TseTech

Tyvek 滅菌袋
Product Information

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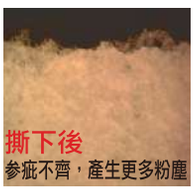
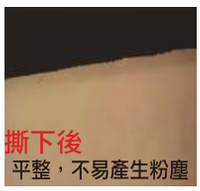
TSE Technologies Corp.

DuPont 授權台灣製造



Medical paper



Tyvek®

TYVEK® / HDPE STERILIZABLE BAGS

Tyvek® 高溫滅菌袋

無菌醫療包裝的唯一選擇！

產品介紹

- 抗微生物 & 細菌孢子滲透性 / 抗撕裂性 / 耐穿刺性 / 防水抗濕性 / 長纖不發塵
- 工廠認證
  - ISO Class 5 高規格無塵製造環境 (Cleanroom Class 100)
  - 符合國際 & 國內標準
    CE / ISO 13485 ,11607 , 11140
    TFDA / GMP
- 滅菌方式
  Steam (最高溫度可達125°C,30分鐘)
  EO / GAMMA / Plasma


滅菌無塵衣


BCAH護目鏡

產品規格

	型號	尺寸(寬 x 長)	包裝
個體袋	T40L1726	170 X 265 mm (外徑) 150 X 215 mm (內徑)	100pcs / 雙層PE袋 1000pcs(10袋)/箱
	T40L2537	250 X 375 mm (外徑) 230 X 325 mm (內徑)	
	T40L3046	300 X 460 mm (外徑) 280 X 405 mm (內徑)	
	T73B4050	400 X 500 mm (外徑) 380 X 450 mm (內徑)	500 pcs(5袋) / 箱
	T73B5065	500 X 650 mm (外徑) 480 X 600 mm (內徑)	200 pcs(2袋) / 箱
	T73B1K1K	1000 X 1000 mm (外徑) 980 X 980 mm (內徑)	50 pcs(2袋) / 箱
管袋	T40L050R ~ T40L800R	寬度 50 / 75 / 100 / 150 / 200 / 250 300 / 350 / 400 / 510 / 600 / 800 mm	長度 100M / 捲
	T73B200R ~ T73B800R	寬度 200 / 300 / 400 / 500 / 600 / 800 mm	長度 100M / 捲

- 材質
  Tyvek® 40L ; 1073B
  HDPE Film
- 保存期限
  正常環境下,滅菌包裝效期3年
- 適用產品
  無塵衣鞋/護目鏡/醫療器械和設備
  注射組件/植體/導管/傷口護理/手術器械...等

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Preliminary Product Specifications and Miscellaneous Properties of DuPont™ Tyvek® 40L

The customer is responsible for determining that the new Tyvek® 40L is suitable for the intended application and to complete the regulatory processes to gain market approval for their specific packaging applications.

Preliminary Product Specifications–Metric

Property	Comparable Standard Test Method	Units	Nominal Value [range] Tyvek® 40L
Basis Weight	ASTM D3776[1]	g/m^2	41 [39-43]
Bendtsen Air Permeability	ISO 5636-3[2]	mL/min	2350 [700-4000]
Mullen Burst	ISO 2758	kPa	690 [550-830]

1. Modified for sample size.
2. Modified to allow for a larger applicable measurement range based on the manufacturer's equipment validation.

For processing instructions, including sealing guidance, please refer to section 4 of the DuPont™ Tyvek® 40L Preliminary Technical Documentation and ISO 11607 Compliance document.

Preliminary Miscellaneous Properties–Metric

Property	Comparable Standard Test Method	Units	Typical Value Tyvek® 40L
Opacity	ISO 2471[1]	%	77
Gurley Hill Porosity	TAPPI T460[2]	sec/100 cc-in.^{2}	6
Thickness	EN ISO 534[3]	µm	127
Tensile Strength, MD	EN ISO 1924-2[4]	N	120
Tensile Strength, CD	EN ISO 1924-2[4]	N	85
Elmendorf Tear, MD	ASTM D1424	N	1.7
Elmendorf Tear, CD	ASTM D1424	N	3.0
Hydrostatic Head	AATCC TM 127[5]	cm H_2O	94
Elongation, MD	EN ISO 1924-2[4]	%	12
Elongation, CD	EN ISO 1924-2[4]	%	16
Spencer Puncture	ASTM D3420[6]	J/m^2	4553

MD = machine direction; CD = cross direction; LRV = log reduction value

1. Modified for different backing standards, area and illumination.
2. Electronic device.
3. Surface 2 cm^2, pressure 50 kPa.
4. Modified for speed, sample width (2.54 cm) and gauge length.
5. Rate of use: 60 cm H_2O/min.
6. Modified for probe size.

Specification Properties of Transition Tyvek® 1073B and 1059B

Metric

Property	Comparable Standard Test Method	Units	Nominal Value [range]	
			Transition Tyvek® 1073B	Transition Tyvek® 1059B
Basis Weight	ASTM D3776[1]	g/m^2	74.7 [71.2–78.0]	64.5 [61.7–67.1]
Delamination	ASTM D2724[2]	N	2.6 [1.8-3.6]	2.6 [1.8-3.6]
Gurley Hill Porosity	TAPPI T460	sec/100 cc	22 [8–36]	22 [8–36]

1. Modified sample size.

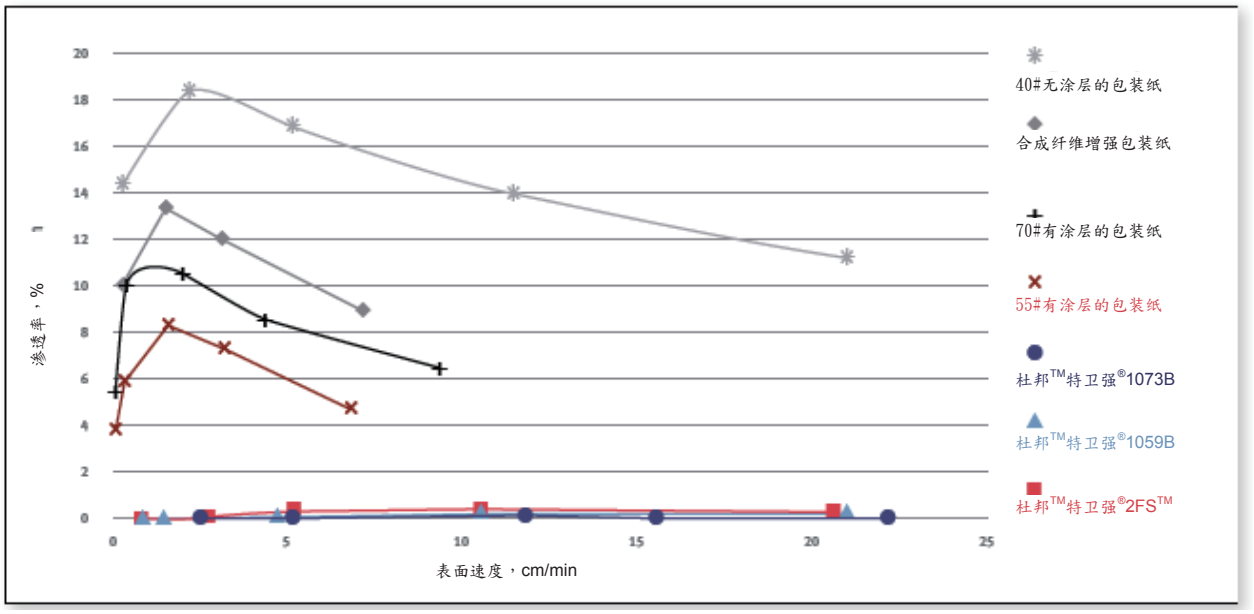
2. Modified for speed, sample width (2.54 cm/1 in.) and gauge length.

