Phase High-Performance Liquid Chromatography (RP-HPLC), Size Exclusion Chromatography (SEC-HPLC), Liquid Chromatography - Tandem Mass Spectrometry (LC-MS/MS), Electrochemiluminescence Immunoassay (ECLIA), Immunoturbidimetry, Real-Time PCR (RT-PCR), Nanoparticle Dynamic Light Scattering (Nano DLS), Electron Microscopy (EM), and Particle Size Analysis (PSA) throughout product development, process validation, stability studies, and final batch release.

These technologies provide superior analytical sensitivity, specificity, and comprehensive characterization of critical quality attributes enabling manufacturers to deliver safe, effective, and reproducible IVD products.

High Performance Liquid Chromatography (HPLC)

HPLC has become one of the most important analytical techniques for the characterization and quality evaluation of antigens and antibodies used as raw materials in the manufacture of immunodiagnostic kits.

RP-HPLC and SEC-HPLC are

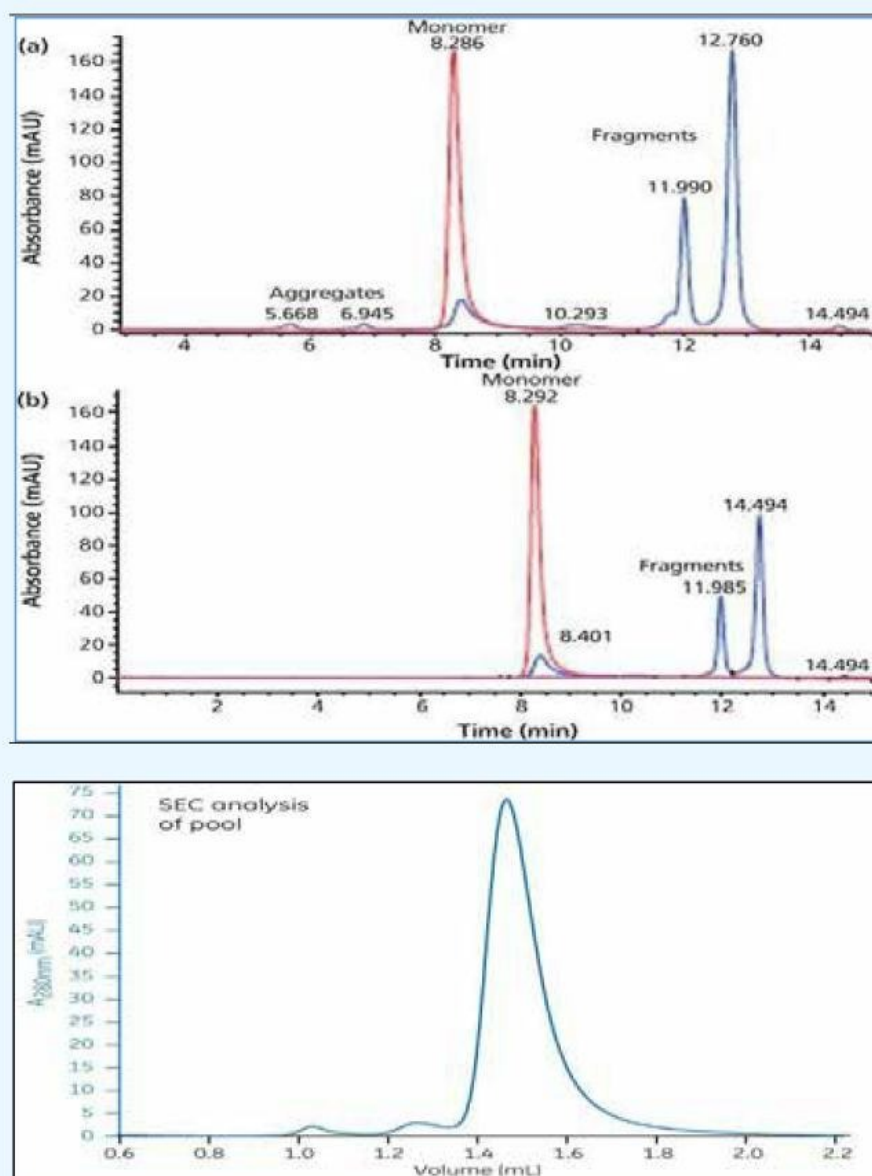


Fig. 1

extensively employed to evaluate the purity, identity, structural integrity, aggregation profile, and stability of antigens and antibodies used in diagnostic reagents.

SEC-HPLC can be used for the characterization and quality evaluation of IVD antigens and antibodies used as a raw material in IVD immunoassays. The technique separates proteins according to their hydrodynamic molecular size and can provide information on the relative proportion of the desired protein species, higher-molecular-weight aggregates and lower-molecular-weight

