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**By reducing analysis time from 5–6 hours to less than 30 minutes per sample, Genedata Expressionist enabled us to overcome a major bottleneck in our analytical support of process development.**

**Tim Nagel**, Ph.D., Scientist, F. Hoffmann-La Roche, Basel, Switzerland

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#### INDUSTRY

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#### ABOUT ROCHE

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#### GENEDATA SOLUTION



**EXPRESSIONIST**

# Automating LC-UV-MS-Based Analytics in Therapeutic Oligonucleotide Process Development

## Background

As a leading biopharma company developing solutions to many of the challenges in healthcare today, Roche is currently developing several oligonucleotide-based drugs to address a range of diseases. Our lab provides analytical support to the process chemistry department, which is responsible for optimizing oligonucleotide synthesis processes. We combine the information-rich data obtained from high-performance liquid chromatography (HPLC) and mass spectrometry (MS) to determine the number, amount, and identity of impurities in crude oligonucleotide samples. These insights are key to optimizing the oligonucleotide solid-phase synthesis process.

The number and complexity of samples combined with the laborious nature of the data analysis generated a significant bottleneck in the analytical process. To overcome this issue, we worked together with Genedata to develop and implement a tailored MS data processing workflow that increased our throughput and the level of characterization while reducing the burden on our MS experts.



## Main Challenges

### Meeting high analytical throughput demands

The exploration of the optimal synthesis conditions generates large numbers of samples requiring fast analytical turnaround to provide timely feedback and accelerate process development. Because it relied on laborious manual operations for impurity quantification and any requested deeper analysis, our previous oligonucleotide analytical procedure was unable to scale efficiently and often led to process bottlenecks.

### Providing comprehensive analytical characterization

Samples generated during the optimization of oligonucleotide synthesis often contain many impurities. This sample complexity translates into the analytical challenge of assessing 20–30 peaks arising from 50–100 closely coeluting impurities. In addition, the iterative nature of the optimization procedure creates a complex and continually changing range of sample components that require a flexible and robust analytical solution to deliver a comprehensive characterization.

### Making the most of analytical resources

Our previous quantification process required intensive supervision and constant adaptation for unknown impurities. The large number of manual operations—such as integrating peaks and creating extracted ion chromatograms (XICs)—in this highly laborious procedure often required 5–6 hours of an analyst's time. This burden limited the ability of our MS experts to perform required deeper characterization in a timely manner.

## Solution

### Automated MS workflows providing detailed information

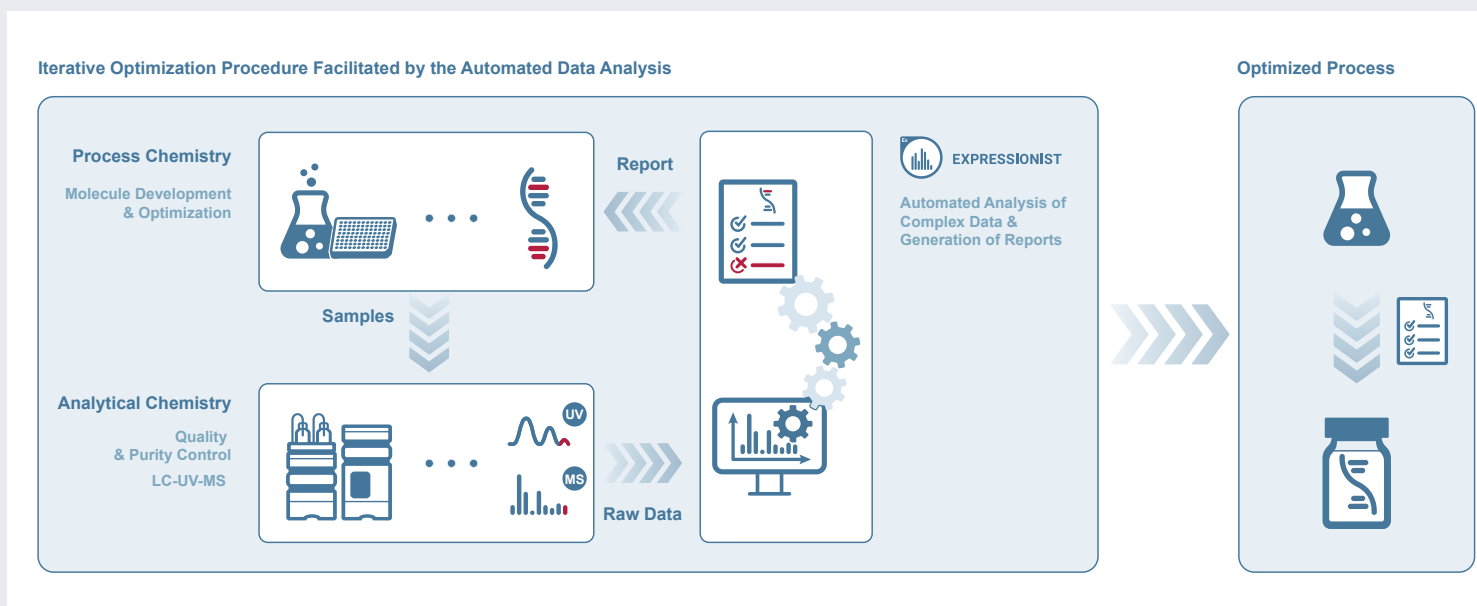
Genedata Expressionist® integrated seamlessly into our analytical process and enabled us to directly import and process raw UV and MS data and combine these data streams for each analysis (Figure 1). The workflow-based approach enabled us to automate routine data processing, analysis, and reporting while still allowing our expert users to bring their expertise to bear on the critical stages of the analysis, such as identifying unexpected impurities (Figure 2).

