

DuPont<sup>®</sup> Tyvek<sup>®</sup> Medical Packaging Transition Project (MPTP) Styles 1073B and 1059B Compliance to ISO 11607-1:2006 & EN ISO 11607-1:2009 as modified by Amd. 1:2014

June 2017

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### Introduction

DuPont<sup>™</sup> Tyvek<sup>®</sup> spunbonded olefin is intended for packaging of terminally sterilized medical devices. To guide the medical device manufacturers and sterile packaging manufacturers in their selection and qualification of materials, as well as design and validation of packaging and packaging processes, the International Standards community has promulgated the ISO 11607-1:2006/Amd.1:2014 & EN ISO 11607-1:2009/ Amd.1:2014 Packaging for terminally sterilized medical devices Part 1: Materials, sterile barrier systems and packaging systems and ISO 11607-2:2006/Amd.1:2014 & EN ISO 11607-2:2006/Amd.1:2014 Packaging for terminally sterilized medical devices Part 2: Validation requirements for forming, sealing and assembly processes. The EN ISO and the ISO versions are identical except for the European Foreword and the Annex ZA providing correspondence with the essential requirements of the European Medical Device Directive. Annex ZA in the EN ISO version was amended in 2009. Subsequent references to EN ISO 11607-1 refer to the amended EN ISO respectively ISO version. (See Appendix A for details concerning the 2014 revisions and amendments.)

As the producer of Tyvek<sup>®</sup> for medical and pharmaceutical packaging, DuPont Medical and Pharmaceutical Protection has compiled documentation which demonstrates the compliance of Tyvek<sup>®</sup> with relevant sections of the EN ISO 11607-1 standard. This will allow medical device manufacturers and sterile packaging manufacturers to focus on the package material production, final package design qualification, and the device package process validation portions of the standard.

This is the fourth Tyvek<sup>®</sup> Compliance to EN ISO 11607-1 document published by DuPont Medical and Pharmaceutical Protection. The first, published in December 2011, was based upon ISO 11607-1:2006, which was reaffirmed in 2010. The second, published in January 2015, was based upon EN ISO 11607-1:2009/Amd.1:2014. Both of these compliance documents, which include Tyvek<sup>®</sup> styles 1073B, 1059B and 2FS<sup>™</sup>, refer the user to the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* for the data supporting compliance.

The third, published in August 2015, and this June 2017 edition of the Tyvek<sup>®</sup> Compliance to EN ISO 11607-1 document apply **only** to Medical Packaging Transition Project (MPTP) material styles 1073B and 1059B. These documents refer the user to data posted on our website at <u>transitiondata.tyvek.com</u>. A new edition of the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* will be published based on the wealth of data that was produced for MPTP. Additionally, compliance is supported by a number of DuPont Technical Information Documents (TIDs) which contain the necessary experimental data. In this preamble, the documents are described and their applicability to the various sections of the EN ISO 11607-1 document are explained. The TIDs, which cover material testing for sterile barrier systems, can be used to demonstrate packaging compliance to this standard. Much of the information in the TIDs is presented in the <u>DuPont Technical Reference Guide for Medical and</u> <u>Pharmaceutical Packaging</u>.

The product characteristics of Tyvek<sup>®</sup> include:

- Outstanding porous microbial barrier
- High strength to weight ratio
- Moisture resistance
- Inertness to most chemicals
- Air and water vapor permeability
- Clean peeling seals
- Low linting due to continuous filaments
- Low fiber tear
- Puncture resistance

These characteristics provide high value in terminally sterilized packaging of medical devices sterilized by a wide variety of methods. Several package configurations containing Tyvek<sup>®</sup> are used within the medical device industry. Packages such as chevron peel pouches and header bags are composed of Tyvek<sup>®</sup> sealed to flat, unshaped, flexible film in a wide variety of length and width dimensions. In addition, Tyvek<sup>®</sup> is commonly used in packages made with a Form-Fill-Seal (FFS) process and equipment using rigid or flexible forming films, as well as lidding material for preformed rigid trays.

We commonly use the terms "coated Tyvek" and "uncoated Tyvek". Coated Tyvek" has an adhesive coating applied to the Tyvek" by sterile packaging manufacturers to seal to the package bottom web to facilitate a peelable seal. Uncoated Tyvek" is used when the bottom web has a sealing layer in its construct to facilitate a peelable seal or when the intent is to produce seals that are not intended to be opened (weld seals).

### Introduction

A variety of converting steps may be required prior to using Tyvek<sup>®</sup> in medical packaging. Some will have the adhesive coated onto the Tyvek<sup>®</sup> prior to use, while most will be printed, slit or die cut before incorporation into the final package.

The permeability and chemical inertness of Tyvek<sup>®</sup> allow its use in a variety of sterilization processes. The sterile barrier systems using Tyvek<sup>®</sup> are commonly sterilized using ethylene oxide, electron-beam and gamma irradiation. In addition, steam sterilization may be used if temperatures are controlled to avoid melting the Tyvek<sup>®</sup>. Tyvek<sup>®</sup> has been shown to meet packaging criteria for steam sterilization under controlled conditions (250°F [121°C] at 30 psi for 30 minutes with temperatures up to 260°F [127°C]). Low-temperature oxidative sterilization methods such as: gas plasma with hydrogen peroxide, vapor phase hydrogen peroxide peracetic acid, ozone and chlorine dioxide, require Tyvek<sup>®</sup> packaging because cellulosic porous materials are adversely affected by these strong oxidizing environments. This document is used to demonstrate the compliance of Tyvek<sup>\*</sup> with the EN ISO 11607-1 standard. Tyvek<sup>\*</sup> sheet material falls under Sections 4, 5 and 7. The MPTP produced extensive data on packages made with Tyvek<sup>\*</sup> that can support manufacturers with Section 6. This document lists each clause from EN ISO 11607-1 that contains a requirement, followed by compliance information for the requirement. There are other DuPont documents that are referred to in this document and they are all available at <u>www.MedicalPackaging.DuPont.com</u> NOTE: There is a tremendous amount of data referenced in this

document that can be viewed and downloaded by clicking on the supplied links. Therefore, it is important to use this document while on a computer with access to the internet.