fragments. A typical antigen SEC-HPLC assessment involves preparation in a suitable buffer, filtration/centrifugation where required, equilibration of the validated SEC column and injection of the sample under predefined chromatographic conditions. The resulting chromatogram is evaluated for the main peak and any additional peaks representing higher- or lower-molecular-weight species (Figures 1 & 2).

Interpretation:

- **Early-eluting peak:** Higher-molecular-weight species/aggregates.

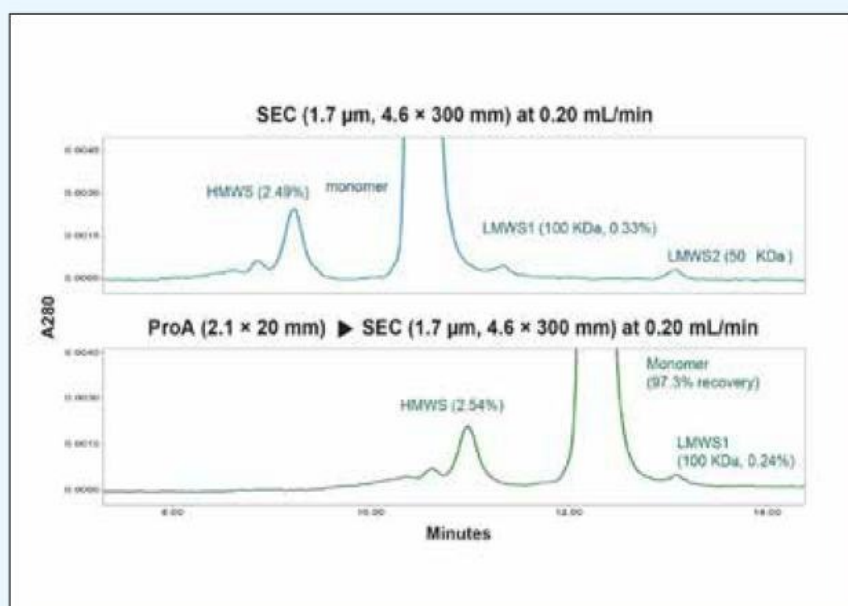


Fig. 2

- **Main peak:** Predominant CRP protein species.
- **Late-eluting peak:** Lower-molecular-weight fragments or degradation products.
- **Peak area %:** Can be used to calculate the relative distribution of the observed species, provided the method is validated for this purpose.

For example, during **release or stability** studies, the SEC-HPLC profile of a test lot can be compared with an approved/reference lot. An increase in aggregate or fragment peaks, or a corresponding reduction in the main peak, may indicate changes in protein stability or product quality and can trigger further investigation.

Within a robust QMS, reliable HPLC analysis depends on validated analytical methods, instrument qualification, calibration, preventive maintenance, system suitability testing, certified reference standards, analyst competency, and data integrity. These quality practices ensure precise release testing and regulatory compliance.

