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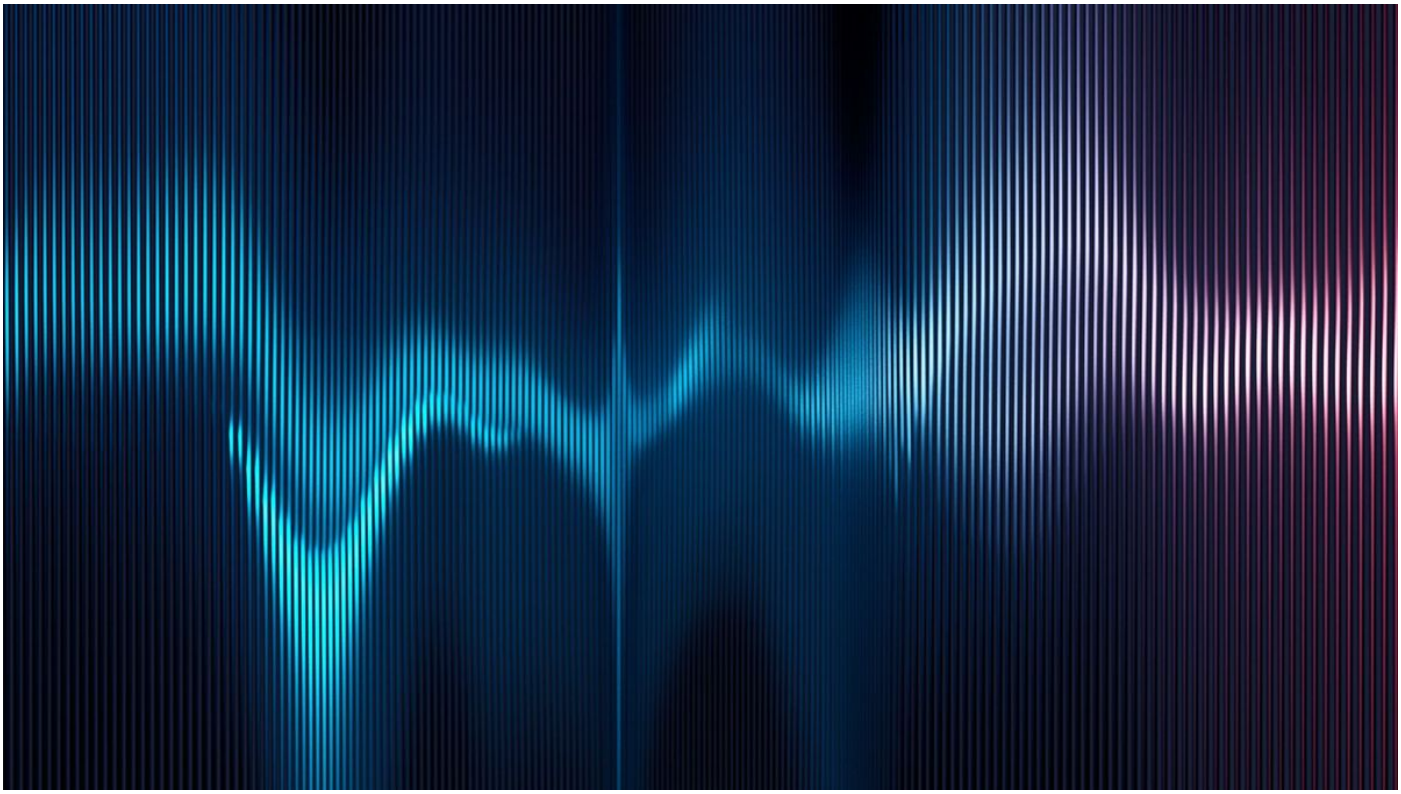
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What's New in NIST 26 for GC–MS and LC–MS/MS Laboratories?

Expanded spectral libraries and new chromatogram-processing tools allow scientists to analyze complete datasets, investigate unknowns, and incorporate retention information within NIST MS Search v4.0.

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The 2026 release of the NIST mass spectral libraries expands compound coverage while introducing a significant change to the accompanying software. NIST MS Search v4.0 can now process complete GC–MS and data-dependent acquisition (DDA) LC–MS/MS files through its new Chromatogram tab.

Previous versions focused on searches involving individual spectra or collections of extracted spectra. The new release brings chromatographic processing, spectral deconvolution, library searching, and follow-up investigation into one environment. Laboratories can use these capabilities with the NIST 26 electron ionization (EI) and tandem libraries, as well as compatible third-party resources.