Property	Comparable Standard Test Method	Units	Typical Values	
			Transition Tyvek® 1073B	Transition Tyvek® 1059B
Microbial Barrier	ASTM F1608 ASTM F2638	LRV % pMax	›5 ‹0.3	›4 ‹0.5
Bendtsen Air Permeability	ISO 5636-3	mL/min	540	540
Moisture Vapor Transmission Rate	TAPPI T523[1]	g/m^2/24 hr	›1600	›1600
Hydrostatic Head	AATCC TM 127[2]	cm H_2O	157	155
Tensile Strength, MD	EN ISO 1924-2[3]	N	205	174
Tensile Strength, CD	EN ISO 1924-2[3]	N	219	185
Elongation, MD	EN ISO 1924-2[3]	%	20	19
Elongation, CD	EN ISO 1924-2[3]	%	24	23
Elmendorf Tear, MD	ASTM D1424	N	3.2	3.0
Elmendorf Tear, CD	ASTM D1424	N	4.0	3.8
Mullen Burst	ISO 2758	kPa	1207	1027
Spencer Puncture	ASTM D3420[4]	J/m^2	9632	7355
Opacity	ISO 2471[5]	%	92	92
Thickness (Individual)	EN ISO 534[6]	µm	199	178

1. Test conditions: 73˚F (23°C), 85% RH.
2. Rate of use: 60 cm H_2O/min.
3. Modified for speed, sample width (2.54 cm) and gauge length.
4. Modified for $^9/_{16}$-in. (14.28-mm) probe.
5. Modified for different backing standards, area and illumination.
6. Surface 2 cm^2, pressure 14.5 psi (50 kPa).

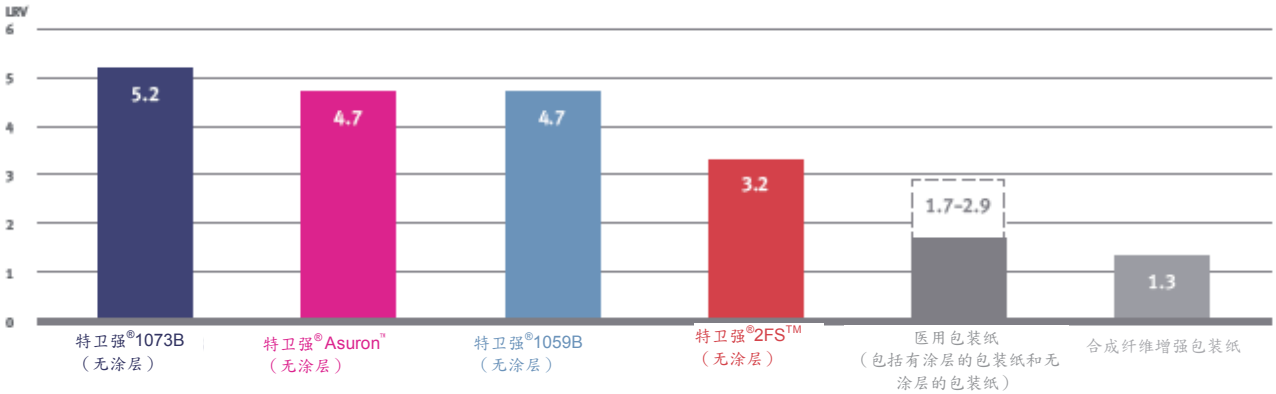
MD = machine direction; CD = cross direction; LRV = log reduction value

Tyvek & 醫療包裝紙的滲透率比較



多孔无菌屏障材料的微粒渗透率（ASTM F2638）

按ASTM F2638《使用气溶胶过滤测量替代微生物屏障的多孔包装材料性能的标准试验方法》测量多孔基材材料防止微粒渗透的能力，微粒渗透与微生物孢子渗透高度关联。所有材料均具有出现最大微粒渗透率（Pmax）的表面速度。渗透率越低，性能越好。



无菌屏障材料的微生物屏障试验（ASTM F1608）

按ASTM F1608《多孔包装材料的微生物分等标准试验方法（开放室法）》测量多孔无菌屏障材料防止细菌孢子渗透的能力。完全不能渗透的对照试样（微生物渗透率为零）在一百万即10^6菌落数（cfu）的挑战下，LRV值为6，即10^6个菌落数（CFU）的以10为底的对数值是6。如果一个与对照试样面临相同挑战的试样允许10个菌落形成单位（cfu）（log10=1）渗入，则其对数下降值（LRV）为5（6-1=5）。因此，对数下降值（LRV）越高，包装材料抗微生物的能力就越强。

灭菌方法的适应性

与医用包装纸和薄膜不同，杜邦™特卫强®适应所有最常用的灭菌方法，包括：环氧乙烷（EO）、伽马射线、电子束、蒸汽（在受控条件下）及低温氧化灭菌方法（例如STERRAD®灭菌系统）。这是因为特卫强®由高密度聚乙烯制成，高密度聚乙烯暴露于灭菌气体和高能灭菌方法中时极为稳定。此外，特卫强®的特别设计使灭菌气体和蒸汽能快速渗透和解析。不论采用哪种灭菌方法，特卫强®均能在微生物屏障和强度方面保持优越的保护性能。

表5 与各种灭菌方法的材料适应性

	杜邦™特卫强®	有涂层、乳胶饱和的医用包装纸	医用薄膜
环氧乙烷（EO）	是	是	否
伽马辐射	是	是	是
电子束辐射	是	是	是
蒸汽	是[1]	是[2]	否
STERRAD®	是	否	否

1. 在30psi（ 250℉-260℉ [121℃-127℃] ）的受控条件下保持30分钟。
2. 可能易脆。

灭菌方法的适应性

环氧乙烷（EO）

环氧乙烷（EO）不易吸附在杜邦™特卫强®上，而且比起从医用包装纸（包括合成纤维增强包装纸）等纤维素材料更为迅速的释放（图10）。经环氧乙烷灭菌后，保留了特卫强®优越的强度和微生物屏障性（表6）。对于5年真实老化后的试验结果，参考第5章“老化后杜邦™特卫强®的性能”。

