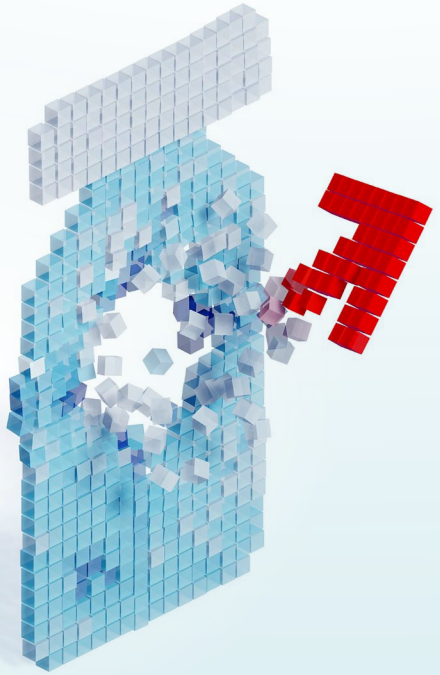
ThermoFisher SCIENTIFIC

Straight through to breakthrough

Thermo Scientific MAM 2.0 Workflow

Powered by the Thermo Scientific Ardia Platform



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Where development and quality control come together

Multi-attribute method (MAM) has been embraced by the biopharmaceutical industry and regulatory leaders in recent years. The ability to analyze multiple product attributes in a single analytical run offers valuable scientific insights, speeds up process development and manufacturing, and deepens the understanding of product quality.

There are a number of compelling reasons for adopting a MAM strategy across all stages of the product cycle, including:

- **Improved efficiency:** The MAM workflow enables the simultaneous analysis of multiple attributes in a single analytical run, significantly reducing the time required for testing.
- **Increased sensitivity:** Use of LC-MS makes it possible to detect extremely low levels of impurities, as well as modifications and variants that may be missed by other analytical methods.
- **Improved specificity:** MAM enables the identification and quantification of multiple product attributes with high accuracy and reliability.
- **Better understanding of product quality:** The MAM approach provides a more comprehensive understanding of biopharmaceutical quality, enabling researchers to identify and deal with potential issues.
- **Regulatory acceptance:** Multi-attribute method has gained regulatory acceptance by organizations such as the US FDA, making it a trusted and approved analytical technique for biopharmaceutical analysis.

A more detailed look at MAM

Comprehensive workflow for assessing Critical Quality Attributes

Closely-aligned with the principles of Quality by Design (QbD), MAM is a mass spectrometry-based peptide mapping method that can quantify multiple potential critical quality attributes (CQAs) in a single analytical run.

Even the smallest modifications in a protein sequence can measurably impact the safety and biological activity of a drug. By directly measuring potential CQAs, important information can be derived for the optimization of production processes—ultimately enhancing product quality, safety, and efficacy.

Traditionally, CQAs are assessed using multiple chromatographic and electrophoretic techniques. In addition to being resource-intensive, these methods are profile-based and often incapable of identifying and quantifying potential residue-specific CQAs.

High resolution MS looks deeper—and saves time, too

By giving you detail on a molecular level that is often not discernable with conventional techniques, high resolution mass spectrometry offers a viable and appealing alternative. As shown in the table on page 5, an appropriately-developed MAM expands the dataset, while considerably reducing the number of individual tests (CEX, CE-SDS, HILIC, ELISA) for specific potential CQAs.

