Adapting for Changing Demands in Compound Management:

with the Brooks Universal LabStore

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"The Compound Management Group designed this amazing storage automation system, made a big investment, and thought it knew exactly what it wanted to do. But when the team started using the system, it found out some things had been missed. This is how the group has adapted the storage system from the time it was purchased."

The Broad Institute is a non-profit research organization in Cambridge, Massachusetts. It was founded 10 years ago by Eli and Edith Broad. The institute is associated with Harvard University, Massachusetts Institute of Technology, and many of the Boston-area hospitals. It has a very collaborative environment.

The Broad Institute is organized into platforms and programs. The programs involve scientific research, and the platforms are the technology groups that support the research. The Compound Management Group is part of the Therapeutic Platform. It has a collection of about 100,000 unique small molecule samples. The group also has some commercially available compounds and other samples created for the medicinal chemistry groups. The Broad has a diverse group of people who access these samples and compounds. Along with the medicinal chemistry groups, the Compound Management Group has many external collaborations. It also has its own internal screening group.

When the original screening lab was designed, the idea was to put drug discovery in one room (see figure 1). There are three integrated High-Res Biosolutions systems for screening, a compound management system, and long-term compound storage. This layout allows a lot of flexibility and enables all compound management and screening in one room. The instruments are on carts and can move from system to system very easily. This project was completed in 2008. At that time, the group also moved from sample tracking in Excel spreadsheets to tracking with an informatics system.

A Brooks LabStore 450 long-term store houses the glass master tubes. All of the compound management was designed around a diversity -oriented synthesis (DOS) library of 100,000 small molecules. These samples were all made using solid-phase synthesis. They were in small quantities and were stored in smaller tubes. The compounds are all dry, and the store was specifically purchased to house them.

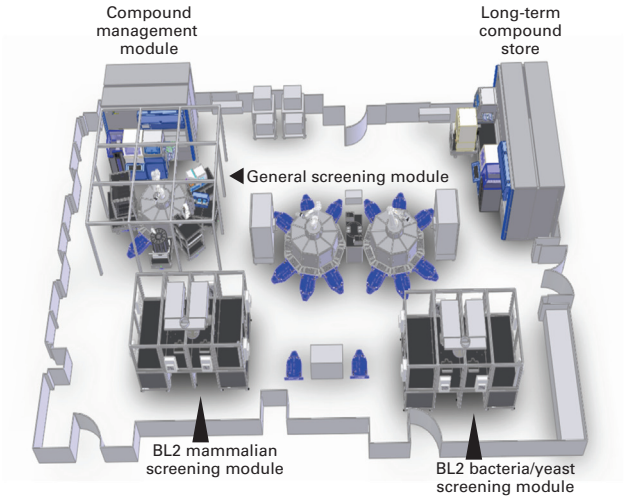

Figure 1: Original Broad screening lab workflow.

Things Went Well for a While

Originally, there was an automation interface on the store with a robotic arm and dock. A technician could roll up a carousel next to the store and pick racks of compounds. After a while, it was clear that compounds were not being accessed as frequently as expected, the picker was very slow, and samples could not be removed any faster with the IO station. So the robotic arm picking system was discarded.

The lab uses Matrix tubes for liquid stock working volumes. There is another store that houses those compounds. It's connected to a six-dock Microstar system. The team can put many different instruments on this system — liquid handlers, cappers, plates sealers, and peelers. Much of the liquid handling is done there. The lab does transfers from master tubes into mother tubes, performs solvent transfers, makes screening libraries, and produces assay-ready plates — all on this system. This workflow started operating in 2008.

Things went well for a while. But the workload with medicinal chemistry groups started to increase and they were creating compounds in much larger quantities. The lab needed a larger container and started using 1-gram, 2D bar coded glass vials. At first, they were stored in racks in a freezer. But that process got unwieldy very quickly. The group also had trouble tracking their locations and things were getting lost.

So the team started loading the vials into trays and putting them into the LabStore 450. Everything was already set up in the informatics system, allowing the inventory to be tracked. But the vials had to be picked manually for retrieval. That work involved using a query tool on the computer. A list of compound bar codes would be entered and a printout of the desired trays and their locations was generated. The trays would be pulled and a technician would find and pick the vials. The process, which was used for several years, was slow, tedious, and highly error-prone. Plus, entire trays of vials were defrosted to retrieve one compound.

