

# Maintaining sample integrity during high throughput processing using a fully automated store-to-plate system

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## Abstract

Billions of pounds have been invested in the generation of large compound libraries by the pharmaceutical industry. Advances in technology have addressed the issues of storing large compound libraries in controlled conditions.

However, the increased demands on these libraries for high-throughput screening require constant processing of compounds in and out of storage, introducing another stage where sample integrity can be compromised.

TTP LabTech have designed comPILER, a fully automated store-to-plate processing system, which can be integrated with their cherry-picking comPOUND store to address the concerns of sample integrity in a high-throughput environment.

## Introduction

Sample integrity in library management and processing is a key concern for many pharmaceutical companies. Although DMSO is a good universal solvent for compound storage, its hygroscopic and volatile properties mean samples are prone to solubility and cross-contamination issues. This can lead to key drug candidates being missed (false negatives) or time and money being wasted on poor drug candidates (false positives).

The issues to be addressed to maintain sample integrity during high throughput processing are:

- thawing from -20°C without exceeding DMSO boiling point and degrading the sample
- ensuring all sample is collected at the base of the tube for access by a liquid handler
- coping with the hygroscopic properties of DMSO: is it better to decap samples and risk moisture ingress over the short term or pierce caps and risk imperfect cap resealing, allowing moisture ingress over the long term?
- cross contamination between samples.

## 1 Safe storage for libraries

Each comPOUND stores 100,000 samples in a self-contained sealed chamber refrigerated to -20°C, providing a dark, dry and inert environment. comPILER maintains a similar level of sample care throughout the thawing, decapping, reformatting and recapping stages.

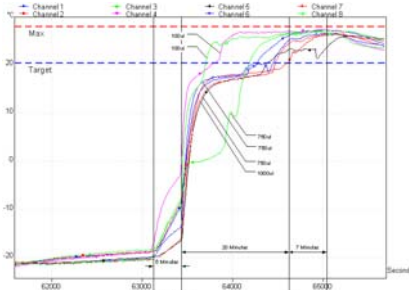
## 2 Sample throughput

comPILER can cherry-pick samples from 12 comPOUND stores at the same time, maximising throughput. It arrays a rack of 96 tubes in under 2 minutes. Each comPILER station can process a rack of 96 tubes in under 2 minutes with no operator intervention.



## 3 Sample care while thawing DMSO

If samples are thawed at too high a temperature, then smaller volumes can easily be heated past the boiling point of DMSO, resulting in degradation of the sample. TTP LabTech tested the response of DMSO while comPILER thawed samples from -20°C. The results below show the samples never exceed +27°C, regardless of the volume in the tube, and all samples reached +20°C with no crystals of frozen DMSO present.



## 4 Centrifuge

After thawing, comPILER's standard process centrifuges each cherry-picked racks of tubes to ensure:

- all sample is collected at the base of the tube ready for reformatting by a liquid handler
- no droplets of liquid are present on the cap when it is removed, to prevent cross-contamination.

## 5 Reliable automated decapping and recapping

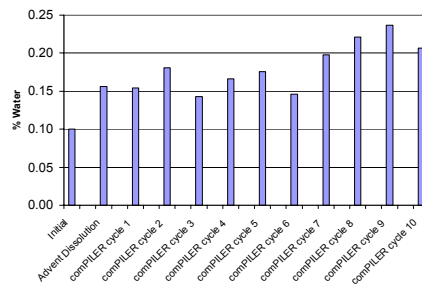
comPILER offers an automated decapping/recapping solution to sample access. The decapper removes caps a row at a time over capped microtubes to prevent any splashing into uncapped tubes. The rack is flushed with argon to form an inert 'plug' against moisture ingress. Racks are then passed to the reformatter. Once the reformatting is complete the rack passes to the recapper, where it is again purged with argon before new caps are stamped on and scanned to ensure correct fit.

This approach has the following advantages:

- high-speed automated decapping or recapping process takes less than 2 minutes
- inert gas 'plug' prevents moisture ingress
- the decapping process is design to prevent cross-contamination by splashing
- samples are uncapped for the minimum amount of time
- can decap and recap racks containing any number of tubes from 1 to 96
- no requirement for specialised septum piercing.

## 6 Measuring water uptake in DMSO by Karl Fischer titration

Wyeth devised a test to measure sample protection during processing by comPOUND/comPILER. They took samples from frozen storage, through the whole processing cycle and back to storage 10 times. Before storage on each cycle the percentage of water uptake in DMSO solvent was measured by Karl Fischer titration (results below). These data demonstrate that water uptake is negligible when samples are processed by comPILER, highlighting its effectiveness for repeated sample processing.



## Conclusion

comPOUND and comPILER have been successfully implemented at Wyeth to provide not only a secure library storage environment, but also to maintain sample integrity reliably while tubes are cherry-picked, processed, presented for reformatting, and then returned to storage.

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