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LIMS & Lab Automation

# It's Not Too Late to Automate Your Structure Verification

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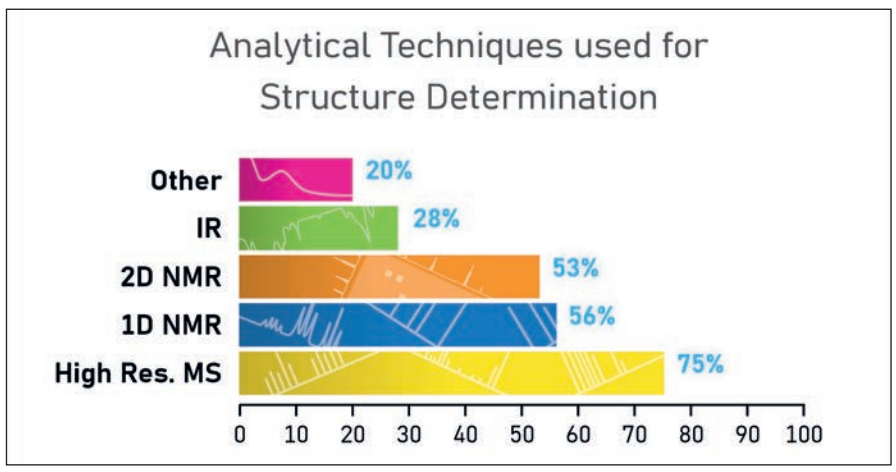
## Analytical Experiments are Carried Out to Answer, Essentially, One Question: What Is In My Sample?

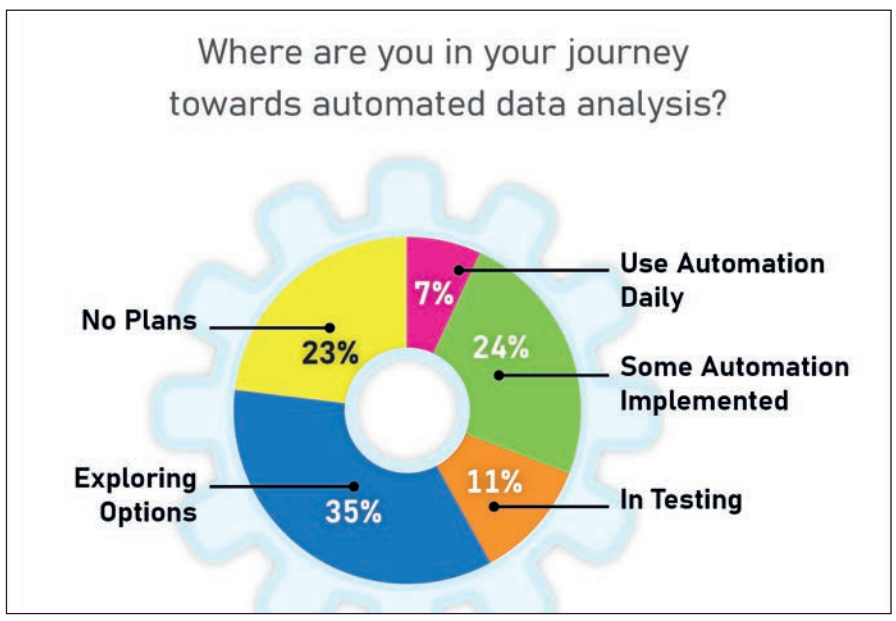
There is nuance based on the work being done - lead optimisation in discovery, impurity control in process development, forced degradation studies, or manufacturing QA/QC. Results may be used to better understand a material, to understand a process, or to reveal its limitations - but the high-level question is still, 'what is it?' Every day, scientists collect vast quantities of NMR, LC/MS, FTIR, Raman spectroscopy, and a variety of spectroscopic and analytical techniques' data to verify or elucidate the identity of chemical (or biochemical) structures and mixture components. Enhancing efficiency in this pursuit thus offers significant gains to individual scientists and their organisations.




## What is Automated Structure Verification?

Automated structure verification (ASV) generally refers to the process of using computational algorithms and software tools to assess the match between a proposed chemical structure and corresponding analytical data.

ASV software analyses experimental data, such as NMR spectra, and compares it with the proposed molecular structures. By applying various algorithms and rules, these tools can detect inconsistencies, errors, or ambiguities in the proposed structures. This verification process saves scientists time in routine analyses, can help with throughput, and reduces the risk of human bias, as we analysts subconsciously try to fit data to the expected structure.




