APPLICATION NOTE

ACD/LABS [ADVANCED CHEMISTRY DEVELOPMENT, INC.]

Workflow for Chemical Characterization and Database Curation for LC/MS and GC/MS Data

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Confident Identification of Known and Unknown Components to Create a Curated Centralized Database

Medical device manufacturers are required to evaluate the biocompatibility of medical devices to manage biological risk. The ISO 10993 series provides the framework for the evaluation of medical device biocompatibility. Medtronic conducts extractable and leachable (E&L) testing in accordance with ISO 10993 Part 18, to create a profile for every medical device they supply. This generates an immense amount of highly regulated analytical data that must be appropriately managed and stored.

Medtronic uses MS Structure ID Suite for their data-handling workflow for confident structure assignments. They then carefully and strategically curate relevant spectral libraries/databases for LC/MS and GC/MS data from reference standards and reference materials that they can search against. The software is used to standardize, integrate, and store their analytical data with its scientific context (structure, metadata, retention time, etc.), allowing them to elucidate each component's structure efficiently and confidently.

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Adding Confidence to Compound Assignments

Various capabilities of the software are used as part of the workflow, increasing confidence in compound assignments.

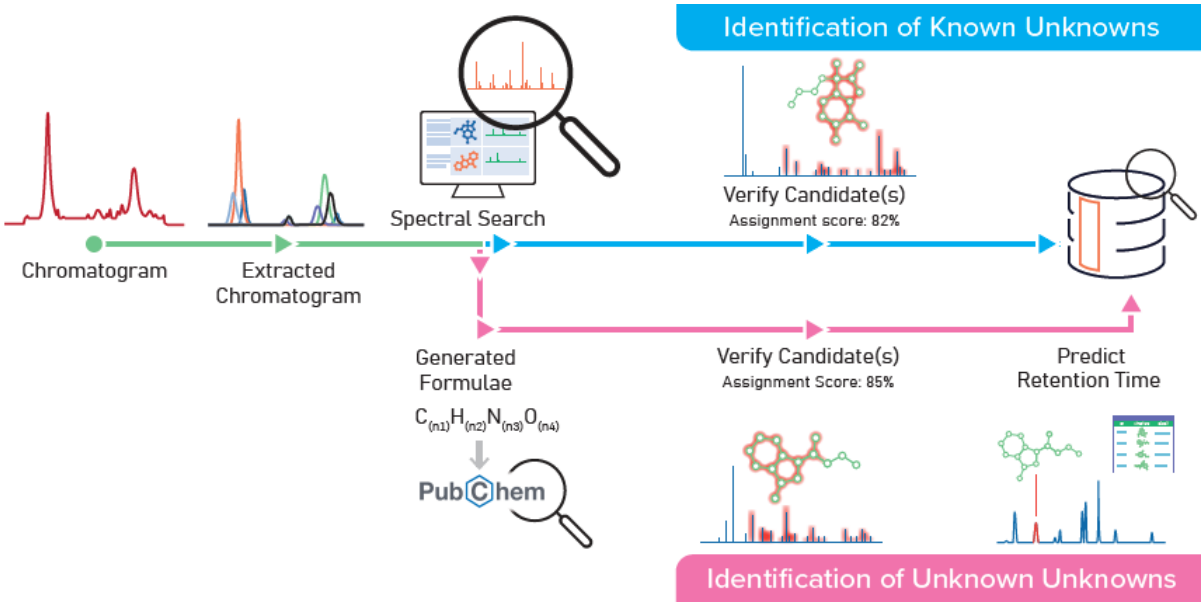

Figure 1. Workflow showing the structure elucidation and verification of known and unknown components using the various capabilities of MS Structure ID Suite software.

Workflow for Known Unknowns

The Intelligent Component Recognition (IXCR) tool is used to screen GC/MS and LC/MS mass spectra samples, search databases to compile structure hits (hit quality index, HQI%), and conduct spectral comparisons via mirrored plots (mass difference).

Depending on the HQI%, further verification of known compounds may be required. Here, the AutoAssignment tool is used to interrogate LC/MS data and top structure candidates to determine an assignment score. This assignment score shows structure and match factor for the compounds, instilling confidence in the assignment.

Workflow for Unknown Unknowns

Following IXCR screening, for cases of true unknown components, ACD/Labs' Molecular Formula Generator tool can propose potential molecular formulae and displays expected isotopic abundance. MS Structure ID Suite is then used to search for a target component's accurate parent mass and predicted molecular formula to generate a ranked structure hit list. The AutoAssignment tool matches predicted fragments to experimental spectra to determine the best structural matches. An additional check is performed with the ChromGenius tool to predict retention time. As the database containing known structures (i.e., with structural similarity and retention time) increases, retention time prediction efficacy also increases.

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Curation of a Centralized Database

Once an accurate structure verification is achieved, the associated analytical and metadata are stored in a centralized database. The workflow complies with regulatory requirements, including 21 CFR Part 11 (i.e., traceability, audit trail, versioning, etc.), and information necessary for regulatory documentation is easily accessed. Scientists have access to live, curated data from any remote location, allowing cross-functional teams to work and make decisions more efficiently. With MS Structure ID Suite, Medtronic consolidates its analytical and metadata in a carefully curated centralized database, ensuring analytical knowledge generated today is retained and leveraged into the future.