### **MPTP Overview**

The DuPont<sup>••</sup> Tyvek<sup>•</sup> Medical Packaging Transition Project (MPTP) is a plan to transition production of Tyvek<sup>•</sup> 1073B and Tyvek<sup>•</sup> 1059B to the latest flash-spinning technology and equipment. The MPTP is a collaborative effort involving sterile packaging manufacturers, medical device manufacturers, regulatory authorities, testing laboratories and contract sterilizers around the world. The MPTP would not be possible without this industry collaboration.

The MPTP includes a systematic method for generating data at Nelson Laboratories, a third-party test laboratory, to prove that Tyvek® produced on newer manufacturing lines (known as Transition Protocol material) is functionally equivalent to Current Tyvek®. The study was initiated to help mitigate requalification and ensure the continuity and flexibility of future supply. In this context, Functional Equivalence means that attributes of Transition Protocol material meet functional and performance requirements.

Positive outcomes from Functional Equivalence testing ensure that Transition Protocol material behaves similarly to Current Tyvek<sup>®</sup> in various downstream processes and applications, even if some attribute data may not be identical. Transition Protocol material produced on the newer manufacturing lines has become commercially available around the globe following U.S. FDA affirmation of Functional Equivalence. Production is done in two locations—Richmond, VA, USA and Contern, Luxembourg—with two polymer supply sources for the United States and two polymer supply sources for Luxembourg.

There are three MPTP study components to demonstrate that all six possible line/polymer combinations are interchangeable for both Tyvek<sup>\*</sup> 1073B and Tyvek<sup>\*</sup> 1059B, two of which involve production and testing of sterilized medical device packages. Those two components are:

1. U.S. FDA Transition Protocol – a study plan based on sound principles of experimental design and statistical analysis for generating data to prove Functional Equivalence by comparing Transition Protocol material and Current Tyvek<sup>®</sup> using 60 different device/package combinations ("cells") with a validated design and a validated forming, sealing and assembly process. The plan has been reviewed and accepted by the Center for Devices and Radiological Health (CDRH) at the U.S. FDA. Over the course of protocol implementation, CDRH reviewed the DuPont analysis of the third-party test laboratory data to determine Functional Equivalence. On October 5, 2015, DuPont received notification from CDRH at the U.S. FDA affirming Functional Equivalence of Transition Tyvek<sup>®</sup> to Current Tyvek<sup>®</sup> for sterile medical packaging. **2. Phantom Protocol** – creation and testing of 18 additional sterilized medical device/package combinations ("cells") that are outside the scope of the U.S. FDA Transition Protocol but have been requested by the industry to support risk assessments.

The third study component is Biocompatibility, Food Contact and Pharmacopeia testing.

To view details about each cell in the MPTP, including package configurations and constructions, as well as sterilization information, go to the <u>MPTP Cell Descriptor Selector Tool</u>.

Industry Summary Reports for each study time point are posted on the website (<u>transitiondata.tyvek.com</u>) as they become available. The Industry Summary Reports contain study background and data summaries. Each of the metrics, including: seal strength, microbial barrier, package integrity and visual inspection will be broken down by seven categories to facilitate individual risk analysis where applicable.

These seven categories are:

- Coated 1073B Pouches/Bags
- Coated 1073B Form-Fill-Seal
- Coated 1073B Lids/Rigid Trays
- Uncoated 1073B Pouches/Bags
- Coated 1059B Form-Fill-Seal
- Uncoated 1059B Pouches/Bags
- Uncoated 1059B Form-Fill-Seal

Test results can also be found using the <u>MPTP Package Test</u> <u>Results Selector Tool.</u>

#### **4. GENERAL REQUIREMENTS**

The numbers in the following sections refer to the specific clauses in EN ISO 11607-1.

#### 4.2. Quality systems

## 4.2.1 The activities described within this part of EN ISO 11607-1 *shall* be carried out within a formal quality system.

Tyvek<sup>°</sup> production facilities located in Richmond, VA, and Luxembourg are ISO 9001:2008 certified. As a requirement for certification, both facilities have a Quality Systems Manual. The Quality Systems Manual is an evergreen document and the controlled copy is kept on file. Our performance against it is the subject of semi-annual audits as part of retaining ISO 9001:2008 Registration, and is available to the auditors of our facilities. Changes to the manual may only be made with appropriate approvals.

The production activities of Transition Protocol material will be carried out within the same formal quality systems in place before the transition. We have quality assurance measures and standard operating procedures for all Tyvek\* manufacturing lines, as required, to manage style and polymer transitions and to prevent cross-contamination.

#### 4.3 Sampling

#### The sampling plans used for selection and testing of packaging systems *shall* be appropriate to packaging systems being evaluated. Sampling plans shall be based upon statistically valid rationale.

Sampling and physical property testing for Tyvek<sup>®</sup> medical packaging styles are conducted per procedures associated with ISO 9001:2008 quality systems registration. Samples of Tyvek<sup>®</sup> are taken at the bonder windup, identified, and delivered to the in-area lab for physical property testing.

All routine physical property tests run on bonded Tyvek<sup>®</sup> are performed in the in-area lab. Testing is intended to satisfy Product Characterization, Process Control, and Measurement Control.

Samples are managed using the laboratory information management system (LIMS). Every sample is identified with a LIMS sample label. The sample label contains all necessary information needed to track a test result back to finished product.

