

Achieving Cost Effectiveness in Point-of-Care Diagnostic Devices With Frangible Seal Technology

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The point-of-care (POC) *in-vitro* diagnostic (IVD) market is continuing to grow, with speculation that IVD could become the leading niche in the medical device industry by 2020 with more than \$65 billion in sales.¹ POC testing is supported by continuous technology improvements and the recognition that rapid test results offer economic benefits and potential patient benefits due to faster turnaround of testing results.

An increasing number of POC device manufacturers are recognizing the value of easily incorporating burst and frangible seal reagent blister reservoirs into lateral flow and lab-on-a-chip/card formats, providing significant cost savings as an alternative to the conventional eyedropper and bottled reagent systems with an added reassurance of test reliability. By integrating frangible seal technology into on-board reagent blisters of POC devices, the device manufacturer can better control performance variability, reduce overall manufacturing and disposal costs, and simplify the

end-user experience.

Incorporating on-board reagent blisters represents a new vision for improving the performance of POC devices while at the same time reducing cost and offering a safe and reliable method for dispensing unit-of-measure volumes. With some up-front consideration of the system dynamics, custom blister designs can be optimized and applied to an entire testing platform, thereby lowering costs across the entire product family.

Considerations for Incorporating Frangible Seals in POC Test Platforms

In order to successfully integrate frangible seal technology, it is critical that frangible seal manufacturers consider the specific requirements of every custom blister reservoir and design a blister solution that considers material compatibility, burst characteristics, reagent volume delivered, and long-term storage requirements. There are many different types of mate-

rials that can be used for reagent blisters and generally can be described as specialized foils and laminates used for cold- and thermo-formed packaging. These materials have various thicknesses and seal strengths that can be customized for use in pierced or burst applications, as well as peelable and hybrid peel-push barriers.

Depending on the form factor and release requirements, a wide range of materials can be processed to create “frangible” blister seal reservoirs with differential weld strengths designed and engineered to either be permanent or break, distort or yield on contact actuation or fail under a specific pressure. The weld strengths are a function of the material properties and applying unique welding processes that are combinations of pressure, temperature and time to meet the seal specification.

A thorough understanding of these specialized material properties and processing techniques allows the blister fabricator to “dial in” the specific burst strength needed for activation—though not fragile enough to rupture prematurely due to routine handling, assembly or shipping activities.

Generally, the design of the blister cannot be done in isolation of other system features such as the microfluidics (“plumbing”), type and style of actuation (mechanical or manual, piston-like or roller/“squeegee”). The best approaches start with well-defined device manufacturer design specifications in order to focus efforts on only those variables that will deliver the required performance.

Reducing Cost for the Manufacturer

There are tangible reductions in overall manufacturing costs achieved by incorporating frangible seal reagent blisters into the testing device.

These include:

- Reduced waste with exact volume



Frangible seal technology simplifies point-of-care diagnostics testing by enabling the controlled release of testing reagents. Photo courtesy of JPac Medical LLC.

delivery of reagent: The reagent blister stores and delivers only the required amount of reagent needed for the determination, so excess reagent to overfill a secondary transfer bottle is not necessary. The liquid volume for single dose reagents can range from 30 microliters (μl) to 5,000 μl . For example, a J-Pac Medical blister was designed to deliver 75 μl ; results showed a mean of 76 μl , standard deviation of 0.33 and coefficients of variation of 0.43 percent.²

- **Reduced inventory costs:** Frangible seal technology reduces the number and cost of separate reagent bottles and applicators, as well as the associated costs of filling, packaging, and labeling (i.e., less inventory management). No secondary packaging, labels or inventory are required. Considering that prices of application bottles alone can start at 20 cents each and a fully filled, sealed, weighed, labeled and boxed bottle can approach a dollar, this can quickly add up to significant savings if blisters are substituted.
- **Improved product simplicity:** Using larger blister cards with multiple reagents (multiplexing) can reduce the number of overall component packaging, assembly steps and complexity of manipulating and dispensing fluids. Frangible seal form factors can be compatible with various reagents, powders, beads, liquids, and solvents, thereby reducing the number of storage and dispensing methods needed. Additional value includes the capability to record lot numbers, expiration dates, and two-dimensional barcodes on the surfaces of the blisters, helping with lot traceability.
- **Greater stability and longer shelf life:** Frangible seals support lower vapor barrier transmission rates, resulting in greater stability and longer shelf life (greater than two years), in some cases eliminating the need

and cost of desiccants.

- **Better ease of integration:** Blisters are easily customized and integrated into many existing platforms; this helps manufacturers create new offerings without drastic—and costly—changes in the product line. Blisters can be filled without dead space air (100 percent fill) or with air to facilitate delivery and fluid clearance. With either method, an exact delivery volume can be specified into the design of the blister and fluid path.

Reducing Cost for the End-User

Similarly, there are cost savings for the end-user when they use devices with on-board frangible seal blisters.³

They may include:

- **Greater simplicity and reduced manual error rates:** Frangible seals remove the guesswork and sampling error associated with manually dispensing liquid reagents. POC test processes can be simplified and made less complex, allowing expanded use by less trained personnel. For example, if a technician is distracted during the dispensing process or running a number of identical tests, any interruption may result in a questioned assay run, the cost of a repeated test, or in the worst case, an inaccurate test result reported.
- **Longer shelf life:** Frangible seals are resistant to ultraviolet light compared to plastics, resulting in a longer shelf life and less obsolescence of product.
- **Saved storage space and inventory management time:** Frangible seals keep reagents together with a reaction pack, so there is no chance of mixing with different lots or separating from the assigned or matched lot. Also, blister incorporation holds the promise of a smaller product “footprint” and better portability.
- **Lower cost of waste:** The reservoirs

are lightweight and disposable components when integrated into the device. There are no extra bottles or packages to throw away, resulting in reduced cost of disposing hazardous or biological waste, which can be expensive.

- **Environmental benefits:** Eliminating plastic storage bottles and eyedroppers reduces the solid waste mass of slowly biodegradable polymers.

These factors further help to drive the economic justification for incorporating on-board frangible seal reagent blisters into new and existing POC IVD medical devices from a manufacturer and end-user perspective.

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With changing economic drivers, fueled by downward cost pressures from healthcare reform, point-of-care diagnostic testing provides significant economic benefits by reducing complexity and saving time. This creates challenges and opportunities for IVD manufacturers to respond quickly and competitively with cost-effective, accurate and precise POC testing platforms.

Frangible seal blisters provide a simple, elegant and cost effective way to rapidly upgrade existing POC test platforms or to roll out new test offerings to keep up with evolving demands, while providing great value from both a manufacturer and end-user perspective. ❖

References

1. “EvaluateMedTech World Preview 2015, Outlook to 2020,” Evaluate, Ltd., Oct. 6, 2015
2. “Frangible Seal Reagent Blisters Deliver Precision Performance to Point-of-Care Diagnostic Testing,” J-Pac Medical LLC. 2015
3. *Ibid*

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