WHITE PAPER

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Medical Packaging Study — Reducing the Risk of Failure through Performance Testing of Packaging Made from Various Materials

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Overview

Packaging for terminally sterilized medical devices, also known as the sterile barrier system (SBS), serves two key functions. The first is to allow for sterilization and the second is to maintain sterility by keeping package integrity, throughout all steps of the value chain, until the point of use in a healthcare setting.

Sterility cannot easily be measured; therefore, package designs and processes must be validated and controlled. ISO 11607 Packaging for terminally sterilized medical devices, Part 1 addressing materials and design, and Part 2 addressing packaging process validation, is a standard recognized by the U.S. Food and Drug Administration (FDA) and harmonized with the essential requirements of the European medical device directives. This standard also lists a number of test methods in Annex B that can be used to perform package or material testing for qualification and validation purposes.

The loss of package integrity can have serious consequences ranging from costly product recalls to compromised patient safety. As one of the first lines of defense against infection during invasive surgical procedures, the SBS is a key component in the successful prevention of healthcare associated infections (HAIs). However, when there is a breach in the package integrity, this line of defense is no longer in place and patients are at greater risk. HAIs are a major problem, causing an estimated 37 000 deaths each year in the EU according to the European Centre for Disease Prevention and Control (ECDC). Selecting a packaging material that provides the highest possible degree of protection and conducting an established testing and validation process are crucial steps to ensuring package integrity and helping to prevent HAIs.

This paper discusses a study that was conducted to evaluate the performance of standard chevron pouches made with either DuPont™ Tyvek® 1073B, Tyvek® 2FS™ or one of five commonly used medical-grade papers (see Table I). A 2D chevron pouch was selected for this study because this configuration has few design variables; therefore, the focus could remain on material performance differences versus design considerations.

A total of 8 715 pouches were tested in two phases. The purpose of Phase 1 was to define the sealing window of the closure seal and perform an evaluation of the seal performance prior to sterilization. This analysis was performed by an independent contract packing service provider.

During Phase 2, the pouches were subjected to visual inspection, seal integrity evaluation (dye penetration and bubble leak testing) and seal strength testing. Package testing was performed pre- and post-sterilization (ethylene oxide[EO] and Gamma); post accelerated aging 1, 3 and 5 years; and post environmental conditioning and subsequent transportation testing. All testing was conducted by an independent accredited laboratory according to recognized standards listed in ISO 11607.

As shown by the data, loss of integrity after transportation testing was reported for three of the five types of medical-grade paper that were evaluated in this study. The integrity failures, which were only observed after Gamma sterilization, were all linked to punctures and/or creases in the paper. None of the pouches made with Tyvek® 1073B or Tyvek® 2FS™ had a loss of integrity.

To assist readers who wish to further explore this topic, a list of test standards/references is provided.

Scope of the study

For this study, the following material selection criteria were applied: focus on premium and/or the most commonly used medical-grade coated papers. For DuPont™ Tyvek®, the medical packaging styles with the highest and lowest basis weight (Tyvek® 1073B and Tyvek® 2FS™) were selected.

A 2D chevron pouch was chosen as the package type because this is a configuration with few design variables. Results would therefore highlight material performance differences and avoid provoking any design discussions. A blood transfusion device was selected because this device can realistically be expected to be packaged in pouches (see Figure 1).

Figure 1. Sample 2D chevron pouch filled with blood transfusion device.

The pouches were purchased from various sterile packaging manufacturers (SPMs) who offer the respective Tyvek® or medical-grade paper in combination with the appropriate film. All films were polyester and polyethylene (PET/PE) based. To allow for peelability, specific PET/PE-based films having an integrated peel layer were used to seal to Uncoated Tyvek®. See Table I for a list of materials used in this study.

Secondary packaging was defined by the contract packing service provider, the company responsible for the filling and sealing activities (closure seal), as well as the organization of sterilization.

Two types of sterilization were performed, ethylene oxide (EO) and Gamma (refer to Table II). Standard cycles were applied according to the contract packing service provider. Because validations often include double cycles, this option was selected.

All package testing in Phase 1 was performed by the contract packing service provider. All package testing in Phase 2 was performed by an independent accredited testing laboratory.

Table I. Materials Used in the Study

Material	Configuration
Uncoated DuPont™ Tyvek® 1073B	Pouch 260 (258) x 160 mm
Uncoated DuPont™ Tyvek® 2FS™	
100g/m^2 Paper / 10 g/m^2 Grid Lacquer	
60g/m^2 Paper / 11g/m^2 Grid Lacquer	
113g/m^2 Reinforced Paper / 13g/m^2 Allover Coating	
85g/m^2 Reinforced Paper / 11.5g/m^2 Allover Coating	
80g/m^2 Reinforced Paper / 3g/m^2 Allover Coating	
Bottom webs for DuPont™ Tyvek®	
PET-O/PE 12/50µm peel	
Bottom webs for medical-grade papers	
PET-O/PE 12/50µm or 60µm	
Shelf (inner) carton	521 x 365 x 187 mm
Transportation carton	548 x 394 x 438 mm
Transfusion set	N/A

Table II. Description of Sterilization Cycle

Sterilization Method	Target Dosage
Ethylene oxide (EO)	Two full cycles with pre-conditioning and aeration RH pre-conditioning: 60% ± 15% EO concentration: ~720 mg/L Temperature: 45 ± 5°C Cycle duration: ~12hrs Max. pressure rate change: 34 mbar/min.
Gamma radiation	Two cycles at min. 25 kGy (effective max. 36.1 kGy) each

Study Phase 1: Sealing window definition and packaging seal evaluation

The purpose of Phase 1 was to define the sealing window of the closure seal and to perform an evaluation of the seal performance of the pouches. Seal performance was determined by machinability, sealing window and seal strength properties. This analysis was performed prior to sterilization by the selected contract packing service provider. Figure 2 provides an overview of the testing that was conducted during Phase 1.

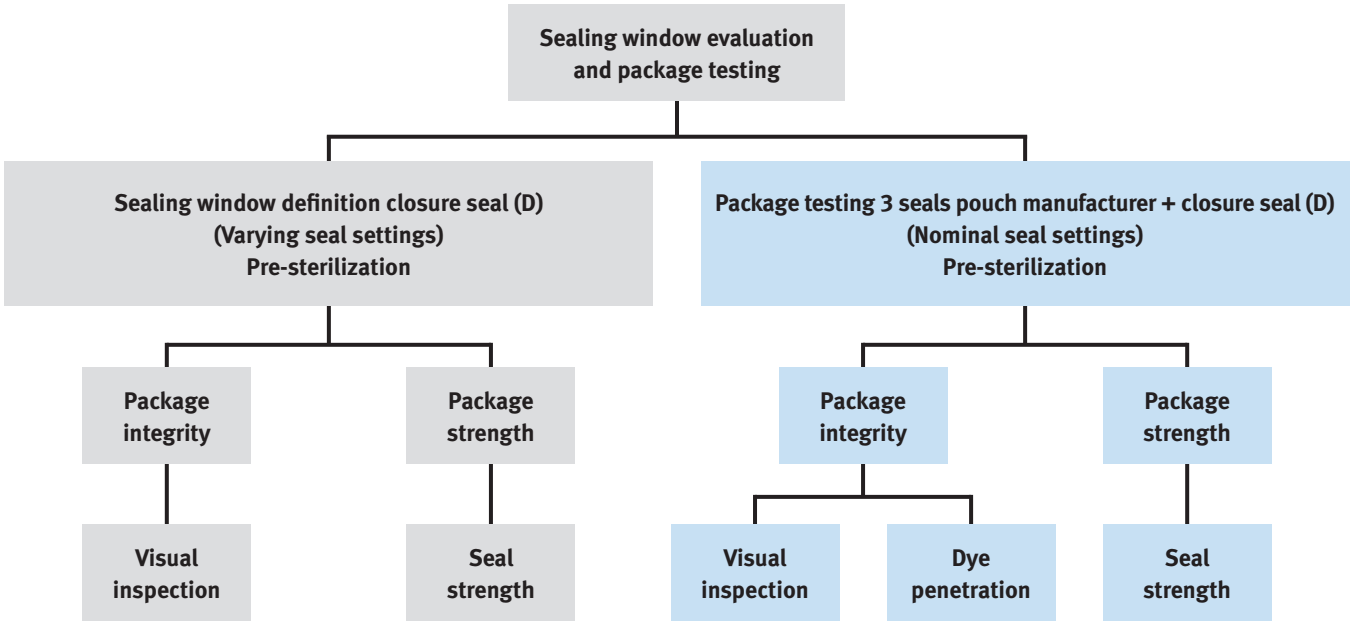


Figure 2. Process flow of testing conducted during Phase 1.