Liquid Chromatography Quadrupole Time-of-Flight Mass Spectrometry (LC / QTOF)

Liquid Chromatography - Mass Spectrometry (LC-MS), particularly high-resolution LC QTOF-MS, provides molecular-level characterization of protein antigens used as raw materials in IVD products. Unlike chromatographic techniques that primarily assess purity or molecular-size distribution, LC-MS can provide information on molecular mass, protein identity, peptide composition and structural modifications.

A typical LC - MS workflow for an IVD antigen involves sample preparation followed by liquid chromatographic separation and high-resolution mass spectrometric detection. For intact-mass analysis, the antigen is introduced into the mass spectrometer using electrospray ionization, generating multiple charged ions. These signals are subsequently deconvoluted to obtain the molecular mass of the antigen.

For more detailed characterization, the antigen may be subjected to enzymatic digestion, such as tryptic digestion, followed by LC-MS/MS analysis. The resulting peptide masses are compared with the expected protein sequence to support **identity confirmation** and **sequence coverage**. This approach can also support the investigation of modifications such as oxidation, deamidation and other product-related variants.

Illustrative LC-MS Characterization of an IVD Antigen

Figure 3 presents an illustrative LC-MS/QTOF characterization workflow consisting of three complementary datasets:

Other Advanced Analytical Technologies

ELISA continues to serve as a fundamental technology for detecting numerous protein biomarkers for infectious diseases, autoimmune disorders and cancer. Quality assurance in ELISA focuses on reagent qualification, pipetting accuracy, incubation control, calibration verification, and internal quality controls.

Electrochemiluminescence Immunoassay (ECLIA) provides exceptional analytical sensitivity, automation, and rapid turnaround for characterization of several biomarkers. A robust QMS around ECLIA methodology and instrumentation ensures reagent traceability, instrument calibration, assay validation, and continuous performance monitoring.

Immunoturbidimetry/Immunonephelometry quantitatively measures antigen-antibody complexes and is widely used for Inflammatory markers, renal markers, liver function marker and specialized cardiac