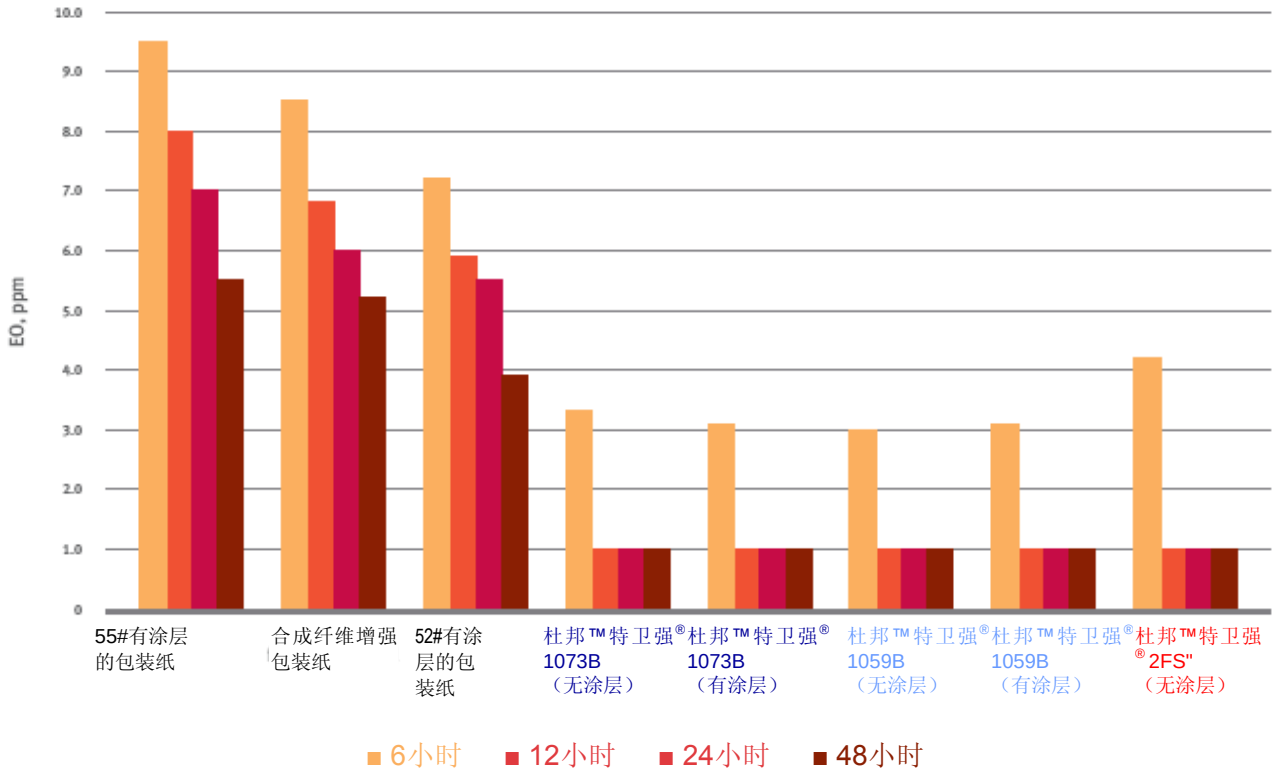


图10　灭菌和通气6、12、24和48小时后多孔无菌屏障材料的环氧乙烷（EO）残余浓度。根据ISO 10993-7进行残余分析。

表6　环氧乙烷（EO）灭菌前后的强度和屏障特性

		抗张强度，MD[1] 磅/英寸（N/2.54cm）	微生物屏障，对数下降值[2]
杜邦™特卫强®1073B	未灭菌	44.0（196）	5.2
	灭菌	46.0（205）	5.3
杜邦™特卫强®Asuron™	未灭菌	38.6（172）	4.7
	灭菌	36.8（164）	4.9
杜邦™特卫强®1059B	未灭菌	37.0（165）	4.7
	灭菌	35.0（156）	4.7
杜邦™特卫强®2FS™	未灭菌	31.0（138）	3.6
	灭菌	33.0（147）	3.3

1. 按照ASTM D5035和EN ISO 1924-2；可根据速度和治具长度进行修改。
2. 按照ASTM F1608测试的对数下降值（LRV）。

用于医疗保健用品灭菌市场的灭菌袋和灭菌卷袋

强生公司的高级灭菌产品（ASP）已采用适于STERRAD®灭菌方法的杜邦™特卫强®4057B品牌防护材料开发出门类齐全的灭菌袋和灭菌卷袋。

高级灭菌产品（ASP）也在其灭菌袋和灭菌卷袋上印有STERRAD®化学指标以简化加工包装的标识。STERRAD®灭菌方法也用于具有特卫强®防护材料制成的普通包装结构的工业器械杀菌。多次循环后应注意选择包装完整性试验方法，因为可能改变材料的抗水性。欲了解有关STERRAD®系统的信息（包括循环时间和性能细节），请访问www.sterrad.com。

辐射灭菌

特卫强®保持优越的微生物屏障特性，而且当暴露于医疗器械行业常用的辐射剂量时，抗张强度、伸长率和颜色仅有微小的变化。与其他多孔材料不同，特卫强®能抗灭菌后发生的脆性，打开包装时，特卫强®保持其低纤维屑磨脱率性能。

因特卫强®为多孔性材料，可将辐射灭菌产生的异味吹出包装。无孔材料则将这些气味封在包装内。

重要的是要注意，虽然特卫强®能轻易承受采用伽马射线或电子束的再灭菌，但医疗器械本身并非如此。如果需要再灭菌，可进行气体灭菌。再灭菌后，特卫强®仍保持柔韧并继续发挥优越的微生物屏障特性。

伽马辐射

暴露于达100kGy的伽马辐射后，特卫强®仍保持优越的微生物屏障特性，对其强度特性的影响亦有限（表7）。暴露于加速老化和真实老化之后的辐射后，仍保持这些特性（第5章"老化后杜邦™特卫强®的性能，表14至16）。

表7 以各种剂量*进行伽马辐射前后，比较杜邦™ 特卫强®医疗包装产品的强度和微生物屏障特性的试验结果

			抗张强度，MD[1] 磅/英寸（N/2.54cm）	微生物屏障，对数下降值[2]
杜邦™特卫强®1073B	未灭菌	-	42.0（187）	5.2
	灭菌	25 kGy	39.1（174）	5.2
		30 kGy	-	5.3
		50 kGy	35.8（159）	5.2
		60 kGy	-	5.4
		100 kGy	23.1（103）	5.1
杜邦™特卫强®Asuron™	未灭菌	-	38.6（172）	4.7
	灭菌	25 kGy	31.3（140）	4.7
		50 kGy	28.6（127）	4.6
杜邦™特卫强®1059B	未灭菌	-	36.7（163）	4.7
	灭菌	25 kGy	28.9（128）	4.7
		30 kGy		5.1
		50 kGy	26.5（118）	4.1
		60 kGy	-	4.5
		100 kGy	19.1（85）	4.2
杜邦™特卫强®2FS™	未灭菌	-	30.8（137）	3.6
	灭菌	30 kGy	25.1（112）	3.6
		60 kGy	21.2（94）	3.4

*25kGy和30kGy为单次剂量；其他为加倍剂量的累计量（即，50kGy代表25kGy的加倍剂量等等）。

1. ASTM D5035和EN ISO 1924-2；可根据速度和治具长度进行修改。

2. 按照ASTM F1608测试的对数下降值（LRV）。

灭菌方法的适应性

电子束

暴露于达100kGy电子束辐射后，杜邦™特卫强®仍保持其优越的微生物屏障特性和强度特性（表8）。老化后电子束灭菌的具体研究还未进行。

然而，因为高密度聚乙烯对辐射的稳定性，我们还未发现除伽马辐射和老化后显示的一些影响外的其他影响（第5章"老化后杜邦™特卫强®的性能，表14至16）。

表8 以各种剂量*进行电子束辐射前后，比较杜邦™特卫强®医疗包装产品的强度和微生物屏障特性的试验结果

			抗张强度，MD[1] 磅/英寸（N/2.54cm）	微生物屏障，对数下降值[2]
杜邦™特卫强®1073B	未灭菌	—	42.0（187）	5.2
	灭菌	50 kGy	35.8（159）	5.2
		100 kGy	21.5（96）	5.2
杜邦™特卫强® Asuron™	未灭菌	—	38.6（172）	4.7
	灭菌	25 kGy	33.8（150）	4.5
		50 kGy	29.2（130）	4.7
杜邦™特卫强®1,059B	未灭菌	—	36.7（163）	4.7
	灭菌	50 kGy	30.4（135）	4.9
		100 kGy	21.2（94）	4.3

*50kGy为单次剂量；100kGy为累计剂量，代表50kGy的加倍剂量。

1. ASTM D5035和EN ISO 1924-2；可根据速度和治具长度进行修改。
2. 按照ASTM F1608测试的对数下降值（LRV）。

等离子体/过氧化氢

特卫强®适用于强生公司高级灭菌产品（ASP）的STERRAD®灭菌系统。这种环保的灭菌替代方法采用低温气体等离子体来避免蒸汽的降解或环氧乙烷（EO）残留。

医用包装纸，包括高压蒸汽灭菌纸袋，不可和STERRAD®系统一起使用，因为纤维素质会中和灭菌剂。多倍剂量低温氧化灭菌后应注意包装完整性试验方法的选择，因为材料的抗水性可能被改变。欲了解有关STERRAD®系统的更多信息，请访问www.sterrad.com。

蒸汽

已经证明特卫强®满足在控制条件下（250℉-260℉[121℃-127℃]，30磅/平方英寸条件下，灭菌30分钟）进行蒸汽灭菌的包装标准。采用特卫强® 进行蒸汽灭菌的包装方案在商业上应用于一些医疗器械和制药厂。

若需要强韧、无纤维毛屑、可蒸汽灭菌的封口盖，特卫强®仍优于医用包装纸。事实上，特卫强®在250℉-260℉（121℃-127℃）、30磅/平方英寸、30分钟的条件下仍保持尺寸稳定性和完整性，且不变色。硬质或半硬质托盘限制了可能的收缩和起皱，可导致封口盖更滑/更紧。

在达260℉（127℃）温度下蒸汽灭菌30分钟后，特卫强®仍保持其抗张强度、微生物屏障特性和葛尔莱法透气度（表9）。蒸汽灭菌后，特卫强®的收缩率低于1.6%（表9，图11）。