### Rapid and scalable platform for high-throughput analysis

Automation of all routine data processing steps—such as blank subtraction, spectrum averaging, and MS quantification—enabled us to streamline and standardize our MS analyses, increasing both throughput and result quality. The highly robust data workflow requires little or no adaptation to process any sample, regardless of purity or complexity.

### A flexible and future-proofed processing workflow

The data workflow presented here was created and optimized for a specific product synthesis process. However, the inherent flexibility of Genedata Expressionist enables us to use this workflow as a template that can easily be adapted for processing other molecules. For example, the compound library used to identify and annotate MS signals can be readily expanded to accommodate new synthetic reagents or reactive groups.



## Benefits

### Accelerated analyses enabling systematic optimization

Genedata Expressionist automated data processing increased analytical throughput by shortening the time required for analysis from 5–6 hours to just 30 minutes in the case of very complex samples. By eliminating analytical bottlenecks, we were able to keep pace with the large number of samples generated by our process chemists systematically optimizing each parameter and step.

### No trade-off between speed and thoroughness of analysis

Deep characterization of impurities at an early stage of synthesis development is key in reducing risks in downstream drug development processes. The additional expert analytical capacity provided by automation of routine data processing tasks enabled us to better characterize unexpected impurities and provide more detailed reports to stakeholders without impacting the overall laboratory throughput.

### Effective application of expert knowledge

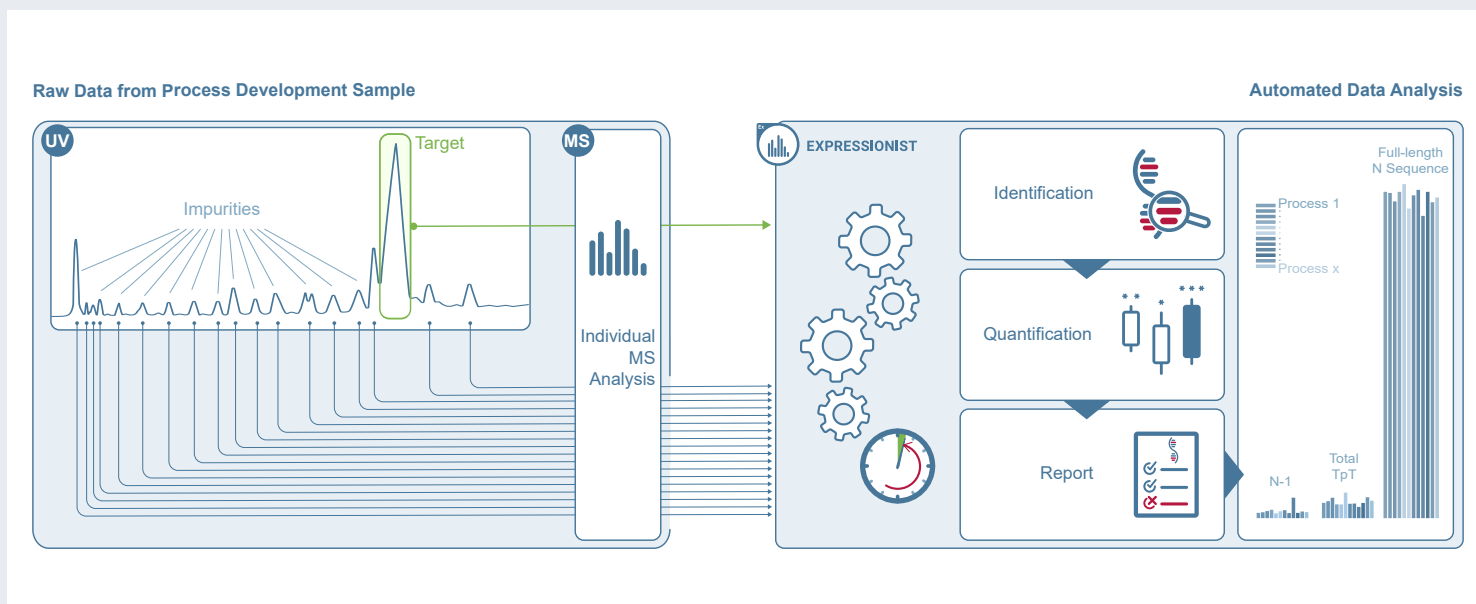
Automating MS data processing removed the burden of performing tedious manual data operations from our analysts. By enabling them to focus on tasks that require their domain expertise and training rather than routine and repetitive manual operations, the Genedata Expressionist workflow not only enabled us to deliver higher-quality results faster, but also generated a more engaging and rewarding workload for our analysts (Figure 3).