Tyvek<sup>\*</sup> is produced in full mill rolls that are approximately 10 feet wide and have a diameter of approximately three feet. These full mill rolls are then slit into multiple smaller packages according to the customer requirements. Full mill rolls are sampled uniformly across their width to calculate roll averages. Test method variance related to equipment and analysis is included in the observed values. Other sampling plans and test methods may yield different values.

See Aligned Test Methods and Sampling Plans for details.

A regular work practice alignment between Richmond and Luxembourg ensures that products are controlled in the same way and that interchangeability will be maintained over time.

Sampling plans used for MPTP are described in the Industry Summary Reports, which are available at <u>transitiondata.tyvek.com</u>

#### 4.4 Test methods

## 4.4.1 All test methods used to show compliance with this International Standard *shall* be validated and documented.

All physical properties of Tyvek<sup>\*</sup> that are used to demonstrate acceptable material for packaging terminally sterilized medical devices are measured by validated DuPont test methods that are comparable to recognized, national and international standards. DuPont conducts testing as described in <u>Aligned Test Methods</u> and <u>Sampling Plans</u>.

Most of the testing for the MPTP has been performed by independent external test laboratories certified under ISO 17025:

<u>Nelson Laboratories</u> <u>NAMSA</u> <u>ISEGA</u>

See MPTP Testing Summary for details.

#### 4.4.2 Test method validation *shall* demonstrate the suitability of the method as used. The following elements *shall* be included:

- Establishment of a rationale for the selection of the appropriate tests for the packaging system
- Establishment of acceptance criteria; pass/fail is a type of acceptance criterion
- Determination of test method repeatability
- Determination of test method reproducibility
- Determination of test method sensitivity for integrity tests

Equipment calibration procedures for quality critical instruments and lab measurement control are conducted per internal procedures associated with ISO 9001:2008 quality systems registration.

The establishment of test methods was based on EN ISO 11607-1 Annex B recommendations for test methodology. The accuracy and reliability of test results are highly dependent on the calibration of test equipment and the control of the testing environment, sampling process, and the testing process. The DuPont standard operating procedure specifies the calibration and control system for the in-area test lab equipment to ensure data is consistently accurate. The test data on routine production samples is used to certify product meets established standards and to control processing conditions that impact physical and chemical properties. All test equipment is calibrated on a specified frequency using gauges traceable to nationally recognized standards or locally developed standards.

The Tyvek<sup>®</sup> in-area lab controls the measurement system by using a standard sample to monitor the repeatability and stability of most instruments in the lab. This provides a reliable method for detecting significant deviations in instrument readings due to instrument failure. Following is a summary of the standard control procedure:

- A standard sample roll is selected from routine production that represents a stable process condition in spinning and bonding.
- Several samples from this roll are tested to establish control limits.
- The standard sample is tested on a regular schedule on each instrument and the results are monitored.
- Corrective action is taken when a drift is detected.

The MPTP U.S. FDA Transition and Phantom Protocols use four key test methods:

#### a. Visual Inspection

Visual inspection has been made according to the visual inspection procedure of the medical device manufacturer during production of the packages and using ASTM F1886 in the test laboratory. ASTM F1886 is a well-established standard in the industry and there is no alternative ISO or EN standard available.

#### b. Seal Strength

Seal strength testing has been done according to ASTM F88, which is widely used in the industry because it is the only seal strength test method with a published precision and bias statement based on a round robin study. The seal strength test method described in EN868-5, also used in Europe, has no published precision and bias statement, which would be the basis for proper validation of the test method. The Sterile Barrier Association (SBA) has undertaken efforts to develop precision and bias statements for some EN test methods. Regarding seal strength, the SBA recommends ASTM F88.

#### c. Package Integrity

There are a number of test methods available for integrity testing. The protocol is based on ASTM F1929—*Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration*.

- ASTM F1929 has a sensitivity down to 50 µm channels, which is the best of all package integrity test methods.
- The method is widely used in the industry.
- There is a documented precision and bias statement available.

#### d. Microbial Barrier

Historically, the microbial barrier performance of Tyvek<sup>®</sup> has been evaluated using ASTM F1608—*Standard Test Method for Microbial Ranking of Porous Packaging Materials* (*Exposure Chamber Method*). ASTM F1608 produces a value and, as such, is ideal for comparison of microbial barrier materials. However, being a microbiological test method, it has relatively high variability and needs a significant amount of time to be performed. For these reasons, DuPont proposed the use of ASTM F2638—*Standard Test Method for Using Aerosol Filtration for Measuring the Performance of Porous Packaging Materials as a Surrogate Microbial Barrier*. ASTM F2638 is a physical test method, which is less difficult to perform and produces data in a much shorter timeframe.

The test method was revised prior to completing the testing with a precision and bias statement. ASTM F2638 has been accepted by the U.S. FDA as a recognized standard and is listed in Annex B of the EN ISO 11607 amendment of 2014. For consistency and to allow comparisons, additional microbial barrier data has been produced on Tyvek<sup>\*</sup> sheets using ASTM F1608.

Other test methods used have been selected based on industry recommendations.

## 4.4.3 Unless specified in test methods, test samples shall be conditioned at $(23 \pm 1)^{\circ}$ C and $(50 \pm 1)^{\circ}$ relative humidity for 24h.

All samples used for product release are tested in a controlled laboratory environment. Because Tyvek<sup>®</sup> is hydrophobic, samples are not stabilized for 24 hours prior to testing.

For MPTP materials, all polymers continue to be virgin highdensity polyethylene (HDPE); the hydrophobic nature of Tyvek<sup>®</sup> will not change. Most of the MPTP testing is done in third-party external test laboratories certified according to ISO 17025. Specific conditioning requirements have been applied, as applicable.

#### **4.5 Documentation**

## **4.5.1 Demonstration of compliance with the requirements of this standard** *shall* **be documented.**

# 4.5.2 All documentation *shall* be retained for a specified period of time. The retention period *shall* consider factors such as regulatory requirements, expiry date and traceability of the medical device or sterile barrier system.