表9 蒸汽灭菌前后，杜邦™特卫强®医疗包装产品的物理性质

			抗张强度MD[1] 磅/英寸（N/2.54cm）	微生物屏障，对数下降值[2]	收缩率[3]，高压灭菌，%	葛尔莱法[4] sec/100 cc
杜邦™特卫强®1073B	未灭菌	—	41.9（186）	5.2	—	24
	灭菌30分钟	250°F（121℃）	43.1（192）	4.8	0.5	24
		255°F（124℃）	48.4（215）	4.8	0.3	26
		260°F（127℃）	48.2（214）	5.2	1.4	25
杜邦™特卫强®Asuron™	未灭菌	—	38.6（172）	4.7	—	40
	灭菌30分钟	—	36.5（162）	4.7	—	34
杜邦™特卫强®1059B	未灭菌	—	35.2（157）	4.7	—	19
	灭菌30分钟	250°F（121℃）	36.0（160）	4.7	1.0	21
		255°F（124℃）	38.7（172）	5.1	0.5	34
		260°F（127℃）	40.2（179）	4.1	1.5	23
杜邦™特卫强®2FS™	未灭菌	—	27.8（124）	3.6	—	18
	灭菌30分钟	250°F（121℃）	26.7（119）	3.1	0.8	20
		255°F（124℃）	28.5（127）	3.1	0.3	20
		260°F（127℃）	29.1（129）	3.3	0.9	17

1. ASTM D5035和EN ISO 1924-2；可根据速度和治具长度进行修改。
2. 按照ASTM F1608测试的对数下降值（LRV）。
3. 杜邦™特卫强®Asuron™仍在进行收缩试验。
4. TAPPI T460和ISO 5636-5。

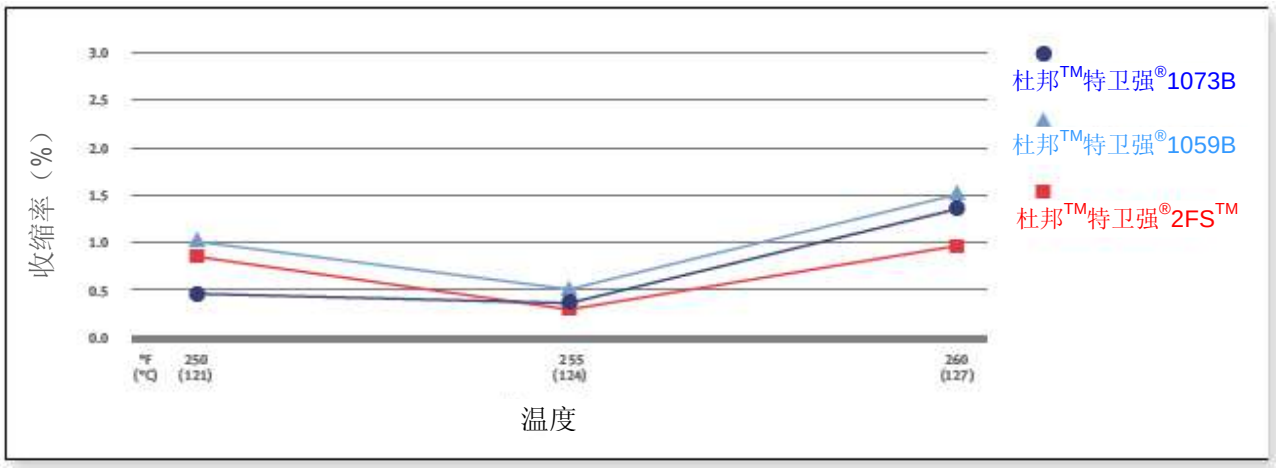


图11 蒸汽灭菌后，杜邦™特卫强®1073B、特卫强®1059B和特卫强®2FS™的收缩试验结果

灭菌方法的适应性

生物兼容性

采用ISO 10993和《美国药典》（USP）的试验方法进行杜邦™特卫强®医疗包装的生物学评价。这些产品满足所有可接受的性能标准。

特卫强®试样通过环氧乙烷、伽马射线和电子束灭菌方法灭菌后，也进行了该测试；该测试证明特卫强®在灭菌后满足所有合格性能标准（表10）。测试结果表明了生物兼容性—即使是在灭菌后。

表10 杜邦™ 特卫强®1073B、特卫强®Asuron™、特卫强®1059B和特卫强®2FS™试样的毒理学结果

所进行的试验	未灭菌	环氧乙烷（EO）	伽马射线（25kGy、50kGy）	电子束辐射（25kGy、50kGy）	STERRAD®
烯烃类聚合物中萃取物的测定[1]	低于最大容许比率				
动物溶血性试验-兔血液-ISO[2,3]	非溶血性				
L929MEM洗脱试验-USP[4]	非细胞毒素				
ISO-动物热原试验-兔（材料引起）[2,5]	非热解				
Kligman最大化试验-SO（CSO与NaCl萃取)[2,6]	非过敏				
组织注射试验-ISO[2,5]	无生物反应				
皮肤刺激试验- ISO[6]	非刺激性				
短期肌肉植入试验-ISO（14天、28天）[7,8]	非刺激性				
USP级VI试验[9]	0%敏感度				

基于以下参考进行试验：

1. 美国联邦法规汇编第21篇177.1520有关烯烃类聚合物的规定，标题21，第1章，1997.
2. 医疗器械的生物评价-第12部分：试样制备和对照材料，EN/ISO 10993-12, 1997.
3. 医疗器械的生物学评价-第4部分：与血液相互作用试验的选择，ISO 10993-4, 1992.
4. 美国药典25，国家处方集20，2002，<87>体外生物反应性试验.
5. 医疗器械的生物评价-第11部分：组织毒性试验，EN/ISO 10993-1995.
6. 医疗器械的生物评价-第10部分：刺激性和敏感度试验，EN/ISO 10993-10, 1996.
7. 医疗器械的生物评价-第6部分：植入后的局部作用试验，ISO 10993-6, 1995.
8. ASTM第13.01卷第13节医疗器械，名称：F 981-93,1994.
9. 美国药典25，国家处方集20，2002，<88>体内生物反应性试验.

DUPONT®
Tyvek®

DuPont™ Tyvek®
Compliance to ISO 11607-1:2006/Amd.1:2014

January 2015

Contents

Preface

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 (or will be) available from ISO, CEN, National Standards Bodies, and Standard Development Organizations.

The major amendments to 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 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™ Tyvek® Transition Protocol that is currently underway.

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

Introduction

DuPont™ Tyvek® 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 use of packaging, the International Standards community has promulgated the ISO 11607-1:2006/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 *Packaging for terminally sterilized medical devices Part 2: Validation requirements for forming, sealing and assembly processes.* Subsequent references to ISO 11607-1 refer to the amended version.

As the producer of Tyvek® for medical and pharmaceutical packaging, DuPont Medical and Pharmaceutical Protection has compiled documentation which demonstrates the compliance of Tyvek® with the materials portion of the 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. The 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 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 *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

The product characteristics of Tyvek® include:

- Outstanding porous microbial barrier
- 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® are used within the medical device industry. Packages such as chevron peel pouches and header bags are composed of Tyvek® sealed to flat, unshaped, flexible film in a wide variety of length and width dimensions. In addition, Tyvek® 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.

Both adhesive coated and uncoated Tyvek® are used in medical packaging. When uncoated Tyvek® is used, the film web contains the adhesive layer to form the seal between the film and the Tyvek®.

A variety of converting steps may be required prior to using Tyvek® in medical packaging. Some will have the adhesive coated onto the Tyvek® 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® allow its use in a variety of sterilization processes. The sterile barrier systems using Tyvek® are commonly sterilized using ethylene oxide (EO) gas, gamma and electron-beam radiation. In addition, steam sterilization may be used if temperatures are controlled to avoid melting the Tyvek®. Tyvek® has been shown to meet packaging criteria for steam sterilization under controlled conditions (250°F to 260°F [121°C to 127°C] at 30 psi for 30 minutes). Emerging low-temperature sterilization methods such as: gas plasma with hydrogen peroxide, vapor phase hydrogen peroxide with peracetic acid, ozone and chlorine dioxide, require Tyvek® packaging because cellulosic porous materials are adversely affected by these strong oxidizing environments.

This document is used to demonstrate the compliance of Tyvek® with the ISO 11607-1 standard. Tyvek® falls under sections 4, 5 and 7. This document lists each clause from 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 www.MedicalPackaging.DuPont.com

ISO 11607-1:2006/Amd.1:2014 Requirements

4. GENERAL REQUIREMENTS

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

4.2. Quality systems

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

Tyvek® 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.

