

High throughput screening (HTS) systems at Boehringer Ingelheim

The Tecan Integration Group (TIG) is currently putting together Boehringer Ingelheim's third fully automated TRAC™-based screening system to meet the growing throughput needs of the screening laboratories at its principal research site in Biberach, Germany.



The HTS automation support team (l to r): Helga Steiner, Michael Karnath and Robert Ries

As one of the world's top pharmaceutical companies, Boehringer Ingelheim invests heavily in research and development, and its laboratories at Biberach are currently focusing on three therapeutic areas: diseases of the CNS, metabolic disorders and respiratory illnesses. The high throughput screening (HTS) group, led by Dr Martin J Valler, is involved in a range of essential functions associated with lead discovery, including assay adaptation, primary screening, dose response, secondary assay development and secondary screening. The HTS automation support team is led by Robert Ries. "We cover automation support for all three screening laboratories here in Biberach. We run our fully automated HTS systems 24 hours a day, five days a week," Robert explained. "The research laboratories design the assay, and it is the day-to-day task of the four of us within the HTS group to program the automated systems to perform the assays to their specifications and required throughput. Throughput is important, because these assays are based on compound libraries from the Boehringer compound collection. There are about 950,000 compounds which we have to test for each disease target, so we require throughputs of between 50,000 and 100,000 datapoints in 24 hours, depending on the assay type. We handle many different screening projects, with different requirements, assay types and technologies, so flexibility in our automation infrastructure is essential in order to support all these demands."

All three TRAC systems in the HTS group are highly customized with numerous integrated devices, and have been designed to have both a very high throughput and flexibility. Operational since 2005, the first of the systems is configured to automate 384-well microtiter plate-based high content screening (HCS) assays, and has a throughput of approximately 40 plates per 24 hours. A Thermo robot is responsible for the plate movement within the system, with a Tecan Freedom EVO® workstation and a Te-MO™ 384 pipetting device for liquid handling.

The second system has been operational since September 2006, and is designed for high throughput cell-based screening, and for biochemical assays in 384- and 1,536-well formats. Per 24 hours, it is capable of a throughput of two hundred and twenty 384-well plates, or more than sixty 1,536-well plates. In addition, this system has integrated storage devices, including cell incubators, to maintain all the assay and compound plates within the system for a 24 hour run.

The new system currently being built by Tecan in Männedorf will be configured for radioactive, biochemical and cell-based assays. A radiometric imaging reader is integrated for radioactive assays, and the concept includes all relevant precautions, such as radioactive shielding.

“TIG is perfect for our customized solutions, because we need a high level of customization in order to truly fulfil all our requirements,” continued Robert. “Very few companies on the market have the flexibility and capability to achieve this high level of customization. Tecan’s inherent flexibility allows us to quickly integrate new devices or replace devices, so that we can upgrade each of our systems at a future date. This is an essential advantage of the TRAC concept because we need to be able to use new technology and new devices as they become available, and particularly to accommodate miniaturization. Over the years we have rapidly miniaturized our assays; we started by using 96-well plates but by 1998 we were using 384 wells and

by 2005 we had progressed to 1,536 as an option. We have to keep up with the very fast pace of progress and, for the smooth and efficient integration of new devices it is important for us to have a partner like TIG.”

“Furthermore, Tecan has FACTS™, a very powerful flexible and modular scheduling software, which allows the integration of every device and technology you might need, including third party devices, whereas most companies are only interested in integrating their own devices. With our long experience in screening automation technology we have our own preferred technologies and devices which are not available from a single company, so it is a great advantage for us to have a partner like TIG to help us

realize the automation and integration of all these components.”

“Service is a vital aspect for us. We need a fast and competent service because our systems need to be as reliable and as stable as possible, so support with a short response time is very important. We have support from both Germany and the TIG in Männedorf, where all the engineers for the mechanical, electrical and software development are available for us. In my experience over the last nine years, each system needs an upgrade every one or two years, and this is a never-ending story. So, just in order to do the development, it is so important to have a stable partner for the future.” Robert concluded: “In this respect, TIG has been ideal for our purposes.”



High throughput screening at Boehringer Ingelheim: robots at work