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Seal Failure or “ False-Positive ” ?

Some medical device manufacturers (MDMs) struggle with the potential of “false-positive” results when performing sterile integrity testing (bubble leak or dye penetration tests) on flexible sterile barrier systems (SBS) containing porous materials. A false-positive result can occur when a flexible pouch containing a porous material is bent, folded or creased, causing internal sheet separation of the porous web. This can happen when a pouch is folded to fit into a shelf container or is folded or bent during distribution stress testing. Sheet separation has been observed in all types of porous sheet materials available in the industry today. Folding is also a common cause of film failure or stress cracking in porous SBS.

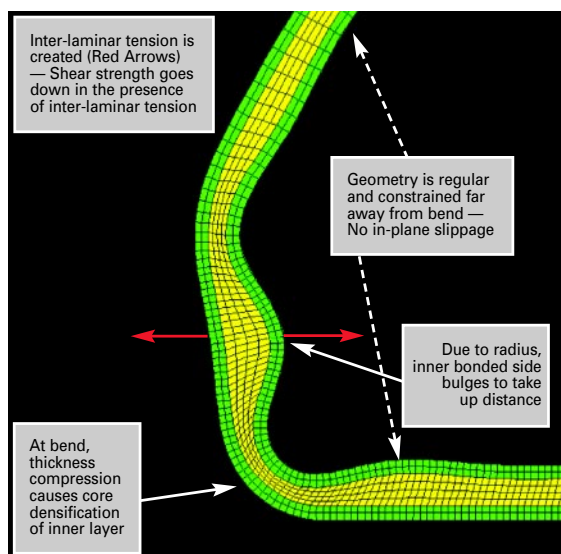
At the request of DuPont Medical Packaging, Ethox Corporation, a contract test facility located in Buffalo, NY, conducted testing that proves sheet separation does not compromise the sterile barrier of DuPont™ Tyvek® medical packaging. The tests showed that any excessive leakage of air or dye is along the transverse direction of the material, not between the porous web and opposing nonporous web material, as would be the case in a seal failure.

When is this found?

The false-positive occurs when evaluating the integrity of a porous SBS using integrity tests such as the American Society for Testing and Materials (ASTM) International F1929 *Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration*, F2096 *Standard Test Method for Detecting Gross Leaks in Porous Medical Packaging by Internal Pressurization (Bubble Test)* and D3078 *Standard Test Method for the Determination of Leaks in Flexible Packaging by Bubble Emission*.

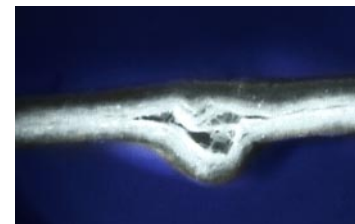
What is it?

Flexible porous sheets may separate internally when folded because the manufacturing process makes the exterior surfaces less flexible than the interior. The process of bending the sheet causes deformation within the flexible inner part of the sheet. This deformation causes tension forces within the sheet that, when sufficiently high, can result in the yielding of the fibers that hold the sheet together. The tighter the bend, the greater forces become until the loads become excessive and the fiber structure holding the sheet together will give and compress on either side of the bend while expanding and creating a gap between internal fibers at the bend. When the sheet is unbent or



(Above) Why porous sheets separate when folded.

(Right) SEM of sheet separation. (50X magnification)



flattened out again, there will still be a less dense area or gap formed in the interior of the sheet. (See Figures above.) These areas in the porous sheet are separations within the softer inner layer between the outer surfaces. The original mass of the fibers is still there, only the bulk density has decreased.

A new issue?

This phenomenon is not new. However, there are several reasons why it may seem to be a new issue. First, and probably most important, is the advent of ISO 11607 *Packaging for terminally sterilized medical devices*. The generation of integrity tests by ASTM International, Subcommittee F02.60, *Medical Device Packaging*, and the industry's heightened awareness of required testing referenced in ISO 11607 both contribute to the increase in reported cases of sheet separation. What's more, the industry now has tools for integrity testing that were not previously available. These tests are more sensitive than those previously used, such as visual inspection or dust drum tests.

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In the past, prior to the advent of the medical device regulations and GMPs, the industry paid little attention to packaging. Stress testing or performance tests to evaluate the package design performance were not common.

As a result, post test sample analysis was not needed nor performed and this phenomenon was never an issue.

A cause?

It is never recommended to fold flexible barrier materials; however, inadvertent folding can happen during distribution and handling. And, packaging system designs based on cost constraints may require a pouch to be folded to fit into an existing shelf container. It may be a good sourcing decision to avoid smaller volume buys of a new, optimum-sized component, but using an improperly sized shelf container that requires the flexible SBS to be folded before loading can result in sheet separation of the porous material and flex cracking of films.

Another factor facing the packaging engineer is the constant pressure to reduce the size of the packaging system because storage space in health care facilities is always at a premium. Additionally, there is pressure to reduce solid waste materials.

Test anomaly

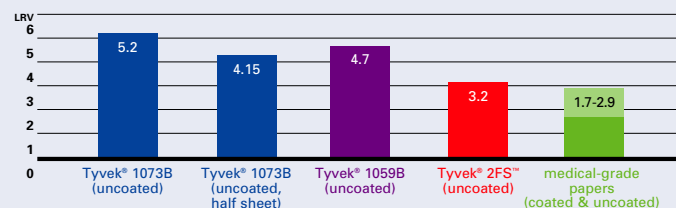
When a material anomaly of this nature is present in a sample during dye leak or bubble leak integrity testing, a false-positive can occur. There is a less resistant path (reduced bulk density) or a more permeable area through which the dye or the air can pass when seeking a route out of the package. The porous member of the package will always reach its bubble point first in the wrinkled or creased fiber separated area. There is little or no loss in the transverse direction or through the web filtration efficiency; thus, the sterile barrier characteristics of the porous sheet have not been compromised.

