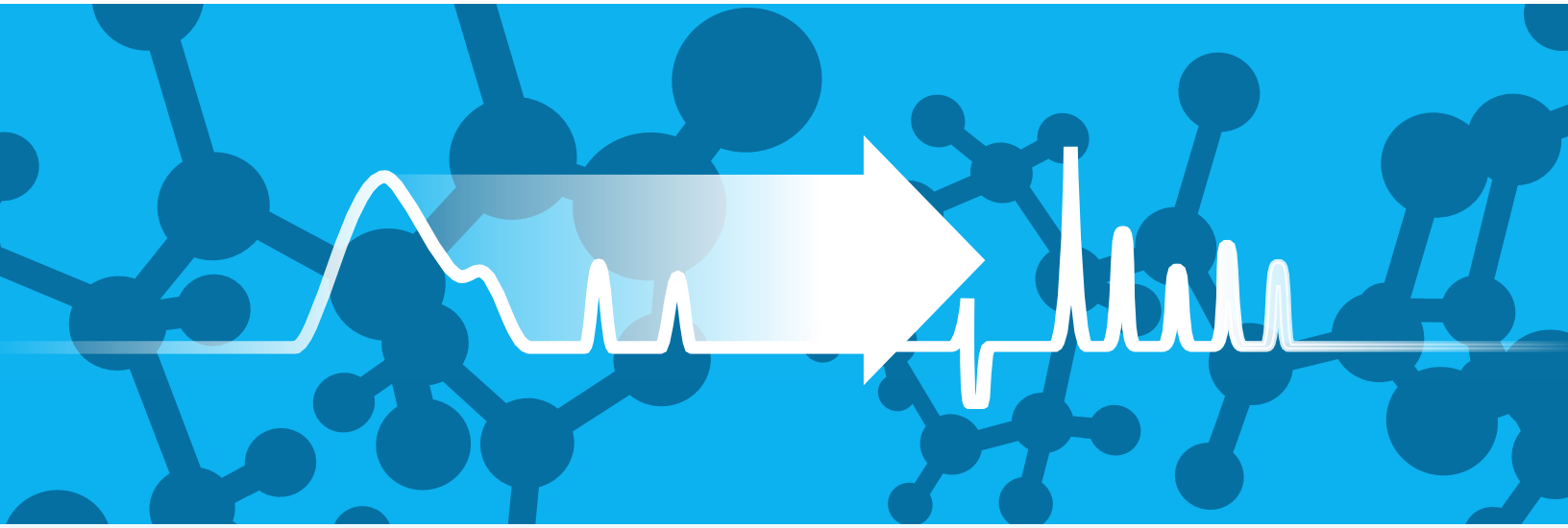
Case Study

Dow AgroSciences Designs Efficiencies into Method Development with Specialized Software



ACD/Labs

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Daniel, Grant, and Erin are among a larger group of scientists at Dow AgroSciences responsible for method development in support of 'Actives to Products R&D'. They undertake projects for early to late stage active ingredient work; and early stage to launch for formulated products.

Dow AgroSciences

In the summer of 2016, the Analytical R&D team at Dow AgroSciences that develops methods for new formulations decided to make changes in their laboratory to enable more efficient screening of method parameters and to implement new best practices across the department for a more consistent, efficient, and effective approach to method development. The methods that this group develops are implemented in labs and facilities all over the world for a variety of applications, including manufacturing and quality control, where they are used hundreds and thousands of times. Successful methods must be robust to ensure successful deployment and to pass validation requirements, as specified by regulatory bodies around the world.

As in the majority of labs, this separations laboratory at Dow AgroSciences is a mixed environment of instruments from different vendors, where analytical chemists use a variety of reverse phase columns for the separation of polar to mid-polarity compounds (C18, C8, phenyl, phenyl hexyl, and other polar embedded columns). The team typically works with new crop protection formulations, usually made up of between four and ten components as well as complex active ingredient samples for impurity profiling with upwards of twenty components. The majority of the methods are developed from scratch with screening of legacy methods for similar active ingredients or formulation types as the first step.

"At best we used to be able to look at two columns at a time, because you wouldn't want to move a method development project from system to system," Erin recalls. "You would develop on one system and then worry about making small changes to the method if moving to another instrument was necessary."

While a project might be completed in two weeks when the scientist's intuition leads him or her to a reliable method at the first try, a complex method could take up to several months to develop and validate. As any chromatographer can attest, every method development project is different. "Sometimes the first method you try works, and there's not a lot of motivation to put more time and effort into it," says Grant. "Other projects may be very difficult, where even once you have optimized a method, you still don't get adequate separation, so you are forced to return to the screening phase and optimize another set of conditions." The typical time frame for a method development project in the lab is 2–4 weeks.