Determination of the sealing window

The first step in Phase 1 was the determination of the sealing window for the final fourth seal, known as the closure seal, for all seven pouch material combinations. A rotary sealing machine with a defined speed of 10 m/min and a contact pressure of 100 N was used. With this machine, temperatures can be varied between 0°C and 220°C.

The sealing window of the closure seal ("D") has been defined as follows:

- An initial seal strength measurement (maximum seal strength in N/15 mm) of the three pre-formed seals (based on 10 pouches; 1 measurement per seal side) of each pouch material combination served as indication for the target seal strength of the closure seal ("D"). The average of all three pre-formed seals (A, B, C), as well as the average of the chevron seal ("C") only was separately noted. See Figure 3.

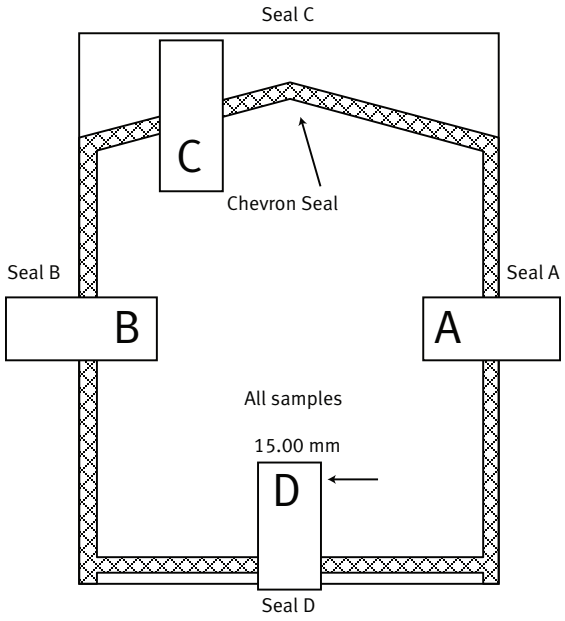


Figure 3. Seal strength sampling locations on the pouch.

- Closure seals were produced at various temperatures, depending on the material combination. Two seal strength measurements and visual evaluation were performed per temperature setting. Absolute minimum requirement for the seal strength was established as 1.5 N/15 mm (based on DIN EN 868-5:2009).
- The sealing process window (temperature range in °C) was determined for the closure seal ("D") based on the seal strength and visual attributes. The seal strength criteria was a minimum of 1.5 N/15 mm, using the pre-formed seal strength "C" as the reference level. Visual attributes were defined as complete seals with no over-sealing or fiber tear. Optimized process parameters (nominal settings) were set within the defined sealing window with no more than ±5°C tolerance.
- All samples for further evaluation were processed with the defined nominal process parameters.

Packaging seal evaluation

Next, all samples were evaluated for machinability, seal strength, seal integrity, visual attributes and peelability. All four pouch seals (A, B, C and D) were assessed. Machinability was an assessment based on the experience of the contract packing service provider. See Table III for other testing details.

Table III. Defined Test Characteristics for Packaging Seal Evaluation at Contract Packing Service Provider

	Test Method	Test Details/Notes	Unit	Acceptance Criteria	Sample Size
Seal strength	SOP based on DIN EN 868-5 Annex D; ASTM F88-09	Test speed 200 mm/min; free tail	N/15 mm Measuring maximum load seal strength Reporting minimum, maximum, mean and standard deviation per seal side	Minimum 1.5 N/15 mm (based on DIN EN868-5: 2009 and on maximum load seal strength)	20 pouches of each material combination Note that 4 separate samples were taken from the seals per pouch; refer to Figure 3 for sampling locations
Seal integrity	SOP based on ASTM F1929-98 (2004)	Dye injected into the pouch, seals wetted for a minimum of 5 seconds and a maximum of 20 seconds Observed for evidence of leakage	Pass/Fail	No fail	20 pouches of each material combination
Visual inspection	DIN EN ISO 11607-2 paragraph 5.3.2b	The following quality properties were considered: intact seal for a specified seal width; no channel or open seals; no punctures or tears; no material delamination or separation; no discoloration	Pass/Fail	No fail	20 pouches of each material combination
Peelability		Manual opening of the pouches	Fiber tear reported	Seal to be opened without difficulty; no fiber tear	20 pouches of each material combination

Phase 1 results

The sealing window temperature range and the optimal process parameters for producing the closure seal ("D") were successfully defined for all seven pouch material combinations. Based on this study, it was found that most of the pouches made with the medical-grade papers generally had a broader sealing window (closure seal "D") than the pouches made with Uncoated Tyvek® and 60g Paper/11g Grid Lacquer. Refer to Figure 4.

However, the final sealing window for all pouch material combinations was defined as the nominal sealing temperature with a tolerance of ±5°C as per the general procedure of the contract packing service provider.

The contract packing service provider rated the pouches made of Uncoated Tyvek® and three of the five types of medical-grade paper pouches as "Excellent" for machinability. The other two medical-grade paper pouches (113g Reinforced Paper / 13g Allover Coating and 80g Reinforced Paper / 3g Allover Coating) were rated as "Good" with a note from the contract packing service provider that these pouches were not of the same visual quality.

Differences in peelability behaviour were observed between the different pouch material combinations but all were found to be within the normal range according to the requirements described in the test procedure from the contract packing service provider.

Seal strength requirements were met by all pouch material combinations (minimum 1.5 N/15 mm). The sample with the highest overall seal strength was the pouch made with 100g Paper / 10g Grid Lacquer, followed by the pouch made with 80g Reinforced Paper / 3g Allover Coating. It is important to note that seal strength levels are influenced by the respective pouch manufacturing specifications, the sealing machines and by the coating/film peel layer type. Refer to Figure 5.

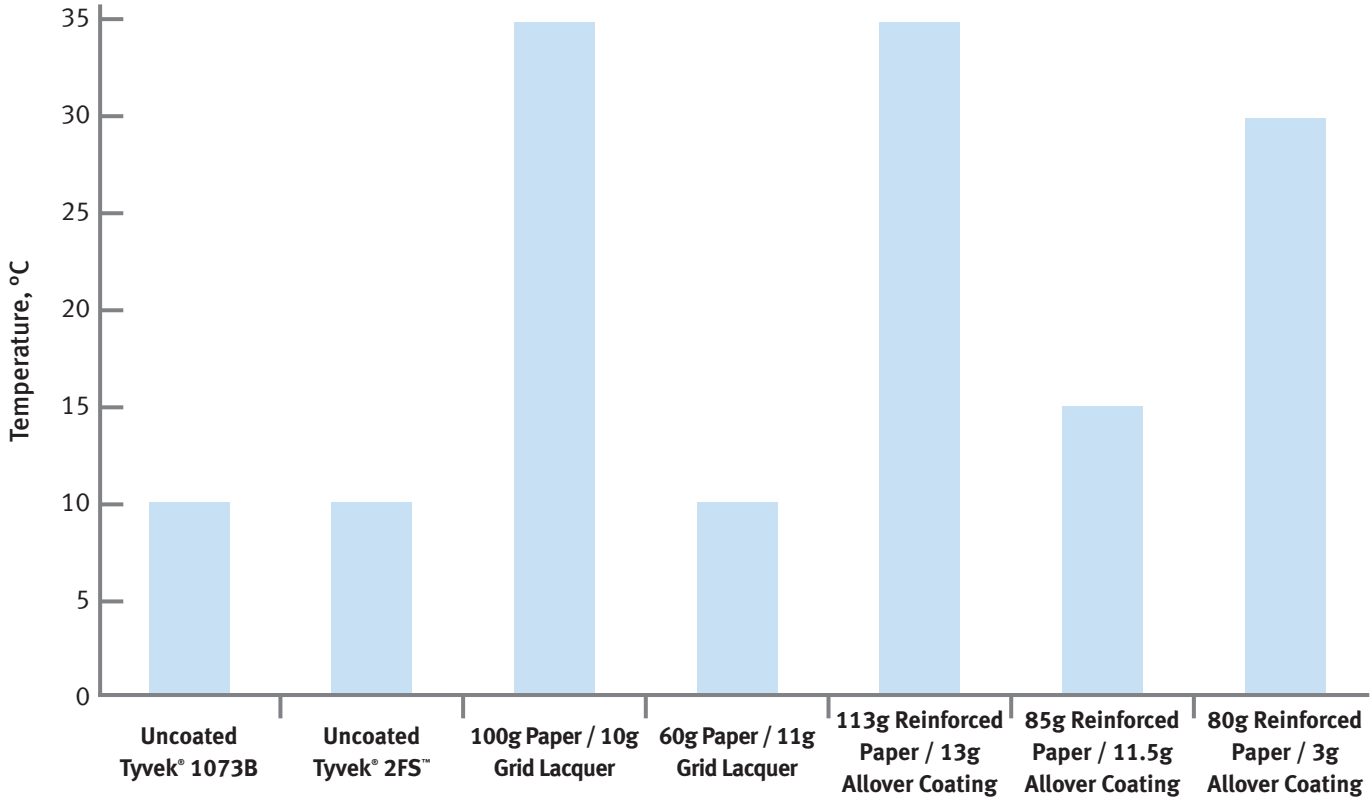


Figure 4. Sealing window of the final closure seal ("D"). Data supplied by contract packing service provider.

