Abstract

A significant modification in the technology used in the manufacture of Tyvek® material found in a wide variety of medical devices and sterile packaging will now require manufacturers of currently approved Tyvek®-based products to re-evaluate them for continued compliance with applicable standards and regulations. This white paper presents the details of the production transition regarding Tyvek®, and summarises the likely steps necessary to ensure the continued recognition of previously approved medical devices and packaging that incorporate Tyvek® material.
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Introduction

Tyvek®-brand polyethylene material has been widely used by manufacturers of certain medical devices and medical device packaging because of its resistance to microbial penetration in sterile applications. However, the DuPont Company, the manufacturer of Tyvek®, is transitioning to a modified manufacturing process in the production of Tyvek®. This modification will require many medical device manufacturers (MDMs) and sterile packaging manufacturers (SPMs) to file formal notifications with their respective EU Notified Body or other national regulatory authorities in connection with previously approved medical devices and packaging that incorporate Tyvek® material. In addition, in some jurisdictions, manufacturers of medical devices that pose the greatest risk to patients may be subject to additional testing in order to maintain their device recognition.

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Medical device sterile packaging requirements and standards

The European Centre for Disease Prevention and Control estimates that over four million patients in the European Union (EU) acquire a healthcare-associated infection each year, directly resulting in at least 37,000 deaths and contributing to as many as 110,000 additional fatalities. Since infections due to poor hygiene account for approximately 20 to 30 percent of all healthcare-associated infections, rigorous hygiene and sterilisation practices are a primary focus of efforts to reduce overall infection rates in healthcare settings.

Most medical devices and apparatus designed to come in direct contact with patients must be sterilised to prevent the unintended transmission of infectious organisms. Typically, sterilisation is achieved through the use of specially-designed, non-reusable packaging materials that provide a barrier against microbial transmission. This sterile barrier system effectively maintains device sterility from the point of initial sterilisation and packaging until the time of use, thereby helping to prevent the spread of infection.

Under the requirements of EU’s directives applicable to medical devices, packaging materials and systems used to preserve the sterility of medical devices must conform to the requirements of the EU’s harmonised version of ISO 11607, Packaging for terminally sterilized medical devices. Part 1 of the standard, ISO 11607-1, addresses requirements for materials used in sterile barrier systems and packaging systems, while Part 2, ISO 11607-2, covers validation requirements for the manufacture and assembly of packaging materials and systems.

Of particular note in ISO 11607-2 is the requirement to revalidate sterile packaging materials and systems when "changes are made to the… packaging materials or packaging processes which comprise the original validation, and affect the sterility, safety, or efficacy of sterile medical devices.” Revalidation is required since packaging characteristics or density could affect the absorption or penetration of sterilising chemicals, the effectiveness of the sterilisation process, the integrity of package sealing or the safety of sterilised devices.

ISO 11607 has become the internationally-accepted standard for sterile packaging materials and systems used with medical devices, and has been adopted by medical device authorities in most countries around the world. Although the U.S. Food and Drug Administration (FDA) does not expressly require demonstrated compliance with ISO 11607, the agency does accept evidence of certification to the standard in support of manufacturers’ 510(k) pre-market submissions for the approval of new medical devices.
Tyvek® and medical device packaging

Originally developed in the U.S. by DuPont in the 1950s, Tyvek® is an engineered material comprised of non-directional fibres that are thinner than a human hair. These fibres are bonded together with heat and pressure (no chemical binders) and spun into sheets using flash-spinning technology, a proprietary manufacturing process. Tyvek®-based materials and packaging have the advantages of being light in weight while also resistant to punctures or tears, as well as providing an effective barrier against liquids. Today, Tyvek® is used in a wide range of applications, including vapour barriers in building construction, garments and shoes, and a variety of packaging material and mailing envelopes.

The earliest application of Tyvek® to medical device packaging occurred in the early 1970s, a time when healthcare facilities were increasingly turning to disposable medical devices as a way of reducing labour costs associated with re-sterilising. DuPont researchers determined that Tyvek® was especially well-suited as a packaging material for disposable medical devices, since it provides greater resistance to microbial penetration than medical grade papers and other sterile packaging materials. Tyvek®’s permeability to air and gas also allows for the infiltration of gas and ethylene oxide, so that medical devices can be sterilised after packaging. Finally, Tyvek® material is strong enough to resist damage that could compromise the condition of previously sterilised devices.