All documents that illustrate the compliance of Tyvek<sup>®</sup> with EN ISO 11607-1 are retained for a specified period of time. This time period varies depending on the type of document and is specified in our quality procedures.

There is no change regarding documentation from standard production as a result of the MPTP. The documentation of MPTP data and the final reports are designated as permanent records.

DuPont maintains a DuPont<sup>™</sup> Tyvek<sup>®</sup> Device Master File at the U.S. FDA and at Health Canada, as well as a DuPont<sup>™</sup> Tyvek<sup>®</sup> Drug Master File at the U.S. FDA. If you are seeking permission to reference one of these master files, please complete and submit the form available in the <u>Tyvek<sup>®</sup> for Medical &</u> <u>Pharmaceutical Packaging Reference Library.</u>

#### 5. MATERIALS AND PREFORMED STERILE BARRIER SYSTEMS

Tyvek<sup>®</sup> has been used to package terminally sterilized medical devices in a variety of global climates since 1972. Because it is made of high-density polyethylene filaments, it is not affected by climatic changes in humidity, temperature, or atmospheric pressure. Because its melting point is 275°F (135°C), steam sterilization should be limited to <260°F (<127°C) temperature cycles. Exposure to UV light should be limited to less than one month. Normal shipping, handling and storage conditions should be used. Compatible ink offerings and labeling systems have been developed and most major manufacturers offer them to the market.

The administration of essential ingredients is conducted per standard operating procedures, specifying responsibility leading to the implementation of a system for the set-up, receipt and release of essential materials. Each shipment of polymer is received with a Certificate of Analysis demonstrating that the specification parameters are met.

#### **5.1 General requirements**

# 5.1.3 The conditions under which the material and/or preformed sterile barrier system are produced and handled *shall* be established, controlled and recorded, if applicable, in order to ensure that:

a) the conditions are compatible with the use for which the material and/or sterile barrier system is designed;

## b) the performance characteristics of the material and/or sterile barrier system are maintained.

Tyvek° is a highly inert material and, once manufactured, it typically does not change unless directly exposed to UV light for more than 30 days.

#### 5.1.4 As the minimum, the following *shall* be considered:

#### a) Temperature range

Toughness and flexibility are retained down to -100°F (-73°C). When exposed to heat, Tyvek<sup>®</sup> begins to shrink at approximately 270°F (132°C) and melts at 275°F (135°C). Under actual processing conditions, the temperature can influence the handling of the web and the range of exposures should be controlled or validated. It is suggested that during processing (slitting, coating, printing, etc.) the web temperature should not exceed 175°F (79°C).

#### <u>Freeze Thaw Dimensional Stability Study</u> <u>Effects of Steam Sterilization</u>

#### b) Pressure range

The ability to perform over a range of pressures is a critical characteristic of Tyvek<sup>®</sup> when incorporated into a sterile barrier system (SBS). Porosity is the fabric characteristic related to pressure an SBS may experience and allows for the equilibration of pressure differentials across a sealed SBS. The extent of the porosity necessary for an SBS is an attribute only a medical device manufacturer can determine based on the sterilization process, shipping, handling and storage the packaging system will be exposed to during its life cycle.

In the frame of the U.S. FDA Transition Protocol and Phantom Protocol, 78 packaging configurations with Tyvek<sup>®</sup> have been evaluated through a wide range of manufacturing and sterilization conditions while meeting Functional Equivalence criteria.

#### c) Humidity range

Tyvek° is hydrophobic and is not affected by moisture. Tyvek° maintains its strength regardless of humidity.

For MPTP materials, all polymers will continue to be virgin high-density polyethylene (HDPE); the hydrophobic nature of Tyvek\* will not change.

#### d) Maximum rate of change of the above, where necessary

As a packaging material, the rate of temperature, pressure and humidity changes are not applicable. These elements must be considered once Tyvek<sup>®</sup> becomes part of an SBS.

In the frame of the U.S. FDA Transition Protocol and Phantom Protocol, 78 packaging configurations with Tyvek" have been evaluated through a wide range of manufacturing and sterilization conditions while meeting Functional Equivalence criteria for pre- and post-sterilization, as well as after accelerated and real-time aging.

#### e) Exposure to sunlight or UV light

Physical properties of Tyvek<sup>®</sup> are degraded with extended exposure (more than 30 days) to direct sunlight (ultraviolet rays).

#### f) Cleanliness

Tyvek<sup>®</sup> is composed of essentially continuous filaments and does not generate a significant amount of lint particles under conditions of ordinary use.

#### Particle Generation Properties

#### g) Bioburden

The process of manufacturing Tyvek<sup>°</sup> allows only short periods of time when the sheet is subject to airborne particulates and microbes; therefore, the bioburden on the surface of the Tyvek<sup>°</sup> is very low. This low bioburden does not add significantly to the required sterilization time. The typical bioburden of all Tyvek<sup>°</sup> medical packaging styles is less than 100 colony forming units (cfu) per ft<sup>2</sup>.

The bioburden of MPTP materials has been determined per ISO 11737-1, with a similar performance to Current Tyvek<sup>®</sup> (pre-sterilization). A testing certificate is available in the <u>Tyvek<sup>®</sup></u> for Medical & Pharmaceutical Packaging Reference Library.

#### h) Electrostatic conductivity

In some processing steps, Tyvek<sup>®</sup> may generate static electricity unless treated with antistatic agents. Styles intended for medical packaging do not contain an antistatic agent. Manufacturers should assess the static electricity produced when processing materials and use static control mechanisms as necessary.

Untreated styles can build a static charge during roll or sheet handling and should not be handled in areas where there is the potential for explosive vapor/air mixtures.