Package integrity?

To evaluate the integrity of a pouch made of uncoated Tyvek® 1073B and polyester (PET)/low density polyethylene (LDPE) exhibiting this anomaly, DuPont Medical Packaging had the microbial ranking test [ASTM International F1608 *Standard Test Method for Microbial Ranking of Porous Packaging Materials (Exposure Chamber Method)*] performed by Ethox Corporation. As a worst-case scenario, the samples were split approximately in half, resulting in a test sample only half as thick as a full sheet of Tyvek® 1073B. The average for the tests was an LRV of 4.15 (a whole sheet of Tyvek® 1073B has an average LRV of 5.2).

To cause sterility loss with a typical delamination channel anomaly in a SBS, a contaminant must enter the channel, migrate up that channel to the point where that channel overlaid the inside of the pouch, migrate through the remaining

layer of the porous material into the pouch and finally land on the device component inside the SBS and survive! Needless to say, the chances of this happening are very remote. The test results show that Tyvek® exhibiting sheet separation still provides an excellent microbial barrier and does not compromise package integrity. Although the test results indicate a small reduction in the LRV of the samples, all of the results were significantly better than those of other commonly used porous materials (see chart below).



Per ASTM F1608. Microbial barrier is the measure of the ability of a porous substrate to prevent bacteria penetration. A completely impermeable control sample (microbial penetration is zero) is challenged with one million or 10^6 colony forming units (cfu). The number of cfu 10^6 has a \log_{10} value of 6. If a sample challenged in the same way as the control allows 10 cfu ($\log_{10} = 1$) to penetrate, then its log reduction value (LRV) is 5 ($6 - 1 = 5$). Therefore, the higher the LRV, the more resistant the packaging is to bacteria and microorganisms.

How to evaluate for false-positives

- Microscopically examine sheet edge in the area of a suspected seal failure.
- Wait for dye to dry and then remove film from substrate. Dye penetrating through a true seal failure will stain the surface of the film.
- Check dye color, which will be more intense through a seal failure than through sheet separation.
- Examine channel edges, which will be more defined in seal failures. (Wicking dye will be viewed through some of the porous substrate and dye color will be less intense.)

It's important to know that when there is a seal failure present, a dye test will produce a very definitive result within less than one second. Dye wicking into the sheet and then crossing the seal area (within the sheet) will occur at a slower pace than dye channeling through the adhesive layer in the sheet surface. In areas exhibiting sheet separation, dye will diffuse into the sheet and edges will not be well defined. When viewed from the porous side of the sample, the dye color will be more intense from the wicking vs. channeling.

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A Team of Experts Focused on Your Needs — Part Three of a Series

This ongoing series of articles is designed to provide you with insights about the education, work experience, industry activities and special skills of each member of the DuPont Medical Packaging Team. We hope that these articles will give you a better understanding of how our team of experts can help you.

In the last issue of *Tyvek® Rx*, we featured Paul Herman, a research technologist. In this issue, we spotlight Raffaella Cristanetti, the new Global Business Manager of DuPont Medical & Industrial Packaging.

Before assuming leadership of the DuPont Medical Packaging Team in January 2005, Cristanetti led the turnaround in the Training Materials product segment of DuPont Safety Resources, one of the fastest-growing DuPont business units, which provides professional consulting and training services to corporations, government agencies and other organizations globally.

During her six-year career with DuPont, she has gained a wealth of experience in a variety of assignments, including: business and financial planning; marketing; corporate policy; and issues management.

Prior to joining DuPont, Cristanetti held various positions with Chevron Corporation in the areas of international business development and government relations. She also has experience in international trade consulting.

Cristanetti graduated magna cum laude with a bachelor's degree in international politics from Georgetown University's School of Foreign Service in Washington, D.C. She also earned a master's degree in international trade and finance, with an honors certificate in international business diplomacy, from the same school. Cristanetti is fluent in English, Italian and Spanish.



Raffaella Cristanetti

"As the new Global Business Manager, I will draw upon my extensive international business experience and rely on my deep commitment to customer focus to ensure that we continually improve the way we do business," said Cristanetti. "I am pleased to be leading this great team of talented individuals and I'm confident that by working together in close partnership with MDMs and SPMs, we will be able to meet the evolving needs of the medical device industry. I am also looking forward to exploring new opportunities in emerging markets."

To speak with Raffaella Cristanetti or any of the other experts on the DuPont Medical Packaging Team, call 1-800-44-TYVEK®. We are committed to providing the support you need to ensure that medical professionals around the world receive the highest quality medical packaging available.

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Conclusion

A round robin interlab research study conducted by ASTM Subcommittee F02.60 for F1929, did not include samples with creases or folds. As a result, the false-positive phenomenon was not observed and therefore was not evident in the final results. This phenomenon needs to be addressed in more detail in the next revisions of ASTM D3078, F1929 and F2096. There also should be a detailed discussion in an annex to address this anomaly.

Demonstrated ways of distinguishing between seal failure and sheet separation include:

- Dye penetration testing;
- High-powered microscopic photos of the edge of the seal that reveal sheet separation within a porous sheet; and
- Waiting until the dye solution has dried and then peeling open the pouch to examine for a blue dye witness mark on the film seal surface.

In closing, whenever a leak in the seal area is observed during a dye or underwater pressure differential integrity test, get a second opinion about what is being observed to fully understand the nature of the leak. Consider doing further verification of the leak to avoid failing a test protocol due to a false-positive observed during a leak test. In addition, to help minimize the occurrence of false-positives in future designs, implement designs which incorporate properly sized shelf containers to avoid folding or bending the flexible package.