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® 1073B, Tyvek® 1059B, Tyvek® 2FS™ (4058B) and Tyvek® 4057B are conducted per procedures associated with ISO 9001:2008 quality systems registration. Samples of Tyvek® 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® 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® 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 (typically 12 samples/full mill roll) to calculate roll averages. Thickness measurements are based on individual values (typically 112 samples/full mill roll) versus full mill roll averages. The average thickness is determined by pooling the ~112 data points from a roll with individual data points from other rolls and averaged. Test method variance related to equipment and analysis is included in the observed values. Other sampling plans and test methods may yield different values.

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® 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 shown in Table I.

ISO 11607-1:2006/Amd.1:2014 Requirements

Table I. Test methods used for measuring material properties

PROPERTY	COMPARABLE STANDARD TEST METHODS		DEVIATIONS FROM STANDARD TEST METHODS
	Richmond, VA	Luxembourg	
Basis Weight	ASTM D3776	EN ISO 536	Modified sample size.
Delamination	ASTM D2724	ASTM D2724	Modified for speed and gauge length.
Gurley-Hill Porosity	TAPPI T460[1]	ISO 5636-5[2]	1. Modified sample size. 2. Modified for sealing fluid characteristics.
Opacity	TAPPI T425	ISO 2471	Modified for different backing standards, area and illumination.
Thickness (individual)	ASTM D1777[1]	EN ISO 534	1. Modified to use 7.15 psi, 0.625-in. diameter presser foot.
Tensile and Elongation	ASTM D5035	EN ISO 1924-2	Modified for speed and gauge length.
Elmendorf Tear	ASTM D1424	EN 21974	—
Hydrostatic Head	AATCC TM 127	EN 20811	Rate of use: 60 cm H_2O/min.
Mullen Burst	ASTM D774	ISO 2758	—
Bendtsen Air Permeability	ISO 5636-3	ISO 5636-3	—
Spencer Puncture	ASTM D3420	ASTM D3420	Modified for $^9/_{16}$-in. (14.28-mm) probe

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 ISO 11607-1 Appendix 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.

ISO 11607-1:2006/Amd.1:2014 Requirements

The Tyvek® 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.

4.4.3 Unless specified in test methods, test samples *shall* be conditioned at (23 ± 1)˚C and (50 ± 1) % relative humidity for 24h.

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

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® with 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.

5. MATERIALS AND PREFORMED STERILE BARRIER SYSTEMS

Tyvek® 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 fibers, it is not affected by climatic changes in humidity, temperature, or atmospheric pressure. Because its melting point is 275°F (135°C), steam sterilization must 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.

ISO 11607-1:2006/Amd.1:2014 Requirements

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® 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 the web temperature should not exceed 175°F (79°C).

b) Pressure range

The ability to perform over a range of pressures is a critical characteristic of Tyvek® 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 processing, shipping, handling and storage the packaging system will be exposed to during its life cycle.

c) Humidity range

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

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® becomes part of an SBS.

e) Exposure to sunlight or UV light

Physical properties of Tyvek® are degraded with extended exposure to direct sunlight (ultraviolet rays).

f) Cleanliness

Tyvek® is composed of essentially continuous fibers and does not generate a significant amount of lint particles under conditions of ordinary use.

g) Bioburden

The process of manufacturing Tyvek® 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® is very low. This low bioburden does not add significantly to the required sterilization time. The typical bioburden of all Tyvek® medical packaging styles is less than 100 colony forming units (cfu) per ft^2.

h) Electrostatic conductivity

In some processing steps, Tyvek® may generate static electricity unless treated with antistatic agents. Styles intended for medical packaging do not contain an antistatic agent. 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 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® medical packaging styles.

5.1.6 The following properties *shall* be evaluated:

a) Microbial barrier

The microbial barrier properties of Tyvek® are superior to medical-grade papers and are well documented in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 3) located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

ISO 11607-1:2006/Amd.1:2014 Requirements

b) Biocompatibility and toxicological attributes

Biocompatibility and other toxicological attributes of Tyvek® medical packaging styles are acceptable and are documented in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

c) Physical and chemical properties

The physical properties of Tyvek® styles intended for medical packaging can be found in specifications and miscellaneous properties tables in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 2) located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html These specifications and miscellaneous properties serve as a guide for medical device manufacturers to determine the level of protection required for a particular device.

Because Tyvek® is made of high-density polyethylene, it is relatively chemically inert. The chemical resistance of Tyvek® to various chemicals is available at http://www2.dupont.com/Tyvek/en_US/assets/downloads/tyvek_handbook.pdf

d) Compatibility with respect to forming and sealing processes

Tyvek® 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 required 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. The strength of a preformed SBS seal should be determined by the manufacturer of that system. The effect of aging on seal strength is documented in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging*, which is available at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

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

Tyvek® 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. The effects of sterilization on Tyvek® medical packaging styles are documented in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 4) located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

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

Tyvek® medical packaging styles should be stored under the same conditions as one would store a medical device. Tyvek® 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. The effects of post-sterilization storage are documented in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 5) located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

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® 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® styles 1059B and 1073B meet the testing requirements of USP 36, <661> as well as the compositional and testing requirements of Section 3.1.3 and Section 3.1.5 of the European Pharmacopoeia.

ISO 11607-1:2006/Amd.1:2014 Requirements

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® and the release standards for Tyvek® 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®; 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.

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

See the specification properties tables in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 2) which is available at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

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

Internal processes specify release limits for cleanliness and particulate matter. Tyvek® does not generate a significant amount of lint particles under conditions of ordinary use. Refer to the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 3), which is available at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

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® medical packaging styles, the established specification properties are Gurley Hill, Delamination and Basis Weight. The specific values for these can be found in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 2), which is available at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html Additional properties that are important when considering alternative materials for your specific applications can also be found in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 2).

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® 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® styles 1059B and 1073B meet the testing requirements of USP 36, <661> as well as the compositional and testing requirements of Section 3.1.3 and Section 3.1.5 of the European Pharmacopoeia.

ISO 11607-1:2006/Amd.1:2014 Requirements

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 Tyvek® medical packaging styles are documented in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* (Section 4) located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

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.

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® 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 Tyvek® are superior to medical-grade papers and are well documented in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

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.

5.3.2 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® 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. The effects of sterilization on medical packaging styles are documented in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

ISO 11607-1:2006/Amd.1:2014 Requirements

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®. 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® 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® 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.

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® rolls from contamination and damage during distribution and handling. There are no restrictions on transport and storage of Tyvek® 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 restrictions on transport and storage of Tyvek® other than avoiding direct exposure to UV light for more than 30 days.

ISO 11607-1:2006/Amd.1:2014 Requirements

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 are contained on every roll of Tyvek® manufactured. The rest of the information can be found in this document and in the *DuPont Technical Reference Guide for Medical and Pharmaceutical Packaging* located at http://www2.dupont.com/Medical_Packaging/en_US/tech_info/index.html

For more information about DuPont™ Tyvek® for medical and pharmaceutical packaging and to find out how we can help you with packaging and regulatory compliance, call us today at 1.800.44.TYVEK or visit us at www.medicalpackaging.dupont.com

You can also find links to other resources in your country and information in other languages at this website.

Comprehensive List of Testing for DuPont™ Tyvek® MPTP

As of December 18, 2017

The DuPont™ Tyvek® Medical Packaging Transition Project (MPTP) includes a systematic method for generating data to prove that Transition Protocol material is functionally equivalent in performance to current Tyvek ®, in an effort to help mitigate requalification.

This document provides a comprehensive listing of all testing that will be conducted for each of the three MPTP study components:

- U.S. FDA Transition Protocol
- Phantom Protocol
- Biocompatibility, Food Contact and Pharmacopeia Testing

It is designed to help you with your risk assessment and change control management procedures by providing an overview of all MPTP testing in one document.

To date, we have posted a wealth of information on our website (www.transitiondata.tyvek.com), including: Transition Protocol Material property data, Phantom Protocol data and Biocompatibility, Food Contact and Pharmacopeia Testing data. We have also posted Industry Summary Reports of package test results for pre- and post-sterilization; 1-, 3-, 5-, 7*- and 10-year accelerated aging; and 1- and 3-year real-time aging. In the future, we will post Industry Summary Reports for other MPTP time points, including: 5- and 10-year real-time aging.*

In addition, we have created the MPTP Package Test Results Selector Tool, which enables you to search for current results from MPTP testing by selecting Tyvek® style and package design. This tool currently features MPTP package test results for pre-sterilization, post-sterilization, 1-, 3- and 5-year accelerated aging and 1-year real-time aging.

