Speeding up drug discovery

Production of dose-response plates and cherry-picking are essential steps in early drug discovery to enable testing of many thousands of compounds. Researchers at Novartis are benefitting from the automated plate generation capabilities of two customized systems based on Freedom EVO® 200 platforms, each equipped with an MCA 384, significantly increasing sample throughput to over 10,000 compounds a day.

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The Novartis Institutes for BioMedical Research (NIBR) screen hundreds of thousands of compounds for subsequent lead optimization in early stage drug discovery. To meet the demands of today's research, its Compound Management Group (CMG) in Basel, Switzerland, has embarked on a Compound Bank initiative to replace its existing hardware infrastructure, collaborating with Tecan to develop an automated system to deliver customized dose-response plates (DRPs). Frank Hoehn, a laboratory head within CMG, explained: "In 2009, we decided to replace the liquid handling module of our old Solution Archives (SolArs) system. We contacted a number of vendors, and Tecan offered us the opportunity to test a Freedom EVO platform with a MultiChannel Arm™ (MCA). The platform's small footprint and high efficiency made the Tecan system an attractive choice, and it also offered the best technical fit for our needs in terms of quality, throughput, variability and software capabilities. The Company's attitude also played a major part in our decision; the Tecan Integration Group (TIG) showed genuine interest and fully engaged with us."

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Yannick Gautier with the DRP system

The CMG purchased two identical DRP systems, designed for automated plating of compounds from Matrix storage tube racks into 96-, 384- and 1,536-well destination plates. Fully integrated with the Company's LIMS, each Freedom EVO platform is equipped with MCA 384, Liquid Handling (LiHa) and Robotic Manipulator (RoMa) Arms, as well as an integrated Cytomat® 24 hotel and docking station (Thermo Scientific), a PlateLoc® Thermal Microplate Sealer (Agilent), a Multidrop® Combi nL (Thermo Scientific) for bulk filling, an argon bath, a customized 96 piercing head, and a variety of MCA 384 adaptor plates. Research investigator Caroline Engeloch commented: "The MCA 384's adaptor plate concept gave us the flexibility to use both disposable tips and washable fixed tips, as well as to switch between 96- and 384-well formats, and we worked with the TIG team to design customized adaptors that can pick two or three rows or columns of tips simultaneously, increasing the throughput of the system. We also needed to be able to use fixed tips on the MCA to pipette directly from Matrix tubes in a 96-well format, without having to uncap and recap the tubes. This required a bespoke piercing head to transfer the entire contents of a 96-tube rack into a 96- or 384-well plate, and Tecan was the only vendor to offer a solution with the flexibility we were asking for."

Caroline continued: "After delivery of the system, we performed site acceptance testing, optimization and validation to ensure that the platform met all our requirements. With no specification to start from for the customized piercing head, there was a lot of

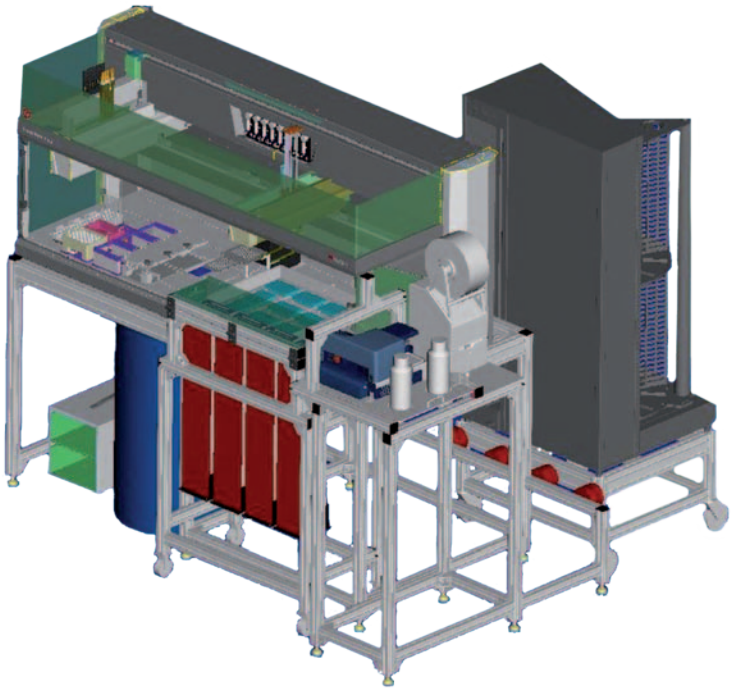
testing to be done, including quality control, reliability, variability and durability of the tips. The system also combines many different dispensing technologies to provide efficient generation of high quality plates and we collaborated closely with Tecan to optimize pipetting and tip washing conditions for our needs, minimizing the volume of wash solution required and reducing cross-contamination."

"The Freedom EVO-based platforms are far more flexible than our old system. The user-friendly software allows us to change and adapt the workflow to our needs, and we can implement new dose-response plate layouts much more quickly. We are also happy with the support we receive and the ease with which we can introduce new protocols; we occasionally need to contact Tecan, but we can implement most of the changes ourselves. This gives us confidence that the system is reliable and working as it should, increasing our productivity and ensuring we can meet our customers' deadlines."

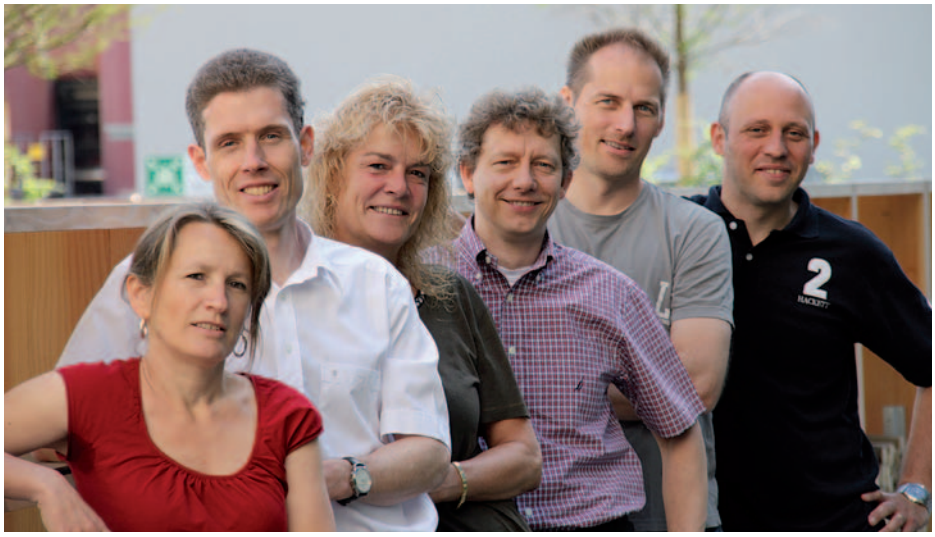
Frank concluded: "Our system is now operational and in routine use, and during the test phase we were able to process 5,000 hits per DRP module – 10,000 per day – increasing our throughput five- to six-fold compared to our old SolArs system. Our goal now is to have the same DRP system on both sides of the Atlantic, helping us to more closely align our processes, and so a similar platform is currently being planned for our site in Cambridge, USA."

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

To find out more about the NIBR, visit **www.nibr.com**



A 3D representation of the Novartis DRP system



The DRP project team. Left to right: Caroline Engeloch, Daniel Baeschlin, Ingrid Beuttenmueller, Frank Hoehn, Thomas Steiner and Yannick Gautier