Frangible Seal Reagent Blisters Deliver Precision Performance to Point-of-Care Diagnostic Testing

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Frangible seal reagent blisters, Point-of-Care (POC) diagnostic testing, In Vitro Diagnostic (IVD) testing, medical diagnostics, precision diagnostics testing, unit-of-measure dispensing, custom blister reservoirs, diagnostics manufacturing

BACKGROUND

The continuing growth of Point-of-Care (POC) *In Vitro* Diagnostic (IVD) testing is supported by technology improvements and the recognition that rapid test results offer economic and patient outcome benefits. The integration of frangible seal reagent blisters into various technology platforms holds promise for more precise and reproducible results compared to currently accepted methods – an important consideration for any end-user. This paper examines the uniform processing and performance of J-Pac Medical's frangible seal Safe Seal™ blisters and compares burst seal strength and dispensing performance versus a conventional eyedropper method. To demonstrate J-Pac Medical's process control over given material sets, a single blister design was created with commercially available foil materials, filled and then sealed using different processing parameters.

SEAL STRENGTH CONTROL

J-Pac Medical manufactures custom blisters for the medical diagnostics industry, each according to specific application requirements. While each blister may have different configurations, shapes and volumes; each sealed blister is designed with differential seal strengths to either be permanent or break, distort, or yield on contact actuation or fail at a defined applied force and deliver a specific amount of fluid to a target. These seal strengths are a function of the material properties and applying unique sealing processes that are combinations of tooling, applied pressure, temperature and time to meet the seal specification.

There are several different types of materials that can be used to fabricate reagent blisters and generally can be described as specialized foils and laminates used for cold- and thermo-formed packaging. These materials have various thicknesses that can be applied to burst push-through, pierced, peelable, and hybrid peel-push barriers.

SEAL STRENGTH RESULTS

A series of identical-shaped blister test coupons were fabricated[1] to demonstrate a range of seal strengths and subjected to a metered tear-test[2]. The Minitab® graph below illustrates the testing results, highlighting three discreet populations of seal strengths that were created reproducibly by making adjustments in the processing parameters.

An understanding of these specialized material properties and processing allows the blister fabricator to "dial-in" the specific seal strength needed for activation but at specific threshold, e.g., not too fragile to rupture prematurely due to routine handling, assembly or shipping activities. This processing control of the seal strength allows the medical device manufacturer to have confidence that the reservoirs will release their contents under defined and controlled conditions. Additional levels of seal strength can be developed and optimized using different material sets and processing conditions, thereby expanding the selectivity of the activation range of the blisters.

PRECISION FILL AND DISPENSING CONTROL

J-Pac Medical's Safe Seal™ blisters are extremely well suited for precise unit-of-measure dispensing of liquids and other reagents, e.g., magnetic and conjugated beads, and are easily integrated with POC platforms including lateral flow, microfluidic Lab-on-Chip/Card formats. By integrating into these platforms, the delivery precision to the target is improved and user sampling errors are eliminated by removing the conventional use of dropper bottles or eyedroppers.

