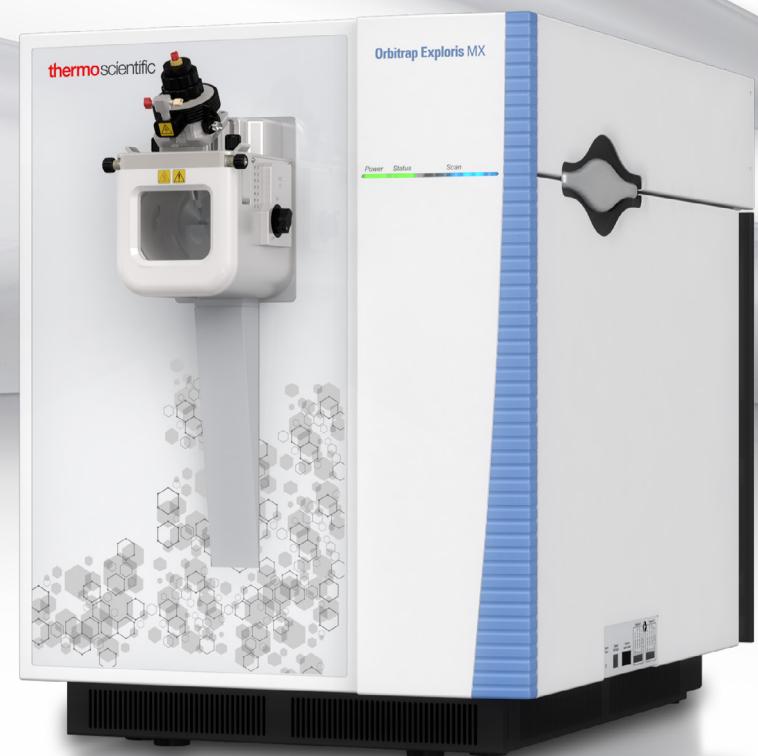


Mass spectrometry

Perfect fit

Orbitrap Exploris MX mass detector



thermo scientific

Fit for purpose mass detection



The Orbitrap Exploris MX mass detector coupled to the Thermo Scientific™ Vanquish™ Flex or Thermo Scientific™ Vanquish™ Horizon UHPLC system delivers fit-for-purpose mass monitoring.

High-quality mass information offers significant advantages in accelerating biopharmaceutical late-stage development, commercialization, manufacturing, and quality control (QC). This information must be easily and reliably obtained, day after day, from site to site, and in a compliant manner.

Welcome to the Thermo Scientific™ Orbitrap Exploris™ MX mass detector, the perfect fit for biopharmaceutical laboratories looking to deploy routine mass monitoring. Beyond the renowned high-resolution accurate mass detection provided by Thermo Scientific™ Orbitrap™ mass analyzers, this fit-for-purpose system is simple to operate and compliance ready with Thermo Scientific™ Chromeleon™ chromatography data system (CDS) software. High-resolution accurate-mass (HRAM) data provide utmost confidence for sequence confirmation, peptide monitoring, intact protein analysis (from small to large molecules, including mAb subunits, reduced mAbs, and intact mAbs under native and denaturing conditions), glycan profiling, as well as oligonucleotides and their impurity mass confirmation. Consistent performance between the Thermo Scientific™ Orbitrap Exploris™ 240 mass spectrometer and Orbitrap Exploris MX detector ensures seamless method transfer from development through to QC.

Ease of Use | Operational Simplicity | Reliability

• Simplicity for scientists and technicians

The Chromeleon CDS software offers built in methods, control, data processing and management that simplify tasks and reduce errors for more ‘right first time’ analyses. A suite of smart tools make work faster and easier, while ensuring reproducible, high-quality mass monitoring.

• Productivity to accelerate commercialization

High uptime boosts productivity. Rapid “set and forget” calibration procedures provide consistent mass stability for at least four weeks at prescribed conditions. Instrument status monitoring and optimized pressure control alert users when maintenance is needed, avoiding unnecessary downtime and repeat analyses.

• Compliance for competitive advantage

Designed for data integrity, data security, and compliance, fully scalable Chromeleon CDS software gives you a competitive edge in meeting global regulatory requirements.

