

Sample Management Special Interest Group Meeting Minutes

Session Chair: David Burns, Abbott Laboratories.

Speaker: Peter Woods, The Automation Partnership,
“Trends in Compound Management from a Systems Perspective”

Peter described that the main driver has been scaling up the quantity of compounds dispensed for most compound management systems. There has always been pressure to deliver materials in a timely and cost efficient manner from vast inventories of compounds contained in multiple systems. Some compound management systems are local to a company, some are global and others centralized. Coordination of systems across multiple sites is critical for an effective drug discovery organization. The responsiveness and flexibility of these compound management systems is always a challenge; especially today given the cost pressures of the pharmaceutical and biotech industry. Peter also mentions that other factors need to be considered when determining the appropriate delivery times for samples. The time to deliver samples is not determined exclusively by the automation hardware. Rather, integration of ordering interfaces, the inventory model and the order validation process all contribute to throughput determinations.

In his presentation, Peter mentioned that there are new demands being introduced due to the attrition rate of potential new drugs from clinical trials. Picking for *in silico* screening, support of chemical profiling and the evolution of compound libraries also will put pressure on the compound management systems. But, the efficiency of these new systems has shifted the bottlenecks back to the assay groups. Compound purity is increasingly becoming important and should always be considered when creating new systems. Pharmaceutical mergers have created logistical problems related to the multiple sites that contain various compound libraries. Thus, there is an important requirement to properly address the infrastructure needs to manage these multiple libraries and consolidate them. Should there be a central hub for the entire library? Should there be a local storage of the library at each site? These questions must be considered when creating compound management systems.

Speaker: Collette Dechard, Merck
“Zeus – An Automated Compound Distribution Center”

Collette described Zeus, the Merck automated compound management system. The system is housed in a very large building specifically designed and built for compound management and took four years to complete. The actual automated platform was designed by The Automation Partnership and is the central repository for all of Merck’s compound collection. Hence the system must service all nine different Merck HTS sites.

Logistically, dry samples are introduced into the system from either an outside compound vendor or internal scientists. These are then transferred to a manual dry store or to the Haywain™ dry sample weighing system before transfer into the automated dry storage system. Samples are requested and processed for delivery via weighing systems before being staged and shipped to the requestor. Samples

can also be weighed for solubilization for single compound/well plate replication – this is typically done annually. Currently, the automated dry storage system contains approximately 3 million tubes and can be used for ad hoc sample requests, secondary requests and PROSET production. The Zeus system is set up as “islands of automation” that allow the flow of samples to proceed around and through an integrated, software-controlled laboratory. The system is flexible, redundant, robust and high throughput. Approximately, 1.2 million samples were dispensed and shipped to Merck’s multiple HTS sites throughout the world.

At the end of her presentation Collette asked the following question “What’s next?” Should screening be centralized or decentralized? Should compounds be screened as mixtures or singles? What aliquot sizes and plate formats should be used. Some of these questions were discussed at the round-table session of this SIG meeting.

Speaker: James Craven, RTS Life Sciences
Tube Picking – How Fast is Fast Enough?

James discussed the new picking system that is being developed at RTS Life Sciences for 384 mini-tube picking. The current picking systems used by RTS are the ABB Flexpickers used to pick tubes from a 96-tube format. These robotic systems are good for the larger tubes but have difficulty picking the 384 mini-tubes currently coming onto the market. The ABB Flexpickers are best suited for sample libraries of around 1 million samples, but prove a slower option for libraries closer to 5 million samples.

RTS has been developing a new picking head that pushes tubes from the top of the source 384 tube plate thru to a receiver plate positioned below. The receiver plate is shifted to an open position on the receiver plate as more tubes are picked until it is full. Picking is very fast during the beginning of picking but slows as more samples are picked since the receiver plate needs to be moved to open locations more frequently.

Original designs were larger picking heads but RTS has settled at a 3 x 3 pin matrix. This matrix is less complex but the picking rate is far lower. It remains to be seen if this is a problem for future compound picking requirements.

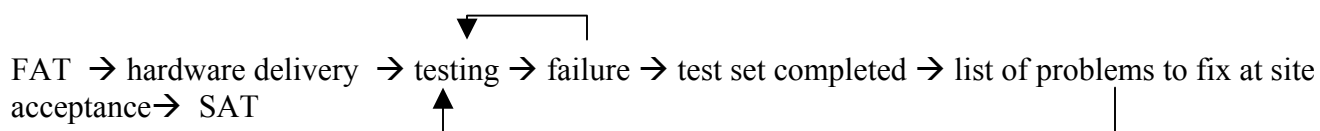
Speaker: Ulrich Schopfler – Novartis
Automated Solution Production – The Project Management Prospective.

Ulrich described the automated storage and distribution system used by Novartis. It is a centralized compound storage operation that is used for dry compound storage and general sample distribution. Compounds are added to the dry store using an automated weighing system to place compounds in a cleverly designed vial with a screw-topped lid for subsequent creation of liquid compound samples. The focus of the Novartis compound management team has always been on quality of the samples entered into the system. Concentration, water content and compound stability are all factors that are considered before samples are introduced into the system. All of the samples entered into the collection are ultimately dissolved into DMSO:water at a 9:1 ratio and stored in the system at 20% RH at 4 deg. C. Compound stability studies designed by the Novartis team indicated that solubility

was the number one concern related to compound storage. Hence, stock solutions from the system have between a three-year life cycle and a six-year life cycle before new powders are used for replacement. During that time frame, suspect compounds are weeded out of the library as rules for excluding compounds are reviewed and often revised. Samples that are water labile are excluded as are compounds that violate Lipinski's rules, as are the following types of compounds: dyes, mercury salts, well know compounds such as beta-lactams and other antibiotics, and many combichem compounds.

Approximately, 200,000 fresh solutions are prepared each year, which essentially refreshes the library every six years. The system uses an automated weighing station utilizing specific vials that include an Archimedes screw in the cap. Sample vials are turned upside down so that the powders are in contact with the cap. The screw is turned by automation and sample is transported out of the vial into a weighing station. Tars, oils and troublesome compounds are not on the system and are weighed by hand. The system reduces the timeframe for processing powders to solutions from 5-6 months to 3-4 weeks. New user requirements are causing challenges for the system. Glass vs. plastic tubes, etc.

Ulrich outlined the process of acceptance for the system.



Any failure at one of the testing steps can set back the acceptance of the system. Hopefully, rigorous testing will prevent any extended delays for the final acceptance.