

Integrated nanoliter dispensing aids drug discovery

Scientists in the ADME Screening, Enzymology and Automation Group at Roche, Switzerland, have successfully integrated a mosquito® nanoliter liquid handling instrument with a Freedom EVO® platform, enabling accurate, precise pipetting at very low volumes.



Pascal Schenk with the Group's Freedom EVO system



The Roche ADME Screening, Enzymology and Automation Group, based in Basel, relies heavily on laboratory automation to efficiently deliver high quality experimental data. Accurate and precise pipetting, sometimes of nanoliter volumes, is required to perform the Group's assays, as Automation Specialist Pascal Schenk, explained: "Test compounds are delivered in DMSO, and this has implications for our enzyme assays, where the overall DMSO concentration must be less than 0.5 %; the total volume of your experiment is dependent on the minimum volume of DMSO that can be accurately and precisely dispensed."

Pascal continued: "Our department has six Freedom EVO 200 platforms, each equipped with a MultiChannel Arm™ (MCA) g6, as well as Te-Stacks™ for nested disposable tips and microplates. We needed

to integrate a liquid handling system capable of dispensing nanoliter volumes with one of these workstations to enable pipetting of sample volumes of less than 1 µl; the mosquito nanoliter liquid handling instrument (TTP Labtech) proved ideal. As the first ever integration of such a system with a Freedom EVO platform, this required a driver to enable communication between the two instruments. We have a very good relationship with the Tecan Integration Group (TIG); the team wrote a driver in just a couple of weeks."

"Integration of the mosquito with a Freedom EVO was a really straightforward process, and was carried out in house. We validated the system by testing a range of liquid classes – including DMSO, acetonitrile, methanol, and aqueous buffer solutions – with both the Liquid Handling (LiHa) Arm and the MCA, as well as calibrating the mosquito for DMSO, checking the accuracy and precision of pipetting to ensure that the correct volumes were dispensed. For our current assays, we use a sample volume of 250 nL, which is easily achievable with a CV of 1 % for both accuracy and precision, and the mosquito's positive displacement pipetting also allows us to dry dispense as little as 25 nL of our test compounds."

"We use the system to prepare assay-ready plates, dispensing 100 nL aliquots of test compounds directly into microplates for screening, as well as generating standard curves. The enzyme reagents used for these procedures can be very expensive and are sometimes in short supply. Integrating the mosquito with the Freedom EVO has enabled the total assay volume to be reduced, significantly decreasing the amount of test compound and other reagents required. Through careful selection of labware and the use of appropriate tips, we had already



“TIG wrote a driver in just a couple of weeks.”

managed to reduce compound requirements from 200 μl per assay to 20-50 μl . Using the mosquito system, just 5 μl is now sufficient to enable serial dilutions to be prepared, delivering further material and cost savings.”

“In addition to enzyme assays, we also assess compound solubility. For the final step in the process, samples are diluted at least 1,000-fold for analysis by mass spectrometry, and the integrated system is ideal for this,” Pascal added. The plate containing the samples for dilution is placed directly on the mosquito, along with a second 384-well plate from the Freedom EVO’s Te-Stack, transferred to the system by the Robotic Manipulator (RoMa) Arm. A low volume of test compound is dispensed into the second plate before the RoMa transfers it to the workdeck of the Freedom EVO, where dilution is performed using the MCA. The MCA allows us to add 200 μl of reagent to the sample, enabling dilution to be performed by dispensing just one large volume of the dilution solvent, rather than by serial dilutions.”

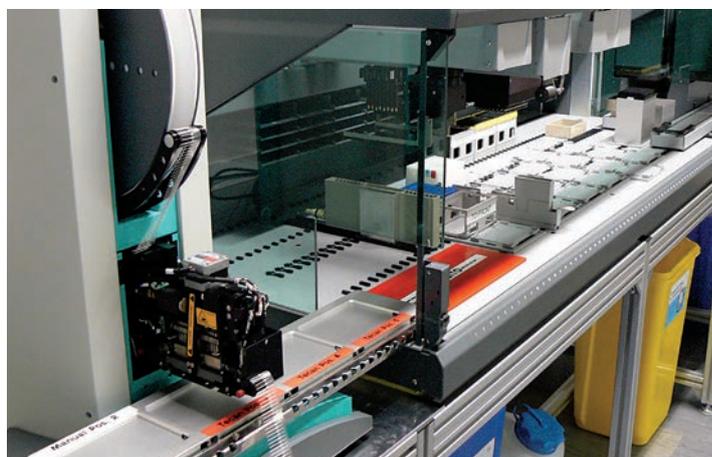
“The driver TIG developed allows us to control everything from Freedom EVOware®, including initializing the mosquito scripts and specifying which of its five deck positions the RoMa should transfer a plate to. To oversee the status of a run, we simply open the mosquito software and the Freedom EVOware side-by-side on the monitor, enabling us to observe both instruments. We have been using the system for almost a year now, and

it is working very well. The project has been a great success,” concluded Pascal.

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

For more information on TTP Labtech’s mosquito, go to www.ttplabtech.com

To learn more about Roche, visit www.roche.com



The mosquito system has been fully integrated into the Freedom EVO workstation



The mosquito provides positive displacement pipetting down to 25 nl