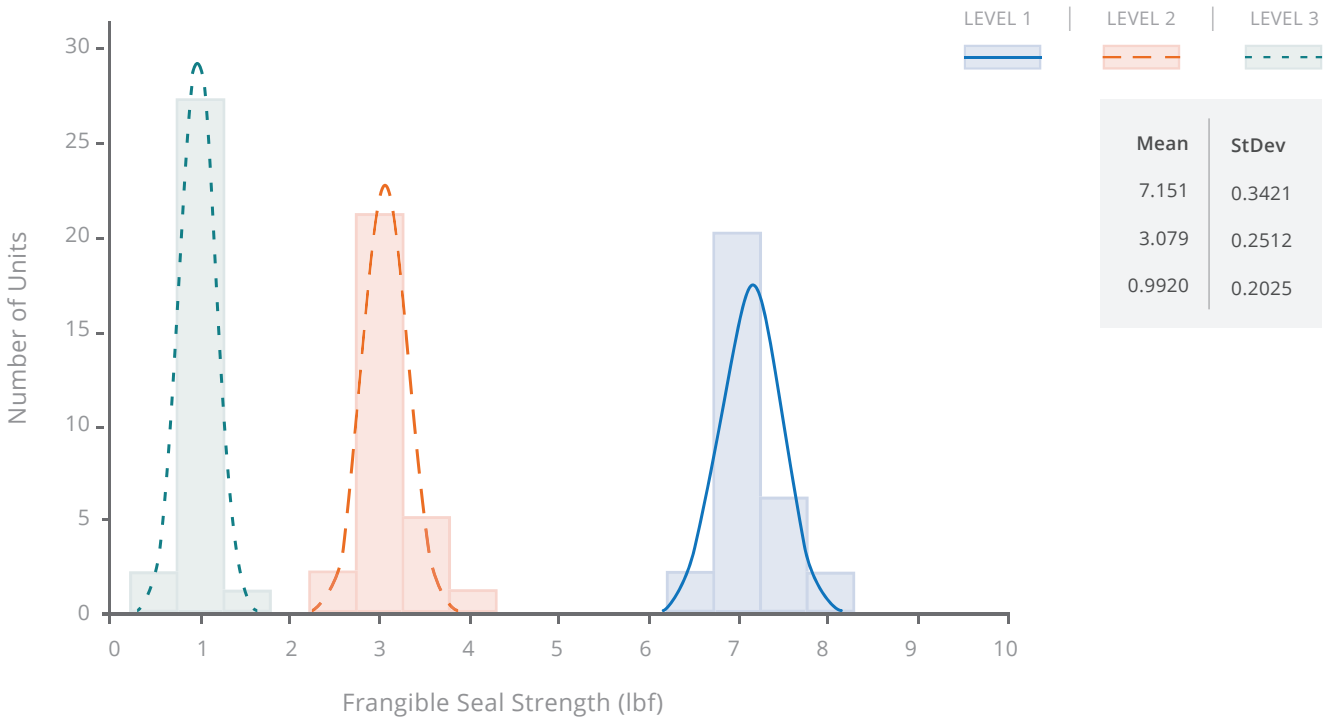
PRECISION FILL AND DISPENSING RESULTS

J-Pac Medical's Innovation Services group designed a frangible seal blister that would deliver 75 µl of distilled water. The blisters were fabricated, filled with a precision pipette, sealed and individually weighed[3]. The blisters were then actuated to release their contents and then weighed again to measure the amount of liquid dispensed. For comparison purposes, a standard manual eyedropper was used to deliver approximately 90 µl of distilled water (3 drops per estimated 30 µl/drop). The resulting data were then analyzed by routine statistical methods.

The graph below illustrates the comparison of fluid delivery between J-Pac Medical Safe Seal™ frangible seal blisters and a conventional eyedropper method. The Safe Seal™ blisters each received a consistent and uniform fill volume and after actuation demonstrate a reproducible and consistent fluid

Controllable Seal Strength - Frangible Seal Technology

Matched Reservoir & Lid Foil



dispense. The eyedropper method was less precise than the blister seals, and was not unlike literature citations describing the variability in delivery using similar methods, citing a range of 34 µl to 63 µl per drop[4].

Precision delivery using J-Pac Medical Safe Seal™ blisters is the preferred method as it reduces the variability compared to eye-dropper methods, reduces potential operator dispensing error, eliminates the cost of supplying excess reagents and eliminates the cost of dispensing bottles and extra packaging.

STORAGE AND STABILITY CONTROL

J-Pac Medical uses medical grade foil laminate materials to fabricate the Safe Seal™ blisters which have extremely low vapor transmission rates, allowing longer reagent shelf life compared to plastic bottles which may have more gas-permeable materials, excessive open bottle head space (more opportunity for oxidation), more surface interaction and chemical reactivity. To illustrate the stability of J-Pac Medical's Safe Seal™ packaging, a population of like blisters was fabricated and filled with distilled water and subjected to an accelerated stability study according to the ASTM F1980 standard[5]. The blisters were weighed together on an OHaus digital scale and stored in a Yamoto DP43 oven, 60°C, 65% RH for the duration of study and weighed at an intermediate time interval.