• Consistent results deliver confidence

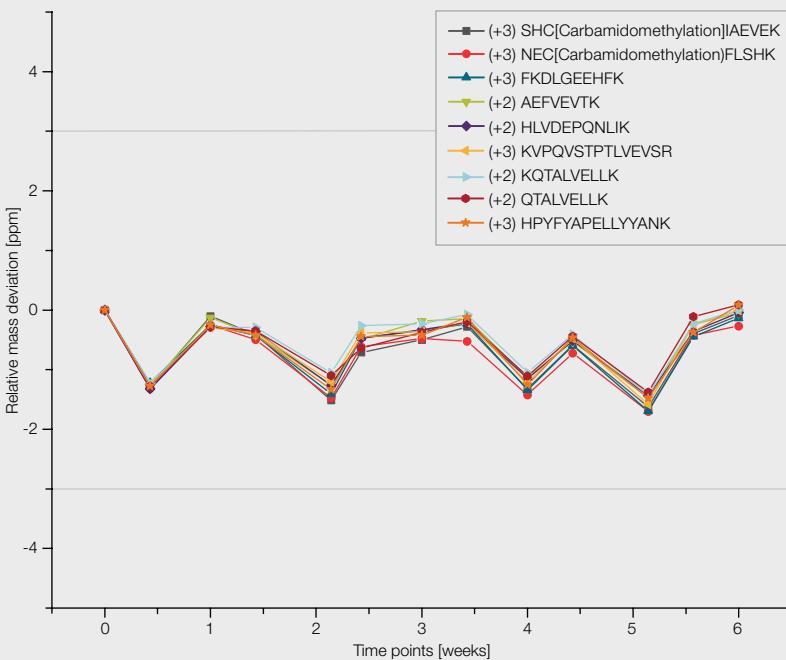
Robust and reliable performance from system to system and from site to site ensure high-confidence results used to make critical decisions. Industry-proven Orbitrap technology, now purposely designed for mass monitoring in future-proof lab operations.

• Seamless method transfer streamlines multi-attribute method (MAM)

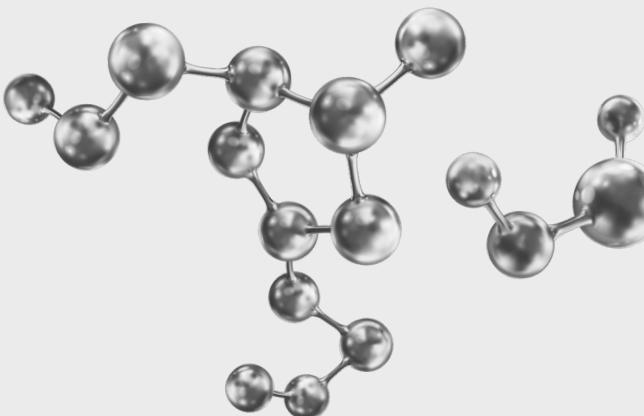
Easy transfer of sophisticated MAM assays from development to manufacturing bridges the gap between development and QC.

• Dedicated global support maximizes your productivity

The dedicated Thermo Scientific™ MAM team maximizes your productivity and confidence with installation, training, and fast service and support. Standardized system performance evaluation test (SET) and installation qualification/operational qualification (IQ/OQ) thoroughly assess system performance with comprehensive installation and post-maintenance acceptance criteria.



Orbitrap Exploris MX mass stability: mass deviation relative to first observed mass in parts-per-million for 9 BSA tryptic peptides monitored over a period of **6 weeks** using the new internal recalibration option. Each data point is an average of 19 individual injections.



Accelerate MAM deployment

Seamless knowledge and method transfer



The Orbitrap Exploris MX mass detector is part of the end-to-end Thermo Scientific™ MAM 2.0 workflow approach for comprehensive characterization and monitoring of biotherapeutics from development to commercialization. Orbitrap Exploris 240 mass spectrometer methods established during development seamlessly transfer to an Orbitrap Exploris MX detector used in manufacturing or by contract partners. In addition to full integration into the high-resolution MAM 2.0 workflow, the usability and low cost of the Orbitrap Exploris MX detector make it the perfect fit for QC and contract labs.

