DuPont™ Tyvek® Medical Packaging Transition Project
2013 Progress Report

June 2013
Presenters

Roseann C. Salasin
Global Marketing Director

Bruce A. Yost, Ph.D.
Global Technical Director

Thierry Wagner
Regulatory Affairs Director

Karen Polkinghorne
Packaging Engineer & MDM Specialist
Agenda

- Transition Project Overview
- Regulatory Update
- Technical Milestones Reached as of June 2013
- Preparing for Full Commercialization
- Closing Remarks
- Q&As
Project Objective – To Ensure Continuity and Flexibility of Future Supply

- Goal of the Transition Protocol is to demonstrate functional equivalence

- Functional equivalence means that the attribute you are measuring may be different, even statistically, but it still meets functional and performance requirements, so that it will perform similarly to current Tyvek® in your process and applications

- More than $30 Million investment by DuPont covering:
  - Global regulatory and industry support
  - Raw materials for multiple line and polymer testing
  - Developmental package creation and testing
  - Transition Protocol package creation and testing
  - Third-party laboratory testing
  - Phantom Protocol
  - Product Stewardship
Components of DuPont™ Tyvek® Medical Packaging Transition Project (MPTP)

- U.S. Food and Drug Administration (FDA) Transition Protocol
- Phantom Protocol
- Product Stewardship
Progress Possible Through Industry Collaboration

- Amcor Flexibles
- ATMI LifeSciences
- Barger, a division of Placon
- Beacon Converters, Inc.
- Bischof + Klein GmbH & Co.
- E-Beam Services, Inc.
- Encaplast srl
- Faxcim Corporation
- Ferric, Inc.
- Mangar Medical Packaging
- MEDIPACK AG
- NAMSA
- Nelson Laboratories
- Nordion
- Oliver-Tolas® Healthcare Packaging
- PeelMaster Packaging Corporation
- Perfecseal, Inc.
- Printpack Inc., Medical Packaging Division
- Rollprint Packaging Products, Inc.
- Sealed Air Nelipak
- SteriPack Asia Sdn. Bhd

- Medical Device Manufacturers (MDMs) around the world who are participating in the MPTP
**Key Regulatory Activities as of June 2013**

**United States**

- U.S. FDA Transition Protocol Amendments made and accepted by the Center for Devices and Radiological Health (CDRH) at the U.S. FDA in October 2012

**Europe**

- 4 largest Notified Bodies, which issued guidance letters for European compliance, received copy of U.S. FDA Transition Protocol Amendments and no issues have been reported. These Notified Bodies are:
  - BSI Assurance UK Ltd
  - SGS United Kingdom Ltd
  - TÜV Rheinland® LGA Products GmbH
  - TÜV SÜD Product Service GmbH
Key Regulatory Activities as of June 2013

Japan

- The MPTP was reviewed in a 3-party consultative meeting held on September 19, 2012. Participants included:
  - Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceutical and Medical Device Agency (PMDA)
  - Association of Registered Certification Bodies (ARCB) under PAL
  - Japan Federation of Medical Device Association (JFMDA)
- Published meeting minutes reference the official Japanese guidance (Yakushokuki) describing the process of reporting partial changes made to medical devices under a minor change notification
- The plan is to review MPTP data with the 3 parties; meeting minutes will be published
- For devices to be sold in Japanese domestic market, MDMs will apply their specific change management process following the official Japanese guidance (Yakushokuki)
Key Regulatory Activities as of June 2013

China

- Criteria established for determining functional equivalence of specification and miscellaneous properties
- SFDA–Jinan is currently performing testing on Transition Protocol materials, including:
  - Basis weight
  - Mullen burst
  - Delamination
  - Hydrostatic head
  - Gurley Hill porosity
  - Microbial barrier
  - Tensile strength, MD/CD
- SFDA–Jinan to issue final report later this year with results of functional equivalence
Global Members of the DuPont Medical and Pharmaceutical Protection Regulatory Team

Michael H. Scholla, Ph.D.
Global Regulatory Director and Acting North American Regulatory Director

Thierry Wagner
EMEA Regulatory Director

Ichiro Ikeda
Asian Regulatory Director

Park Qian
Regulatory Affairs Manager, China
Technical Milestones Reached as of June 2013