Expanded EI and Tandem Libraries

The NIST/EPA/NIH EI Mass Spectral Library now contains 431,280 spectra representing 382,185 compounds. This marks a 10% increase in compound coverage from the previous release. More than 153,000 of the included spectra were measured at NIST.

The NIST 26 Tandem Mass Spectral Library has grown by 33%. It contains more than 3 million nominal- and accurate-mass spectra from approximately 576,000 precursor ions, covering more than 65,000 compounds. The collection includes product-ion spectra generated primarily through positive and negative electrospray ionization, with some atmospheric pressure chemical ionization data.

These additions increase the likelihood of finding a direct library match. However, compound count alone does not determine identification performance. Spectral quality, ionization conditions, collision energy, precursor selection, and retention information continue to shape the reliability of a result.

NIST now distributes the EI and tandem libraries as separate products. Laboratories can install both on the same computer and access them through one copy of MS Search v4.0.

Complete GC–MS File Processing

The Chromatogram tab represents the most substantial workflow change in the new software. It incorporates capabilities based on the Automated Mass Spectral Deconvolution and Identification System, better known as AMDIS.

GC–MS data often contain overlapping signals, background ions, and low-abundance components obscured by more intense compounds. Deconvolution separates these contributions into component spectra before submitting them for library searching.

MS Search v4.0 can process GC–MS files containing either nominal- or accurate-mass data. Because the AMDIS algorithm operates with whole-number mass values, the software encodes accurate-mass measurements for processing and restores them for display and subsequent investigation.

Scientists can process data with or without retention index constraints. The software also supports the creation of retention index calibration files for semi-standard non-polar columns. When users zoom into part of a reconstructed total ion chromatogram, the hit list updates to display the components within that retention-time window.

Selected components can then move into other MS Search views for further evaluation, including Hybrid Search. This connection reduces the need to export individual spectra and move between separate programs during an unknown-identification workflow.

DDA LC–MS/MS Analysis Within MS Search

The Chromatogram tab also processes DDA LC–MS/MS data in the open mzML format. Scientists whose instrument software does not export mzML files can convert their data using a compatible tool such as MSConvert.

The workflow draws on NIST's XIC Analyzer, which uses extracted ion chromatograms to support the identification and quantification of LC–MS/MS features. Users can process a complete file with conventional library searching or apply Hybrid Search during the analysis.

Large LC–MS/MS files can require substantial processing time. MS Search v4.0 allows chromatographic analysis to run in the background while the user works in other tabs, although the software processes one chromatographic file at a time.

This capability may prove useful in metabolomics and other small-molecule workflows where laboratories need to evaluate many precursor and product-ion spectra across one dataset.

Stronger Support for Unknown Identification

Hybrid Search remains important when a library does not contain an exact spectrum for the measured compound. The method combines fragment-ion similarities with neutral-loss information to identify related library compounds and estimate the difference between the query and reference structures.

MS Search v4.0 translates the resulting mass difference into possible elemental additions or losses. The hit list can display the proposed formula change, its relative frequency among high-scoring results, and a predicted elemental composition for the unknown.

Scientists can transfer a proposed spectrum–structure pair to MS Interpreter for further assessment. This workflow does not replace confirmation with reference standards or orthogonal evidence, but it can narrow the range of plausible candidates.

Retention Data Add Another Constraint

The NIST 26 GC Method/Retention Index database contains approximately 527,000 values covering 216,000 compounds. Experimental retention indices are available for many compounds represented in the EI library.

NIST also provides artificial intelligence-predicted retention index values, known as AIRI values, for compounds in the EI library. When a search uses a retention constraint and no experimental value is available, MS Search v4.0 can apply the AIRI value.

Combining spectral similarity with retention behavior can help distinguish candidates that produce comparable EI spectra. Scientists must still consider column chemistry, method conditions, and

prediction uncertainty when evaluating the result.

A Shift From Individual Spectra to Complete Workflows

NIST 26 expands its reference collections, but the larger change lies in how scientists can use them. MS Search v4.0 moves beyond individual-spectrum searching to support complete GC–MS and DDA LC–MS/MS datasets.

For laboratories considering an upgrade, the key question is whether the new Chromatogram tab can streamline existing deconvolution, library-searching, and unknown-identification workflows. Its value will depend on data formats, instrument configurations, retention index practices, and the level of manual review required for each application.

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