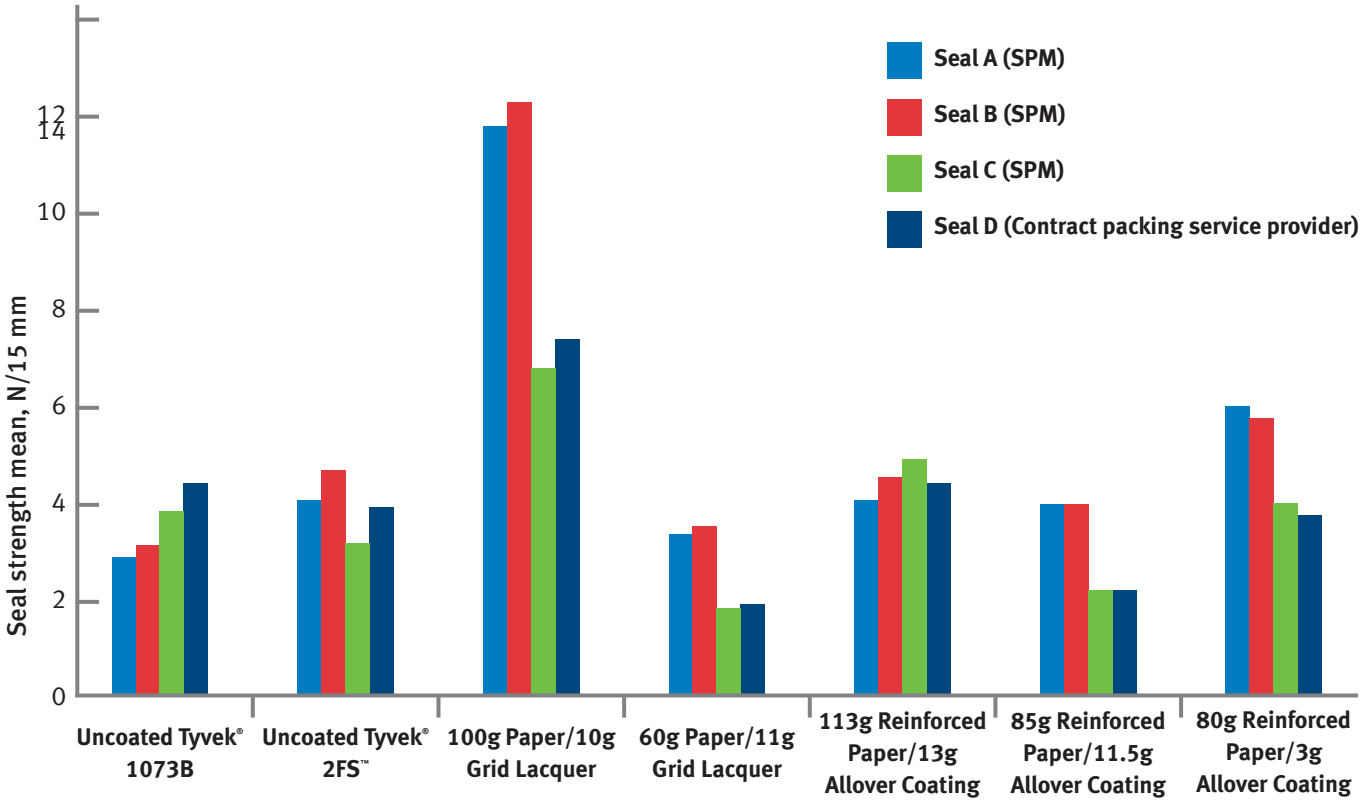


Figure 5. Seal strength comparison for all pouches and all seals (A, B, C and D). Data supplied by contract packing service provider.

All samples of the seven pouch material combinations passed the dye penetration test, confirming the integrity of all seals (A, B, C and D). In addition, all samples passed the visual inspection.

Table IV provides a quick reference summary of all test results from Phase 1.

Next steps

With the completion of Phase 1 testing and the confirmation that all seven pouch material combinations met the specified requirements, Phase 2 could be initiated. Pouches being sent to the independent accredited laboratory for Phase 2 testing were filled with the blood transfusion device and the closure seal ("D") was made by the contract packing service provider according to the defined nominal process parameters.

The filled, sealed pouches were then packed in qualified shelf cartons and transport boxes compatible with the respective sterilization method and subsequently sent to a contract sterilizer to be sterilized with either EO or Gamma radiation. These pouches were then sent to the independent accredited laboratory for Phase 2 testing.

Additionally, the contract packing service provider sent unfilled, non-sterilized pouches to the independent accredited laboratory to be tested as reference.

Table IV. Summary of Phase 1 Test Results

		Test Materials						
Test or activity	Sterilization method	Uncoated Tyvek® 1073B	Uncoated Tyvek® 2FS™	100g Paper / 10g Grid Lacquer	60g Paper / 11g Grid Lacquer	113g Reinforced Paper / 13g Allover Coating	85g Reinforced Paper / 11.5g Allover Coating	80g Reinforced Paper / 3g Allover Coating
Machinability	N/A	Excellent	Excellent	Excellent	Excellent	Good	Excellent	Good
Sealing window final seal temperature range (°C)		115-125	125-135	130-165	150-160	130-165	140-155	135-165
Nominal sealing condition (°C)		120 ± 5	130 ± 5	135 ± 5	155 ± 5	150 ± 5	150 ± 5	145 ± 5
Seal strength seal A (SPM) N/15 mm		min: 2.52 max: 3.40 mean: 2.90 standard deviation: 0.27	min: 2.26 max: 5.80 mean: 4.10 standard deviation: 1.17	min: 11.31 max: 12.67 mean: 11.88 standard deviation: 0.40	min: 2.99 max: 3.77 mean: 3.40 standard deviation: 0.23	min: 3.81 max: 4.41 mean: 4.12 standard deviation: 0.18	min: 3.65 max: 4.33 mean: 4.00 standard deviation: 0.19	min: 6.07 max: 7.32 mean: 6.51 standard deviation: 0.30
Seal strength seal B (SPM) N/15 mm		min: 2.56 max: 3.63 mean: 3.16 standard deviation: 0.34	min: 2.88 max: 6.26 mean: 4.72 standard deviation: 1.00	min: 11.41 max: 13.35 mean: 12.30 standard deviation: 0.46	min: 2.96 max: 4.36 mean: 3.54 standard deviation: 0.41	min: 4.14 max: 5.08 mean: 4.61 standard deviation: 0.27	min: 3.65 max: 5.55 mean: 4.05 standard deviation: 0.42	min: 5.87 max: 6.90 mean: 6.38 standard deviation: 0.31
Seal strength seal C (SPM) N/15 mm		min: 3.77 max: 4.96 mean: 4.43 standard deviation: 0.31	min: 2.37 max: 6.04 mean: 3.92 standard deviation: 1.00	min: 5.95 max: 8.44 mean: 7.39 standard deviation: 0.62	min: 1.71 max: 2.52 mean: 1.96 standard deviation: 0.21	min: 3.17 max: 5.25 mean: 4.48 standard deviation: 0.54	min: 2.37 max: 3.19 mean: 2.65 standard deviation: 0.23	min: 3.51 max: 5.16 mean: 4.57 standard deviation: 0.37
Seal strength seal D (contract packing service provider) N/15 mm		min: 3.20 max: 4.93 mean: 3.87 standard deviation: 0.49	min: 2.47 max: 4.55 mean: 3.19 standard deviation: 0.51	min: 6.24 max: 7.58 mean: 6.79 standard deviation: 0.32	min: 1.50 max: 2.78 mean: 1.88 standard deviation: 0.31	min: 3.88 max: 6.30 mean: 4.94 standard deviation: 0.48	min: 2.01 max: 2.61 mean: 2.29 standard deviation: 0.15	min: 3.59 max: 4.46 mean: 4.01 standard deviation: 0.28
Dye penetration final seal		passed	passed	passed	passed	passed	passed	passed
Visual		passed	passed	passed	passed	passed	passed	passed
Peelability		good; no fiber tear	good; no fiber tear	good; no fiber tear	good; no fiber tear	good; no fiber tear	good; no fiber tear	good; no fiber tear

Study Phase 2: Final package performance evaluation

Phase 2 addresses the package performance of the pouches filled with the blood transfusion device. All pouch material combinations tested in Phase 1 were also tested in Phase 2. Refer to Table I for material details.