- Completed Developmental material assessments
- Successfully produced and tested Transition Protocol material
- Shipped materials to participating Sterile Packaging Manufacturers (SPMs) for conversion
- Participating MDMs have begun creating packages
- Publishable cell descriptor information collected and compiled; now available
- Conducted formal DuPont Product Stewardship review
- Nelson Laboratories and NAMSA ready for MPTP testing
Effects of Sterilization and Aging on Mechanical and Microbial Barrier Properties—Developmental Materials

Developmental 1073B and 1059B materials
- Represent the different manufacturing lines and polymers
- Control = Tyvek® 1073B or Tyvek® 1059B

Sterilization
- EO (2X)
- Gamma (25 kGy, 50 kGy)
- Electron-beam (25 kGy, 50 kGy)
- Steam (127°C for 30 minutes)

Test environments
- Pre-sterilization
- Post-sterilization
- Accelerated aging (1, 3, 5 years)
1073B Developmental Materials vs. Control Material

ASTM F1342
Control = DuPont® Tyvek® 1073B
Center point is zero
1059B Developmental Materials vs. Control Material

![Graph showing puncture strength comparison between developmental and control materials after various sterilization methods.](image)

- **Puncture** (lb)
  - 3.5 Pre-Sterilization
  - 3.5 Steam
  - 3.5 Ethylene Oxide (EO)
  - 3.5 Gamma @ 50 kGy
  - 3.5 Electron-beam @ 25 kGy
  - 3.5 Electron-beam @ 50 kGy

**Legend**:
- Red: Developmental
- Orange: Developmental: 1 year accelerated aging
- Red Diamond: Developmental: 3 year accelerated aging
- Red Star: Developmental: 5 year accelerated aging
- Blue: Control
- Blue Circle: Control: 1 year accelerated aging
- Blue Diamond: Control: 3 year accelerated aging
- Blue Star: Control: 5 year accelerated aging

**NOTES**:

- ASTM F1342
- Control = DuPont® Tyvek® 1059B
- Center point is zero

6/10/2013
1073B Transition Protocol Material

Transition Protocol typical values represent data from 200 rolls across different line and polymer combinations from a limited number of manufacturing campaigns. Values will be refreshed, as necessary, upon data collection from additional campaigns and long-term variability discernment.

*Based on customer feedback, upper limit was not specified.
1059B Transition Protocol Material

Transition Protocol typical values represent data from 100 rolls across different line and polymer combinations from a limited number of manufacturing campaigns. Values will be refreshed, as necessary, upon data collection from additional campaigns and long-term variability discernment.

*Based on customer feedback, upper limit was not specified.
1073B Transition Protocol Material

Transition Protocol typical values represent data from 200 rolls across different line and polymer combinations from a limited number of manufacturing campaigns. Values will be refreshed, as necessary, upon data collection from additional campaigns and long-term variability discernment.
1073B Transition Protocol Materials

Transition Protocol typical values represent data from 200 rolls across different line and polymer combinations from a limited number of manufacturing campaigns. Values will be refreshed, as necessary, upon data collection from additional campaigns and long-term variability discernment.

*Thickness variability target is equal to or less than incumbent product.
1059B Transition Protocol Materials

Transition Protocol typical values represent data from 100 rolls across different line and polymer combinations from a limited number of manufacturing campaigns. Values will be refreshed, as necessary, upon data collection from additional campaigns and long-term variability discernment.
1059B Transition Protocol Material

Transition Protocol typical values represent data from 100 rolls across different line and polymer combinations from a limited number of manufacturing campaigns. Values will be refreshed, as necessary, upon data collection from additional campaigns and long-term variability discernment.

*Thickness variability target is equal to or less than incumbent product.
# 1073B and 1059B Transition Protocol Materials

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Microbial Barrier</td>
<td>ASTM F1608</td>
<td>LRV</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td>&gt;4</td>
<td>&gt;4</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Microbial Barrier</td>
<td>ASTM F2638</td>
<td>% pMax</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
<td>&lt;0.3</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>

Notes: 1073B and 1059B Transition Protocol typical values represent data across different line and polymer combinations from a limited number of manufacturing campaigns. Values will be refreshed, as necessary, upon data collection from additional campaigns and long-term variability discernment.
Package Creation and Testing

- Qualified designs and validated processes

- Sealing conditions
  - Upper
  - Lower
  - Nominal

- Test environments
  - Pre-sterilization
  - Post-sterilization
  - Accelerated aging (1, 3, 5, 7 and 10 years)
  - Real-time aging (1, 3, 5 and 10 years)

