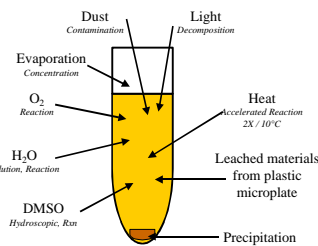


Minimizing Compound Exposure

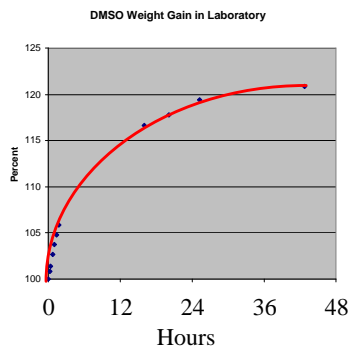
W. Steven Fillers, Ph.D., TekCel, Inc., Hopkinton, MA

Compound Exposure (Unsealed Microplate Well)



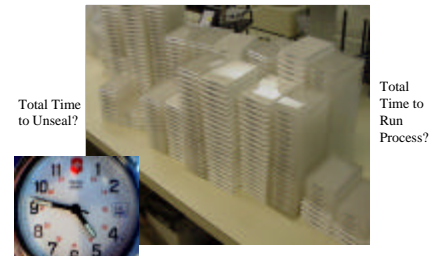
Introduction

The quality of a chemical compound stored in DMSO can be degraded by a wide variety of conditions that normally exist in the laboratory. TekCel introduces the SealTite seal for use in the PlateServer and PlateStore fully automated microplate storage and retrieval system designed to maximally preserve the compound library. Beyond the low temperature and inert atmosphere utilized for storage and processing, the TekCel system minimizes the time that compounds are exposed to the agents that compromise sample integrity.



Fresh DMSO is very hygroscopic, gaining 5% water in less than 2 hours exposure to normal laboratory atmosphere. The sample is almost saturated within 24 hours total exposure.

How Long Are Your Compounds Exposed? (Before and During Process)

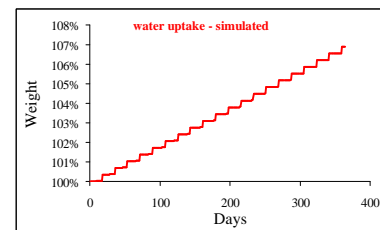


Total Time to Unseal?

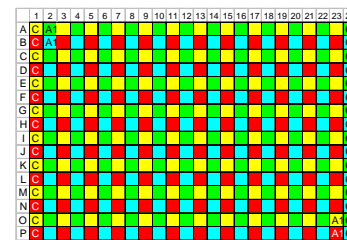
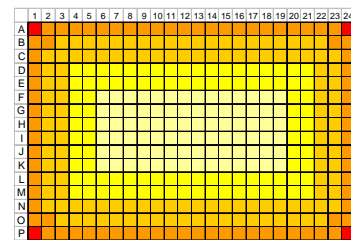
Total Time to Run Process?

Typical library replication processes involve removal of large numbers of sealed microplates from cold storage, time for temperature equilibration, time to manually removal of the seals, time for loading the microplates into the replication automation, time to run the replication automation process, time to reseal the microplates and then time to return to the storage location. During much of this time, the compounds are exposed to conditions that lead to degradation of the sample.

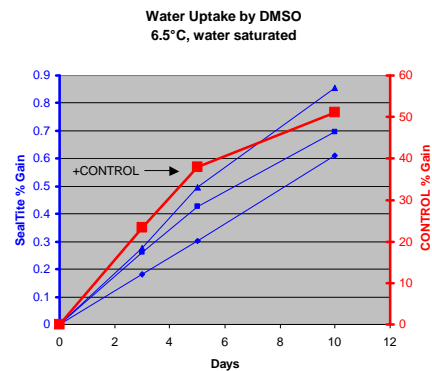
| Input | Result |
|------------------------------|----------------------------|
| closed rate 0.0014 g/day | 6.9% increase/year |
| open rate 1 g/day | 6.3% Increase while open |
| frequency of opening 18 days | 0.6% Increase while closed |
| Time open 6 hour | |



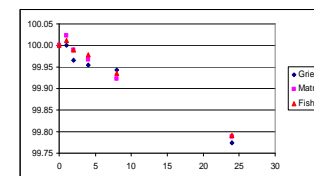
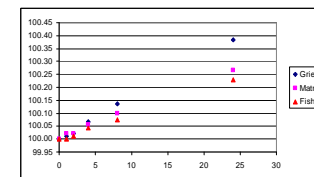
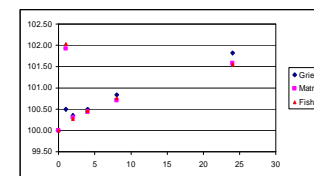
Most degradation occurs while the microplates are uncovered. This model represents the cumulative degradation across 20 screening campaigns during one year of storage. The vast majority of water uptake by DMSO occurs during the processing times when the storage microplates are uncovered. It is important to minimize the open time. (customer calculation)



Effects on sealed microplate samples have a characteristic pattern. Peripheral wells and especially the corner wells demonstrate the greatest changes while interior wells are minimally influenced. One approach to minimize some of these edge effects is to arrange empty control wells on the perimeter of the microplate. One example would be to invert two of the four source microplates when reformating into a 384-well configuration. In the figure above, note the locations of the A1 positions for each of the color coded 96-well source plates. The control wells are arranged on opposite ends of the new 384-well storage plate eliminating all corner positions and minimizing the number of samples stored on the edge of the microplate.



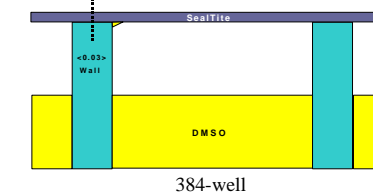
Storage conditions within a laboratory refrigerator represent a worst case scenario with regard to water uptake by DMSO. Unsealed samples will gain more than 40% in weight in just one week while SealTite sealed samples on average gain less than 0.5%.



SealTite effectively seals in extreme conditions. Fresh DMSO samples in a variety of 384-well microplates are sealed with SealTite and incubated for 24 hours at 37°C, 95%RH (top panel), 20°C, 45%RH (middle panel, compare to figure at far left), or 20°C, 10%RH (bottom panel). Data are weight as a % of initial weight. n=1 (customer data)



The TekCel HTS system provides low temperature storage and processing in an inert environment. Exposure of compound libraries is minimal due to the high level of integration of the storage automation to the assay process.



Cross contamination is minimal with the SealTite system.

1. TekCel automation does not agitate the microplates to the point of splashing sample onto the seal surface.
2. SealTite placement and removal is vertical which minimizes the spread of materials on the seal and the surface of the microplate.
3. The placement precision of SealTite in the PlateServer automation is within 0.01 of an inch, one third the width of the wall of a 384-well microplate.
4. Condensation on the seals is primarily solvent (pure DMSO).

Summary

1. Compound libraries must be protected from the laboratory environment.
2. Exposure time should be minimized.
3. No seal is perfect but careful management can maximize effectiveness
4. Cross contamination can be minimized
5. Fully automated storage and sample processing can be accomplished in inert atmospheres.

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