Due in large part to these unique properties, Tyvek® has become an important packaging material option for sterile medical devices and is widely used by device manufacturers worldwide. In addition to its application in the packaging of medical devices, Tyvek® is now also used to package disposable syringes and as a material in the construction of medical grade trays and pouches. It is even used as a packaging material for pharmaceuticals.
The Tyvek® Medical Packaging Transition Project

DuPont manufactures a number of different styles of Tyvek® for the packaging of sterile medical devices, the two most popular being Tyvek® 1073B and Tyvek® 1059B. Tyvek® 1073B is a robust packaging material offering increased resistance to microbial penetration and greater protection against damage from heavy devices or devices with sharp points. Tyvek® 1059B is a packaging material intended for use in sterile packaging applications for smaller medical devices without sharp edges. As originally manufactured, both Tyvek® styles 1073B and 1059B comply with the material requirements of ISO 11607-1. Accordingly, medical device packaging comprised of either of these two Tyvek® styles are presumed compliant with material properties for a sterile packaging as required under the EU’s directives applicable to medical devices, as well as applicable regulations in other jurisdictions around the world.

In 2011, DuPont notified medical device manufacturers and sterile packaging manufacturers of its plans to eventually adopt a new flash-spinning technology in the manufacturer of Tyvek® to help ensure the company’s capabilities to meet anticipated future demand. According to the company, the change in manufacturing technology would potentially trigger the need to revalidate sterile packaging materials and systems previously tested to the requirements of ISO 11607. At a minimum, the transition to a new manufacturing technology would require manufacturers to update their documentation to reflect the change and potentially to adapt and revalidate the process.

To aid medical device and sterile packaging manufacturers with the transition and possible revalidation of packaging materials, DuPont launched the Tyvek® Medical Packaging Transition Project (MPTP) in 2011. Working in conjunction with device and packaging manufacturers, regulatory authorities, Notified Bodies (including TÜV SÜD Product Service) and contract sterilisers around the world, the company conducted extensive testing with Tyvek® material produced using its new manufacturing process to determine its functional equivalence with Tyvek® material manufactured with the earlier version of flash-spinning technology. Testing conducted by DuPont as part of the MPTP has included assessments of the effects on the microbial barrier properties of the new Tyvek® from sterilisation, and from one year real-time aging and one, three and five year accelerated aging.

Under the MPTP, DuPont has also worked closely with regulatory authorities in the EU, the U.S., China, Japan, Canada and other countries. The goal of these discussions has been to provide regulators with testing data showing functional and biocompatibility equivalence between Tyvek® produced under the new process and Tyvek® produced using legacy technology. These discussions have also enabled DuPont to anticipate and address other issues that could potentially create additional hurdles for manufacturers seeking revalidation of their packaging materials.
Required actions for maintaining EU Notified Body certification

The exhaustive and detailed efforts taken under the auspices of DuPont’s MPTP have now provided medical device and sterile packaging manufacturers with a clear path for maintaining existing approvals of sterile packaging materials and systems made of Tyvek® in most jurisdictions. Currently, it appears that the requirements for maintaining EC-certification issued by an EU Notified Body will involve the greatest effort for medical device and sterile packaging manufacturers. In most cases, the changeover from legacy Tyvek® to new Tyvek® will require manufacturers to prepare a notification of Significant Change to their existing certification. At a minimum, manufacturers of medical devices and sterile packaging will be expected to:

1. Initiate a formal change assessment and risk assessment process consistent with the requirements of ISO 11607-2 and NBOG BPG 2014-03;
2. Document the rationale for accepting the functional equivalency conclusions of DuPont’s testing and protocol assessment as they apply to their specific product; and
3. If further testing is deemed appropriate, identify and complete the specific testing that must be conducted;
4. Update the applicable medical device design file with all relevant documentation, including a Significant Change notification.

In the case of Class III medical devices, manufacturers will be required to submit their updated medical device design dossier and Significant Change notification to their respective EU Notified Body immediately upon the completion of the above steps. The Notified Body will then review all submitted documentation and make a determination whether the manufacturer’s submitted data is sufficient to support the changeover to the new Tyvek® material.

For lower risk devices categorised as Class Ia and IIa and IIb, it is expected that Notified Bodies will not require manufacturers to immediately submit their Significant Change notification and supporting documentation for review. Instead, these documents will be examined by the Notified Body during its next regular scheduled audit.