Thermo Scientific™ BioPharma Finder™ software identifies and evaluates relevant product quality attributes (PQAs) via high-throughput analytics. MAM 2.0 powered by Thermo Scientific™ HyperBridge™ software allows data to be accessed by connected labs from development through QC. The MAM target peptide workbook built from the list of identified peptides can be used to monitor PQAs throughout the entire drug development process upon incorporation into a Chromeleon processing method. The processing method along with the instrument method, injection sequence, view setting and report template can all be stored into a MAM eWorkflow for easy and direct transfer to QC via Chromeleon CDS Enterprise software.

MAM 2.0 offers:

- Fast decision making based on high-confidence PQAs obtained using industry-leading HRAM Orbitrap technology
- Seamless knowledge and method transfer across instruments, departments, and sites using BioPharma Finder software, compliance-ready Chromeleon CDS enterprise software, and HyperBridge server or cloud

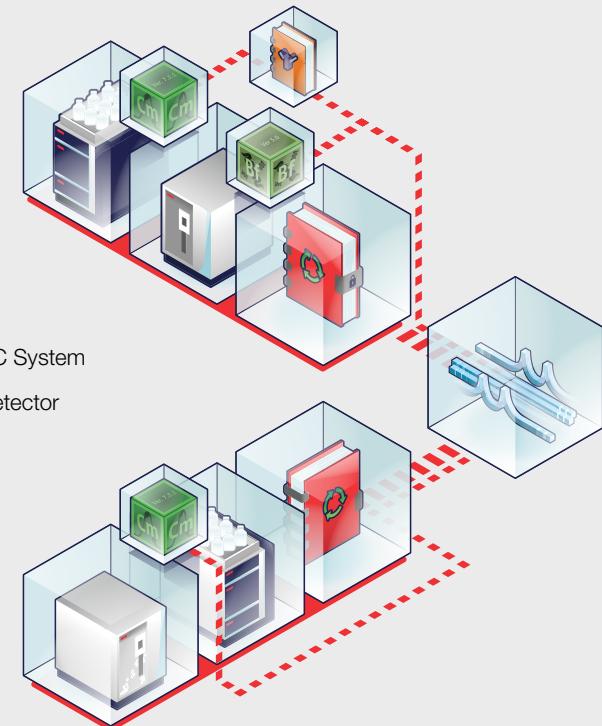
DEVELOPMENT

- Vanquish Flex/Horizon UHPLC System
- Orbitrap Exploris 240 Mass Spectrometer
- Chromeleon CDS
- MAM Workbook
- BioPharma Finder Software
- MAM eWorkflow

HyperBridge Software

QC

- MAM eWorkflow
- Vanquish Flex/Horizon UHPLC System
- Orbitrap Exploris MX Mass Detector
- Chromeleon CDS



Maximize productivity, accelerate approval and release

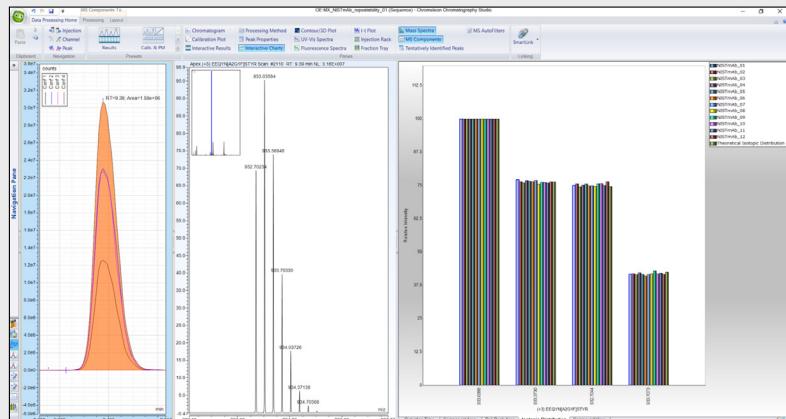
Compliance-ready MAM monitoring of peptide quality attributes

Post-translational modifications (PTMs) and process-induced modifications can occur during upstream and downstream bioprocessing, formulation, and storage. Any PTMs impacting safety or efficacy are critical quality attributes (CQAs) that must be monitored and controlled. Liquid chromatography mass spectrometry (LC-MS) MAM offers simultaneous, direct, site-specific identification and quantitation of a broad set of peptide CQAs. With the ability to replace multiple assays used during drug development and manufacturing, MAM can accelerate approvals, increase product and process knowledge, reduce development time, and reduce lot release assay cost and time.

