Novartis embraces full automation

Basel-based Novartis Pharma AG has completed a year-long collaboration with the Tecan Integration Group, developing a fully automated Freedom EVO®-based system for antibody formulation screening.

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In 2007, as part of the FDA Quality by Design initiative, the Biologics Section of Novartis Pharma AG in Switzerland created an automation laboratory to prepare and screen antibody formulations, meeting the high throughput demands of its analytical workload. Principal Scientist Olivier Graf explained: "To cope with the ever-increasing sample numbers, we had two options; introduce automation, or outsource the analysis to an external service provider. We chose automation, giving us full control of our data, and speeding up sample preparation, integration and delivery of results to our clients. Automation is more cost-effective and avoids the need to transfer methods to an external company, which can be complicated and time consuming, particularly if different chromatographic data systems are in use."

"We began collaborating with the Tecan Integration Group (TIG) around mid-2010, and the project took about a year to complete. We already knew which analytical instruments and modules we needed to incorporate, and that our techniques were working well, but integrating everything into the system was still a considerable technical challenge. We needed a system that was as compact as possible, with error handling systems, macros that start the chromatographic data systems automatically, and data management capabilities; the robotics and third-party devices required made the system really complex. The TIG proposal was straightforward, incorporating all the third-party instruments and integrating them with the Tecan software."

Novartis chose a customized solution consisting of two Freedom EVO 200 systems coupled back-to-back, one dedicated to liquid handling for sample preparation, the other to logistics. The sample preparation platform is equipped with an eight-channel Liquid Handling Arm and a MultiChannel Arm™ (MCA) 96, as well as a Robotic Manipulator (RoMa) Arm for maneuvering plates. A RoMa Arm on the logistics platform enables transfer of 96-well sample plates via a Te-Link™ module to the sample preparation workstation for dilution, or to the analytical instruments for analysis. Integrated third-party modules — including barcode readers, a high speed thermoshaker, a shaker-incubator, a capper/decapper, a plate sealer, a centrifuge, and a plate hotel — enable complex preparation methods involving digestion, reduction and alkylation to be performed. For sample analysis, the system incorporates a UV/Vis spectrophotometer for quantification of proteins, a dynamic light scattering system for protein characterization, a capillary electrophoresis instrument, and five HPLCs. The entire set-up is controlled by Tecan's Pegasus software package.

Associate Scientist Sébastien Heitz continued: "We already had a Freedom EVO 200 liquid handling platform, which was chosen for its capability to handle RoboColumns® (Atoll) and increase the speed of the sample purification process. We receive antibody suspensions in BD Falcon™ tubes, purify them on this workstation using RoboColumns with Protein A, and then transfer them to our customized system for all the subsequent steps. The antibody solutions may or may not be formulated, or may contain excipients such as sucrose or trehalose, and the sample concentrations will also vary. This affects the viscosity of the solution. To address this issue, the new system has specialized liquid classes for our protocols. Working at maximum capacity, we carry out either one run of 192 samples or two runs of 96 samples in one week, depending on the run time of the analytical method."

Olivier added: "Pre-automation, we were limited by the number of samples we could handle. Fully automating our processes has allowed us to carry out all the projects in house in preference to outsourcing the work, with significant cost savings. We have employed additional staff, who focus on data interpretation rather than time-consuming manual pipetting and loading samples onto instruments, and can deal with even the smallest requests from our customers. Automation has also streamlined and simplified mobile phase preparation; instead of several analysts preparing the same mobile phase for different instruments, scientists simply request sample analysis and the results are available the next day."

"Working with TIG was fantastic. The team was really receptive to any last-minute changes, implementing these very quickly, and the software programmer was always highly proactive. It was all very straightforward, a really interesting and nice collaboration. With Tecan, we accomplished our big challenge; developing a customized, fully automated platform that does everything we need," concluded Olivier.