## Boosting Scientists Workflows Across Industries

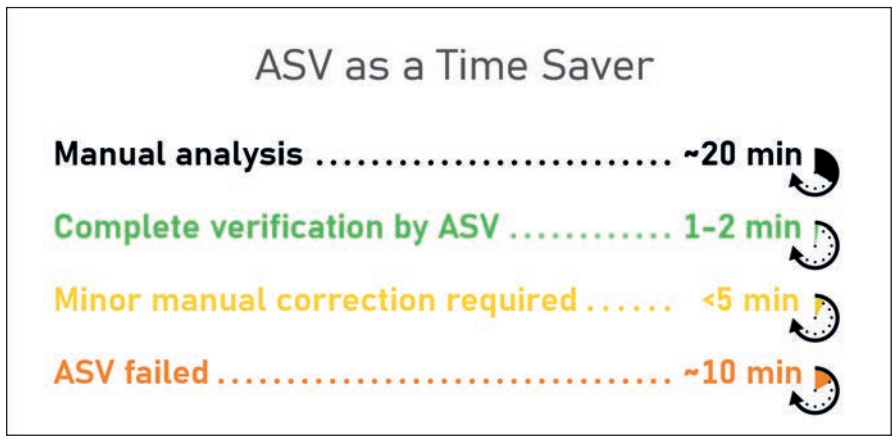
ASV can benefit a wide variety of fields in which structure verification plays a significant role. This includes the pharmaceutical industry from drug discovery, through to development, and even manufacturing QA/QC. It's also valuable in analytical labs like CROs and environmental testing, as well as regulatory agencies, academic institutions, and patent offices.

At Novartis, Associate Director/Chemical Structure Investigation Group Lead, Dorina Kotoni reported that her team have implemented ACD/Labs ASV by NMR, for molecules smaller than 800 Daltons across research and development. In their workflow, analysts review the generated results which are then reported directly to the chemist, to a database, or to an ELN record, based on their needs.

She reports that the team has saved a significant amount of time from their 'ASV engine' deployment. She estimates that for manual verification an experienced analyst, on average, would spend 20 minutes on processing and interpreting NMR data per submission. When the ASV engine successfully delivers a structure confirmation result, the analyst only spends a minute or two on review, which represents a 90% time savings. When minor manual corrections are necessary, the analyst may spend 5 minutes on the analysis - less than half the time required for manual analysis. Even when ASV does not generate a result or data processing is incomplete, it still saves the analyst time "because the peak picking is done", Kotoni adds.

***"After 2 years we are seeing 60–65% of successful automated verifications and the software is learning as we feed more data into it… Even failed verifications save the analysts time because they don't have to process the datasets from scratch."***

*Dorina Kotoni, Novartis*

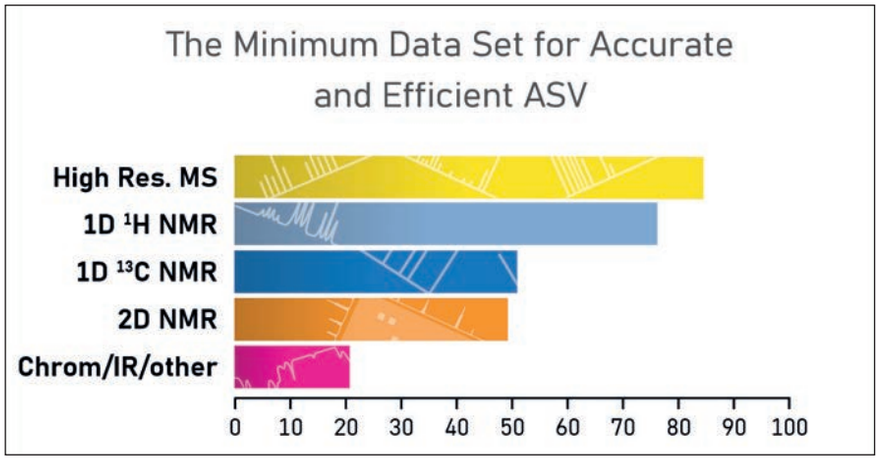



## Cut Down on Data Needed for Structure Determination

Structure determination requires the use of data from a variety of analytical techniques. The amount of data required also depends on how much structural information you have—is it a novel compound requiring elucidation or are you verifying the presence of an expected structure? The exact combination of techniques also depends on the type of compounds you anticipate are present.