The Orbitrap Exploris MX detector adds unprecedented simplicity, robustness, and HRAM-enabled confidence to MAM workflows. In addition to operational productivity, integrated Chromeleon CDS software provides superior MS data-processing tools and comprehensive controls for regulated labs.

Why MAM?

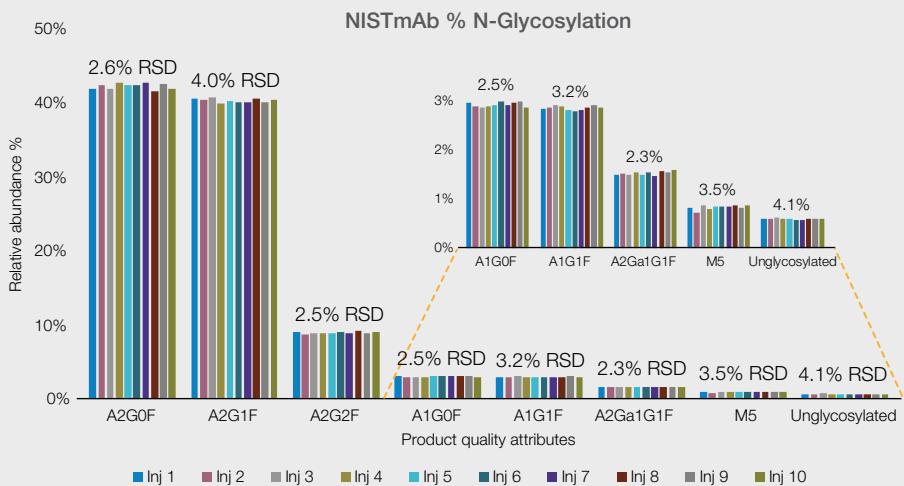
Embraced by industry and regulatory leaders, MAM is key to the future of high-quality biotherapeutics. MAM adoption across all stages of development and manufacturing enables efficient and comprehensive understanding of processes and products by replacing many assays with one. Thermo Fisher Scientific has developed a fit-for-purpose MAM solution—now drug developers have the partner they need to aid them in deploying MAM.



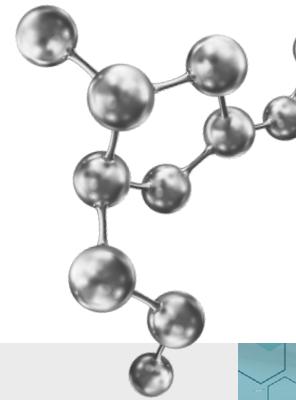
Customizable result view in Chromeleon CDS software. The panes represent the glycopeptide EEQYN(A2G1F)STYR displaying the overlaid integration of the XICs of the four most abundant isotopes (left), the single scan Full MS mass spectrum (middle), and the isotope distribution across 12 sequential injections showing excellent alignment with the theoretical isotope intensities.

Wide applicability

The enhanced Orbitrap Exploris MX-based MAM workflow is applicable for monitoring PTMs such as glycosylation, deamidation, and oxidation, peptides for sequence confirmation, and glycan profiling.



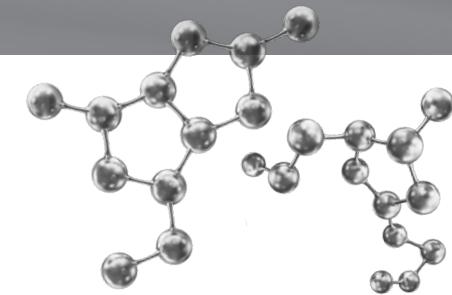
Example view for the N-glycan profile report of NISTmab reference standard. The report displays the percent modification level representing relative abundances of seven glycoforms of the glycopeptide EEQYN*STYR as well as the unmodified peptide monitored across ten sequential injections.



