

comPOUND D2: a simple approach to increasing store capacity

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Introduction

Storage and delivery of compounds for pharmaceutical research is a complex and dynamic process. Designing and implementing an automated storage and retrieval system must encompass many important requirements, such as cost, flexibility, sample integrity, throughput, current and future size of compound library, storage vessels being used, and its physical location within the screening facility.

Most storage technologies try to meet all these criteria, but this often leads to compromises and a lack of flexibility, particularly when facing marked increases in the number of samples and changes within the companies needs.

The comPOUND® modular tube store (TTP LabTech) is a flexible, self-contained system that can be installed almost anywhere, and is easily expanded. Samples are stored individually in a dark, dry and inert environment, enabling library subsets to be selected using high-speed cherry-picking.

This poster discusses how the comPOUND D2 store has been configured at Millennium: The Takeda Oncology Company with other automated systems to meet the varied demands of a robust and growing pipeline of investigational drug candidates.

1. comPOUND D2: Providing Sample Integrity

The comPOUND store provides a secure environment to maintain the integrity of collections of precious material. Samples are stored individually under nitrogen in a hermetically sealed chamber at -20°C; providing a dark, dry and inert environment.

Individual storage of tubes allows true cherry-picking, so unwanted samples are not disturbed. Cherry-picking times are absolute, so campaigns can be forecast accurately.

Each comPOUND module stores 100,000 x 1.4 ml or 200,000 x 0.5 ml microtubes, or a mixture of both for maximum flexibility. comPOUND modules track every tube by imaging their 2D barcodes on the way into the store and on the way out, making it impossible to obtain the wrong sample. This also allows each tube to be stored anywhere within the storage environment regardless of its contents.

Microtubes are delivered to racks at the front of the comPOUND module and can be automatically loaded on to a comSTACKER. This stacking unit expedites the loading and unloading of racks and allows for walk-away processes that can be run overnight. comPOUND's unique pneumatic transport system also allows it to deliver samples remotely. In some installations this feeds samples to an automated processing system, or it can deliver to a laboratory on a different floor of the building.

2. Growth of Storage Capacity at Millennium

Millennium Pharmaceuticals, Inc. introduced automated compound management in 2003 with their first two comPOUND modules, which were based at different sites in the US and UK to support lead optimization. Each of these initial stores was a D1 module, holding up to 100,000 1.4 ml tubes.

The Compound Management department was centralised in the US in 2005 and the UK system was relocated to Cambridge, MA, to house both chemical and biological libraries. At the same time, both comPOUND modules were converted to D2 units – thus doubling the storage capacity available without involving a large capital expense. The upgrade process can readily be done in the field, without the need to thaw stored samples, as it involves modifications to only the front indexer and turntable which are both outside the environmentally-controlled interior.

Since then, Millennium have added a further two comPOUND D2 modules to provide a maximum library capacity of 800,000 tubes.

3. Compound Management at Millennium



Millennium currently store around 410,000 tubes which are a mixture of 1.4 ml and 0.5 ml sizes. The 1.4 ml tubes are generated from internally synthesized compounds and 0.5 ml tubes are all new vendor compounds.

Having tubes at both half and full height maximizes storage capacity within each comPOUND module while maintaining sufficient volume for the expected compound life cycle.

The 4 comPOUND modules support both lead optimization and creating new HTS plates and focused libraries when necessary. Transferring from individually picked 2D tubes means only the samples required are pulled, avoiding unnecessary thaw cycles and allowing quicker cherry picking than from plates.

Previously, when Millennium picked 80 compounds they generally needed to pull 80 plates from storage. Now just the compounds needed are collected in one rack of 80 tubes ready for further processing. Racks of retrieved tubes can also be arrayed in user-specified formats to simplify subsequent automated plate creation. Each comPOUND module is equipped with a comSTACKER unit to facilitate overnight runs.

4. Further Developments to the Compound Management Process at Millennium

Millennium have recently introduced automated assay-ready plate preparation and plate storage to their processes to support the increasing demands of their HTS campaigns. The comPOUND modules continue to ensure the long term integrity of Millennium's chemical and biological libraries. The stores are used to generate mother plates for HTS campaigns, new formats for focussed libraries and to support lead optimisation – in short, they form the primary storage and fulfilment option for requests to Millennium's CM department.



Conclusion

Millennium Pharmaceuticals, Inc. have successfully implemented an automated compound management system that has had the flexibility to be expanded at a pace compatible with their growth over the last seven years.

The modular format of TTP LabTech's comPOUND system allows companies to control their investment in compound management according to their needs for library size, throughput, location and flexibility. Modules can easily be added and linked, or simply upgraded to increase storage capacity.