We will continue to share data and post new information on our website, and update the MPTP Package Test Results Selector Tool as new data becomes available.

* Eleven cells are designated for 7- and 10-year accelerated aging and for 10-year real-time aging.

DuPont™ Tyvek® MPTP Package Testing

As of December 18, 2017

Protocol	No. of Cells	Package Format†	Sterilization Method*	Test Methods	Tests - Description	Pre-Sterilization	Post-Sterilization	Accelerated Aging Conditions (Years)	Real-Time Aging Conditions (Years)
FDA	6	Coated 1073B Pouches/Bags	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
FDA	6	Coated 1073B FFS	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
FDA	9	Coated 1073B Lids/Rigid Trays	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5; one cell 7, 10 also	COMPLETED: 1, 3 In progress: 5; one cell 10 also
FDA	6	Uncoated 1073B Pouches/Bags	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5; one cell 7, 10 also	COMPLETED: 1, 3 In progress: 5; one cell 10 also
FDA	3	Coated 1073B Pouches/Bags	Gamma	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5; two cells 7, 10 also	COMPLETED: 1, 3 In progress: 5; two cells 10 also
FDA	3	Coated 1073B FFS	Gamma	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5; one cell 7, 10 also	COMPLETED: 1, 3 In progress: 5; one cell 10 also
FDA	6	Coated 1073B Lids/Rigid Trays	Gamma	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5; five cells 7, 10 also	COMPLETED: 1, 3 In progress: 5; five cells 10 also
FDA	3	Uncoated 1073B Pouches/Bags	Gamma	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
FDA	3	Coated 1073B FFS	Electron-beam	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
FDA	3	Uncoated 1073B Pouches/Bags	Electron-beam	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
FDA	3	Coated 1059B FFS	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
FDA	6	Uncoated 1059B Pouches/Bags	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
FDA	3	Uncoated 1059B FFS	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	1	Coated 1073B Pouches/Bags	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	1	Coated 1073B FFS	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	2	Coated 1073B Lids/Rigid Trays	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	1	Uncoated 1073B Pouches/Bags	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	2	Coated 1073B Lids/Rigid Trays	Gamma	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	1	Uncoated 1059B Pouches/Bags	EO**	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	3	Coated 1073B Lids/Rigid Trays	Steam	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	2	Uncoated 1073B Pouches/Bags	Steam	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	1	Coated 1073B Lids/Rigid Trays	Dry Heat	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	1	Coated 1073B Pouches/Bags	Low Temp. H_2O_2	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5, 7, 10	COMPLETED: 1, 3 In progress: 5, 10
Phantom	1	Coated 1073B Lids/Rigid Trays	Low Temp. $C_2H_4O_3$	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	1	Coated 1059B FFS	Gamma	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Phantom	1	Coated 1059B FFS	Electron-beam	ASTM F1886M, F88‡, F1929, F2638	Visual, Seal Strength, Package Integrity (Dye), Microbial Barrier	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5	COMPLETED: 1, 3 In progress: 5
Total	78	Coated & Uncoated 1073B & 1059B♦				ALL	ALL	eleven cells 7 & 10 also	eleven cells 10 also

NOTES:
† Packages made at upper, lower and nominal sealing conditions for three lots of Transition Protocol material and three lots of current Tyvek®.
* Sterilization cycles are described in cell descriptors which can be found using the MPTP Cell Descriptor Selector Tool at www.Transition.Tyvek.com.
** EO residuals are measured and compared between Transition Protocol material and current Tyvek®.
‡ ASTM F88 technique per cell per medical device manufacturer's (MDM's) standard practice.
♦ Specific material combinations are described in cell descriptors which can be found using the MPTP Cell Descriptor Selector Tool at www.Transition.Tyvek.com.

Phantom Protocol Material Testing

As of December 18, 2017

DUPONT Tyvek

Property	Test Method(s)	Sterilization Method/Details	Pre-Sterilization	Post-Sterilization	Accelerated Aging Conditions (Years)	Real-Time Aging Conditions (Years)	Status
MD Tensile Strength & Elongation	ASTM D5034	EO; 25, 50 & 100 kGy gamma; 25, 50 & 100 kGy electron-beam; steam; STERRAD® 100S; vapor hydrogen peroxide	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5, 7, 10	COMPLETED: 1, 3 In progress: 5, 7, 10	Aging work in progress
CD Tensile Strength & Elongation	ASTM D5034	EO; 25, 50 & 100 kGy gamma; 25, 50 & 100 kGy electron-beam; steam; STERRAD® 100S; vapor hydrogen peroxide	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5, 7, 10	COMPLETED: 1, 3 In progress: 5, 7, 10	Aging work in progress
Puncture Strength	ASTM F1342	EO; 25, 50 & 100 kGy gamma; 25, 50 & 100 kGy electron-beam; steam; STERRAD® 100S; vapor hydrogen peroxide	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5, 7, 10	COMPLETED: 1, 3 In progress: 5, 7, 10	Aging work in progress
Microbial Barrier	ASTM F1608	EO; 25, 50 & 100 kGy gamma; 25, 50 & 100 kGy electron-beam; steam; STERRAD® 100S; vapor hydrogen peroxide	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5, 7, 10	X	Aging work in progress
Microbial Barrier	ASTM F2638	EO; 25, 50 & 100 kGy gamma; 25, 50 & 100 kGy electron-beam; steam; STERRAD® 100S; vapor hydrogen peroxide	COMPLETED	COMPLETED	COMPLETED: 1, 3, 5, 7, 10	COMPLETED: 1, 3 In progress: 5, 7, 10	Aging work in progress
Differential Scanning Calorimetry (DSC)			•	X	X	X	COMPLETED
Attenuated Total Reflectance - Fourier Transform Infrared Spectroscopy (ATR-FTIR)			•	X	X	X	COMPLETED
Area Shrinkage (%) after Steam Sterilization		steam: 121°C, 123°C, 125°C, 127°C, 129°C, 131°C	X	•	X	X	COMPLETED
Gurley Hill Porosity (GHP) after Steam Sterilization	"Modified GHP" ISO 5636-5	steam: 121°C, 123°C, 125°C, 127°C, 129°C, 131°C	X	•	X	X	COMPLETED
Hydrostatic Head (HH) after Low-Temperature Oxidative Sterilization	AATCC TM 127 EN 20811	STERRAD® 100S; vapor hydrogen peroxide	X	•	X	X	COMPLETED
Dimensional Stability Study	MD/CD Tensile Strength, Puncture Resistance, Microbial Barrier ASTM F2638	Steam Sterilize - Freeze (-80°C) - Thaw - Freeze (-80°C) - Thaw - Test	X	•	X	X	COMPLETED
Particle Generation	"Modified Gelbo" ISO 9073-10		•	X	X	X	COMPLETED
Printability	Flexography Thermal Transfer		•	X	X	X	COMPLETED
Parker Surface Smoothness			•	X	X	X	COMPLETED
Surface Energy	Contact Angle Dyne Pen		•	X	X	X	COMPLETED
Coefficient of Friction	Dynamic Static		•	X	X	X	COMPLETED
Color	L,a,b Measurements	EO; 100 kGy gamma; 100 kGy electron-beam; steam; STERRAD® 100S; vapor hydrogen peroxide	•	•	X	X	COMPLETED
Low-intensity UV Stability	Various Properties†		•	X	X	X	COMPLETED

NOTES: • = Will be tested
X = Will not be tested
† = Tests included: Basis weight, Delamination, Gurley Hill porosity, Spencer puncture, MD/CD tensile strength, MD/CD elongation.

Biocompatibility, Food Contact and Pharmacopeia Testing*

As of December 18, 2017

DUPONT Tyvek.