Realize HRAM confidence in intact mAb mass confirmation

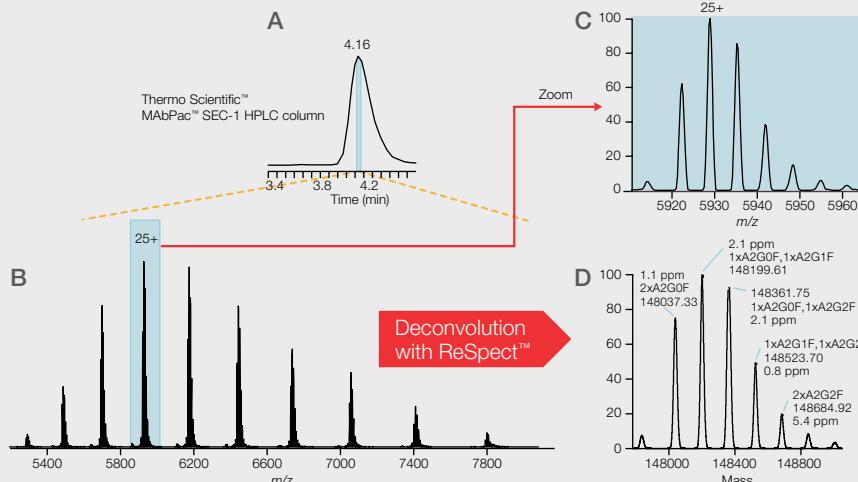
High-sensitivity mass determination up to m/z 8000

Confirming the molecular weight of large intact proteins under native and denaturing conditions is essential to biotherapeutic production and QC. With optional mass range up to m/z 8000 and HRAM data quality, the Orbitrap Exploris MX detector is the ideal choice for rapid, high-confidence molecular weight profiling, even for complex mAb glycoforms at low concentrations.



Why analyze native proteins

Analysis under non-denaturing conditions allows characterization of proteins in their near-native biological states. Previously, obtaining this information required multi-step labor intensive isolation and purification. Using native MS, quality attributes can be directly assessed with minimal need for sample preparation, rapidly providing mass information for all proteins in a sample.

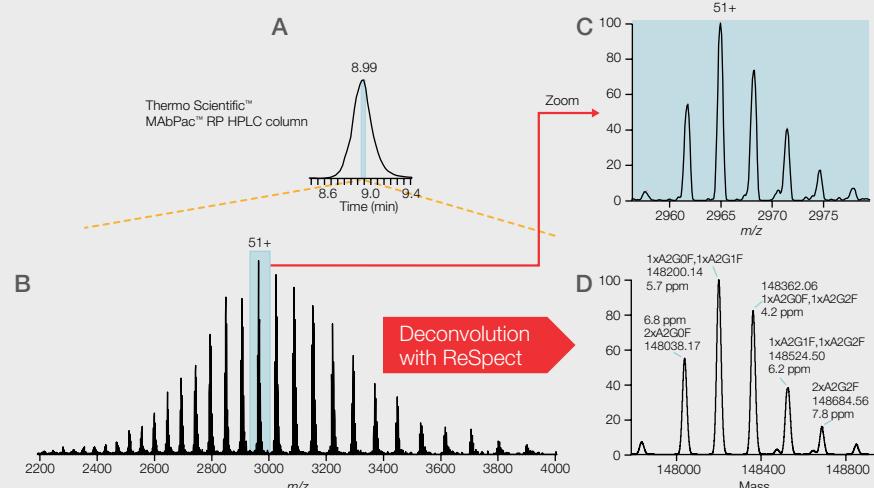


LC-MS analysis of intact NISTmAb reference standard under native conditions:

(A) Sample analysis was performed by size exclusion chromatography (B) following mass detection with the mass range set to m/z 2500–8000. The Full MS spectrum represents an average of 3 scans. (C) The zoom into the most abundant charge state showcases the baseline resolved glycoform pattern (D) resulting in the deconvoluted spectrum with a closely matching pattern providing mass accuracies below 6 ppm.

Chromeleon CDS software streamlines molecular weight determination

Complementary deconvolution algorithms optimized for isotopically resolved and unresolved data provide accurate molecular weights for intact proteins, in both denaturing and native conditions, and at low abundances. The automated parameter optimizer makes it easy to obtain trusted results.