Over the last few years, the number of compound requests has gone up dramatically. The group was getting more requests, and it has larger numbers of vials. Picking 60 compounds manually became very difficult. The 100,000-compound DOS library was also nearing completion and the new compounds were arriving in vials. The team reached a point where it had 28,000 vials in the store that were picked manually.

The manual picking was slowing turnaround time. In 2012, for non-urgent samples, turnaround time had reached 15 to 20 days because of the backlog. The group realized it needed an automated process to retrieve the vials.

No Longer a Dreaded Task

When the DOS library production stopped, some extra lab space came available that could be used for a vial store. But lab space was at a premium and room was also needed for liquid handlers and work space. Brooks was asked about adding the capability to pick vials out of the existing LabStore, since it was only about one-third full. After removing the old automation interface, another screening system was built in front of the store. This worked well for the screeners, but made storage access difficult. So the vial picker was placed in the corner of the lab.

When the group started the installation, it had to upgrade the lab's software to support the new hardware. This work required about 4 days and was completed in May 2013. The vial picker was installed in June and needed about 3 days to install and test.

Now, picking vials is no longer a dreaded task. In the past, there were problems with multiple people picking vials at the same time. It was almost impossible to keep things straight. The new picker, plus some other changes, has cut the previous 20-day turnaround time to less than 1 week (see figure 2). It has also eliminated any picking errors.

In closing, the group did encounter two issues in the transition that caused picking errors. First, automated picking wasn't anticipated when the first vials were loaded in the store. Many of the chemists were not used to working with bar codes and taped paper labels on the side of the vials. The labels caused the vials to stick in the tray. They also would parafilm the vial cap, which also caused picking problems.

Question: Why is the new turnaround time 5 days and not quicker?

Corrie: That is the average turnaround time. It includes large jobs such as making assay plates for our entire 100,000-plate library. Many of our picks are faster. Smaller orders take only 1 or 2 days.

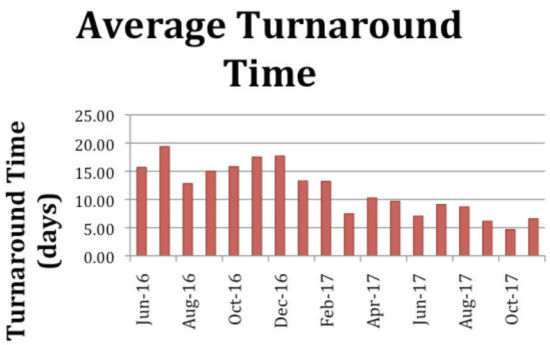

Figure 2: Average turnaround time dropped from almost 20 days to under 1 week.

About the Author

Corrie Aghia is a senior research associate in the Compound Management Group at the Broad Institute. She also worked as an automation engineer in ArQule's discovery department. Corrie received a bachelor of science degree in biomedical engineering from Boston University.

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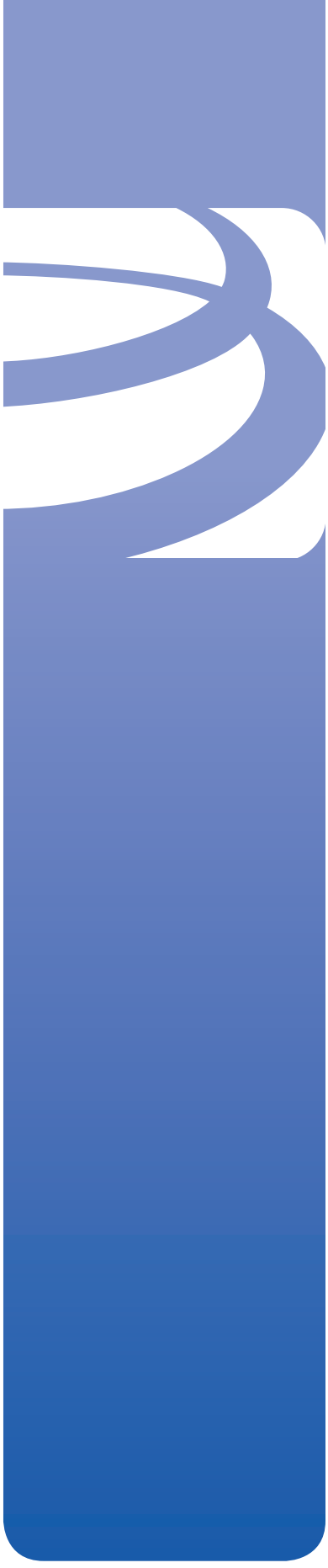

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