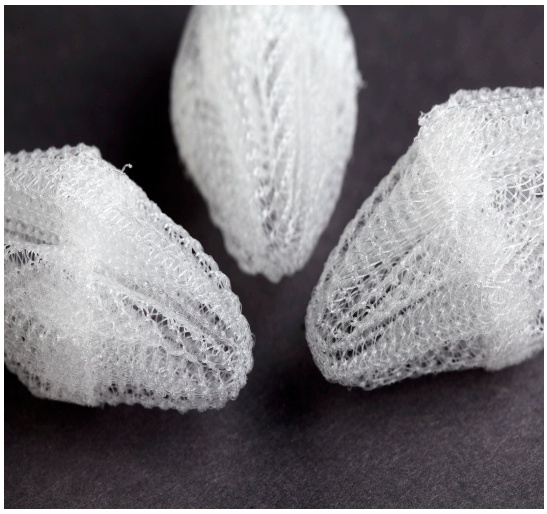
Resorbable Polymer Implants: Attention to WIP Exposure

Purpose



This white paper is meant to identify critical considerations related to WIP Exposure vulnerabilities of resorbable polymers. A structured and disciplined assessment of the different contributors to the Overall Exposure Risk will enable a fact based decision pathway that will result in the establishment of a repeatable and capable manufacturing, packaging and sterilization processes that reduce device degradation. The result will be a consistently performing, efficacious product with optimized shelf life.

Background and Challenges

Implants that are made from resorbable polymers offer the ideal scenario for surgical repair. The device provides support to a surgically repaired site to enable critical wound healing of the affected tissues, and then the implant is absorbed by the body through routine body functions. No mass from the implant remains once it is totally absorbed.

The challenging part is that the same sensitivity of the polymer to breakdown in the human body is also taking place during the fabrication, packaging and sterilization of the device. This degradation occurs during manufacturing processing time (Work-In-Process) and needs to be assessed and controlled in order to provide a consistently performing resorbable polymer implant with an optimized expiry dating claim.

A broad range of resorbable polymers are available that display total absorption profiles from roughly 2 weeks up to 2 years. These polymers include Polyglycolide (PGA), Polylactide (PLA), and Polydioxanone (PDO) just to name a few. The decomposition of these materials can be driven most notably by moisture and/or Oxygen, but also can include sensitivities to light, heat, and other factors. The shorter the critical wound

healing time the polymer is designed to accommodate, the more critical WIP Exposure control will be to the overall performance of the resorbable implant.

Manufacturing Requirements

The manufacturing and supply chain of a typical resorbable implant will include polymerization, extrusion or injection molding, kitting with other components, packaging, sterilization, and distribution. All these areas of production can negatively affect the ultimate performance of the device if exposure to environmental elements is not limited. A systematic understanding of the link between WIP Exposure and Product Performance/Shelf Life can be established, and controls put in place to ensure identified WIP Exposure limits are not exceeded.

As part of polymer and product development, a WIP exposure study should be performed to establish data that links WIP exposure to implant performance and Shelf Life. The goal is to set acceptable "WIP Exposure" windows for each critical assembly process step such that a documented overall exposure time will be established that will ensure finished product that is compliant to performance and shelf life claims. These WIP exposure windows should be challenged individually and sequentially through the supply chain (low and high exposure at each step), and implant efficacy measured as determined to set viable limits. Once limits are established, a WIP Exposure Log should be maintained for each processing step such that overall exposure is known for each lot/sub-lot of resorbable product. This exposure log can identify lots that may be at risk towards the end of the supply chain such that special handling may be instituted to ensure the Overall Exposure Limit is not exceeded. The WIP Exposure Log should be maintained as part of the Device History Record (DHR).

In establishing and controlling WIP exposure, there are a number of methods that can be utilized that will minimize polymer degradation:

- A manufacturing dry clean room that maintains low humidity as an ambient condition will help to limit WIP Exposure Degradation.
- For most resorbable polymer products, a dry nitrogen environment will stop or significantly slow any ongoing degradation. A nitrogen storage chamber should be available to store exposed product in case of unanticipated delays/stoppages in processing. In addition, flowing nitrogen over any exposed resorbable product can inhibit the impact of moisture and oxygen in the ambient environment.
- In most cases, Nitrogen-flushed foil pouches provide an effective storage and shipping format for the in-process resorbable implants.
- The resorbable components should be packaged in small quantities within a larger processing lot such that only a small number of components are exposed at any one time. The key to a successful flow is the rapid processing of product once

opened to the environment, and the rapid return of product to barrier packaging that will slow or stop the degradation clock.

- Minimize handoffs where at all possible. It is more desirable to perform all functions in a single facility than it is to be shipping these sensitive products from site to site.
- Refrigeration of packaged, in-process resorbable components can also help to maintain implant efficacy.

Sterilization Optimization

Most of the resorbable polymer implants are sterilized via Ethylene Oxide (Eto). This presents the challenge of providing a breathable packaging format that performs through the sterilization cycle, but the need remains for a high barrier final format that will maintain a dry, and possibly alternate gas (like Nitrogen) environment that will maintain implant efficacy. Additionally, the packaged product must perform through transit and distribution, and provide easy aseptic transfer in the OR.

Additionally, the Eto Process itself will impact resorbable polymers. The Eto process utilizes steam to raise the load temperature and create the most advantageous environment for Eto sterilization to take place. With this introduced steam entering the package and impacting the resorbable implant, it is important that the overall cycle be developed to minimize any latent moisture that might remain in the package post processing. This can be accommodated through extended aeration, or with the addition of some sort of drying/vacuum drying cycle.

Unique Packaging Requirements

Historically, a Foil to Foil Pouch with Tyvek Header has been the preferred package format for resorbable products. This format can provide the needed barrier properties discussed above, but typically requires intricate inner packaging components to provide protection to the product and enable aseptic transfer. This format is especially complex when the resorbable implant is packaged with an inserter and/or other instrumentation that requires a 3-Dimensional infrastructure within the pouch.
Most recently, vented tray concepts are in development that provide the protection and handling simplicity of a tray that incorporates an easily placed barrier patch over vent to complete the barrier package post sterilization. This format incorporates all the performance advantages of a rigid tray/lid package while providing the final barrier packaging seal convenience of the header bag.

Process Controls to Reduce Degradation

With packaging identified, the logistics of integrating WIP Exposure Controls to the Eto Flow becomes a critical concern. With any product destined for Eto Processing, the package feature that allows for the Eto Sterilant to enter and exit the package will also allow for moisture and oxygen to enter the package and potentially impact the resorbable implant. If the Eto Sterilization is not on site, then shipping to the sterilizer must be orchestrated such that a minimum amount of time is spent in transit and in queue at the sterilizer so as to minimize this portion of WIP Exposure. As most sterilizers will not create the final barrier seal in any package format, the product will also need to be returned post-processing in an expedient manner again to minimize WIP Exposure.

About the Author

Rick Crane has more than 30 years of experience in the healthcare products industry. He brings strong general management skills demonstrated across operations, R&D, program management, technical sales, and marketing organizations. Crane is an Ameristar Packaging Competition Gold Star Award Winner for Medical Device Package of the Year, and is a patent holder. He has a Bachelor of Science from Ursinus College.

About J-Pac Medical

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