LC-MS analysis of NISTmAb reference standard under denaturing conditions:

(A) Sample analysis was performed by reversed phase chromatography (B) following mass detection with the mass range set to m/z 2000–5000. The Full MS spectrum represents an average of 3 scans. (C) The zoom into the most abundant charge state showcases the baseline resolved glycoform pattern (D) resulting in the deconvoluted spectrum with closely matching pattern providing mass accuracies below 10 ppm.

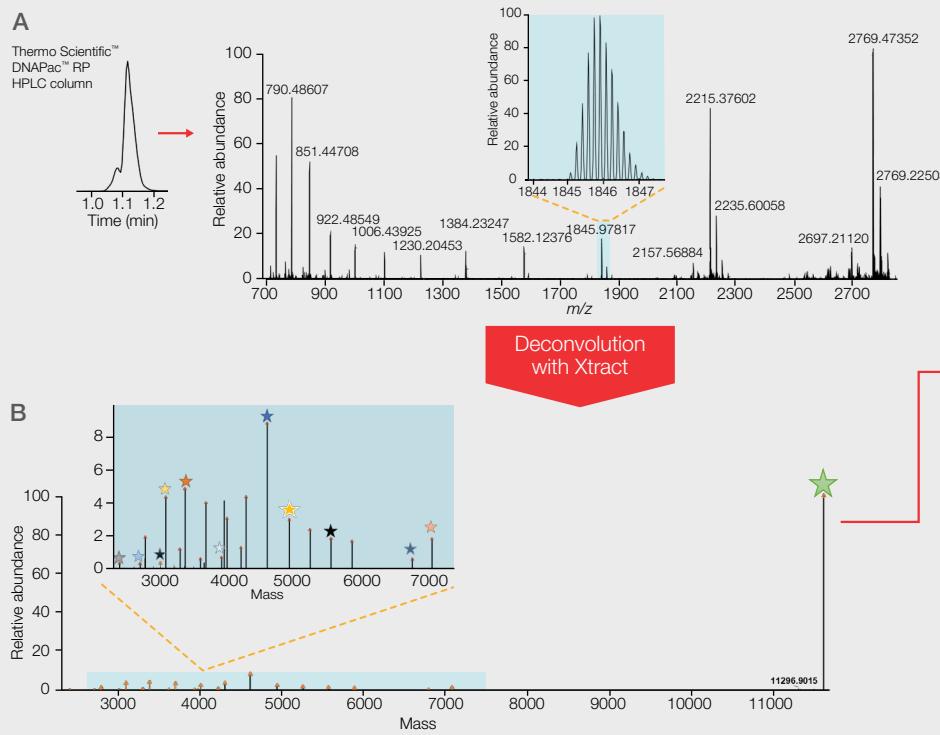
Oligonucleotide analysis

Intact mass monitoring of oligonucleotide sequences

The advancement of oligonucleotide therapeutics is driving needs for easier and more reliable characterization approaches. The Orbitrap Exploris MX detector is an ideal solution for sensitive and robust intact mass monitoring of oligonucleotide sequences and their low-level production related impurities. Compared to low-resolution instruments which only provide average molecular weight, HRAM data enables resolution of very closely related intact oligonucleotide sequences. Unlike software that relies on traditional peak picking algorithms, Xtract™ and ReSpect deconvolution algorithms implemented in BioPharma Finder software make use of the Sliding Window feature intact and provide mass deconvolution on a chromatographic time scale to identify failed oligonucleotide sequences and process related impurities, even at low levels or in poorly resolved chromatographic peaks.

Why is oligonucleotide analysis challenging?

The complexity, diversity, and size of oligonucleotides and potential impurities makes analyses challenging. HRAM LC-MS is the technique of choice due to its mass accuracy, reproducibility, robustness, sensitivity, and speed. HRAM capability is indispensable in verifying that an oligonucleotide has the expected molecular weight.



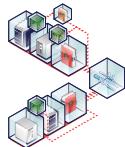
BioPharma Finder software uniquely handles oligonucleotide nomenclature and custom modifications

BioPharma Finder software provides an intuitive set of tools to support sequence modifications at each subunit of the oligonucleotide, including the nucleoside base, backbone-linker, and 2' ribose positions. Custom building blocks can easily be inserted into existing sequences or utilized for future sequence creation. Chemical modifications can also be created and searched to identify unexpected or variable modifications of the target sequence.