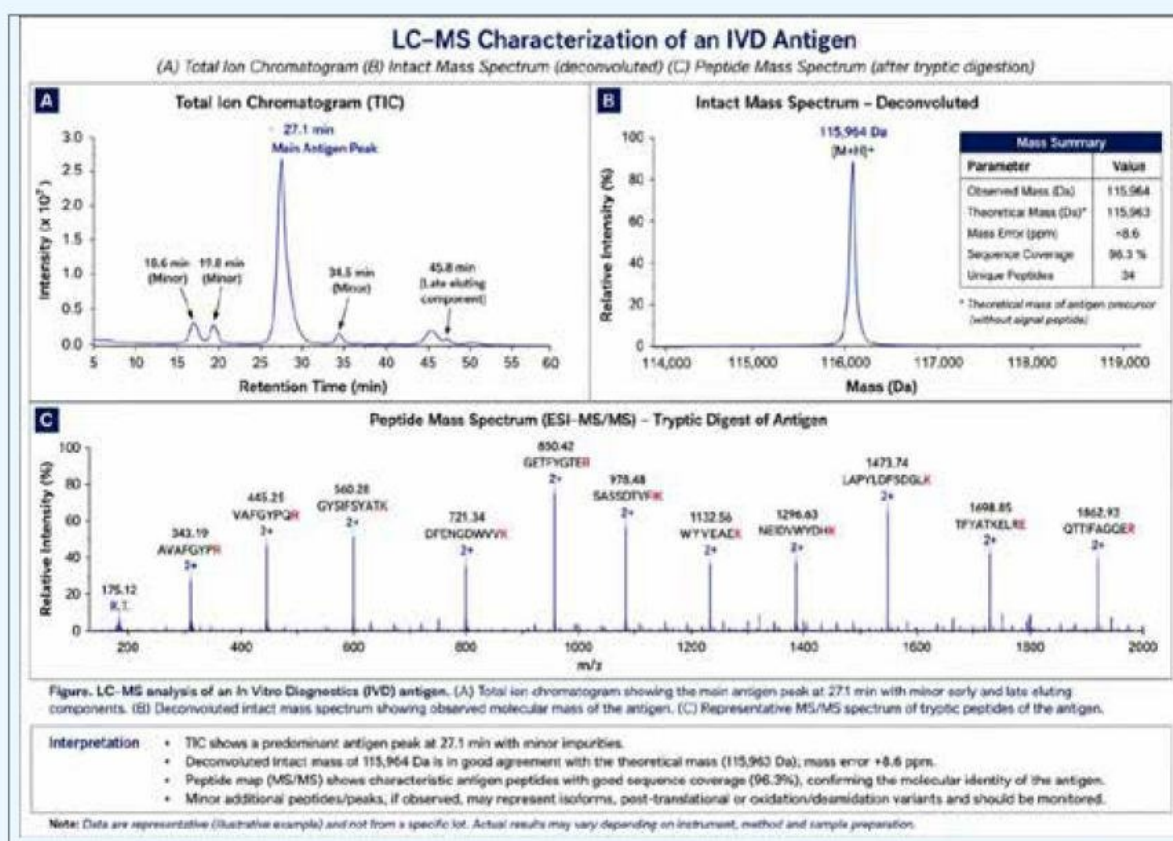


Fig. 3: LC-MS analysis of an IVD antigen. (A) Total ion chromatogram showing the predominant antigen peak at 27.1 min with minor early- and late-eluting components. (B) Deconvoluted intact-mass spectrum showing an observed molecular mass of 115.964 KDa. (C) Representative LC-MS/MS peptide spectrum following tryptic digestion, demonstrating characteristic antigen peptides.

markers. Reliable performance in immunoturbidimetry depends on calibration, reagent stability, interference evaluation, and routine analytical quality control.

Real-Time Polymerase Chain Reaction (RT-PCR) has transformed molecular diagnostics by enabling rapid and highly sensitive detection of nucleic acid markers for infectious pathogens and genetic targets. Under a robust QMS, validated assays, qualified instruments, contamination control, positive and negative controls, and comprehensive documentation ensure analytical accuracy and reproducibility.

Nanoparticle Dynamic Light Scattering (Nano DLS) characterizes nanoparticles, biologics, latex particles, and lipid nanoparticles by measuring particle size,

hydrodynamic diameter and polydispersity index, ensuring consistent product performance.

Electron Microscopy (TEM and SEM) provides ultra-high-resolution imaging for characterization of viruses, extracellular vesicles, nanoparticles, and biological structures, supporting product development, failure investigations, and advanced morphological analysis.

Particle Size Analysers determine particle size distribution of nanoparticle-based diagnostic materials, ensuring consistent assay sensitivity, stability, and reproducibility.

Quality Management - The Future of IVD

The future of the IVD industry

lies in the seamless integration of advanced analytical technologies with digital quality management systems. Automation, Laboratory Information Management Systems (LIMS), Artificial Intelligence (AI), Machine Learning (ML), predictive maintenance, advanced analytical software, electronic laboratory notebooks (ELN) and electronic Quality Management Systems (eQMS) are transforming how manufacturers monitor product quality throughout the product lifecycle.

Digital quality ecosystems enable real-time data acquisition, automated trend analysis, predictive quality assessment, risk-based decision-making, remote instrument monitoring, and enhanced regulatory compliance while strengthening data integrity and operational efficiency.

Quality Management Systems and Advanced Analytical Technologies: Shaping the Future of the IVD Industry

Introduction
The IVD industry is evolving rapidly with the emergence of native proteins, recombinant proteins, monoclonal and recombinant antibodies, multiplex immunoassays and molecular diagnostics. Ensuring consistent product quality and analytical reliability is more critical than ever.

A robust Quality Management System (QMS) ensures quality throughout the product lifecycle—from design to post-market—delivering safe, effective and reliable diagnostic solutions.