To find out more about Tecan's customized solutions, visit **www.tecan.com/tig**

To find out more about Novartis, visit **www.novartis.com/innovation/research-development/index.shtml**
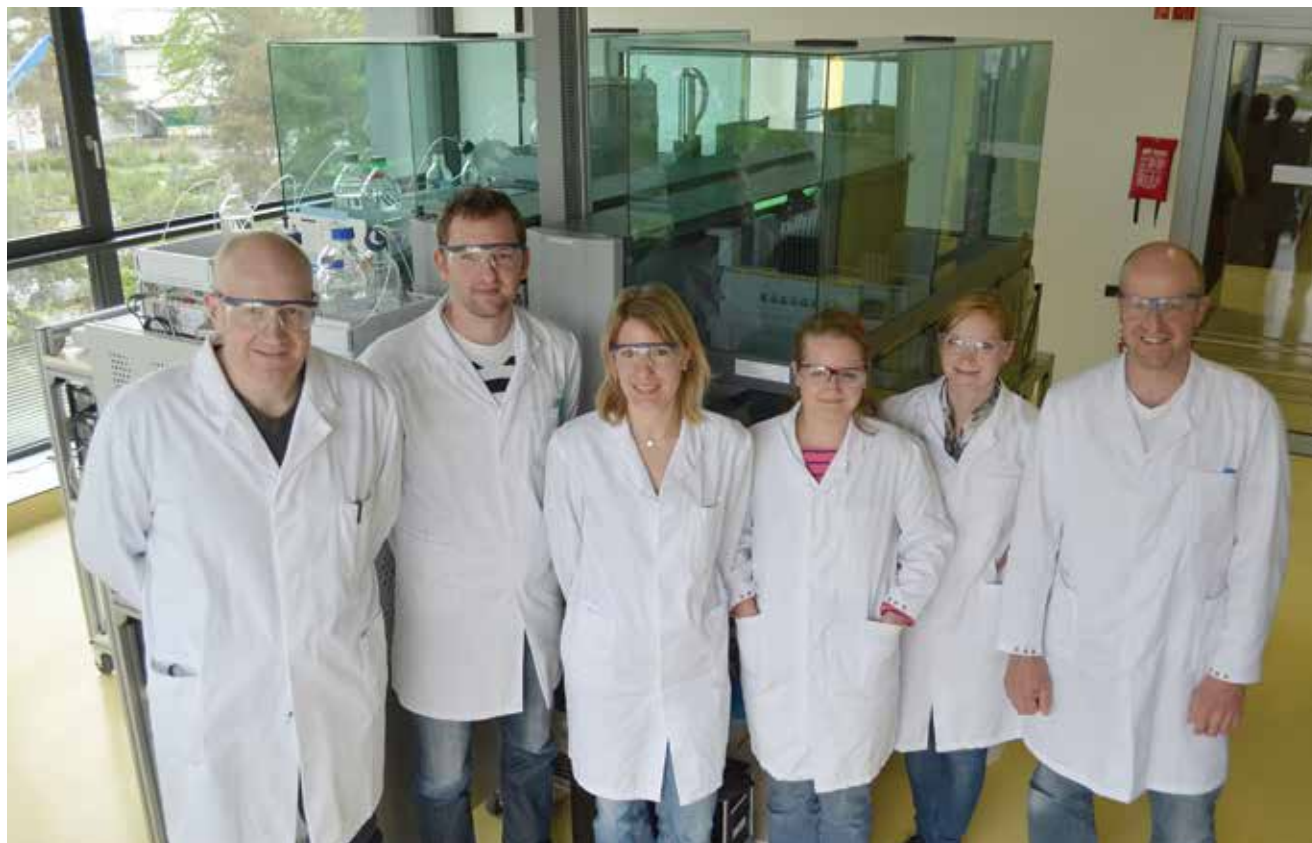
The Novartis team with its customized solution for antibody formulation screening. Left to right; Olivier Graf, Sébastien Heitz, Vanessa Seyfried, Sabine Dehm, Kim-Sarah Schneider, Gilles Thoma