# 5.1.5 The source, history and traceability of materials, especially recycled materials, *shall* be known and controlled to ensure that the finished product will consistently meet the requirements of this part of EN ISO 11607.

The source, history and traceability of incoming and outgoing materials are controlled by our quality control procedures. Recycled materials are not used to manufacture Tyvek<sup>®</sup> medical packaging styles.

No change in our approach to handling materials; Tyvek<sup>®</sup> will continue to be manufactured without recycled materials.

#### 5.1.6 The following properties *shall* be evaluated:

#### a) Microbial barrier

The microbial barrier properties of MPTP materials are available at the following link:

Microbial Barrier Properties of 1073B and 1059B

#### b) Biocompatibility and toxicological attributes

Biocompatibility and other toxicological attributes of MPTP materials are acceptable and are documented in Biocompatibility, Food Contact and Pharmacopeia Testing

#### c) Physical and chemical properties

The physical and chemical properties of MPTP materials are documented at the following links:

<u>Transition Protocol Materials Specification</u> and Miscellaneous Properties Data Sheet (English)

Transition Protocol Materials Specification and Miscellaneous Properties Data Sheet (Metric)

Infrared Spectrum "Fingerprinting" via ATR-FTIR

Differential Scanning Calorimetry

Bar Charts of Specification and Miscellaneous Properties:

Specification Properties of 1073B

Specification Properties of 1059B

Miscellaneous Properties of 1073B

Miscellaneous Properties of 1059B

Because Tyvek<sup>®</sup> is made of high-density polyethylene, it is relatively chemically inert. The chemical resistance of Tyvek<sup>®</sup> to various chemicals is available at the following link:

#### <u>Product Handbook for DuPont<sup>™</sup> Tyvek<sup>®</sup></u>

#### d) Compatibility with respect to forming and sealing processes

Tyvek<sup>®</sup> has been used as a packaging material for medical devices since 1972. It is customary for the user of a sterile barrier system (SBS) to specify the strength requirements for its use. It is intended that the package or SBS strength selected will be sufficiently strong so as to assure SBS integrity through the user's distribution, handling and storage systems until the end of the indicated shelf life. The strength of a preformed SBS seal should be determined by the manufacturer of that system as well as required process parameters (i.e., sealing window) to ensure that the product meets the established seal specifications. Sealing fingerprints of Transition Protocol material have been evaluated in comparison to Current Tyvek® during the development phase. These evaluations have been performed for uncoated 1073B pouches with a 100-gauge Nylon/HDPE film and uncoated 1059B form-fill-seal blister packs with a 100-gauge multilayer nylon with a peelable sealant. Functional Equivalence between Transition Protocol material and Current Tyvek<sup>®</sup> has been determined using 78 different device/package combinations ("cells") with a validated forming and sealing process. The comparison of seal strength and the effects of aging on seal strength are documented in the Industry Summary Reports.

## e) Compatibility with respect to the intended sterilization process(es)

Tyvek<sup>®</sup> medical packaging styles are compatible with all approved sterilization methods, including: ethylene oxide, electron-beam, gamma irradiation, steam (under controlled conditions), and low-temperature oxidative sterilization processes.

#### Material Sterilization Details

Effects of Steam Sterilization

Hydrostatic Head and Surface Energy

## f) Any shelf-life limitations for pre-sterilization and post-sterilization storage

Tyvek<sup>®</sup> medical packaging styles should be stored under the same conditions as one would store a medical device. Tyvek<sup>®</sup> should not be exposed to direct sunlight for more than 30 days.

Tyvek° is capable of maintaining package integrity and sterility for at least five years.

#### Industry Summary Reports

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1073B (ASTM F2638)

Effects of Sterilization and Real-time Aging on Microbial Barrier for 1073B (ASTM F2638)

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1059B (ASTM F2638)

Effects of Sterilization and Real-time Aging on Microbial Barrier for 1059B (ASTM F2638)

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1073B (ASTM F1608)

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1059B (ASTM F1608)

## 5.1.7 Materials, e.g. wrapping materials, paper, plastic film, nonwovens, reusable fabrics, *shall* meet the following general performance requirements:

#### a) Materials shall be non-leaching and odorless under specified conditions of use to such an extent that neither performance nor safety is impaired and the medical devices with which they are in contact are not adversely affected.

Tyvek<sup>®</sup> medical packaging styles meet the extractable or composition requirements of various regulations such as 21 CFR 177.1520, Commission Regulation (EU) N° 10/2011.

Tyvek<sup>®</sup> styles 1059B and 1073B meet the testing requirements of USP <661> as well as the compositional and testing requirements of Section 3.1.3 and Section 3.1.5 of the European Pharmacopoeia.

#### Biocompatibility, Food Contact and Pharmacopeia Testing

Testing certificates and regulatory letters are available in the <u>Tyvek\* for Medical & Pharmaceutical Packaging</u> <u>Reference Library</u>.

## b) Materials *shall* be free of holes, cracks, tears, creases, or localized thickening and/or thinning sufficient to impair functioning.

Standard operating procedures (SOPs) are used within the manufacturing facilities to identify and correct visual anomalies. A summary of the SOPs describing the types of anomalies seen in Tyvek<sup>®</sup> and the release standards for Tyvek<sup>®</sup> medical packaging styles are listed below. Corrective actions when an anomaly is detected are also defined.

**Inspecting, grading, segregating and dispositioning of product** SOPs define the roles and responsibilities required to deliver the best product possible to our customers, including: guidelines for inspecting, grading, segregating and dispositioning Tyvek<sup>\*</sup>; specifications for moving sheet and stationary sheet; inspections tables describing anomalies, their causes, detection methods; and instructions related to segregating and dispositioning product when anomalies are detected.

#### Anomaly descriptions and possible causes

SOPs are designed to give a detailed description and definition of each known anomaly, the frequency of occurrence, and detection process. There are two categories of anomalies:

#### Minor:

An anomaly that does not affect performance but should be eliminated. This anomaly will be recorded and action taken to correct and prevent the anomaly. This type of anomaly will ship to customers.

