Case Study

Accelerating Analytical Workflows: ChemisTwin Portal for Automated Structure Verification in Quality Control

Lauren Lytwak,[1] Albert Farre Perez,[2] Sarah Srokosz,[3] Dimitris Argyropoulos,[2] Shahriar Jahanbakht[2], Hans De Bie[2]
1 MilliporeSigma, Round Rock, USA, 2 Sigma-Aldrich (Merck KGaA), Buchs, Switzerland, 3 ACD/Labs, Toronto, Canada

Physical Reference Materials Are a Burden for Scientists, Their Organizations, and the Environment

In the last several decades, the use of highly pure physical reference materials has become a standard for structure verification and quantification of active compounds and excipients. Like other physical materials in the lab, these reference materials must be purchased from a supplier and are thus limited by availability as well as processing and shipping times. Once the physical material is received, scientists must prepare the standard for analysis, perform the measurement, process the resulting data, and finally dispose of the material in a suitable way.

The Vision: On-Demand Reference Data

As industry-leading suppliers of physical reference materials, MilliporeSigma (known as Merck KGaA, Darmstadt, Germany outside of the US and Canada) recognized that when they send a customer a physical reference material, what the scientist ultimately cares about is its corresponding data. This led them to realize that if users could access high-quality pre-processed data on-demand, they could eliminate the costly, error-prone steps of physical material handling for their customers. Given how frequently these workflows are performed in many industries, the potential time and resource savings offered by such a solution are significant.

A Digital Twin Powered by NMR Workbook Suite

And thus, the ChemisTwin™ portal[1] began to take shape: an online platform containing an extensive database of digital reference materials (dRMs), serving as digital twins of their catalog of >25,000 physical reference materials. As a starting point, they chose to target routine structure verification workflows using NMR data because of its prevalence across industries and distinct advantages over other analytical techniques.

ChemisTwin leverages NMR Workbook Suite's NMR prediction capabilities in the creation of the dRMs and its automated structure verification technology of NMR Workbook Suite to automatically compare the sample with the dRM and compile the results in a detailed report.

Putting It to the Test

To assess the time saving benefits of ChemisTwin, three quality control scientists at MilliporeSigma were provided the raw the ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of ibuprofen as a *.jdx file. They were asked to record the time it took to verify ibuprofen as the main component of the spectrum and discriminate the closely related compounds considered as impurities according to Pharmacopeia[2] (Figure 1) using their conventional manual analysis method as well as ChemisTwin (Table 1).

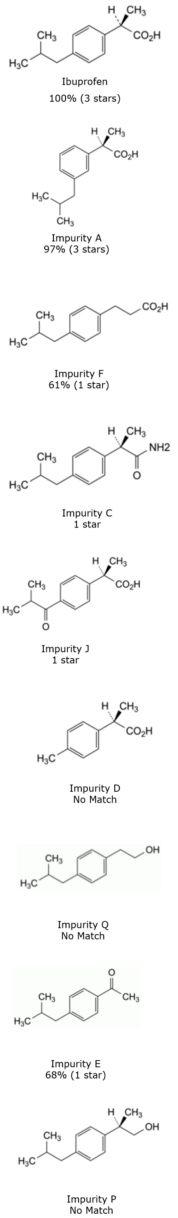

Figure 1. Structure of ibuprofen and related compounds along with the corresponding match factor from ChemisTwin.

ACD/Labs®

Table 1. Overview of the steps in the manual analysis method and the ChemisTwin method.

Manual Method	ChemisTwin Method
1 Spectral processing (referencing, peak picking, peak integration, etc.) 2 Spectral interpretation 3 Comparison with literature data	1 *.jdx file uploaded to ChemisTwin 2 Qualitative verification analysis workflow was selected, along with the dRMs corresponding to the nine structures shown in Figure 1

Outcomes—Reliable Structure Verification in Half the Time

In all cases, the scientists were able to correctly identify ibuprofen as the main component of the sample and discriminate the eight impurities. However, the conventional QC approach took 2 to 3 times longer than using ChemisTwin, which cut analysis time down by 53% on average (Table 2).

Table 2. Results of the manual conventional quality control method versus ChemisTwin for identity verification of a target compound versus its closely related compounds using NMR spectroscopy

QC Member	Manual QC (min)	ChemisTwin (min)	Time Savings
1	10.6	5.2	51%
2	32.3	9.4	71%
3	20.8	13.1	37%
		Average Time Savings	**53%**

ChemisTwin Results

ChemisTwin provided a table on the result page containing proton assignments, along with the sample and the dRM predicted spectra, considering the sample's experimental conditions (solvent and instrument frequency), and the match factor score between the sample and the corresponding dRM.

ChemisTwin was able to identify ibuprofen as the most likely main component of the sample with the highest match factor (100%, 3 stars). Ibuprofen Impurity A was listed with a high match factor (97%) due to high similarity of the spectra (0.1 ppm difference in few peaks). However, this can be conclusively ruled out with visual comparison of the spectra in the ChemisTwin interface. The related compounds C, E, F, and J were determined to be unsatisfactory matches (match factor <75%, 1 star) suggesting that those compounds are highly unlikely to be the main component of the sample. This can be also intuited by the spectral difference and the table of assignment report. Finally, impurity D, Q, and P found no match (match factor <50%) with the sample spectrum.

Realizing Benefits Beyond Data Analysis

ChemisTwin streamlines the verification process, providing accurate results in a fraction of the time required by traditional methods. Furthermore, its digital nature eliminates the need for extensive manual interpretation and literature comparison, enhancing efficiency and reducing the potential for errors. In addition to these benefits to analysis efficiency, the use of ChemisTwin eliminates the need for handling of physical reference materials, which reduces the environmental impact of such analyses and provides scientists and their organizations further time savings that have yet to be quantified. Overall, ChemisTwin represents a valuable tool for quality control in compound identification via NMR spectroscopy, offering improved speed, accuracy, and sustainability.

References

1. Merck - ChemisTwin Portal. (2024, April 4). MilliporeSigma. https://chemistwin.com/
2. Ph. Eur. 11.0, 3062—3064 (04/2024)