A more detailed look at MAM

Required CQA Characterizations	MAM	Analytical Techniques						
		SEC	CEX	rCE-SDS	nrCE-SDS	HILIC	ID ELSIA	HCP ELSIA
Aggregation	○	●	Indirect	●	●	○	○	○
CDR Tryptophan Degradation	●	Indirect	○	○	○	○	○	○
C-terminal Amidation	●	○	Indirect	○	○	○	○	○
C-terminal Lysine	●	○	●	○	○	○	○	○
Cysteine Adducts	◐	○	◐	○	○	○	○	○
Deamidation	●	○	Indirect	○	○	○	○	○
Disulfide Isoforms	◐	○	Indirect	○	○	○	○	○
Disulfide Reduction	◐	○	○	○	●	○	○	○
Fregmentation (Peptied Bond)	◐	◐	○	●	●	○	○	○
Fucosylation	●	○	○	○	○	○	○	○
Galactosylation	●	○	○	○	○	○	○	○
Glycation	●	○	○	●	●	○	○	○
HCP	●	○	○	○	○	○	○	●
High Mannose	●	○	○	○	○	●	○	○
Hydroxylysine	●	○	○	○	○	○	○	○
Identity	●	○	●	○	○	○	●	○
Methionine Oxidation	●	○	○	○	○	○	○	○
Mutations & Misincorporations	●	○	○	○	○	○	○	○
Non-concensus Glycosylation	●	○	○	◐	◐	○	○	○
Non-glycosylated Heavy Chain	●	○	○	○	○	○	○	○
N-terminal pyroGlutamate	●	○	Indirect	○	○	○	○	○
O-lined Glycans	◐	○	○	○	○	○	○	○
Residual Protein A	●	○	○	○	○	○	○	○
Signal Peptide	●	○	○	○	○	○	○	○
Thioether	●	○	○	○	○	○	○	○
Trisulfide	◐	○	○	○	○	○	○	○
Unusal Glycosylation	●	○	Indirect	◐	◐	●	○	○

Quality attribute characterization analyses covered by the MAM.

● Yes ◐ Maybe ○ No

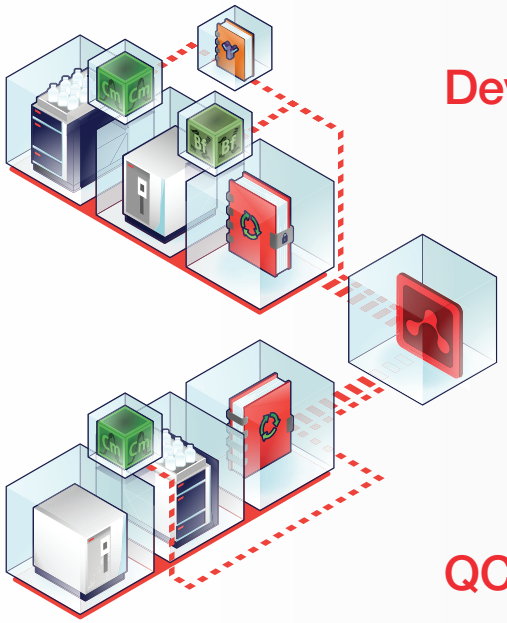
Take a confident step forward with Thermo Scientific MAM 2.0 workflow

Thermo Fisher Scientific™ MAM 2.0 workflow has been developed in close partnership with the biopharmaceutical industry to address some of the limitations of the original multi-attribute method and ensure confident, effective and efficient implementation of MAM workflows.

A complete, end-to-end solution, MAM 2.0 integrates the power of Thermo Scientific™ Orbitrap™ mass analysis, a compliance-ready enterprise data system, and dedicated global support.

MAM 2.0 enables:

- Faster, smarter decision making based on high-confidence information of multiple product quality attributes (PQAs) from development through QC
- Seamless knowledge sharing and method transfer across instruments, functions, departments, and sites throughout the whole organization
- Maximum uptime and high productivity through application focused training and services conducted by Thermo Fisher Scientific MAM experts



Development

QC

- **Connectivity**
- **Purpose built**
- **Ease of use**
- **Compliance-ready**
- **Training and support**

Critical success factors for successful MAM

Reproducibility

Exceptional reproducibility is essential to ensure that the results obtained from different experiments or labs are consistent and reliable. This confidence allows researchers to validate findings, compare results across studies or labs, and build with assurance upon existing knowledge.

Transitioning to the QC environment

Implementation into the QC environment involves demonstrating the method's accuracy, precision, linearity, specificity and other parameters to regulatory agencies. Specialized training is required, as well as dedicated support.