Hardware upgrade and implementation of new best practices

The team upgraded their hardware so they could screen multiple columns and solvents at once and coupled it to their Agilent HPLC running ChemStation software.

"We set up a system with seven different stationary phases," says Daniel. "The intention was that as a best practice all projects would start with a screen to generate data packages that could be leveraged for further development and optimization either using software or by traditional 'manual' means."

Part of the motivation for the upgrade was also to leverage the ACD/Labs method development software already available but being under-utilized in the

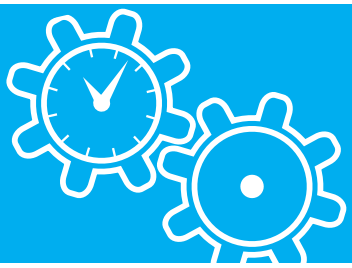
organization. While two ACD/Labs method development software tools were available to scientists, only ACD/LC Simulator was being used regularly.

Grant had good experience with the simulation software since he had been using it routinely for many years, but there was little experience with the more complex, full method development toolset. "I wouldn't be without the simulation software," Grant says, "It's a pleasure to work with. We build a model, make all the changes we intend to the method and then see what the chromatogram would look like using the software. The vast majority of the time, I'm pretty happy with the accuracy [predicted retention times of peaks versus experimental]. When we come across inaccuracies, it's usually due to overlapping peaks that were difficult to assign."

With the hardware changes complete, on-site training helped the group get started using the full capabilities of ACD/AutoChrom.

The impact of implementing specialized method development software

The team's favorite example of the impact of the software on their work was the first project they worked on during training. Several months had been spent working on a method to resolve some critical pairs of peaks with unsatisfactory separation. When the same example was used in training, they were able to generate a method using the software, with more than adequate separation, in two days.



"We had spent several months developing a method without successfully resolving a critical pair of peaks. Using the software we managed to generate a method that resolved those peaks in less than 48 hours."

- Erin Gemperline

With their new systems in place and fully functional, the team is happy with the changes they have implemented, and the software is used on a daily basis. Data collected from the new set of standard screening methods is now used to develop and optimize their separations. Online control of their Agilent instrument means that the software does not simply suggest the next set of experiments to screen; the next experiments are communicated to the instrument and executed. All the while, the team has complete control over optimization cycles with the ability to make adjustments as necessary.

The group notes that when looking at a mixture of four components with one detector, there's not a huge advantage to using the method development software connected to the instrument, because they can keep track of the data easily enough themselves. In this case, using the software in offline mode [not connected to the instrument] or with just LC Simulator can be sufficient to help simulate separations. However, when a complex sample has 20 or more peaks, and they have to use two or three different channels (UV, MS, diode array, etc.) to detect all the peaks, manually keeping track of all the data becomes more cumbersome and the software greatly facilitates the process.

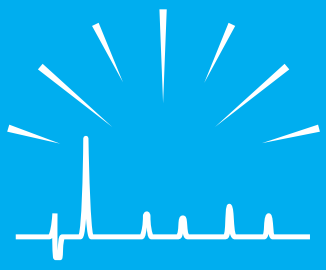
In addition to a more systematic approach to method development, Erin, Grant, and Daniel identified a number of advantages the software delivers over their previous process:

- The software ensures that all the appropriate data is vetted even when/if a legacy method is employed.
- Data are kept well organized—particularly important in more complex studies. The ability to navigate from experiment design down to a single peak is not only possible, but simple.
- Automatic component tracking has led to greater confidence in their results. While routine examination of automatically tracked peaks (to ensure accuracy) does not necessarily reduce the amount of time spent on peak tracking, they benefit from finding components they might otherwise have missed.

Conclusions

"The software provides a systematic approach that has a high probability of converging on an acceptable answer. Whereas the old way (where you start with what you're used to doing) can be very successful and very efficient, it can also be indeterminate and may never lead to a conclusion," says Grant Von Wald.

"Despite the complexity of the software, the final methods it produces are worth the time and effort. We've had good success and the methods we get are of high quality," Erin concludes.



"The real test of a method is if it's still performing the way we expected it to months after we developed it. I measure success by the satisfaction level of our partners in the manufacturing Quality Control labs. With our systematic approach to method development using ACD/Labs tools, I expect our sister labs to be more satisfied as well."

- Grant von Wald

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