A study protocol was established, outlining the test parameters required for the evaluation of the pouches. All protocol non-compliance results were required to be reported.

Prior to Phase 2 testing, the pouches were subjected to sterilization by either EO or Gamma radiation (double cycles). Unfilled, non-sterilized pouches were tested as reference.

Package testing was performed by an independent accredited laboratory at the following conditions: pre- and post-sterilization; post accelerated aging 1, 3 and 5 years; and post environmental conditioning and subsequent transportation testing.

As shown in Figure 6, packages were tested for integrity and strength. All samples were visually inspected and tested for seal strength and for seal integrity by both dye penetration and bubble leak tests. See Table V for testing details.

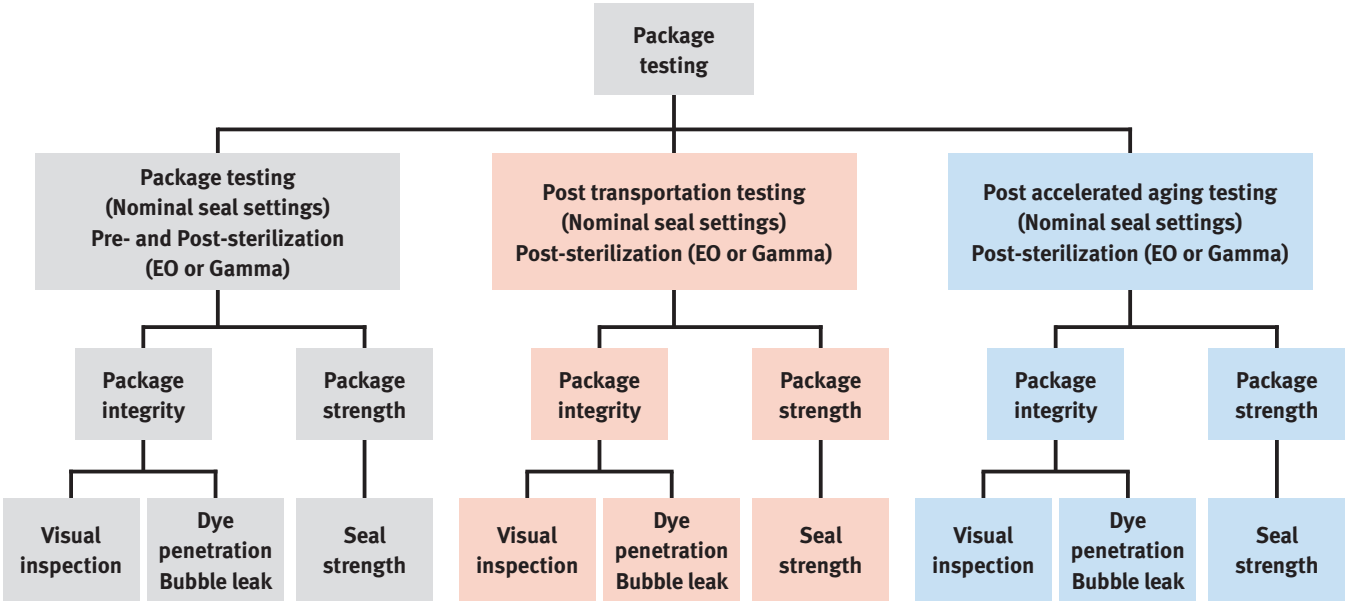


Figure 6. Process flow of testing conducted during Phase 2.

Table V. Defined Test Characteristics for Final Package Performance Evaluation

	Test Method	Test Details/Notes	Unit	Acceptance Criteria	Sample Size
Visual inspection	ASTM F1886-09	The following quality properties were considered: wrinkles; channels; non-uniform seal width; foreign particles; visible bubbles in the seal area; any abnormal observations or colour changes of the materials	Pass/Fail	No fail (all fails to be reported)	15 filled pouches sterilized by EO 15 filled pouches sterilized by Gamma radiation 30 filled pouches post environmental conditioning and transportation testing* 30 filled pouches each post accelerated aging 1, 3 and 5 years* 15 unfilled, non-sterilized pouches of each material combination
Seal integrity—dye penetration	ASTM F1929-98 (2004)	The method has been validated to detect defects down to 50 micron Dye injected into the pouch, seals wetted for a minimum of 5 seconds and a maximum of 20 seconds Observed for evidence of channels, seal creep and any leakage See Figure 7	Pass/Fail	No fail (all fails or half channels to be reported)	15 filled pouches sterilized by EO 15 filled pouches sterilized by Gamma radiation 30 filled pouches post environmental conditioning and transportation testing* 30 filled pouches each post accelerated aging 1, 3 and 5 years* 15 unfilled, non-sterilized pouches of each material combination
Seal integrity—bubble leak	ASTM F2096-04	The method has been validated to detect defects down to 125 micron Pouch is submerged in water and internal pressure is gradually increased Observed for evidence of bubbles seen coming from a potential pouch failure See Figure 8	Pass/Fail	No fail/no leakage during testing from the seals or the surface of the pouch Leakage areas to be documented and photographed	15 filled pouches sterilized by EO 15 filled pouches sterilized by Gamma radiation 30 filled pouches post environmental conditioning and transportation testing* 30 filled pouches each post accelerated aging 1, 3 and 5 years* 15 unfilled, non-sterilized pouches of each material combination
Seal strength, N/15 mm converted in lb/inch	ASTM F88/ F88M-09	Test speed 200 mm/min; free tail	N/15 mm Measuring average seal strength (80% of the curve) and maximum load seal strength Seals were analysed based on the location (e.g., all "A1" seals were evaluated together) Statistical values calculated of the maximum/average seal strength were mean, standard deviation and coefficient of variance	1.2 N/15 mm (according to DIN EN 868-5:2009, based on maximum load seal strength)	10 filled pouches sterilized by EO 10 filled pouches sterilized by Gamma radiation 20 filled pouches post environmental conditioning and transportation testing** 20 filled pouches each post accelerated aging 1, 3 and 5 years** 10 unfilled, non-sterilized pouches of each material combination Note that 7 separate samples were taken from the seals per pouch; refer to Figure 9 for sampling locations

*15 filled pouches for EO and 15 filled pouches for Gamma Sterilization
**10 filled pouches for EO and 10 filled pouches for Gamma Sterilization

Figure 7. Dye penetration testing on pouches.

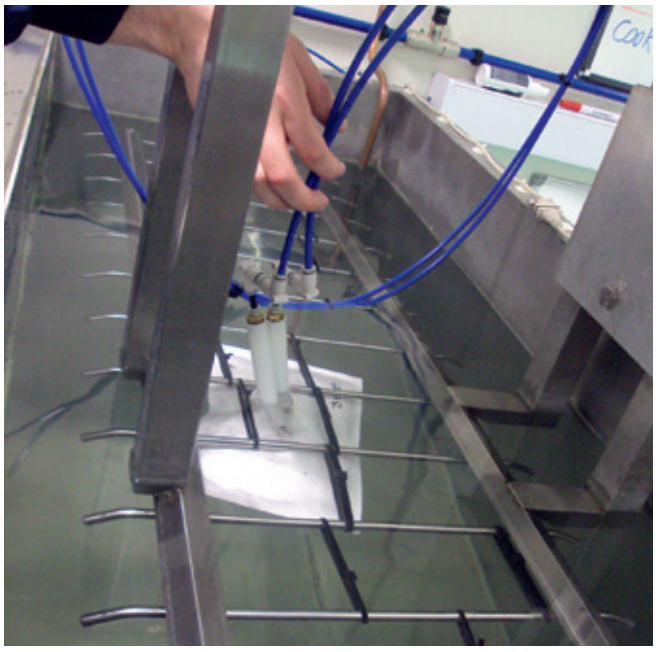


Figure 8. Bubble leak testing on pouches.