- Package testing
  - Visual inspection (ASTM F1886M)
  - Package integrity (ASTM F1929)
  - Seal strength (ASTM F88)
  - Microbial barrier (ASTM F2638)

- Paired data set comparisons
Effects of Sterilization and Aging on Mechanical and Microbial Barrier Properties—Transition Protocol Materials

- Transition Protocol 1073B and 1059B materials
  - Represent the different manufacturing lines and polymers
  - Control = Tyvek® 1073B or Tyvek® 1059B

- Sterilization
  - EO (2X)
  - Gamma (25 kGy, 50 kGy, 100 kGy)
  - Electron-beam (25 kGy, 50 kGy, 100 kGy)
  - Steam (127°C for 30 minutes)
  - Low-temperature oxidation (2 methods)

- Test environments
  - Pre-sterilization
  - Post-sterilization
  - Accelerated aging (1, 3, 5, 7, 10 years)
  - Real-time aging (1, 3, 5, 7, 10 years)
Product Stewardship Testing Underway on Transition Protocol Material

- Cytotoxicity
- Endotoxins
- Skin irritation and sensitization
- Bioburden
- U.S. and European Pharmacopeia/Food Contact
- Extractables and leachables
Product Stewardship – Final Results for All Polymer Sources

U.S. Food Contact
- 21 CFR 177.1520 – Meet Test Requirements

European Pharmacopeia
- EP 3.1.5 – Meet Test Requirements
- EP 3.1.3 – Meet Test Requirements
Additional Data to Be Generated Per Industry Requests

- Particle generation
- Chemical resistance (ISO 11607)
- Steam and low-temperature oxidative sterilization behaviors
- Dimensional stability study (steam–freeze–thaw–freeze–thaw)
- DSC, FTIR
- Surface energy
- Dynamic/static coefficient of friction
- Printing (flexo and thermal)
- Low-intensity UV stability
- Parker (surface) smoothness (both sides)
- Baseline color and color after aging
Preparing for Commercialization

- Information to assist with Risk Assessments
  - Regulatory guidance
  - Developmental material data
  - MPTP Cell Descriptor tool
  - Executive Summary Reports

- Controlled sales of Transition Protocol material

- Expected timing for full commercialization of Transition Protocol material
# U.S. FDA Transition Protocol Test Matrix

<table>
<thead>
<tr>
<th>Style</th>
<th>Pouches and Bags</th>
<th>Form-Fill-Seal</th>
<th>Rigid Trays</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EO</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coated</td>
<td>1073B</td>
<td>1 2 3 4 5 6</td>
<td>7 8 9 10 11 12</td>
</tr>
<tr>
<td>Uncoated</td>
<td>1073B</td>
<td>22 23 24 25 26 27</td>
<td></td>
</tr>
<tr>
<td><strong>Gamma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coated</td>
<td>1073B</td>
<td>28 29 30</td>
<td>31 32 33</td>
</tr>
<tr>
<td>Uncoated</td>
<td>1073B</td>
<td>40 41 42</td>
<td></td>
</tr>
<tr>
<td><strong>Electron-beam</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coated</td>
<td>1073B</td>
<td>43 44 45</td>
<td></td>
</tr>
<tr>
<td>Uncoated</td>
<td>1073B</td>
<td>46 47 48</td>
<td></td>
</tr>
<tr>
<td><strong>EO</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coated</td>
<td>1059B</td>
<td>49 50 51</td>
<td></td>
</tr>
<tr>
<td>Uncoated</td>
<td>1059B</td>
<td>52 53 54 55 56 57</td>
<td>58 59 60</td>
</tr>
</tbody>
</table>
# Phantom Protocol Test Matrix

