

From the Medicinal Chemist's Bench to the Assay Plate

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Introduction

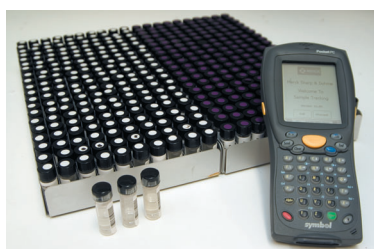
With the increased need to reduce the turn-around time from when a compound is synthesised to when target, off target and ADME assay data becomes available to medicinal chemistry programs, there is a need for the reliable and rapid flow of samples from the chemistry laboratories into a variety of assay ready plates. To meet these needs we have introduced a streamlined process for collecting, storing and cherry picking samples from our medicinal chemistry teams.

Collection and reformatting of samples

The samples are prepared as DMSO solutions by the chemist in vials with coloured dots to identify the primary assay and a bar-code label containing the Merck corporate identifier, L-XXXXXXXX-000A001.

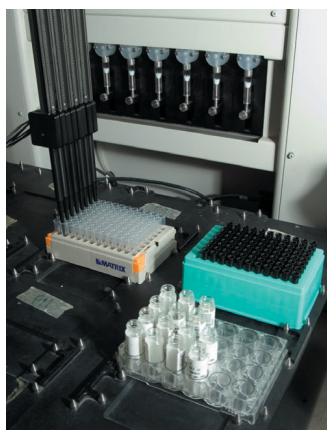
The samples are collected during a daily round of the labs and are scanned using a handheld bar code reader which logs the lab, the L-number and the primary target assay at point of collection (Figure 1).

Figure 1 Samples and handheld bar code reader



The DMSO solutions are then transferred to Matrix 1.4ml 2D coded V-bottomed tubes using the 8-span liquid sensing probe of a Beckman Biomek FX with disposable tips (Figure 2), generally 200ul of a 10mM solution are transferred.

Figure 2 Beckman Biomek FX with disposable tips

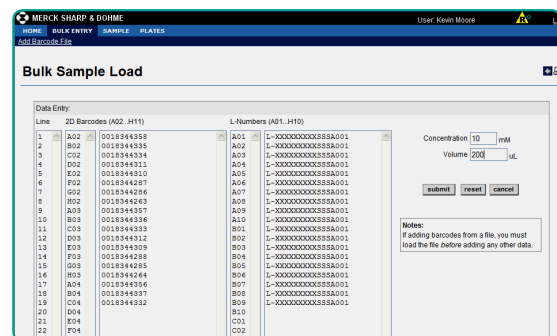


Database

A key part of the process is the in house built database (autopicker) that associates the L-number with the 2D bar code on the tube. This software is web based and is therefore available on any office PC. In order to make the initial link between the L-number with the 2D bar code, a rack of tubes is scanned using commercially available scanner and decoder software whose output is a text file containing both the decoded 2D barcode and the tube location in the rack.

The input page of the database allows for the input of this text file and then the L-numbers can be scanned in directly from the bar code label on the vial into the database hence the link is made between the 2D tube code and the L-number (Figure 3). At this point both the concentration and the load volume can also be entered.

Figure 3 Input page of database



Loading the tubes in to ComPOUND

Once the tubes have been filled they are transferred to be stored in our tube storage system. For this we chose ComPOUND from TTP LabTech. ComPOUND can hold up to 100,000 tubes which are stored in a controlled environment (nitrogen atmosphere from ambient to -20°C). The primary unit is the ComPOUND storage module which can operate either alone or with other units where larger storage capacity or higher throughput is required. ComPOUND software provides an easy and foolproof interface between the module(s) and any existing LIMS or Compound Management System. ComPILER is a remote arrayer unit that assembles racks up to 15m away from the ComPOUND module: it can easily be automated as part of a secondary robotic platform. In our case it's integrated with a Hamilton Swap and three hotels (ComMOTION) allowing for 24 96-well tubes boxes to be handled without human intervention (Figures 4 & 5).