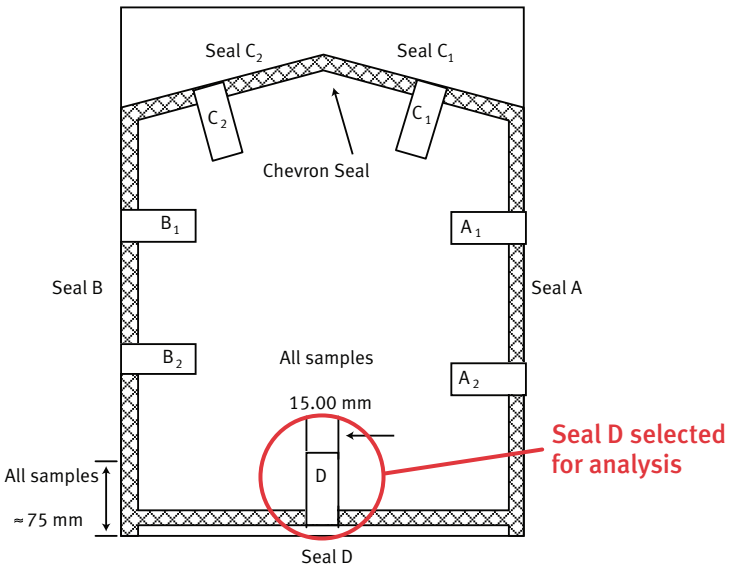


Figure 9. Seal strength sampling locations on pouches.

Transportation testing

Prior to the transportation testing, the conditioning of the respective filled and sterilized pouches was carried out per ASTM D4332-01 environmental conditioning for a total of seven days, as shown in Table VI (conditions partly adapted based on ASTM D4169, ISO 2233 and ISTA 2A as recommended by the independent accredited laboratory in order to reflect worldwide distribution worst case conditions).

After environmental conditioning, transportation testing was carried out in accordance with ASTM D4169-09 and associated international testing standards as described in Table VII. Worldwide distribution with different means of transport has been assumed as a base for the selection of the test level and conditioning. The test has been based on Assurance Level I (high level of test intensity and low probability of occurrence) of ASTM D4169-09 Distribution Cycle 13 (DC-13).

Table VI. Pouch Environmental Conditioning

Anticipated Condition	Temperature (°C ± 2°C)	Relative Humidity (% RH)	Duration Time (hours)
Lab Ambient	Ambient	Ambient	6
Frozen or winter ambient	-35°C ± 2°C	—	72
Ambient	Ambient	Ambient	6
Tropical (Wet)	38°C ± 2°C	85% ± 5%	72
Desert (Dry)	60°C ± 2°C	30% ± 5%	6

Table VII. Transportation Test Standards Sequence

Sequence	Test Schedule	Test Method / Standard
1	Conditioning	ASTM D4169, ASTM D4332
2	A: Manual Handling – First Sequence	ASTM D4169, ASTM D5276 / ISTA 2A*
3	C: Vehicle Stacking	ASTM D4169, ASTM D642
4	E: Vehicle Vibration – Truck and Air	ASTM D4169, ASTM D4728 Method A
5	F: Loose Load Vibration	ASTM D4169, ASTM D999 Method A1
6	A: Manual Handling – Second Sequence	ASTM D4169, ASTM D5276 / ISTA 2A*

* ISTA drop test heights were used with the ASTM drop test sequence.

Acceptance criteria before further testing

Pouches were required to meet the following acceptance criteria before any further testing was conducted in Phase 2.

- Post conditioning:
  - The external shipper box shall not show any signs of deterioration after pre-conditioning. The closing tape must remain in position in all locations of the shipper.
- Post transportation:
  - Some slight damage to the sides and corners of the shipper box is allowed; however, the external shipper box and the manufacturer's closing joint must remain intact. Minor damage is allowed on the internal/intermediate cartons.
  - No damage is allowed on the pouches.
- Post transportation test pouch sampling:
  - All pouches were inspected visually. Damaged pouches were recorded.
  - On non-visibly damaged pouches, if folds/creases were found on the porous top web, the pouches were subjected to bubble leak testing.
  - Pouches with possible seal breaches were subjected to the dye penetration test.
  - The remaining pouches were tested for seal strength and seal visual inspection.

Accelerated Aging

Accelerated aging was performed according to ASTM F1980-07 Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices. The aging is based on the assumption that chemical reactions follow the Arrhenius reaction rate function. Based on modelling kinetics of materials, this function states that a 10°C increase or decrease in temperature of a homogenous process results in a 2x or $^1/_2$ x change, respectively, in the rate of a chemical reaction (Q10 = 2). This applies to shelf life as the equation. See Figure 10.

Subsequent package testing was performed after a 1-, 3- and 5-year equivalent accelerated aging period.

Accelerated	Time $_{RT}$
Time =	$T / Q_{10}^{(T_1-T_{RT}) / 10}$
T = Claimed shelf life period in days T_1 = Aging temperature (= 55°C) T_{RT} = Room temperature (normal environmental temperature) (= 22°C) Q_{10} = Reaction rate coefficient (= 2.0)	

Figure 10. Accelerated aging time calculation based on Arrhenius reaction rate equation.

Phase 2 results

Visual inspection
(post all environments: pre-sterilization; post-sterilization [EO, Gamma]; post transportation testing [EO, Gamma]; and post accelerated aging 1, 3 and 5 years [EO, Gamma])

Of the seven pouch material combinations, all five of the medical-grade papers showed yellowing in different degrees after Gamma sterilization and post Gamma accelerated aging (see photos in Figure 11). This shows that Gamma radiation has a negative impact on the aesthetics of the pouch, probably related to the degradation of cellulose or other ingredients.

None of the pouches made with Uncoated Tyvek® 1073B or Uncoated Tyvek® 2FS™ showed any discoloration.

Seal quality—visual, integrity and strength
(post all environments: pre-sterilization; post-sterilization [EO, Gamma]; post transportation testing [EO, Gamma]; and post accelerated aging 1, 3 and 5 years [EO, Gamma])

All tested pouch material combinations passed the seal quality visual inspection pre-sterilization; post-sterilization (EO, Gamma) post transportation testing (EO, Gamma); and post accelerated aging 1, 3 and 5 years (EO, Gamma).

All tested pouch material combinations also passed the dye penetration test pre-sterilization; post-sterilization (EO, Gamma); post transportation testing (EO, Gamma); and post accelerated aging 1, 3 and 5 years (EO, Gamma). However, one pouch made with 80g Reinforced Paper / 3g Allover Coating had a partial seal channel post accelerated aging 5 years (Gamma).

Figure 11. Medical-grade papers show yellowing after being sterilized by Gamma radiation. None of the pouches made with Tyvek® 1073B or Tyvek® 2FS™ showed any discoloration.

In addition, some of the paper pouches showed seal creep. This was mainly observed with pouches made with 113g Reinforced Paper / 13g Allover Coating after EO and Gamma sterilization. Although the seal strength of these paper pouches was not initially lower than the seal strength of most of the other pouches, this observed seal creep indicates the need to review and define seal strength requirements for this material combination in such a way as to ensure that the seal remains intact under real-world conditions.

Bubble leak testing (post Gamma sterilization and post transportation testing) revealed integrity failures for pouches made with three out of the five medical-grade papers. Details are provided under "Package performance post environmental conditioning and transportation testing" on page 17. In addition, one of the 60g Paper / 11g Grid Lacquer pouches failed bubble leak testing post accelerated aging 3 years (Gamma). The root cause for this integrity failure post accelerated aging 3 years cannot be identified, but demonstrates the fragile nature of this pouch material combination.

Seal strength (closure seal "D")

In this paper, only the seal strength results of closure seal "D" are discussed. Closure seal "D" was selected for analysis because it was produced on the same sealing machine for all pouch samples being tested thereby reducing the impact of different variables on the results. It is important to note, however, that there are still other variables to consider, such as the sealing parameters that have been individually defined, as well as the seal medium/sealant (different coatings on the five medical-grade papers versus film with peel layer to be sealed to Uncoated Tyvek®).