<table>
<thead>
<tr>
<th></th>
<th>Style</th>
<th>Pouches and Bags</th>
<th>Form-Fill-Seal</th>
<th>Rigid Trays</th>
</tr>
</thead>
<tbody>
<tr>
<td>EO Coated</td>
<td>1073B</td>
<td></td>
<td></td>
<td>X74</td>
</tr>
<tr>
<td>EO Uncoated</td>
<td>1073B</td>
<td>X61</td>
<td></td>
<td>X75</td>
</tr>
<tr>
<td>Gamma Coated</td>
<td>1073B</td>
<td></td>
<td></td>
<td>X62</td>
</tr>
<tr>
<td>Gamma Uncoated</td>
<td>1073B</td>
<td></td>
<td></td>
<td>X63</td>
</tr>
<tr>
<td>Electron-beam Coated</td>
<td>1073B</td>
<td></td>
<td></td>
<td>X72</td>
</tr>
<tr>
<td>Electron-beam Uncoated</td>
<td>1073B</td>
<td></td>
<td></td>
<td>X73</td>
</tr>
<tr>
<td>EO Coated</td>
<td>1059B</td>
<td></td>
<td></td>
<td>X78</td>
</tr>
<tr>
<td>EO Uncoated</td>
<td>1059B</td>
<td>X77</td>
<td></td>
<td>X71</td>
</tr>
<tr>
<td>Steam Coated</td>
<td>1073B</td>
<td></td>
<td></td>
<td>X65</td>
</tr>
<tr>
<td>Steam Uncoated</td>
<td>1073B</td>
<td>X69</td>
<td>X70</td>
<td>X66</td>
</tr>
<tr>
<td>Dry Heat Coated</td>
<td>1073B</td>
<td></td>
<td></td>
<td>X68</td>
</tr>
<tr>
<td>Low Temp. $H_2O_2$ Coated</td>
<td>1073B</td>
<td></td>
<td></td>
<td>X71</td>
</tr>
<tr>
<td>Gamma Coated</td>
<td>1059B</td>
<td></td>
<td></td>
<td>X72</td>
</tr>
<tr>
<td>Electron-beam Coated</td>
<td>1059B</td>
<td></td>
<td></td>
<td>X73</td>
</tr>
</tbody>
</table>

6/10/2013
MPTP Cell Descriptor Tool—at www.Transition.Tyvek.com
Example Result from Search of MPTP Cell Descriptor Tool

DuPont™ Tyvek® 1059B – Uncoated – Pouch – EO

English Units

Package Configuration
Chevron peel pouch

Top Web
DuPont™ Tyvek® 1059B
Perfecseal® Uncoated

Bottom Web
Perfecflex® 35793-E
48-gauge PET/1.5 mil PE Film

Sterilization
EO deep draw
Number of cycles: 2
Total time per cycle (including pre- and post-conditioning): 20 hours and 0 minutes
EO exposure time per cycle: 2 hours and 0 minutes
EO concentration: 500 ppm
Maximum temperature: 145°F
Maximum relative humidity: 100%
Maximum pressure rate change: 0.65 psi/min
MPTP Cell Descriptor Tool—at www.Transition.Tyvek.com

Select package attributes to search for specific cell descriptions from the MPTP test matrix. Your results will be available for you to download as a PDF.
Example Result from Search of MPTP Cell Descriptor Tool

DuPont™ Tyvek® 1073B – Coated – Thermoformed tray – Gamma

Metric Units:

**Package Configuration**

Thermoformed tray with coated lid

**Top Web**

DuPont™ Tyvek® 1073B
Oliver-Tolas® XHale® 10MP Coated

**Bottom Web**

800 micron PETG tray

**Sterilization**

Gamma

Number of Exposures: 2
Minimum total dose of 54 kGy
Maximum total dose of 72 kGy
Executive Summary Reports

Summary of the passes and fails for seal strength, package integrity, microbial barrier and visual inspection

<table>
<thead>
<tr>
<th>Summary Report Number</th>
<th>Estimated Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 — Pre-sterilization and Post-sterilization, T=0</td>
<td>1Q 2014</td>
</tr>
<tr>
<td>2 — Accelerated Aging (1, 3, and 5 Years) and Real-time Aging (1 Year)</td>
<td>1Q 2015</td>
</tr>
<tr>
<td>3 — Real-time Aging (3 Years) and Accelerated Aging (7 and 10 Years)*</td>
<td>4Q 2016</td>
</tr>
<tr>
<td>4 — Real-time Aging (5 Years)</td>
<td>4Q 2018</td>
</tr>
<tr>
<td>5 — Real-time Aging (10 Years)*</td>
<td>4Q 2023</td>
</tr>
</tbody>
</table>

*Eleven cells designated for extended accelerated aging (7 and 10 years) and real-time aging (10 years).
Executive Summary Reports—Pass/Fail Summary for Seal Strength