C

Level	Sequence Name	Modification	Monoisotopic Mass	Theoretical Mass (Da)	Matched Mass Error (ppm)	Average Mass	Relative Abundance	Sum Intensity
# 1	Component 38 mer		11609.9590	11609.9815	1.9	11615.38	100.00	2.01E+08
# 2	Component 38 mer	23v5 Truncation,1sPhosphorylation	4613.7638	4613.7733	2.1	4615.91	8.82	1.77E+07
# 3	Component 38 mer	27v5 Truncation,1sPhosphorylation	3385.5471	3385.5541	2.1	3387.12	4.84	9.71E+06
# 4	Component 38 mer	24v5 Truncation,1sPhosphorylation	4300.7089	4300.7157	1.6	4302.71	4.36	8.75E+06
# 5	Component 38 mer	28v5 Truncation,1sPhosphorylation	3096.5017	3096.5077	2.0	3097.94	4.34	8.71E+06
# 6	Component 38 mer	26v5 Truncation,1sPhosphorylation	3698.6034	3698.6117	2.2	3700.33	4.00	8.03E+06
# 7	Component 38 mer	25v5 Truncation,1sPhosphorylation	4011.6605	4011.6693	2.2	4013.53	3.05	6.12E+06
# 8	Component 38 mer	22v5 Truncation,1sPhosphorylation	4942.5147	4942.8258	2.2	4945.12	2.98	5.99E+06
# 9	Component 38 mer	21v5 Truncation,1sPhosphorylation	5255.4668	5255.6834	2.6	5258.33	2.37	4.76E+06
# 10	Component 38 mer	20v5 Truncation,1sPhosphorylation	2792.4574	2792.4617	1.5	2793.76	1.93	3.87E+06
# 11	Component 38 mer	20v5 Truncation,1sPhosphorylation	5568.9252	5568.9410	2.8	5571.54	1.82	3.66E+06
# 12	Component 38 mer	15v5 Truncation,1sPhosphorylation	7077.1747	7077.1916	2.9	7080.48	1.80	3.61E+06
# 13	Component 38 mer	19v5 Truncation,1sPhosphorylation	5881.9837	5881.9989	2.5	5884.73	1.67	3.35E+06
# 14	Component 38 mer	24v5 Truncation	4220.7394	4220.7493	2.4	4222.71	1.29	2.59E+06
# 15	Component 38 mer	27v5 Truncation	3305.5425	3305.5877	1.6	3307.12	1.20	2.41E+06
# 16	Component 38 mer	25v5 Truncation	3931.6941	3931.7020	2.2	3933.53	0.69	1.39E+06
# 17	Component 38 mer	26v5 Truncation	3618.6358	3618.6454	2.7	3620.32	0.59	1.19E+06
# 18	Component 38 mer	16v5 Truncation,1sPhosphorylation	6788.1327	6788.1486	2.3	6791.31	0.59	1.18E+06
# 19	Component 38 mer	28v5 Truncation	3016.5373	3016.5414	1.3	3017.94	0.36	7.28E+05
# 20	Component 38 mer	30v5 Truncation	2408.4509	2408.4493	0.7	2409.58	0.33	6.69E+05
# 21	Component 38 mer	29v5 Truncation	2712.4962	2712.4993	0.3	2713.76	0.31	6.20E+05

Oligonucleotide intact mass confirmation analysis of a 38mer oligonucleotide at a resolution setting of 120,000. (A) Full-MS spectrum with a zoom into the -8 charge state is shown (insert) as well as the (B) resulting spectrum after deconvolution with a zoom into the lower abundant signals (insert). (C) Exemplified, signals in the deconvoluted spectrum are assigned to the masses in the displayed BioPharma Finder result list (colored asterisks), showing the Full length product (FLP) (highest abundance; green asterisk) as well as identified low level impurities.



MAM 2.0 workflow

Seamless knowledge and method transfer across instruments, departments, and sites using BioPharma Finder software, compliance-ready Chromeleon CDS enterprise software, and HyperBridge server or cloud.

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