Seal strength requirements (min. 1.2 N/15 mm) for closure seal "D" were met for all pouch samples in terms of the maximum load single values as defined in the test protocol. For pouches made with 60g Paper / 11g Grid Lacquer, the seal strength was below 1.2 N/15 mm based on the mean average for several environments: pre-sterilization; post-sterilization (EO); post accelerated aging 1, 3 and 5 years (EO); post transportation testing (EO); and post accelerated aging 1 year (Gamma). The seal strength tested post Gamma sterilization for this paper showed an overall increase.

Seal strength behaviour analysis (closure seal "D")

The objective of this analysis was to evaluate the seal strength behaviour for pouches made of each material combination, comparing the strength pre-sterilization versus the different environments (post-sterilization [EO and Gamma], post accelerated aging 1, 3, 5 years and post transportation testing).

The recorded maximum seal strength value in N/15 mm was selected for the analysis (F_{max}) because the maximum seal strength is the force that must be overcome in order to open a seal.

To evaluate the potential change in seal strength for the various environments, the difference between pre-sterilization versus the various environments was calculated using the formula shown here:

F_{max} difference (N/15 mm) = F_{max} post-sterilization (N/15 mm) – F_{max} pre-sterilization (N/15 mm)

The mean is then calculated (out of 10 measurements F_{max} difference per condition).

Result interpretation:

→ If F_{max} difference mean value is >0 (positive) = seal strength has increased post-sterilization and/or post other environments

→ If F_{max} difference mean is <0 (negative) = seal strength has decreased post-sterilization and/or post other environments

→ If F_{max} difference mean is =/≈ 0 (equal or next to zero) = no/only slight change in seal strength post-sterilization and/or post other environments

The analysis has been made using Minitab® statistical software. The results are displayed in boxplot graphs (see Figures 12 and 13). Additionally, one-way Analysis of Variance (ANOVA), using 95% confidence interval, has been run to assess if the changes in seal strength are significantly different comparing the environments, following confirmation that the F_{max} difference values calculated post all environments presented a normal distribution.

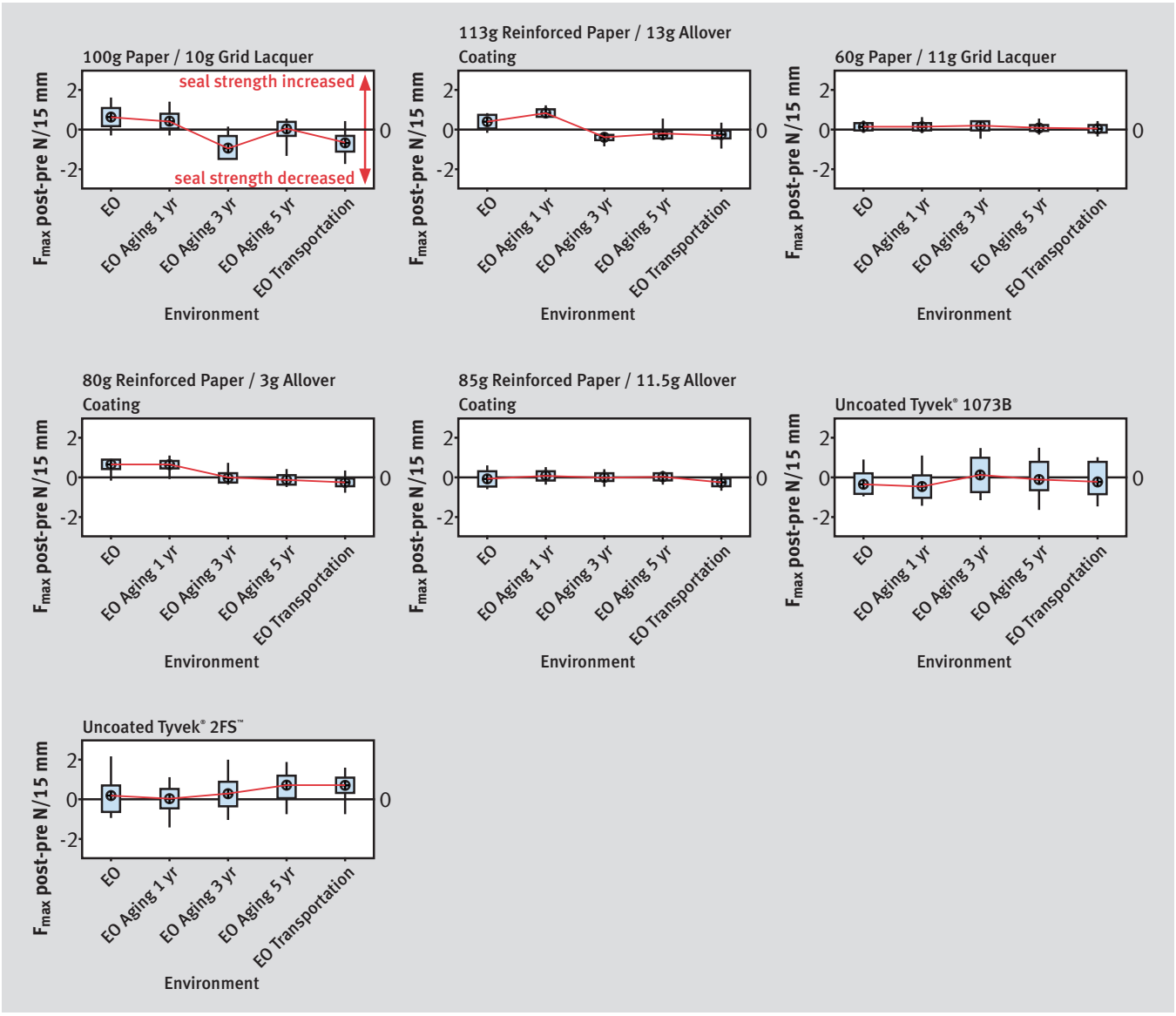


Figure 12. Boxplot for seal strength F_{max} difference in N/15 mm for closure seal "D" post EO sterilization, post accelerated aging and post transportation testing analysis

Post EO sterilization and other environments

As shown in Figure 12 and supported by the one-way ANOVA analysis, the change in seal strength was significantly different for the pouches made with 113g Reinforced Paper / 13g Allover Coating; pouches made with 100g Paper / 10g Grid Lacquer; and pouches made with 80g Reinforced Paper / 3g Allover Coating.

It is important to note that, in general, the acceptance limit for changes in seal strength varies depending on the specific application requirements of sterile packaging users.