Regardless of the risk class assigned to a given device, medical device and sterile packaging manufacturers must also concurrently review and evaluate the provisions of their quality management system for continued compliance with the requirements of ISO 13485, Medical devices - Quality management systems - Requirements for regulatory purposes.
## Required actions in other jurisdictions

Below is a brief summary of the current transition status in other key jurisdictions:

### United States

In October 2015, the U.S. FDA has affirmed the functional equivalence of Tyvek® styles 1073B and 1059B produced with the new technology. With affirmation of functional equivalence, the modification will simply be interpreted as a change in material lot, and medical device and sterile packaging manufacturers will not be required to file amended 510(k) applications for currently approved devices in most cases.

### China

China’s Food and Drug Administration conducted its own independent testing in 2013 on Tyvek® manufactured with the new technology and has concluded that “For the DuPont Tyvek® products manufactured with DuPont’s latest flash-spinning technology and current manufactured DuPont Tyvek® products, all the testing results meet the criteria of functional equivalence and non-inferiority under the DuPont Validation Protocol.” Therefore, no additional testing is required.

### Japan

Japan’s Ministry of Health, Labor and Welfare (MHLW), in conjunction with the Pharmaceutical and Medical Device Agency (PMDA), recommends that medical device manufacturers review and update relevant documentation as necessary, and submit a change notification to authorities. The change notification is not expected to result in a subsequent audit or investigation.

### Canada

Health Canada has developed a unique notification process to specifically address the Tyvek® changes. Under this process, manufacturers of Class III and Class IV medical devices using Tyvek® affected by the manufacturing technology change must submit to Health Canada written notice attesting that the configuration and sterilisation process identified in DuPont’s testing is directly applicable to their product. Manufacturers of Class III and Class IV devices are only required to submit a Medical Device License Amendment Application in cases where differences in the packaging configuration or sterilisation process could negatively impact device sterility over the stated shelf-life.
Other transition considerations

Despite their comprehensive scope, the functional equivalence studies conducted by the MPTP do not address every potential variable in how Tyvek® may be used in a specific application. For example, some sterile packaging manufacturers may prescribe sterilisation using chlorine dioxide, a sterilisation modality that differs from those evaluated under the MPTP. In such cases, medical device and sterile packaging manufacturers will likely be required to conduct additional testing to demonstrate functional equivalence with legacy Tyvek® in connection with a specific use in a currently approved product.

The notification received by DuPont from the U.S. FDA affirming the functional equivalence of transition and legacy Tyvek® in October 2015 signals the beginning of commercial sales of the transitioned advanced material. The company has not announced a specific timetable for phasing out the production of legacy Tyvek®, and is expected to work with individual manufacturers to assure continued access to legacy Tyvek® during the transition period. However, market dynamics and production logistics could lead to excess demand for legacy Tyvek® during the transition period, resulting in temporary shortages, delays in shipments and price fluctuations.

In addition, testing laboratories may not have adequate capacity to handle the anticipated demand for transition testing. This is particularly important in the EU, where only a handful of EU Notified Bodies have issued guidance letters allowing them to process Significant Change notifications. Further, regulatory authorities may be delayed in processing change notices to existing certifications and approvals.

For these reasons, medical device and sterile packaging manufacturers are urged to complete the regulatory review process as soon as possible to determine whether revalidation testing of their specific products is required to maintain compliance with applicable regulations and requirements. Prompt attention to transition requirements will enable manufacturers to quickly incorporate new Tyvek® into their production processes, reducing the risk of production interruptions and helping to ensure the continued flow of product to customers.
TÜV SÜD Product Service GmbH is one of the five EU Notified Bodies that participated in DuPont’s MPTP, and has issued a guidance letter on the transition for compliance with EU requirements. TÜV SÜD has also developed a generic digital Tyvek® Transition Submission Form that will take medical device and sterile packaging manufacturers step-by-step through the evaluation and revalidation process. TÜV SÜD’s Tyvek® Transition Submission Form provides an effective blueprint for navigating the transition process, and is an efficient and cost-effective method for achieving continued compliance. The questionnaire is available digitally for a fee of 850 EUR plus VAT and can be used by companies for all their medical devices affected by the transition.

For more information about TÜV SÜD’s Tyvek® Transition Submission Form, please contact your local TÜV SÜD representative.
GLOSSARY OF ACRONYMMS

EU – european union
FDA – food and drug administration
MDM – medical device manufacturers
MHLW – ministry of health, labor and welfare

MPTP – medical packaging transition project
PMDA – pharmaceutical and medical device agency
SPM – sterile packaging manufacturers

FOOTNOTES


[4] The complete results of DuPont’s testing of the new Tyvek® is available at www.transition.tyvek.com (as of 31 August 2015).


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