Cytotoxicity (ISO 10993-5)	PASS: • Pre-sterilization • Post-sterilization and 5- and 10-year accelerated aging (EO, 100 kGy gamma, 100 kGy electron-beam, STERRAD® 100S, vapor hydrogen peroxide, steam)	COMPLETED
Endotoxins (USP ‹85›)	PASS (pre-sterilization)	COMPLETED
Skin irritation and sensitization (ISO 10993-10)	PASS (pre-sterilization)	COMPLETED
Bioburden (ISO 11737-1)	Similar performance to current Tyvek® (pre-sterilization)	COMPLETED
Extractables and leachables (ISO 10993-18: Infrared spectroscopy; ICP-MS; GC-MS; UPLC-MS)	Pre-sterilization: • No major bands of interest (Infrared spectroscopy) • Met all requirements (ICP-MS; GC-MS; UPLC-MS) Post-sterilization (EO, 100 kGy gamma, 100 kGy electron-beam, STERRAD® 100S, vapor hydrogen peroxide, steam): • No major bands of interest (Infrared spectroscopy) • Met all requirements (ICP-MS; GC-MS) • UPLC-MS testing—see**	COMPLETED
U.S. Food Contact		
21 CFR 177.1520	PASS (pre-sterilization, EO, 100 kGy gamma, 100 kGy electron-beam, STERRAD® 100S, vapor hydrogen peroxide, steam)	COMPLETED
U.S. Pharmacopeia		
USP ‹88› Class VI	PASS (pre-sterilization)	COMPLETED
USP ‹661›	PASS (pre-sterilization, EO, 100 kGy gamma, 100 kGy electron-beam, STERRAD® 100S, vapor hydrogen peroxide, steam)	COMPLETED
European Food Contact		
EC Reg. 10/2011	PASS (pre-sterilization, EO, 100 kGy gamma, 100 kGy electron-beam, steam)	COMPLETED
European Pharmacopeia		
EP 3.1.5 and EP 3.1.3	Meets the compositional and extractable requirements (pre-sterilization)	COMPLETED
EP 3.1.5 Selected Testing: (1) Identification A: IR Spectrometry (2) Hexane Solubility	PASS (EO, 100 kGy gamma, 100 kGy electron-beam, STERRAD® 100S, vapor hydrogen peroxide, steam)	COMPLETED
Japanese Food Sanitation Law		
Specifications and Standards for foods, food additives and other materials (Notification No. 370 of MHLW III-D-2)	PASS (pre-sterilization)	COMPLETED

NOTES: * Generated for 1073B and/or 1059B Transition Protocol material and Tyvek® 1073B and/or 1059B current material.

** Under extraction conditions of 70°C for 24 hours in purified water, a compound tentatively identified as an "oxygenated unsaturated hydrocarbon" was found to exceed the 0.1 µg/mL concentration allowance by ~0.01-0.25 µg/mL.

Date: 01 NOV 2016 Tel: +65 68851346 Fax: +65 67732912

Client's Ref: 2016-09-20-PSB Email: Yin-Pheng.LEONG@tuv-sud-psb.sg

1. GENERAL

1.1 STUDY TITLE

In vitro Cytotoxicity Study of Tyvek Steam Pouch

1.2 TEST ITEM IDENTIFICATION (Based on information provided by sponsor)

Test item name	:	Tyvek Steam Pouch
Test item identification	:	Lot No.: 6071
Sterilization condition	:	YES, STEAM (non-sterile as received)
Date of manufacture	:	NA
Expiry Date	:	NA

1.3 REFERENCE ITEM IDENTIFICATION

High Density Polyethylene panel (Negative Control)
Zinc sulphate solution (Positive Control)

1.4 CHARACTERISTICS OF TEST ITEM (Based on information provided by sponsor)

Name of Test Item	Tyvek Steam Pouch
Physical description	Solid, bag (as seen) Thickness of transparent & non-transparent portions : 0.2mm (by measurement)
Composition	HDPE
Homogeneity	NA
Purity	NA
Quantity received	1 piece

Date: 02 NOV 2016 Tel: +65 68851323 Fax: +65 67784301

Client's Ref: Email: Yang.LI@tuv-sud-psb.sg

1. GENERAL

1.1 STUDY TITLE

In vitro haemolysis study of Tyvek Steam Pouch using rabbit blood (direct contact)

1.2 TEST ITEM IDENTIFICATION

(Based on information provided by sponsor)

Test item name	:	Tyvek Steam Pouch
Batch / Lot No	:	6071
Sterilization condition	:	YES, STEAM (non-sterile as received)
Quantity	:	1 piece
Homogeneity	:	NA
Density	:	NA
Manufacture date	:	NA
Expiry date	:	NA

1.2.1 Material Composition

Composition	:	HDPE

1.2.2 Physical Features / Properties

Physical features/ Properties	:	Solid bag (as seen)

Tyvek Steam Pouch
White Rabbit Intracutaneous Irritation Study
STUDY REPORT

Client: Sterileright Packaging Mfg Inc.

Testing Institution: Master Laboratory Co., Ltd.

October 2016

Report No.: MS-201609-117-T02

IACUC No.: MS20160921

Test article registration date：09.20.2016

Experimental starting date：09.26.2016

Experimental completion date：09.29.2016

Animal in-housing: 09.19.2016

Extraction of test article: 09.23.2016

Observation of dermal reaction: 09.26.2016~09.29.2016

Study Announcement

1. The study report is valid for the test article used only.
2. The study report could not be recopied or extracted only if the permission from Master Laboratory Co., Ltd.
3. The study report is invalid without the endorsement of Master Laboratory Co., Ltd.

SIGNATURE OF STUDY PERSONNEL

Experiment coordinator/executor: Cheng-Ming Chang/ Kuo-Shu Huang and Ying-Chun Chen

Study Director

Cheng Ming Chang
Cheng Ming Chang DVM

11.05.2016
Date

Facility Management

Alan Hsieh
Alan Hsieh

11.05.2016
Date

Tyvek Steam Pouch
Guinea Pig Skin Sensitization Study
(Maximization Test)
STUDY REPORT

Client: Sterileright Packaging Mfg Inc.

Testing Institution: Master Laboratory Co., Ltd.

November 2016

Report No.: MS-201609-118-T03

IACUC No.: MS20160922

Test article registration date: 09.20.2016

Experimental starting date: 10.04.2016

Extraction of test article date: 10.01.2016、10.08.2016、10.22.2016

Test article administration during induction phase:10.04.2016、10.11.2016

Test article administration during challenge phase: 10.25.2016

Observation of skin response: 10.27.2016~10.28.2016

Study Announcement

1. The study report is valid for the test article used only.
2. The study report could not be recopied or extracted only if the permission from Master Laboratory Co., Ltd.
3. The study report is invalid without the endorsement of Master Laboratory Co., Ltd.

SIGNATURE OF STUDY PERSONNEL

Experiment coordinator/executor: Cheng-Ming Chang/ Kuo-Shu Huang and Ying-Chun Chen

Study Director

Cheng Ming Chang
Cheng Ming Chang DVM

10. 15. 2016
Date

Facility Management

Alan Hsieh
Alan Hsieh

10. 15. 2016
Date

Statement

Subject product: Sterilization Packaging
Manufacturer:
Address:

The verification of test report is done by Intertek and the result complies with the requirements of EN ISO 11607-1:2011/EN868-3:2009 / EN868-5:2009.

Raymond Yin

TD and Team Leader (A)

Intertek Testing Services Shenzhen Ltd.
Guangzhou Branch
Block E, No.7-2 Guang Dong Software
Science Park, Caipin Road, Guangzhou
Science City, GETDD, Guangzhou, China

intertek
Total Quality. Assured.

CERTIFICATE OF REGISTRATION

This is to certify that the management system of:

Main Site:

has been registered by Intertek as conforming to the requirements of:

ISO 13485:2016

The management system is applicable to:

Manufacturing of packaging for sterilized medical devices.

Certificate Number:
25013-01

Initial Certification Date:
29 April 2015

Certificate Issue Date:
28 April 2018

Certificate Expiry Date:
28 April 2021

SCC Accredited CB-MS
OCSM
Accrédité CCN
TM

Calin Moldovean
President, Business Assurance

Intertek Testing Services NA Ltd.,
1829, 32nd avenue, Lachine, QC, H8T 3J1,
Canada

CE Technical Documentation Review Report

Organization:

Report Number
20150610601

Examination Date
June 16, 2015

Examination Intent:

Examination the completeness of the Technical Documentation According to the requirements of the MDD 93/42/EEC Annex VII

Product(s): Sterilization packaging, Medical crepe paper, Non-woven sterilization wraps, Indicator tapes and ID Bands

Classification: Class I

Review Result:

During the examination of the provided Technical File of Sterilization Packaging, Medical crepe paper, Non-woven sterilization wraps, Indicators tapes and ID bands no Non-compliance according to the requirements of the MDD 93/42/EEC Annex VII was detected.