STORAGE AND STABILITY RESULTS

The result shown highlights an extremely low mass loss (<1%) of fluid over the period of the accelerated testing. This reflects J-Pac Medical's proficiency in processing these materials for products that require a long shelf life and long term stability.

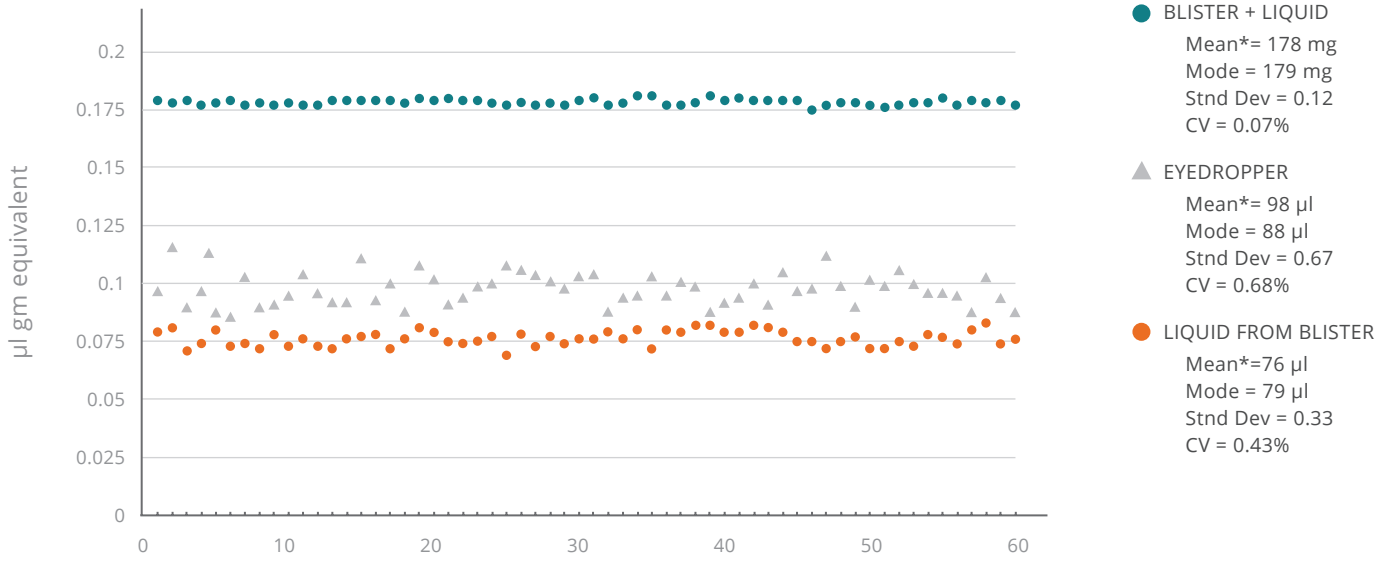
J-Pac Medical's Safe Seal™ blisters provide the confidence that even after extended periods of time, the blisters repeatedly and reliably hold and dispense reagents in unit-per-measure fashion. J Pac's Innovation Services Group has undertaken further testing with different solvents and alcohols and can make this information available when complete.

SUMMARY

It is important that POC IVD test manufacturers work closely with J-Pac Medical to consider the specific requirements of every custom blister reservoir and design a blister solution that considers burst characteristics, reagent volume delivered, long-term storage requirements and material compatibility. Accurate filling and dispensing by design – in