Table 1. Seal Strength Cell Summary, Sealing Condition = Low, Pre-Sterilization

<table>
<thead>
<tr>
<th>Tyvek® Style</th>
<th>Coating Type</th>
<th>Sterilization Type</th>
<th>Pouches and Bags</th>
<th>Form-Fill-Seal</th>
<th>Rigid Trays</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>EO</td>
<td>Pass</td>
<td>Fail</td>
<td>Pass</td>
</tr>
<tr>
<td>10738</td>
<td>Coated</td>
<td>Gamma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Electron-beam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Steam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dry Heat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low Temp H₂O₂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Uncoated</td>
<td>EO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gamma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Electron-beam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Steam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Coated</td>
<td>EO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10598</td>
<td></td>
<td>Gamma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Electron-beam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Uncoated</td>
<td>EO</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Numbers of MPTP cells will be indicated in each box, as appropriate. There are no cells in the MPTP for this category.
Executive Summary Reports—Change in Mean Seal Strengths

Figure 1. % Change in Mean Seal Strengths, Test* vs. Control**—Coated 1073B Pouches and Bags, Pre-Sterilization

*Test = Transition Protocol material
**Control = Current Tyvek® 1073B
Controlled Sales of Transition Protocol Material

Make Transition Protocol material available in advance of full commercialization (estimated 1Q 2015) to:

- Support MDM efforts to complete internal risk assessments prior to commercialization
- Enable MDMs to qualify material for new device packaging
- NOT intended for packaging of existing commercial devices until applicable regulations in the country of sale are met
Transition Protocol Material Controlled Sales Process

Material will be available to SPMs beginning in mid- to late July

MDMs will purchase through their SPMs

DuPont will randomly fill orders from all line/polymer combinations

There will be complete traceability:
- Unique identifiers (e.g., SKUs) from DuPont to SPMs
- DuPont labeling and documentation will appropriately identify materials
<table>
<thead>
<tr>
<th>Phase 5</th>
<th>Phase 6</th>
<th>Phase 7</th>
<th>Phase 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>2Q 2013 to 3Q 2014</td>
<td>4Q 2014 to 4Q 2015</td>
<td>2016 to 2018</td>
<td>2019 to 2023</td>
</tr>
</tbody>
</table>

**MPTP package creation & sterilization**

Full commercial launch of new materials begins after regulatory affirmation of functional equivalence

Publish specification and miscellaneous Transition Protocol material properties

Complete real-time aging for Year 1

Executive summary of package evaluation—pre- and post-sterilization
Commercialization of Transition Protocol Material

What can MDMs do to be ready?

• Initiate your change management process, including risk assessments and associated documentation

• Use controlled sales material to complete any additional testing as determined by your own risk assessments

• Ensure that you are ready to accept Transition Protocol material when it becomes commercially available (estimated 1Q 2015)
  – Discuss your plan and forecasted needs with your SPMs

• Discuss any questions or concerns with members of the global DuPont Medical and Pharmaceutical Protection Team
DuPont Medical and Pharmaceutical Protection — Global MDM Support Team

Jose Arevalo
North America and Central America

Leslie Love
North America

Karen Polkinghome
North America

Nicole Kaller
EMEA

Helmut Scheckenbach
EMEA

Eric Schmohl
EMEA

Joong Siong Bong
ASEAN

Coy Li
China

Daniel Lim
ASEAN

Norihiko Matsuda
Japan
Now More Ways Than Ever to Stay Informed

- wwwTransitionTyvekcom
- Global webcasts – live or available on-demand for up to a year
- Tyvek® Rx eNewsletter
- Face-to-face seminars
- Trade and technical forums
- Individual meetings with SPMs and MDMs
A Note of Appreciation

Thank you for your business, your continued support and your confidence in DuPont

We are committed to support you throughout this transition

Together, we can continue to meet the needs of a growing population for safe and sustainable medical packaging
Thank you!

Thank you for attending today’s Webcast: U.S. FDA Agreed Upon Protocol Testing Underway for Tyvek® Transition Project!

Today’s webcast will be archived for one year for on-demand viewing within this environment.

For any additional questions, please contact us:

Daphne Allen, Editor, Pharmaceutical & Medical Packaging News at daphne.allen@ubm.com

Or a member of the DuPont team at www.Transition.Tyvek.com