comPOUND: The Future of comPOUND Management

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Introduction

Current compound management practices have evolved to support both primary and secondary screening projects from a centralized repository storing a combination of plates and tubes.

Storage of both tube and plate formats is inefficient and adds to the complexity of these repositories, making them expensive to implement and more importantly difficult to expand or relocate. Also, new sample submission becomes a protracted process, which can lead to delays of several months before the samples are available for HTS.

Plate storage is usually considered the only way to support the throughput requirements of primary screening. However, plates compromise sample integrity by introducing uncontrolled exposure to the environment and multiple freeze/thaw cycles. In addition, quality control of plate based material is almost impossible. This causes false positives and negatives, which are not picked up until the secondary screening stage.

Plate storage also limits the flexibility of a library, requiring the entire library to be screened in each HTS campaign. A more efficient approach to primary screening would be to only screen against library subsets that are chemically relevant to the target, but this would require ultra high throughput cherry-picking of tubes.

In this poster we describe an innovative large-scale tube-based compound management approach to maximize lab space; improve compound stability; enable rapid generation of custom screening sets; while providing background QC and real time library integration of new chemical entities.

1. Compound storage past and present

In the past, compound storage systems were usually defined at the preliminary stages of procurement. The size of the library had to be known in advance of commissioning it. Due to legacy vessels, storage systems were often designed to accommodate multiple formats, which slows system throughput. As automation got smarter it became clear that standardizing on one storage vessel format made sense by increasing system reliability, improving throughput speeds and reducing the sample management burden.

Today, it is possible to specify the minimum requirements for an automated storage system. Many vendors provide 'modular' stores, allowing customers to upgrade and expand as they need to.

However, there still persists a misconception that, while the primary library compounds are stored in tubes to ensure sample integrity, quantities of each sample must then be transferred into plate storage ready to meet the throughputs required by screening.

2. Compound stability in tubes and plates

There are many factors that affect the quality of stored compound samples, including:

- Physical contaminants (dust)
- Decomposition due to light
- Concentration (evaporation)
- O_2 reactions
- H_2O dilutions or reactions
- Precipitation
- Freeze/thaw cycles

Keeping individual compound samples in tubes or plates in a cold, dark, dry and inert atmosphere will reduce all of these effects significantly enabling practical long term storage of samples.

However, defrosting and exposure to the atmosphere is still an area where sample integrity can be compromised. This issue is significantly reduced when cherry-picking individual tubes as *only* the sample of interest is removed from the storage system. With a plate *all* the samples in the plate must be thawed and exposed to gain access to an individual sample.

3. Compound storage for the future

The proven comPOUND automated storage system from TTP LabTech meets the requirements for maximising sample integrity whilst providing ultra high speed cherry picking of individual samples in microtubes.

Each comPOUND unit provides modular, self-contained storage so customers can add modules as their library requirements grow. ***Uniquely, adding more modules to a system actually increases the throughput rates.*** Samples can be delivered remotely so units do not need to be located in the lab.

4. Ultra high throughput cherry-picking

It is often thought that samples must be held in plate storage to meet the throughputs required with very large libraries. However, the comPOUND/comPILER system offers ultra high cherry-picking rates of only the samples needed for each screen, direct from the primary library, while preserving sample integrity.

Previously installed systems have demonstrated full processing of 20,000 tubes in an 8 hour period with only 10 comPOUND stores

5. Scaling up

The throughput of a comPOUND system quickly reaches steady state, so it is simple to scale up to 24 hour operation or to add more modules. The table illustrates possible throughputs:

No of stores	Library size[2]	Hours/day	Throughput
5	500,000	24	**30,000**
10	1,000,000	24	**60,000**
15	1,500,000	24	**90,000**
20	2,000,000	24	**120,000**

[2]Assuming 1.4mL tubes. Doubles for 500uL tubes

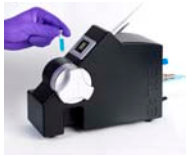
7. Maximising Lab Space

Large arrays of comPOUND stores can be distributed where it is convenient for the user. Sample tubes are then transported using pneumatic technology to the point of use.

7. Compound quality control

Delivering the right compound at the right time is only part of the process. Knowing the volume and quality of the compound is of equal importance and has been hard implement.

TTP LabTech's LAB2LAB system integrates with comPOUND to automatically take individual tubes from storage and send them to HPLC, GC/MS or NMR for analysis. Unexpected screening results can be quickly checked to provide full analytical feedback in a matter of minutes.



Conclusion

The proven comPOUND tube storage system offers true cherry-picking of samples at throughputs capable of satisfying the requirements for custom screen set generation.

Picking screen sets this way also preserves sample integrity both for the primary library and the subsets used for screening

Integration of comPOUND with LAB2LAB gives the end user full analytical capabilities.

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