#### Major:

An anomaly that does affect performance and must not ship. This anomaly will be recorded and action taken to correct and prevent the anomaly. This type of anomaly will not ship to customers.

#### Tracing and clearing of anomalies

Once a major anomaly is detected, the anomaly must be traced and cleared per SOPs. This prevents unacceptable material from shipping to customers.

A regular work practice alignment between Richmond and Luxembourg ensures that products are controlled in the same way and that interchangeability will be maintained over time.

## c) Materials *shall* have a basis weight (mass per unit area) which is consistent with the specified value.

See the specification properties tables available at:

Transition Protocol Materials Specification and Miscellaneous Properties Data Sheet (English) Transition Protocol Materials Specification and Miscellaneous Properties Data Sheet (Metric)

The target and the range for basis weight are not changing for Transition Protocol materials.

## d) Materials *shall* exhibit acceptable levels of cleanliness, particulate matter and linting.

Internal processes specify release limits for cleanliness and particulate matter. Tyvek<sup>®</sup> does not generate a significant amount of lint particles under conditions of ordinary use.

#### Particle Generation Properties

Static/Dynamic Coefficient of Friction

Parker Surface Smoothness

#### e) Material *shall* comply with established specific or minimum physical properties such as tensile strength, thickness variation, tear resistance, air permeance and burst strength.

For Tyvek<sup>®</sup> medical packaging styles, the established specification properties are Gurley Hill, Delamination and Basis Weight.

Transition Protocol Materials Specification and Miscellaneous Properties Data Sheet (English)

Transition Protocol Materials Specification and Miscellaneous Properties Data Sheet (Metric)

#### f) Materials *shall* comply with established specific chemical characteristics (such as pH value, chloride, and sulfate contents) to meet the requirements of the medical device, packaging system or sterilization process.

Tyvek<sup>\*</sup> medical packaging styles meet the extractable or composition requirements of various regulations such as 21 CFR 177.1520, Commission Regulation (EU) N° 10/2011. Tyvek<sup>\*</sup> styles 1059B and 1073B meet the testing requirements of USP <661> as well as the compositional and testing requirements of Section 3.1.3 and Section 3.1.5 of the European Pharmacopoeia.

Biocompatibility, Food Contact and Pharmacopeia Testing

#### g) Materials *shall* not contain or release material known to be toxic in sufficient quantity to cause a health hazard either before, during or after sterilization under the conditions of use.

The toxicological attributes of MPTP materials are documented at the following link:

Biocompatibility, Food Contact and Pharmacopeia Testing

## 5.1.8 In addition to the requirements given in 5.1.1 through 5.1.6, adhesive-coated materials *shall* meet the requirements listed below.

Adhesive coated Tyvek\* is sold by sterile packaging manufacturers and each will require a different set of process conditions to give the required package strength and integrity. The medical device manufacturer must validate the processes used for the coated product they are using.

The U.S. FDA Transition Protocol and Phantom Protocol included Tyvek<sup>\*</sup> styles that had been coated by three sterile packaging manufacturers (see <u>Cell Descriptors</u> for details) and tested for Functional Equivalence. Detailed reports with additional information are available from converters that apply the adhesive coatings.

## 5.1.10 In addition to the requirements given in 5.1.1 through 5.1.7, reusable containers *shall* meet the requirements given below.

Tyvek<sup>®</sup> is not designed to produce reusable containers.

#### 5.2 Microbial barrier properties

## 5.2.1 The impermeability of a material *shall* be determined in accordance with Annex C.

Tyvek° is not considered to be an impermeable material.

## **5.2.2 Demonstrating that the material is impermeable** *shall* satisfy the microbial barrier requirements.

Tyvek° is not considered to be an impermeable material.

## **5.2.3** Porous materials *shall* provide an adequate microbial barrier to microorganism in order to provide integrity of the sterile barrier and product safety.

The microbial barrier properties of MPTP materials are available at the following link:

Microbial Barrier Properties of 1073B and 1059B

#### 5.3 Compatibility with the sterilization process

#### 5.3.1 It shall be demonstrated that the materials and preformed sterile barrier system are suitable for use in the specified sterilization process(es) and cycle parameters.

Functional Equivalence between Transition Protocol material and Current Tyvek<sup>®</sup> has been determined using 78 different device/package combinations ("cells") with a validated sterilization process meeting the respective acceptance criteria as specified by the medical device manufacturer. Packages included pouches, bags, form-fill-seal and rigid tray applications; and sterilization methods included ethylene oxide, electron-beam, gamma irradiation, steam, dry heat, and lowtemperature oxidative sterilization processes.

To view details about sterilization processes included in the MPTP test protocols, go to the <u>MPTP Cell Descriptor</u> <u>Selector Tool</u>.

Results are available in the Industry Summary Reports.

#### 5.3.2 Sterilization compatibility should be determined using a sterilizer designed, constructed and operated in accordance with the requirements of the relevant International or European Standards.

All sterilization processes included under the MPTP U.S. FDA Transition and Phantom Protocols are validated processes performed on sterilizers in accordance with relevant standards and regulations.

# 5.3.3 The performance of the materials *shall* be evaluated to ensure that the material performance remains within specified limits after exposure to all the specified sterilization processes.

Tyvek<sup>®</sup> medical packaging styles are compatible with all approved sterilization methods, including: ethylene oxide, electron-beam, gamma irradiation, steam (under controlled conditions), dry heat and low-temperature oxidative sterilization processes.