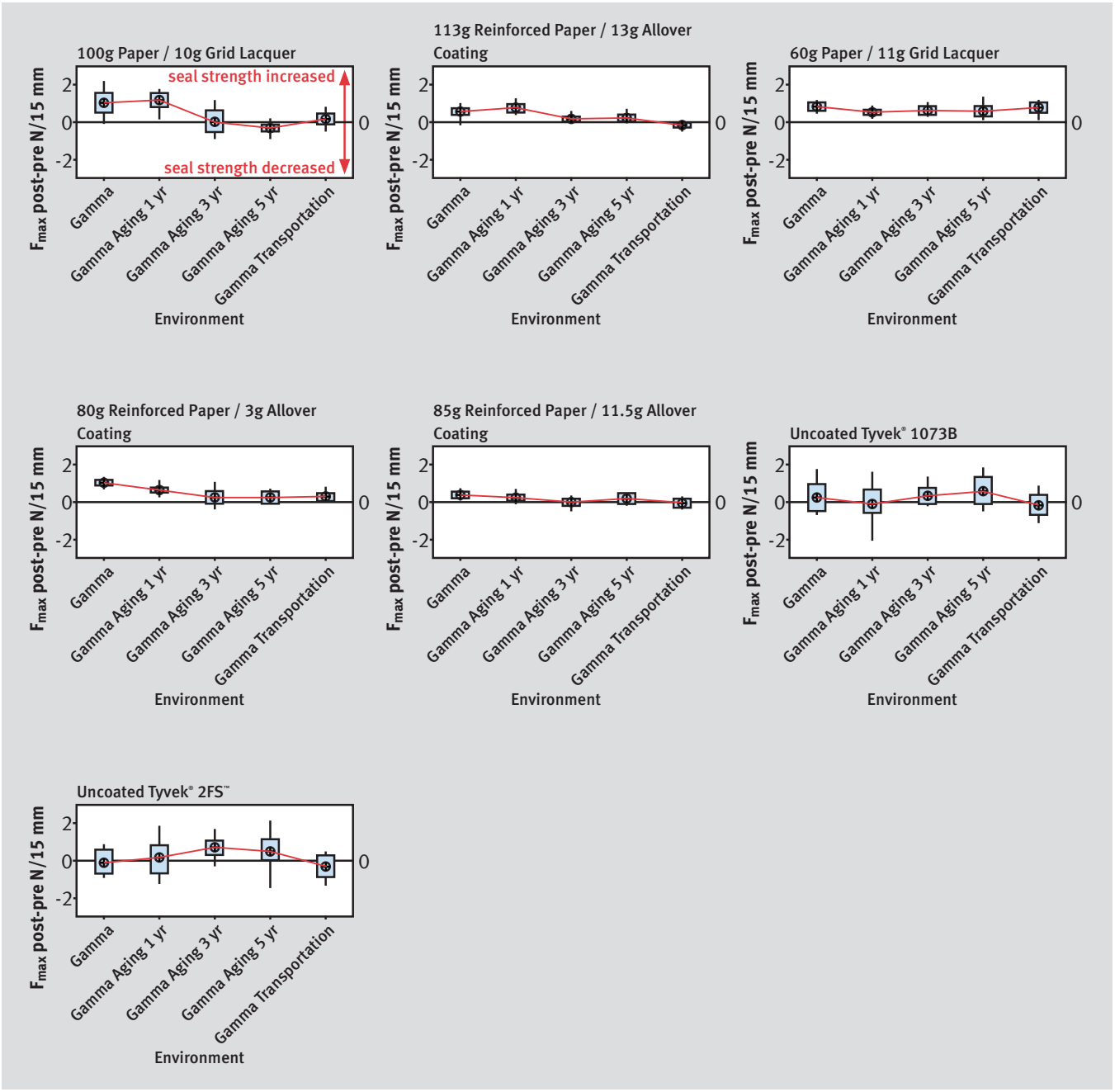


Figure 13. Boxplot for seal strength F_{max} difference in N/15 mm for closure seal "D" post Gamma sterilization, post accelerated aging and post transportation testing analysis.

Post Gamma sterilization and other environments

As shown in Figure 13 and supported by the one-way ANOVA analysis, the change in seal strength was significantly different for the pouches made with Uncoated Tyvek® 2FS™; 113g Reinforced Paper / 13g Allover Coating; 85g Reinforced Paper / 11.5g Allover Coating; 100g Paper / 10g Grid Lacquer; as well as 80g Reinforced Paper / 3g Allover Coating.

For pouches made with all five papers tested, the seal strength increased post Gamma sterilization and post 1-year accelerated aging versus pre-sterilization. Conversely, seal strength tended to decrease post 3-year accelerated aging for pouches made with four of the five papers. The pouches made with Uncoated Tyvek® 1073B and Uncoated Tyvek® 2FS™ showed almost no change in seal strength post Gamma sterilization, post 1-year accelerated aging and post transportation testing. Seal strength for pouches made with Tyvek® increased post 3- and 5-year accelerated aging.

The data for the paper pouches suggests that seal strength first increased post-sterilization but then decreased over time. This trend could not be confirmed on pouches made with Uncoated Tyvek®. One explanation for the difference in behaviour when reviewing the seven pouch material combinations is that the various materials and sealants used (peel film or coating) may react differently to Gamma radiation.

It is important to note that, in general, the acceptance limit for changes in seal strength varies depending on the specific application requirements of sterile packaging users.

Package performance (Post environmental conditioning and transportation testing)

Integrity failures were reported for pouches made with three out of the five medical-grade papers: 60g Paper / 11g Grid Lacquer; 113g Reinforced Paper / 13g Allover Coating; and 80g Reinforced Paper / 3g Allover Coating. Several pouches made with each of these medical-grade papers did not pass the bubble leak test post environmental conditioning and transportation testing (see Figures 14-17).

The pouch made with the lowest basis weight medical-grade paper (60g Paper / 11g Grid Lacquer) had the highest integrity failure rate. There was one case of a punctured pouch post accelerated aging (Gamma) where the root cause could not be identified.

Integrity failure of paper pouches after transportation testing has only been observed post Gamma sterilization. All integrity failures were linked to punctures and/or creases in the paper.

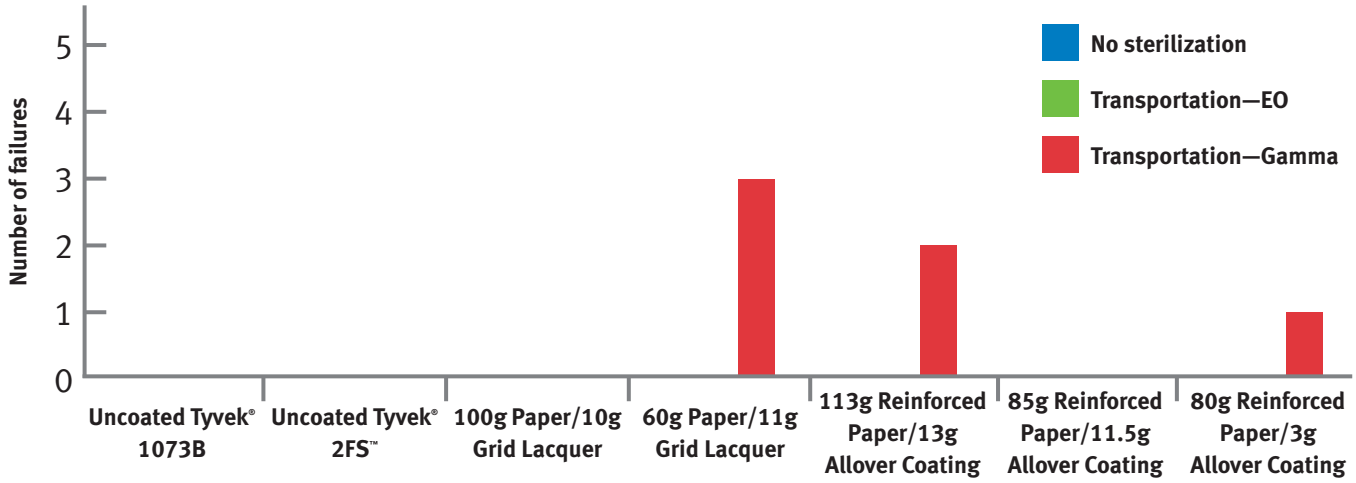
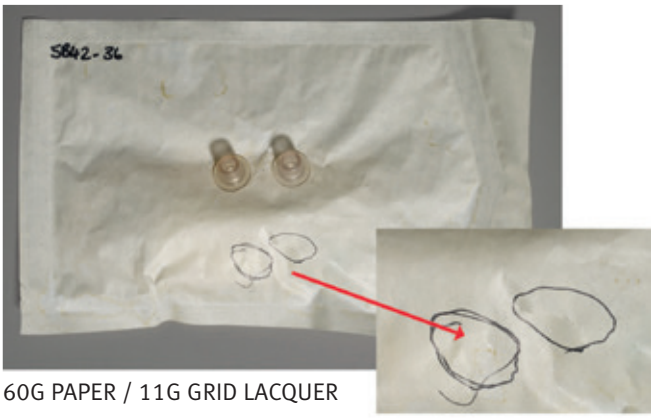
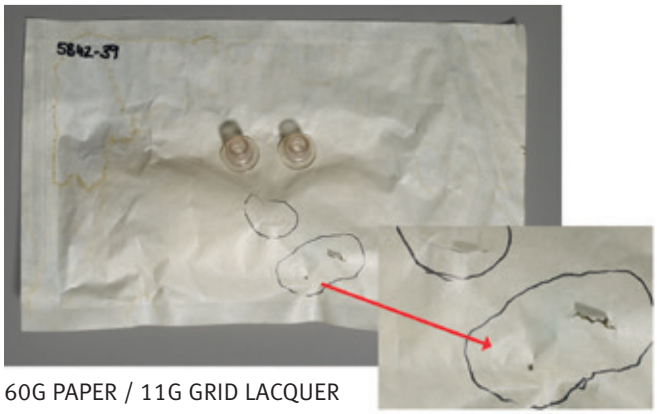


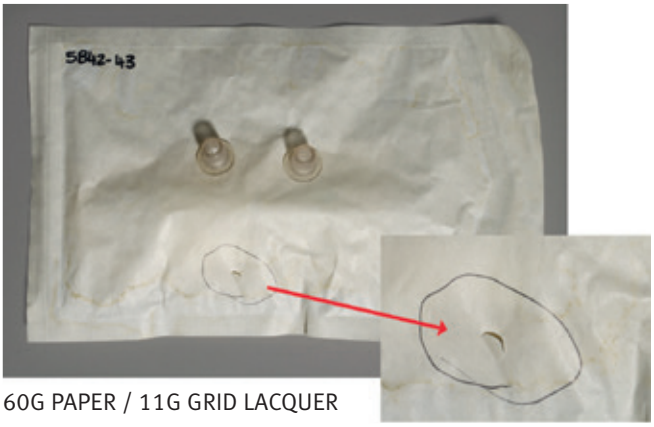
Figure 14. Bubble leak test results post transportation testing, based on 15 samples of each pouch material combination.