We surveyed the audience of approximately 400 scientists from discovery and development who attended our Structure Elucidation & Verification Symposium to learn more about what analytical techniques they're using to identify chemical structures. We found the hierarchy of techniques to be high-resolution mass spectrometry (HRMS), followed by 1D $^{1}H$ and /or $^{13}C$ NMR, then more time-consuming 2D NMR, IR, and finally, other experiments such as LC/MS, UV/Vis, and Raman spectroscopy data.

In addition to time savings gained in data processing and analysis, ASV also presents the opportunity to save time and resources by cutting down on the number of experiments needed to confidently verify a structure.




The minimum data set that is necessary for accurate and efficient ASV is not generally defined. However, this same audience mostly agreed that HRMS and 1D $^{1}$H NMR data, which can both be obtained relatively quickly, are generally necessary. Whereas more time-consuming experiments such a 1D $^{13}$C NMR, 2D NMR, and chromatography may be skipped, particularly for structures that are previously known.

But this doesn't mean that those working with novel structures cannot benefit from ASV. For this subset, the benefits of databasing spectral data are immediate and real. While no commercial database will contain the novel structures being investigated in your organisation. The accuracy of NMR prediction for novel chemical space can be improved with the addition of even small amounts of your own curated data.

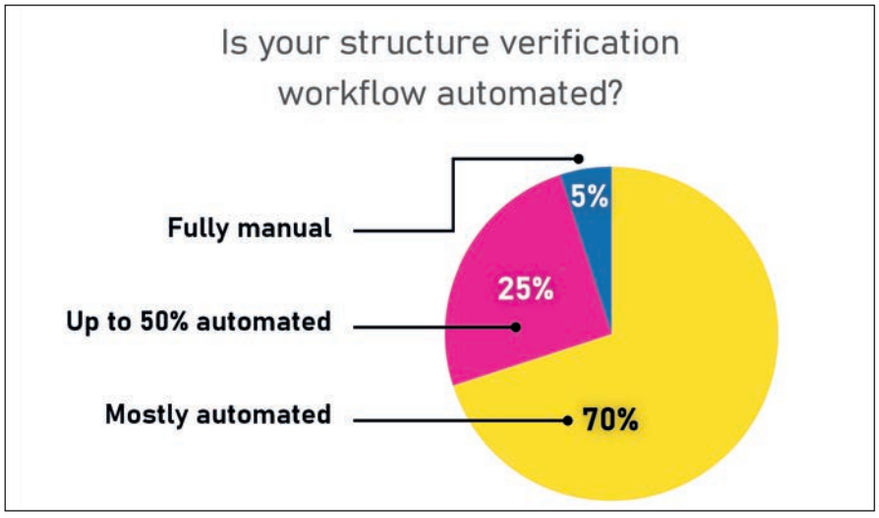
***"Accurate prediction is very important for our automated structure verification process and we've seen excellent results from training the NMR predictors DB with or own data over the years."***

*Celine Nguyen-van-dau, Sanofi*

## The Path to ASV is Made Up of Many Steps

With the ever-increasing number of stories of automation in scientific workflows, it's easy to feel intimidated and overwhelmed. However, while some organisations have begun to adopt and benefit from ASV, we found that most of our Structure Elucidation & Verification Symposium audience (70%) are still only doing manual structure verification. All the while, 20% have less that half of their structure verification automated and only 5% reported fully automated structure verification.

At the same time, we asked this audience where they were in their journey towards automated data analysis, including ASV. The large majority (77%) reported that they are adopting automation, with most being in the early or middle stages of their implementation.




While only 7% report using automation in their daily workflows, they are not the only ones reaping the benefits of automation. The overall time savings of even partially automated structure elucidation and verification can add up quickly in a variety of environments.

In open-access labs, minimised experiment time frees up instrument time and can distribute analysis time savings across a variety of diverse teams within an organisation. Similarly, the large quantity of samples in high-throughput structure verification workflows mean the time and resources saved with ASV can be substantial.

So, while modern workflows still rely heavily on manual structure determination, it appears that the industry is overwhelmingly in favour of adopting automated data analysis to free up scientists' time for more novel pursuits.

For those in a similar situation to almost a quarter of the audience who have no immediate plans to automate their data analysis, it's essential to recognise that the gap between organisations embracing automation and those lagging behind will continue to widen. Therefore, now is an opportune moment to consider how ASV can help alleviate bottlenecks in your workflows.

For decades, ACD/Labs has been committed to supporting scientific experts from many of the world's leading biopharmaceutical and chemical companies in identifying, verifying, and elucidating chemical structures.

Our experts and flexible software solutions can help you strategically build towards your organisation's automated data analysis goals.