Multi-site information sharing and elimination of variance

In a global organization, the same drug may be analyzed in different stages at various sites, requiring secure, compliant connectivity and data transfer within the enterprise network. The information shared must be in a consistent format, and methods must be thoroughly tested for robustness and reproducibility to eliminate any potential for variance.

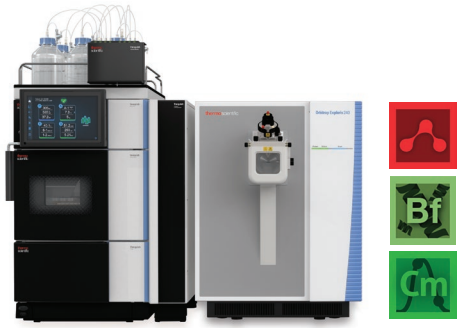
"I approach drug development with a quality lens. Understanding the critical process parameters used to manufacture drugs and monitoring the critical quality attributes of a product boils down to streamlined solutions that give you as much reproducible and high-sensitivity data as possible. The Thermo Scientific MAM workflow does that."

- **Dr. Jared R. Auclair,** *Vice Provost Research, Economic Development and Director of Bioinnovation, Northeastern University Biopharmaceutical Analysis and Training Laboratory (BATL)*

MAM 2.0: A scalable LC-MS platform to future proof your biotherapeutic development and QC

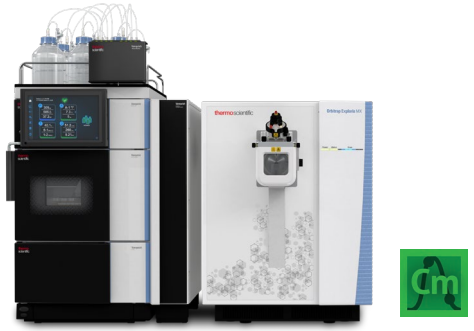
Research & Development

Attribute Characterization
Product Quality Attribute Monitoring



Manufacturing & QC

Critical Quality Attribute Monitoring
New Peak Detection



Bring attribute characterization and monitoring to the next level of confidence

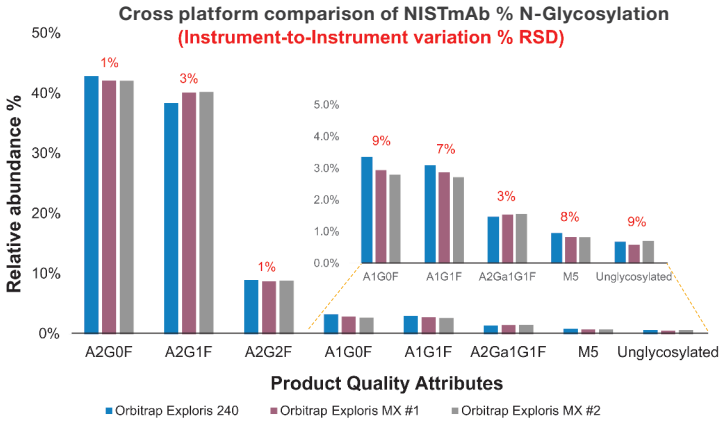
- Achieve **confident, comprehensive characterization of PQAs using industry-proven Orbitrap technology and intelligent data processing algorithm.**
- **Accelerate method optimization** through seamless local and global collaboration within a fully-integrated enterprise data platform that provides secure central data storage, fast data review with dynamic versioning, comprehensive and customizable reporting and easy method transfer.
- Ensure **accurate detection and quantification of targeted attributes** using composite scoring and intelligent peak integration, routinely achieving <10% RSD on low abundant post translation modifications (PTMs).
- Obtain **sensitive and confident detection of new peaks**, avoiding false positives and false negatives.