60G PAPER / 11G GRID LACQUER

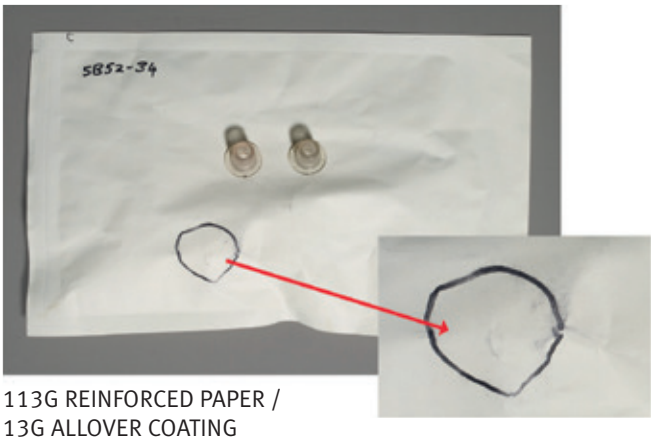


60G PAPER / 11G GRID LACQUER

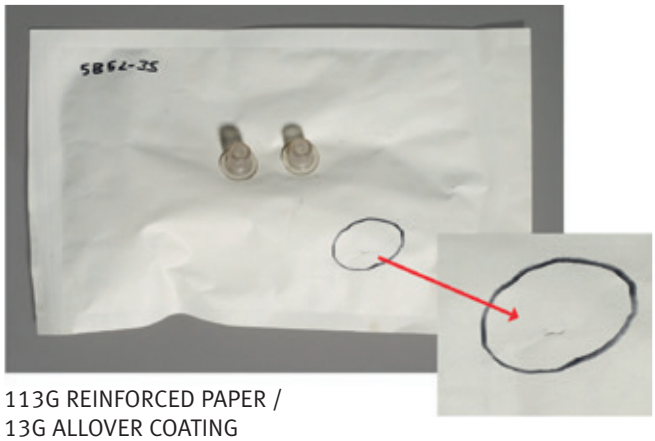


60G PAPER / 11G GRID LACQUER

Figure 15. Three pouches made with 60g Paper / 11g Grid Lacquer had integrity failures.

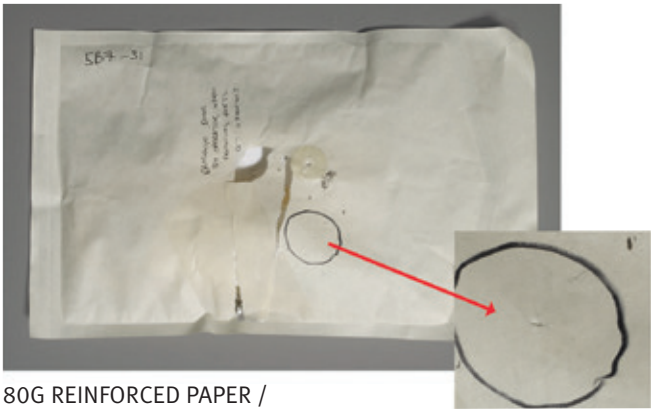


113G REINFORCED PAPER /
13G ALLOVER COATING



113G REINFORCED PAPER /
13G ALLOVER COATING

Figure 16. Two pouches made with 113g Reinforced Paper / 13g Allover Coating had integrity failures.



80G REINFORCED PAPER /
3G ALLOVER COATING

Figure 17. One pouch made with 80g Reinforced Paper / 3g Allover Coating had an integrity failure, as shown by the arrow in the circle. The other visible damage in the center of the pouch was caused by manipulation of the sample after bubble leak testing during removal.

To further investigate the risk of integrity failure during handling, storage and distribution, another study could follow: performing microbial barrier testing on pouches that had undergone transportation testing. Because the sensitivity of the bubble leak integrity test is limited, a microbial barrier test (such as ASTM F2638 or ASTM F1608) on the pouch materials could demonstrate if there is a potential loss of barrier in the area of creases and folds.

Conclusions

All pouches in this study passed the seal strength and seal integrity tests during the preliminary evaluation and after sterilization, aging and transportation testing. However, seal creep was detected on some of the medical-grade paper pouches.

More importantly, integrity failures were reported for pouches made with three out of the five papers due to punctures on the material itself after Gamma sterilization, environmental conditioning and transportation testing.

This data generated by the independent accredited laboratory demonstrates that design validation, including package performance testing, is essential to detect potential integrity failures prior to a product being distributed on the market.

Physical and climate testing in the context of the transportation testing demonstrated the difference in performance of the various pouches, underscoring the critical importance of using the most appropriate packaging materials and design to ensure a safe and compliant packaging solution, thereby reducing the risk of product recalls.

The findings of the study further indicate that Gamma sterilization has a visible impact on pouches made with medical-grade paper, leading to yellowing and integrity failures.

The seal strength analysis showed that Gamma radiation has a higher impact on seal strength than EO sterilization. This points out the need to consider potential changes in seal strength post-sterilization or aging to ensure that the sterile barrier system keeps its integrity and functionality until the point of use.

Drawing on the information from this study, it is clear that defining a comprehensive testing strategy is essential to ensure a safe and reliable sterile barrier system compliant with regulations and relevant standards. Sterile barrier systems are an integral part of a sterile medical device and as such an essential element of clinical procedures to prevent and control healthcare associated infections.

References

Standard / Reference	Description
ASTM D4169-09	Standard Practice for Performance Testing of Shipping Containers and Systems
ASTM D4332-01(2006)	Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing
ASTM D4728-06	Standard Test Method for Random Vibration Testing of Shipping Containers Method A
ASTM D5276-98(2009)	Standard Test Method for Drop Test of Loaded Containers by Free Fall
ASTM D642-00(2010)	Standard Test Method for Determining Compressive Resistance of Shipping Containers, Components, and Unit Loads
ASTM D999-08	Standard Methods for Vibration Testing of Shipping Containers Method A1
ASTM F1608-00	Standard Test Method for Microbial Ranking of Porous Packaging Materials (Exposure Chamber Method)
ASTM F1886-09	Standard Test Method for Determining Integrity of Seals for Medical Packaging by Visual Inspection
ASTM F1929-98(2004)	Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration
ASTM F1980-07	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
ASTM F2096-04	Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)
ASTM F2638-12	Standard Test Method for Using Aerosol Filtration for Measuring the Performance of Porous Packaging Materials as a Surrogate Microbial Barrier
ASTM F88/F88M-09	Standard Test Method for Seal Strength of Flexible Barrier Materials
DIN EN 868-2:2009	Sterilization wrap – requirements and test methods
DIN EN 868-5:2009	Appendix D; Packaging materials and systems for medical devices that are to be sterilized
EN ISO 11607-1:2006/2009	Requirements for materials, sterile barrier system and packaging systems
EN ISO 11607-2:2006	Validation requirements for forming, sealing and assembly processes
ISO 2233:2000	Packaging -- Complete, filled transport packages and unit loads -- Conditioning for testing
ISTA 2A:2011	Simulation test for individual packaged-products less than 150 lbs
Test report	Medical Packaging Performance Study - Technical study report

The information provided herein corresponds to our knowledge on the subject at the date of its publication. This information may be subject to revision as new knowledge and experience becomes available. The data provided fall within the normal range of product properties and relate only to the specific material designated; these data may not be valid for such material used in combination with any other materials or additives or in any process, unless expressly indicated otherwise. The data provided should not be used to establish specification limits or used alone as the basis of design; they are not intended to substitute for any testing you may need to conduct to determine for yourself the suitability of a specific material for your particular purposes. Since DuPont cannot anticipate all variations in actual end-use conditions DuPont makes no warranties and assumes no liability in connection with any use of this information. Nothing in this publication is to be considered as a license to operate under or a recommendation to infringe any patent rights.

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