Intertek Testing Services
Shanghai Ltd.
Tel: +86 21 61810067
Fax: +86 21 61810069

Jerry Guan, Manager—Medical Device
Intertek Business Assurance China

MINISTRY OF HEALTH AND WELFARE
REPUBLIC OF CHINA (TAIWAN)

Issue Date: JUN 15 2016 No: 065204

GMP Certificate

Name of Manufacturer：
Address of Manufacturer：

GMP Registration Number：GMP1256
Expiry Date：February 25, 2019
Scope of Registration：Sterilization Wrap

The above-mentioned manufacturer has been inspected periodically by the Ministry of Health and Welfare and found to be in compliance with the medical device Good Manufacturing Practice (GMP) requirements (based on ISO 13485). This certificate is hereby issued pursuant to Paragraph 3, Article 57 of the Pharmaceutical Affairs Act.
This certificate may not be used as a product license.

Signed by Chiang, Yu-Mei

Director General
Food and Drug Administration
Under the delegated authority of
Tzou-Yien Lin, M.D., Minister
Ministry of Health and Welfare
Republic of China (Taiwan)

MN 000442

HYTECH
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無塵室規劃設計/設備/耗材

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Factory TEL:886-3-3181661 FAX:886-3-3181660

CERTIFICATE OF COMPLIANCE

This is certify that the cleanroom quality assurance of：

Project Title：Cleanroom System construction ISO Class 5
Project NO：SOG-1060050
Certificate NO：C10604014
Original Certification Date：August 11, 2017
Certification Date：August 11, 2017
Effective Date：August 12, 2017
Measuring Instrument：

1. Laser Particle Counter. Model:LASAAIRⅢ-310C
2. Temp & Humi meter. Model: TES-1365

LASAAIRⅢ-310C Instrument Calibration Date :February 23,2017
TES-1365 Instrument Calibration Date :March 15,2017

We certify that we have tested the cleanroom in accordance with Institute of Environmental Sciences IES-RP-CC006.2 Testing Cleanroom method tests for Classification ISO Class 5 and Temperature Humidity control complies with the requirement of the ISO-14644.

Authorized ： _____ Issued date： 2017. 8. 12

Wuxi Medical Instrument Factory 9/7/17

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS

Warning Letter 320-17-49

September 7, 2017

Mr. Chongjiu Li
General Manager
Wuxi Medical Instrument Factory
No. 86, East Street, Zhangjing, Xibei Town,
Wuxi City, Jiangsu, 214194, China

Dear Mr. Li:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Wuxi Medical Instrument Factory at No. 43 Xixin Road, Zhangjing, Xibei Town, Wuxi City Jiangsu, from March 6 to 10, 2017.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See 21 CFR, parts 210 and 211.

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

We reviewed your March 31, 2017, response in detail and acknowledge receipt of your subsequent correspondence. Your response failed to commit to comprehensive actions to address the violations observed during the inspection.

During our inspection, our investigator observed specific violations including, but not limited to, the following.

1. Your firm failed to establish written procedures for production and process controls designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess (21 CFR 211.100(a)).

You failed to adequately validate the process used to manufacture your sterile (b)(4). During the inspection, you could not provide process qualification batch records and quality control test documentation. You provided only a protocol and a summary report with insufficient data. Batch records for your commercial product also failed to document all significant process parameters (e.g., (b)(4) times), order of ingredient addition, sampling frequency, and sample size. You lacked assurance that in-process materials and finished drug products met predetermined manufacturing and quality requirements.

The purpose of validation is to determine whether your processes can operate within established parameters to assure consistent batch uniformity, integrity, and drug quality. Reliable and well-documented batch operations are essential to ensuring process control and drug quality.

See FDA's guidance document, *Process Validation: General Principles and Practices*, at https://www.fda.gov/downloads/drugs/guidances/ucm070336.pdf (https://www.fda.gov/downloads/drugs/guidances/ucm070336.pdf).

In response to this letter, provide:

- A data-driven and scientifically sound program that identifies and controls all known sources of variability, such that your production and packaging processes will consistently meet appropriate parameters. This includes, but is not limited to, evaluating suitability of equipment for its intended use, assuring quality of input materials, and determining the capability and reliability of each manufacturing process step and control.
- Revised procedures that establish an ongoing program for monitoring process control and detecting variation throughout the product lifecycle.
- An updated master batch record for manufacturing sterile (b)(4) that requires specific processing details in order to fully document each significant manufacturing step.

2. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality and purity (21 CFR 211.160(b)).

You did not perform growth promotion testing on each batch of microbiological growth media you prepare for settle plate, bioburden, and sterility testing. In addition, you do not have a written procedure to ensure that prepared media consistently meets appropriate standards of quality and purity.

In response to this letter, provide your procedures to ensure that media used for settle plate, bioburden, and sterility testing is prepared consistently and promotes microbial growth.

3. Your firm failed to clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(a)).

On March 7, 2017, our investigator observed that your firm had stored clean (b)(4) tubing in an open container in your Apparatus Storage room. It was to be used to transfer (b)(4) during batch manufacture. The exposed tubing ends were not covered to protect against dust or other contamination of your terminally sterilized drug product. You lacked procedures for maintaining, cleaning, and sanitizing this tubing to prevent contamination.

In response to this letter, provide your procedures for maintaining, cleaning, and sanitizing all equipment used in manufacturing your drugs.

4. Your firm failed to maintain adequate written records of major equipment maintenance (21 CFR 211.182).

During the inspection, you provided our investigator with records documenting (b)(4) sanitization of your (b)(4) loop. The records, covering January to March, 2017, were signed by two employees, and indicated that sanitization had been completed and verified contemporaneously throughout this period. However, our investigator found that these operations were not documented at the time of their actual performance, but were instead created and completed on March 7, 2017, the second day of the inspection.

Your response acknowledges this data integrity issue and indicates that you have taken some remediation steps. In response to this letter, provide:

A. A comprehensive investigation into the extent of the inaccuracies in data records and reporting. Identify omissions, alterations, deletions, record destruction, non-contemporaneous record completion, and other deficiencies. Describe all parts of your facility's operations in which you discovered data integrity lapses, and provide an evaluation of the nature of the data integrity deficiencies.

B. A current risk assessment of the potential effects of the observed failures on the quality of your drugs.

C. A management strategy for your firm that includes the details of your global corrective action and preventive action plan. Your strategy should include: a comprehensive description of the root causes of your data integrity lapses, the interim measures you have taken or will take to protect patients and to ensure the quality of your drugs while remediation is ongoing, and the long-term measures you will take to ensure the integrity of your company's data. Include a status report for any of the above activities already underway or completed.

CGMP Consultant Recommended

Based upon the nature of the violations identified at your firm, we strongly recommend engaging a consultant qualified as set forth in 21 CFR 211.34, to assist your firm in comprehensively meeting CGMP requirements. Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for fully resolving all deficiencies and ensuring ongoing CGMP compliance.

Conclusion

Violations cited in this letter are not intended as an all-inclusive list. You are responsible for investigating these violations, for determining the causes, for preventing their recurrence, and for preventing other violations.

Until you correct all violations completely and we confirm your compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as a drug manufacturer.

Failure to correct these violations may also result in FDA refusing admission of articles manufactured at Wuxi Medical Instrument Factory, No. 43 Xixin Road, Zhangjing, Xibei Town, Wuxi City, Jiangsu, into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Under the same authority, articles may be subject to refusal of admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351(a)(2)(B).

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your violations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov or mail your reply to: (mailto:CDER-OC-OMQ-Communications@fda.hhs.gov)

Joseph Lambert, Pharm.D.
Compliance Officer
U.S. Food and Drug Administration

White Oak Building 51, Room 4359
10903 New Hampshire Avenue
Silver Spring, MD 20993
USA

Please identify your response with FEI 3006851654.

Sincerely,
/S/
Thomas J. Cosgrove, J.D.
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

More in 2017
(/ICECI/EnforcementActions/WarningLetters/2017/default.htm)