Improve confidence and productivity on a MAM platform designed for QC

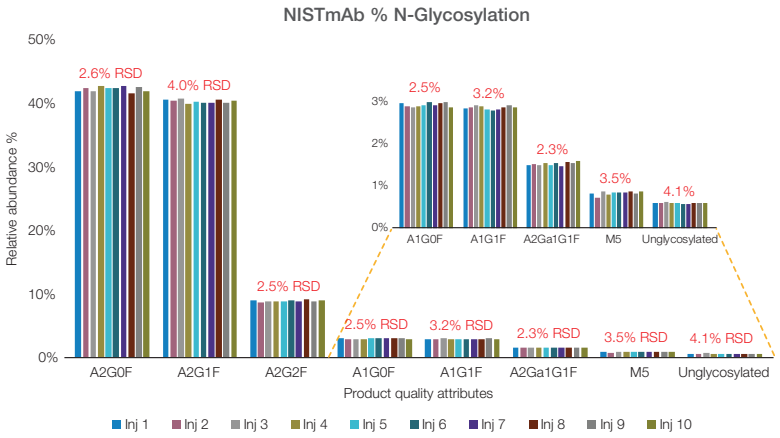
- Ensure **accurate and consistent CQA monitoring and new peak detection** using the same industry-proven Orbitrap technology, now purposely designed for QC with ease of operation, robust and consistent unit-to-unit performance, and extended life-cycle.
- Meet modern regulatory requirements with a single compliance-ready Thermo Scientific™ Chromeleon™ chromatography data system (CDS), providing **ease of administration and complete audit trail** for all analytical processes from data acquisition to data storage, and processing through report generation.
- **Reducing the need for method re-development** in QC through direct transfer from development, saving time and money.
- Simplify operations with **automatic workflow execution** for users of all levels.

Consistent methods and results from development to QC

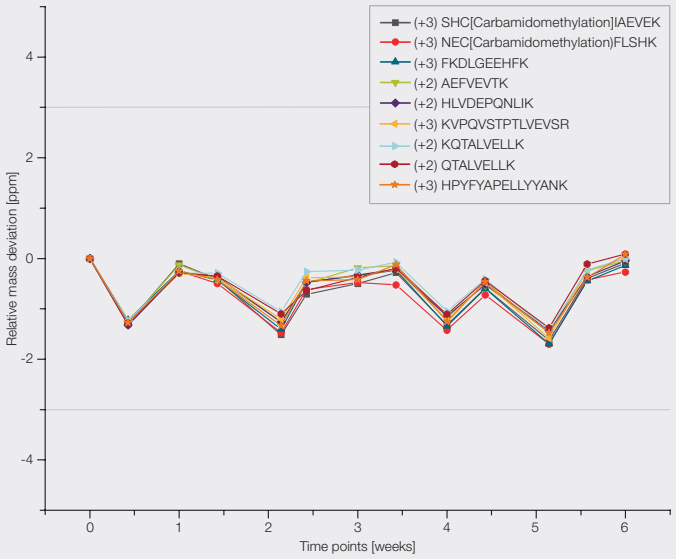
The new Thermo Scientific™ Orbitrap Exploris™ MX mass detector has been purposely designed—and optimized—for MAM workflows. Built on the same platform as Thermo Scientific™ Orbitrap Exploris™ 240 mass spectrometer, it simplifies your routine operations without compromising data quality. Enables direct transfer from development to QC.



Cross-platform consistency demonstrated in the relative abundance measurement of NISTmAb N-glycosylation between Orbitrap Exploris 240 mass spectrometer and Obritrap Exploris MX mass detector. Data were averaged from 10 replicate injections per instrument. RSDs are <9%.



Outstanding reproducibility of NISTmAb CQAs monitoring on Orbitrap Exploris MX mass detector across 10 technical replicates. RSDs are <5%.



Stable mass accuracy on Orbitrap Exploris MX mass detectors: <3 ppm mass deviation **over 6 weeks** with one-point calibration.