Material Sterilization Details

Cell Descriptors

Industry Summary Reports

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1073B (ASTM F2638)

Effects of Sterilization and Real-time Aging on Microbial Barrier for 1073B (ASTM F2638)

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1059B (ASTM F2638)

Effects of Sterilization and Real-time Aging on Microbial Barrier for 1059B (ASTM F2638)

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1073B (ASTM F1608)

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1059B (ASTM F1608)

<u>Tyvek<sup>®</sup> 1073B Current vs. Transition Material</u> <u>Comparisons (Accelerated Aging)</u>

<u>Tyvek<sup>®</sup> 1059B Current vs. Transition Material</u> <u>Comparisons (Accelerated Aging)</u>

<u>Tyvek<sup>®</sup> 1073B Current vs. Transition Material</u> <u>Comparisons (Real-Time Aging)</u>

<u>Tyvek<sup>°</sup> 1059B Current vs. Transition Material</u> <u>Comparisons (Real-Time Aging)</u>

Effects of Steam Sterilization

Hydrostatic Head and Surface Energy

## **5.3.4 Specified sterilization processes may** include multiple exposures of the same or different sterilization processes.

The MPTP protocol packages were exposed to multiple sterilization cycles (1, 2 or 3 times) as specified by the medical device manufacturer for the validation of the respective device/ package configuration. To view details about sterilization processes and number of cycles included in the MPTP test protocols, go to the <u>MPTP Cell Descriptor Selector Tool</u>.

#### 5.3.5 Determination of suitability for the intended purpose shall include consideration of material variations that will occur during normal routine supply.

MPTP protocol packages were made with three lots of Current Tyvek<sup>®</sup> and three lots of material from all line/polymer combinations of Transition Protocol material using a wide variety of representative coatings and bottom webs available globally in the trade.

#### 5.4 Compatibility with the labeling system

#### The labeling system shall:

#### a) remain intact and legible until the point of use;

Ink manufacturers have developed specific inks to print on medical packaging styles of Tyvek<sup>®</sup>. To achieve consistent, high-quality print, the appropriate ink must be used.

- b) be compatible with the materials, sterile barrier system and medical device during and after the specified sterilization process(es) and cycle parameters and *shall not* adversely affect the sterilization process;
- c) not be printed or written in ink of a type which can be transferred to the medical device nor react with the packaging material and/or system to impair the utility of the packaging material and/or system nor change colour to an extent which renders the label illegible.

The labeling of product made by the Tyvek<sup>®</sup> manufacturing plants is aimed at meeting the needs of our customers and contractors. It must further account for and trace product through all manufacturing steps. Labels are applied to rolls of Tyvek<sup>®</sup> during the inspection and packaging operations. These labels provide sufficient information to identify the product and to trace product processing at the manufacturing site using the package number (bar-coded) as the primary identifier.

Because the label is removed prior to final processing; the reaction of the ink and label material is not applicable.

No printing and labeling issues have been reported from the 78 cells in the MPTP.

Printing Trials

#### 5.5 Storage and transport

# 5.5.1 Materials and preformed sterile barrier systems *shall* be packaged to provide the protection necessary to maintain the performance characteristics during transport and storage.

The material wrapping system used by DuPont is designed to provide the necessary protection to the rolls through the global supply chain. This would include transport by rail, truck, ocean containers and air. The rolls are wrapped with a polyethylene stretch film in either an axial or barrel method.

These methods of wrapping protect the Tyvek<sup>®</sup> rolls from contamination and damage during distribution and handling. There are no known restrictions on transport and storage of Tyvek<sup>®</sup> other than avoiding direct exposure to UV light for more than 30 days.

# 5.5.2 Materials and preformed sterile barrier systems *shall* be transported and stored under conditions that ensure that the performance characteristics remain within specified limits.

This can be accomplished by:

- a) demonstrating retention of these characteristics under defined storage conditions;
- b) ensuring that storage conditions remain within specified limits.

There are no known restrictions on transport and storage of Tyvek<sup>®</sup> other than avoiding direct exposure to UV light for more than 30 days.

#### 6. DESIGN AND DEVELOPMENT REQUIREMENTS FOR PACKAGING SYSTEMS

Previous versions of this document did not address the information required in EN ISO 11607-1 Section 6 because DuPont is only a material manufacturer. However, in conducting the MPTP, we now have extensive data on 78 different medical device packages that contain Tyvek\* styles 1073B or 1059B.

#### transitiondata.tyvek.com

The study was conducted on packaging for medical devices already in the marketplace with qualified designs and validated processes. Packages were made with Current Tyvek<sup>\*</sup> styles and also with Transition Protocol materials. The results indicate that the materials are functionally equivalent when assessed for seal strength, microbial barrier, package integrity and visual inspection. Most importantly, the packages were made at the lower, nominal and upper sealing process windows and produced functionally equivalent seal strength measurements before and after sterilization. Functional Equivalence was also confirmed after sterilized packages were subjected to accelerated aging conditions equivalent to 1, 3, and 5 years as well as 1-year real-time aging.

#### Industry Summary Reports

MPTP has caused many to consider the requirements found in clause 5.7 of ISO 11607-2 regarding validation and revalidation. For information on revalidation, please refer to the article in *Journal of Validation Technology* titled <u>"Sterile Barrier Systems:</u> <u>Managing Changes and Revalidations/IVT"</u> written by Wagner and Scholla.

## 6.2.5 The results of the design and development processes shall be recorded, verified and approved prior to the release of the product.

The concept of Functional Equivalence of Tyvek<sup>\*</sup> may only apply to medical packaging applications with documented and validated designs.