YASHRAJ
BIOTECHNOLOGY LTD.
Solution. Quality. Trust.

Native Proteins

Recombinant Proteins

Monoclonal Antibodies

Recombinant Antibodies

Multiplex Immunoassays

Molecular Diagnostics

QMS Across the Product Lifecycle

Design & Development
Manufacturing & Process Control
Validation & Verification
Product Release & Distribution
Post Market Surveillance
Critical Improvement

Quality Risk Management | Change Control | CAPA | Data Integrity Training | Documentation

Advanced Analytical Technologies in IVD

HPLC (SP-HPLC & SEC-HPLC)

- Purity & identify
- Aggregates & fragments
- Stability monitoring

LC-QTOF-MS / LC-MS/MS

- Molecular mass & identity
- Peptide mapping & sequence coverage
- Post-translational modifications

ECLIA

- High sensitivity
- Wide dynamic range
- Automation & right results

Immunoassay / Immunophenotyping

- Quantitative measurement
- Reliable & reproducible
- Small clinical applications

ELISA

- Specific detection
- High quality control
- Automation & right results

Real-Time PCR (RT-PCR)

- Highly sensitive
- Accurate results
- Automation & right results

Nano DLS

- Ultra-high resolution
- Low noise
- Automation & right results

Electron Microscopy (TEM / SEM)

- Ultra-high resolution
- Low noise
- Automation & right results

Benefits of Advanced Analytical Technologies Under a Robust QMS

- Enhanced analytical sensitivity & specificity
- Comprehensive characterization
- Reliable release & stability evaluation
- Regulatory compliance (ISO 13485, NDR, etc.)
- Consistent quality & clinical performance
- Stronger patient safety & trust

Quality Management: The Future of IVD

The future of the IVD industry lies in the seamless integration of advanced analytical technologies with digital quality management systems.

Automation
Reduced manual errors, improved accuracy & efficiency

LIMS & ERM
Real-time data capture & traceability

AI / ML
Predictive analytics & intelligent decision making

Real-time Monitoring
Continuous process & instrument monitoring

Predictive Maintenance
Minimize downtime & ensure reliability

QMS
End-to-end quality workflow & compliance management

Data Integrity
ALCOA+ principles ensuring trust in every data point

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Conclusion

Advanced analytical technologies have fundamentally transformed the quality evaluation and release testing of modern IVD products. While conventional analytical methods remain valuable, advanced technologies such as RP-HPLC, SEC-HPLC, LC-MS/MS, ECLIA, RT-PCR, Nano DLS, Electron Microscopy, and Particle Size Analysis provide comprehensive characterization of critical quality attributes that are essential for today's complex diagnostic products.

However, these technologies can only deliver their full value when implemented within a robust Quality Management System. By integrating advanced analytical platforms with risk-based quality management, digital technologies, and continuous improvement principles, the IVD industry can ensure analytical

excellence, regulatory compliance, product consistency, and patient safety. Pioneering organizations like Yashraj Biotechnology Ltd. continue to set benchmarks by harmonizing state-of-the-art analytical platforms with robust QMS principles to empower diagnostic kit developers worldwide with reliable, high-performance raw materials. Together, QMS and advanced analytical technologies are shaping the future of the IVD industry by enabling innovative, reliable, and high-quality diagnostic solutions that support precision medicine and improve global healthcare. Looking ahead, continued integration of artificial intelligence, automation, and data-driven analytical platforms is expected to further enhance IVD product development and quality evaluation. Standardized analytical workflows, stronger data integrity, and greater interoperability between

laboratory systems will support faster decision-making while maintaining regulatory compliance. By combining technological innovation with robust quality management practices, the IVD industry can achieve greater efficiency, reproducibility, and reliability, ultimately accelerating the delivery of safe and high-quality diagnostic solutions to meet evolving global healthcare needs..

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