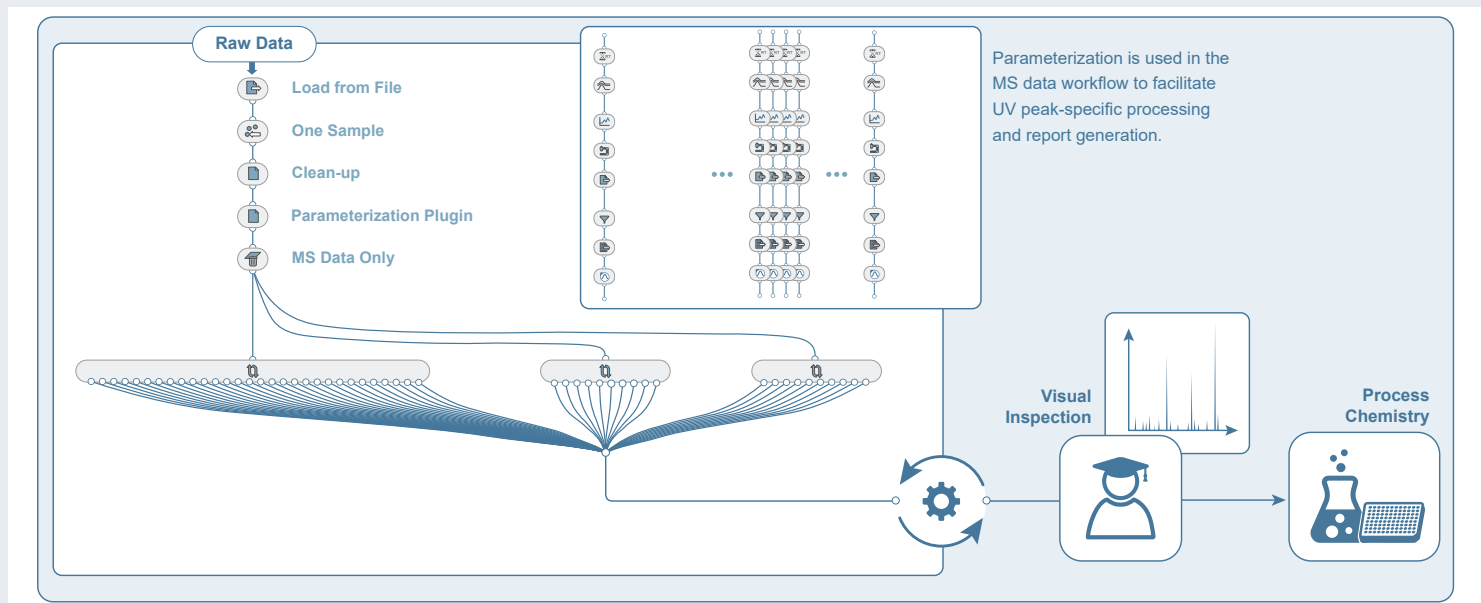
## Summary

Working in close collaboration with Genedata, we developed a streamlined data processing workflow for LC-UV-MS-based analysis of the large number of samples generated during optimization of oligonucleotide drug synthesis. Implementing this workflow enabled us to keep pace with throughput demands and increased the quality of support that we deliver to our colleagues working in process chemistry.

Automating the data processing workflow increases the number of process-related impurities identified in each analysis, providing our colleagues with in-depth overviews that facilitate the development of efficient synthetic processes.

The implemented solution minimizes user intervention and frees our scientists from performing tedious routine work, enabling MS experts to focus on challenges that require their specialist knowledge, such as developing workflows when new processes are being investigated or troubleshooting if unexpected impurities are observed.





3 Automation of routine processing enables experts to leverage their specialist knowledge where it is required.



“The ability of Genedata Expressionist to automate the routine operations of our quantification process greatly enhanced our ability to focus on higher impact and more rewarding deep analysis activities.”

Marwa Le Truong, Scientist, F. Hoffmann-La Roche, Basel, Switzerland

GENEDATA SOLUTION



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NEXT STEPS

To find out more about Genedata Expressionist for mass spectrometry data analysis, please visit [www.genedata.com/products-services/expressionist](http://www.genedata.com/products-services/expressionist).

For a conversation about your MS data analysis needs or to schedule a live demonstration, please contact us at [expressionist@genedata.com](mailto:expressionist@genedata.com).