#### 6.3 Performance testing

For mechanical properties of MPTP materials, see material comparisons:

Specification Properties of 1073B

Specification Properties of 1059B

Miscellaneous Properties of 1073B

Miscellaneous Properties of 1059B

Transition Protocol Materials Specification and Miscellaneous Properties Data Sheet (English)

<u>Transition Protocol Materials Specification</u> and Miscellaneous Properties Data Sheet (Metric)

CFDA –Jinan Sheet Functional Equivalence Confirmation

<u>Tyvek<sup>®</sup> 1073B Current vs. Transition Material</u> <u>Comparisons (Accelerated Aging)</u>

<u>Tyvek\* 1059B Current vs. Transition Material</u> <u>Comparisons (Accelerated Aging)</u>

<u>Tyvek<sup>\*</sup> 1073B Current vs. Transition Material</u> <u>Comparisons (Real-Time Aging)</u>

<u>Tyvek<sup>®</sup> 1059B Current vs. Transition Material</u> <u>Comparisons (Real-Time Aging)</u>

#### 6.4 Stability testing

Extensive stability data has been generated for sheets and packages:

Material Sterilization Details

Effects of Steam Sterilization

Freeze Thaw Dimensional Stability Study

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1073B (ASTM F2638)

Effects of Sterilization and Real-time Aging on Microbial Barrier for 1073B (ASTM F2638)

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1059B (ASTM F2638)

Effects of Sterilization and Real-time Aging on Microbial Barrier for 1059B (ASTM F2638)

Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1073B (ASTM F1608) Effects of Sterilization and Accelerated Aging on Microbial Barrier for 1059B (ASTM F1608) Tyvek\* 1073B Current vs. Transition Material Comparisons (Accelerated Aging) Tyvek\* 1059B Current vs. Transition Material Comparisons (Accelerated Aging)

<u>Tyvek\* 1073B Current vs. Transition Material</u> <u>Comparisons (Real-Time Aging)</u>

<u>Tyvek\* 1059B Current vs. Transition Material</u> <u>Comparisons (Real-Time Aging)</u>

Industry Summary Reports

#### 7. INFORMATION TO BE PROVIDED

#### 7.1 The following information *shall* be provided with the material, preformed sterile barrier systems or sterile barrier systems.

- the name or trade name and address of the manufacturer or his authorized representative;
- the type, size or grade;
- batch number or other means of tracing the manufacturing history;
- the intended sterilization process(es);
- the expiry date, if applicable;
- any known restrictions on handling or use (e.g. environmental conditions) if applicable;
- for reusable materials and/or preformed sterile barrier systems, the frequency and nature of the maintenance;
- whether the materials and/or preformed sterile barrier systems are intended for single use or reuse;
- if instructions for use are supplied, they shall contain the date of issue or the latest revision.

#### 7.2 When national or regional regulations require additional information with the material, preformed sterile barrier systems or sterile barrier systems which are placed on the healthcare market, this additional information *shall* be provided.

Dashes 1-3 of clause 7.1 are contained on every roll of Tyvek<sup>\*</sup> manufactured. The rest of the information can be found in this document and in the <u>DuPont Technical Reference Guide</u> for <u>Medical and Pharmaceutical Packaging</u>.

No change in labeling except to allow identification of Current Tyvek<sup>®</sup> and Transition Protocol material.

## Appendix A—2014 Revisions and Amendments to EN ISO 11607-1

ISO 11607-1 and -2 were published in 2006 and amended in 2014 to address the comments that were received during their reaffirmation ballot in 2010. These amendments were published by ISO in July 2014 and are available from ISO, CEN, National Standards Bodies, and Standard Development Organizations. The EN ISO and the ISO versions are identical except for the European Foreword and the Annex ZA providing correspondence with the essential requirements of the European Medical Device Directive. Annex ZA in EN ISO 11607-1 was amended in 2009. The 2014 amendments includes a new annex ZA for both parts.

#### The major amendments to EN ISO 11607-1 are:

#### Introduction, 2nd paragraph, 3rd sentence:

Replace 'This part of ISO 11607 is harmonized with EN 868-1' with 'This part of ISO 11607 replaces EN 868-1'.

#### Addition to the Clause 1, Scope:

'This part of ISO 11607 does not apply to packaging materials and/or systems used to contain a contaminated medical device during transportation of the item to the site of reprocessing or disposal.'

#### Changes to Clause 3 Definitions:

**3.4 closure integrity-** 'characteristics of the closure which ensure that it prevents the ingress of microorganisms, demonstrated under test conditions which consider sterilization process, handling, distribution, transport and storage'

**3.8 microbial barrier**- 'property of the sterile barrier system which ensures that it prevents the ingress of microorganisms, demonstrated under test conditions which consider sterilization process, handling, distribution, transport and storage'

**3.19 seal integrity-** 'characteristic of the seal which ensures that it prevents the ingress of microorganisms, demonstrated under test conditions which consider sterilization process, handling, distribution, transport and storage'

#### 7.0 Information to be supplied- Additions

7.1'— the name or trade name and address of the manufacturer or his authorized representative;'

'— whether the materials and/or preformed sterile barrier systems are intended for single use or reuse;'

'— if instructions for use are supplied, they shall contain the date of issue or the latest revision.'

The single largest change to EN ISO 11607-1 is a complete revamping of Annex B. This includes additions and deletions of test methods. Most importantly, they have been arranged in a new table B1 which lists the methods and standard guides according to the following headers:

- Attribute/Characteristics
- Reference
- Title of reference
- Test method has statement of precision and/or bias, repeatability and reproducibility
- Test method only has statement of precision and/or bias
- Guidance, Standard Practice

Included in the addition of test methods is ASTM F2638-Standard Test Method for Using Aerosol Filtration for Measuring the Performance of Porous Packaging Materials as a Surrogate Microbial Barrier. This test method is used in the DuPont<sup>™</sup> Tyvek<sup>®</sup> Transition Protocol that is currently underway.

There are several more editorial changes to EN ISO 11607-1 that are contained in the Amendment for clarity. None of these amendments influence our compliance documentation.

For more information about the DuPont<sup>™</sup> Tyvek<sup>°</sup> Medical Packaging Transition Project (MPTP), visit transition.tyvek.com and transitiondata.tyvek.com.

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