J-Pac Medical Safe Seal™ Reagent Blister Filling and Dispensing Efficiency

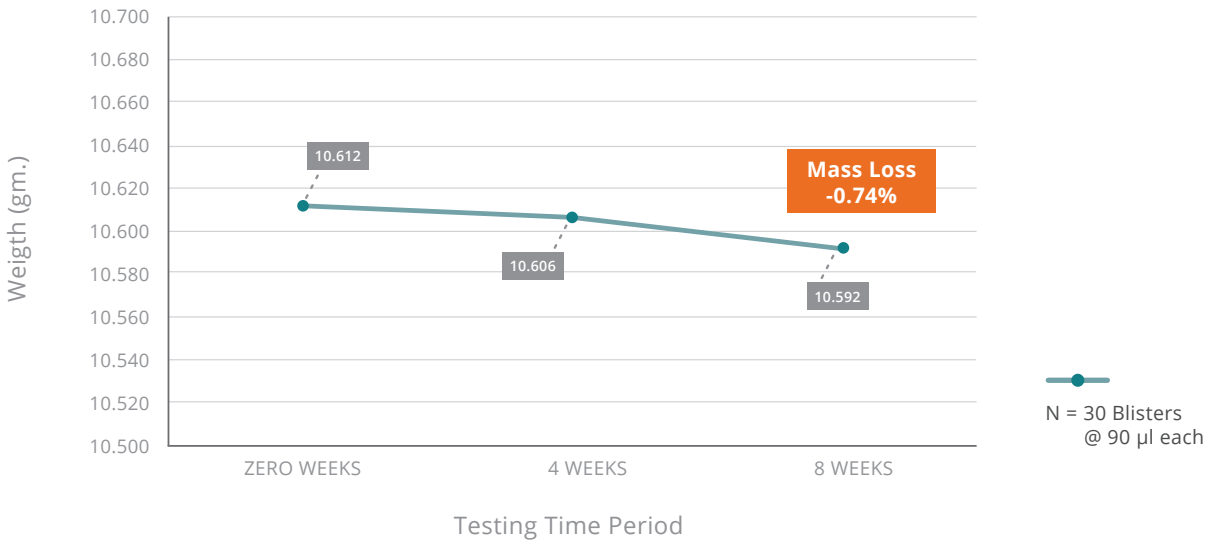
Target Dispense 75 µl vs. Eyedropper (3 Drops, est. 90 µl)



Methodology: 1. ● Blister samples filled with water (SG = 1.00, r.t.), sealed and weighed (gms); 2. Blisters actuated, releasing liquid and weighed, 3. ● Difference represents volume dispensed (µl), 4. ▲Compare against standard three drops applied manually with eyedropper and weighed. *N=60.

Accelerated Evaporation Testing of Safe Seal ™ Reagent Blisters

Two Year Equivalent Period, 60° C, 65% RH



single or multiplex formats - allows tests to be consistent and reproducible, and burst pressure and pin-point release of the reagent from the blisters can be designed into the shape for either manual or mechanical actuation. Safe Seal™ blisters are easily customized and integrated into many existing platforms – this helps manufacturers create new offerings without drastic changes in the product line.

There are tangible reductions in overall manufacturing and end-user costs by incorporating frangible seal reagent blisters, including:

- Eliminating the cost of separate reagent applicator bottles, associated costs of filling, packaging and labeling, and managing less inventory. Further, using larger blister cards with multiple reagents (multiplexing) can reduce the number of overall components and associated costs
- The reagent blister stores and delivers just the right amount of reagent needed for the application, so excess reagent is not required. The liquid volume for single dose reagents can range from 30 µl to 5,000 µl
- The materials used have low vapor barrier transmission rates, resulting in greater stability and longer shelf life (> 2 years), in some cases eliminating the need and cost of desiccants.

In conclusion, the application of frangible seal technology to reagent blisters enables greater control over unit-of-measure release of testing reagents and provides improved performance characteristics and practical implications when compared to current drop bottle formats.

These features translate into benefits for the POC device manufacturer by lowering packaging costs, increasing reagent stability, lower manufacturing and packaging costs, providing a smaller disposable footprint, and easy, accurate and precise fluid transfer.

[1] Blister fabrication and performance metrics were provided by J-Pac Medical's Innovation Services Group.

[2] Protocol using Chatillon Digital Force Gauge available upon request.

[3] Protocol available upon request. Equipment utilized: Mettler Toledo Auto Rep "E" Repeating Dispenser with 1.0 ml tip, OHaus AV213 digital scale

[4] Reliability of drop size from multi-dose eye drop bottles: is it cause for concern? German EJ1 http://www.ncbi.nlm.nih.gov/pubmed?uid=10396391&cmd=showdetailview&indexed=google

[5] ASTM F1980 - 07(2011); Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices

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