Figure 4 ComPOUND / ComMOTION combination

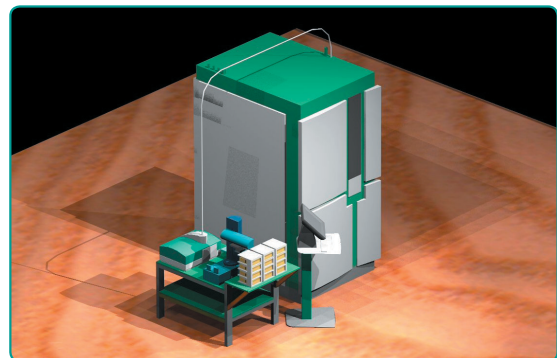
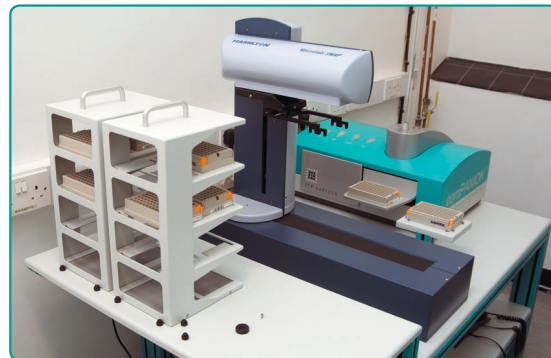
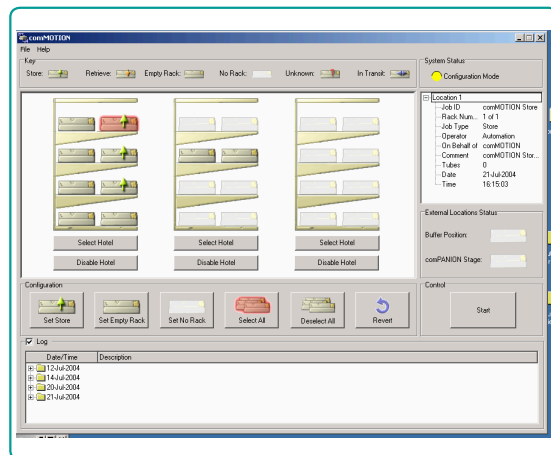


Figure 5 ComMOTION



The ComPOUND / ComMOTION combination is controlled by a single PC with a touch screen. To store samples it is simply a matter of configuring the very visual interface (Figure 6) with the number of tube boxes to store and then touch start.

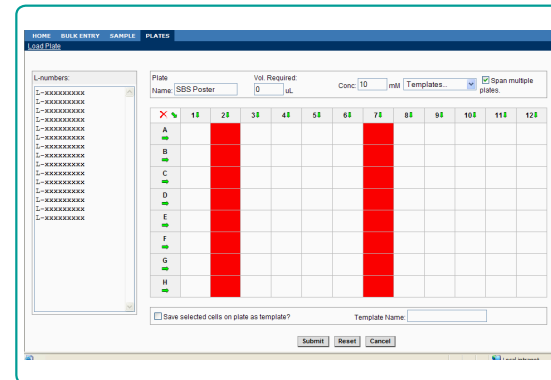
Figure 6 PC touch screen



Retrieval of tubes for ComPOUND

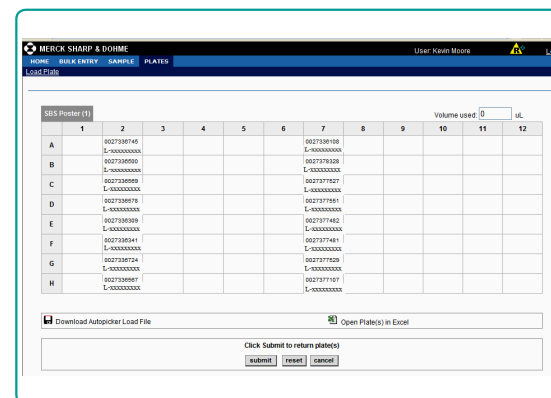
In order to retrieve samples to be plated out for assays, it is first necessary to place an order in the autopicker database, from our office PC a list of L-numbers from any source can be copied into the order page, at this stage you can pick the tube layout in the box and the volume you wish to remove (Figure 7).

Figure 7 Order page



The database gives you a visual plate map (Figure 8) containing the 2D identifier and the L-number, this information can be exported to Excel. At this stage the database can automatically send the order text file to ComPOUND, which will either process the order on receipt or schedule it to run later if it is already running a job. The racks are outputted to the hotels.

Figure 8 Visual plate map



From Tube to Assay plate

The tube racks are then plated on the Beckman Biomek FX (Figure 9), using the 8-span probe (Figure 10) and by running predetermined assay specific programs the 384-well & 96-well assay plates are prepared. These plates are sealed and delivered to the assay team. The tubes are returned to ComPOUND using the same procedure as described above.

Figure 9 Biomek FX



Figure 10 Beckman Biomek FX with deck set out for assay plate preparation



Conclusions

The use of 2D bar-coded tubes along with the combination of ComPOUND / ComMOTION, a Beckman Biomek FX and an in-house built database has allowed us to streamline the process to store, retrieve, prepare assay ready plates and store again.

Acknowledgements

We would like to thank the whole TTP LabTech team under the leadership of Dr. Jas Sanghera for their hard work and dedication in providing us with the ComPOUND / ComMOTION combination which evolved to meet our needs.