

ACD/LABS [ADVANCED CHEMISTRY DEVELOPMENT, INC.]

## Automated Structure Verification for High-Throughput Quality Control in Pharmaceutical R&D—Part 2



**Tatiana Didenko**  
Principal Scientist

Tatiana and the rest of the Structural Chemistry Group at Amgen support the medicinal chemists by providing in-depth NMR characterization of small molecules and maintaining high-throughput NMR for structure characterization.

### Why ASV?

Amgen have been using the automated structure verification (ASV) capabilities of NMR Workbook Suite™ for many years, but the technological advancement of other components of their NMR workflows have recently underscored its value to Tatiana and her team.

### Implementation of the Universal Database

In 2020, they implemented their Universal Database (UDB): a Spectrus database that acts as one location for all small molecule analytical data. It integrates LC/MS and NMR data from a variety of workflows and sources, including open-access instruments. The database is integrated with their ELN and core registration workflows. The live analytical data can also be easily searched by anyone in the organization or used in AI/ML applications.

Because the data in the UDB can be so easily proliferated across the organization, the data and corresponding analyses it contains must be accurate and high-quality. Because of this new emphasis on data and analysis quality, they have found ASV particularly beneficial because it:

- 1 Improves decision-making in structure verification while reducing errors in sample submission
- 2 Provides more comprehensive proof of structure for samples being submitted for assays and to the Sample Bank
- 3 Adds value by providing the chemists a better tool for characterizing newly synthesized compounds

## High-Throughput NMR

Amgen also has a sophisticated high-throughput NMR (HTNMR) workflow in which every step is highly streamlined. The acquisition setup is initiated by simply scanning a barcode on the 96-well plate. This also imports all the metadata assembled in an SDfile. Samples are then delivered automatically to the instrument's cyroflow cell. They use NMR supersequences to record multiple spectra at once and cut down on acquisition time.

To streamline the data analysis, they rely on batch ASV for automated processing and analysis. Tatiana notes that ASV generally provides accurate results for even large, complex structures using only 1D  $^1\text{H}$  and  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectra, however they sometimes use  $^1\text{H}$ - $^1\text{H}$  COSY as well.

## High-Throughput Quality Control Using ASV

Based on this workflow, Tatiana and her team can perform high-throughput quality control (HT-QC) for compounds in the sample bank or commercial/externally synthesized compound or libraries to:

- Confirm the structure
- Check material integrity
- Generate consistent NMR data for use in-house or in patents/publications

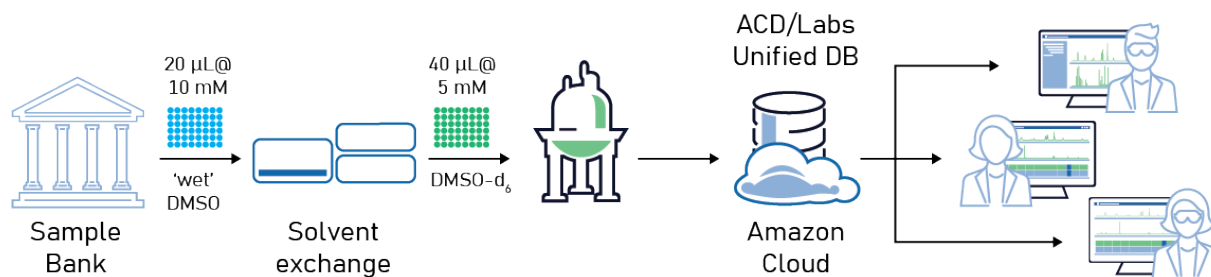


Figure 1. Amgen's high-throughput quality control workflow.

With this HT-QC workflow shown in Figure 1, Tatiana and her team can analyze up to 25 compounds per day, which works out to 5000 compounds in a year. For a 96-sample well plate, they can provide results in 5 business days. They add the analyzed data and results to the UDB, where it can be viewed and used by others in the organization, or employed in AI/ML applications.