Expert MAM support at every level

- A MAM focused team of application scientists, service engineers, and software experts are available to support you at every step of your MAM journey.
- A standardized system performance evaluation test (SET) is used by service engineers to thoroughly assess the performance of the liquid chromatography-mass spectrometry (LC-MS) system at installation and subsequent maintenance appointments, ensuring consistent high-quality results.
- Combination of on-site and remote trainings are conducted by MAM application experts, customizable to meet your needs.
- A support process quickly connects you with the right MAM expert.

01 PLAN

Prepare your lab for a greater connection

Comprehensive hardware and software solution

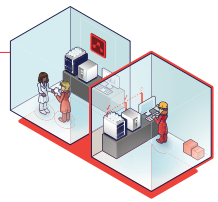
Step-by-step plan for implementation

02 SETUP

Here to help you get up and running

Expert installation

Rigorous performance evaluation testing



03 TRAIN

Start with a master class on MAM 2.0

On-site and remote training

Fully customizable curriculum

04 SUPPORT

Peer-supported science from beginning to end

Global support team of MAM experts available when you need them

05 ADVANCE

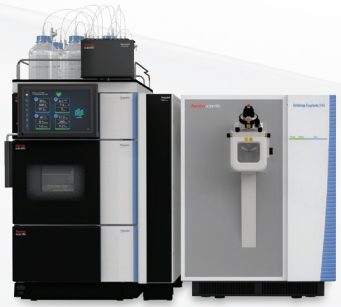
Where development and quality control come together

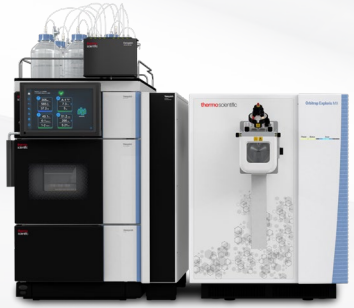
Collaborate with us to continue to develop MAM

A purpose-built MAM solution with industry-proven technology

MAM 2.0 overcomes historic barriers to implementation. The workflow includes hardware and software tailor-made for development and QC to provide consistent and reproducible high-quality results to bring your next biotherapeutic candidate straight through to breakthrough.

Thermo Scientific™ Orbitrap Exploris™ 240 Mass Spectrometer with Thermo Scientific™ Vanquish™ Flex or Horizon UHPLC system offers exceptional spectral clarity, delivers the high confidence required to reliably identify and quantitate quality attributes and new peaks in a development environment.





Orbitrap Exploris MX mass detector (Full MS only) with Vanquish Flex or Horizon UHPLC System is purposely designed for QC, provides ease of operation, extended life cycle, robust and consistent unit-to-unit performance. Built on the same platform as Orbitrap Exploris 240 mass spectrometer, Orbitrap Exploris MX mass detector ensures accurate, consistent CQA monitoring and new peak detection with direct method transfer.

The Thermo Scientific™ Ardia™ platform is designed for scientists running chromatography and mass spectrometry analyses and enables them to combine, aggregate, compare, interrogate and share information via a common digital language. It allows for the highest uptime, security, and global compliance standards in the sharing of previously siloed data.

Thermo Scientific™ Chromeleon™ CDS software is built for LC-MS in QC, offers full suite of compliance tools to support for GMP, data integrity and 21 CFR Part 11 regulations, and provides automatic execution of entire MAM workflow for simplified and consistent operation.

Thermo Scientific™ BioPharma Finder™ software delivers confident and comprehensive attribute characterization and seamless collaboration through centralized data storage, compares and tracks changes using dynamic versioning, and turns peptide mapping data into meaningful results with enhanced dynamic reporting features.

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The way to move biopharma forward

Increasing the speed of biotherapeutics development will unlock a future that delivers needed therapies to patients faster. A future where we can create complex drug therapies that cure complex diseases in less time and subsequently at lower cost. With an approachable process for implementation, enterprise-level connectivity, and the industry's only mass spectrometer engineered for MAM, Thermo Scientific MAM 2.0 is the MAM solution you need to get to this future state. Reach out to our MAM experts today.

Learn more at **thermofisher.com/MAM**