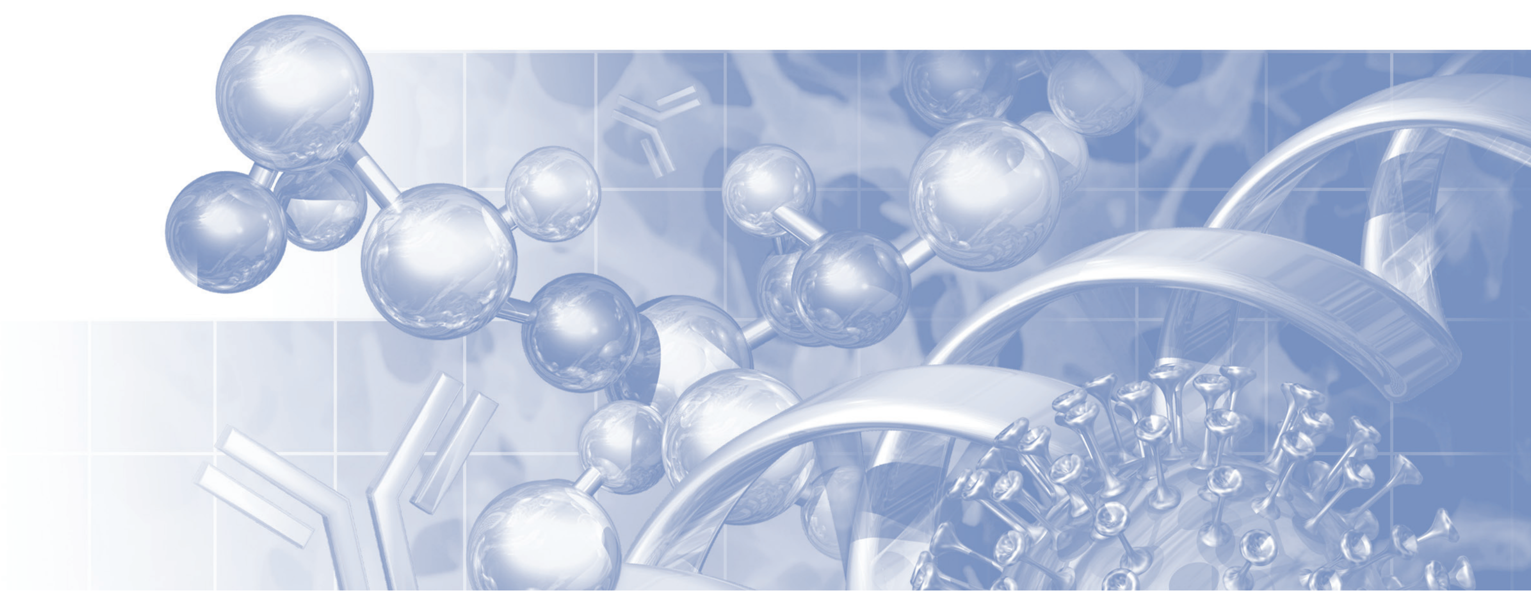
Life Sciences

Validation Guide

USTR3092

Pall® Powder Handling Bags with PD2 Film



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A. General Description of the PD2 Film and Articles

All of the layers in PD2 are made from "medical grade" materials, meaning that they comply with industry standards and are subject to strict change controls.

The structure of the film is as follows:

Outer layer	50 µm mLLDPE + permanent antistatic
Inner layer	100 µm MDPE/LDPE
Contact layer	50 µm mLLDPE + permanent antistatic

mLLDPE: metallocene linear low-density polyethylene

MDPE: medium-density polyethylene

LDPE: low-density polyethylene

Figure 1
Pall powder handling bags made of PD2 film

B. Properties of the PD2 Film

B1. Mechanical Testing

The following tests were carried out on PD2 film to check its ability to withstand mechanical stress.

Test Type and General Description	Test Reference	Summary Description of Test Reference
B1.1. Gelbo Flex Determines the flex resistance of materials by the formation of pinholes.	ASTM F392/F392M-11	This test covers the flex crack resistance of materials by the formation of pinholes. Specimens (=sealed film tube) are twisted and horizontally folded at a constant rate and at 900 test cycles. The speed is 45 cycles per minute. In general the formation of pinholes is determined by use of colored turpentine and allowing it to stain through the pinholes onto a white backing.
B1.2. Thickness	WI-01493	The film is placed in a calibrated digital Determines the thickness of the film system that measures the thickness of the film.
B1.3. Strength and Elongation A measure of the force required to stretch a material to its breaking point.	WI-01647 ASTM D882-02	This test method covers the determination of tensile properties of plastics in the form of thin sheeting, including film, less than 1.0 mm (0.04 in.) thick. This test covers the maximum strength, elongation at break and the young modulus to measure the stiffness of the material.
B1.4. Puncture Resistance Puncture resistance testing predicts the durability of the film while in use. Films with high puncture resistance correspond with material that can absorb the energy of an impact by both resistance to deformation and increased elongation. Puncture resistance, measured in energy units, evaluates the film strength and extensibility properties.	WI-01633 ASTM D2582-00-1	A pressing bar with a fixed diameter will be pushed through the film at a constant speed. The pressure force, needed to break the film, will indicate the puncture resistance of the film.
B1.5. Dart Impact Test method covers the determination of the energy as part of mechanical properties that causes plastic film to fail under specified conditions of impact of a free-falling dart.	WI-01635 ASTM D1709	Described are two testing methods depending on the size of the striker, which are determined by the impact resistance of the material. The standard technique is a staircase method to drop a weight and increase or decrease depending in pass or fail. Standard apparatus and striker has been described.
B1.6. Tear Resistance Determines the tear resistance of flexible plastic film and sheeting at very low rates of loading.	WI-01649	Test is designed to measure the force to initiate tearing.

B2. Physical Testing

Test Type and General Description	Test Reference	Summary Description of Test Reference
B2.1. Surface Resistivity	ASTM D257	Antistatic properties refer to the material ability to resist to tribocharging. The surface resistivity of a material is numerically equal to the surface resistance between 2 electrodes forming opposite sides of a square. The size of the square is immaterial. The surface resistivity gives information on discharge. The surface resistivity is measured on inside and outside surface.

B3. Chemical and Biological Testing

The purpose of these tests was to evaluate the biological suitability of the materials of construction of PD2 film.

Test Type and General Description	Test Reference	Summary Description of Test Reference
B3.1. Biological Reactivity – *In Vitro* Evaluates the response of mammalian cell cultures to extracts of polymeric materials.	USP <87> ISO 10993-5	Post gamma irradiation extracts are obtained by placing the test and control materials (extracts) in separate cell culture media under standard conditions. Cells are observed for visible signs of toxicity (such as change in size or appearance of cellular components or a disruption in their configuration) in response to the test and control materials.
B3.2. Biological Reactivity – *In Vivo* Evaluates the response in animals to exposure of polymeric materials.	USP <88> Class VI	USP Biological Reactivity Test – *in vivo* for Class VI Plastics, is a series of three tests: systemic toxicity, intracutaneous reactivity and implantation. The first two are designed to determine the systemic and local, respectively, biological responses of animals to plastics and other polymers by the single dose injection of specific post gamma irradiation extracts prepared from a sample. The implantation test is designed to evaluate the reaction of living tissue to the plastic and other polymers by the implantation of the sample itself into animal tissue.

B4. Physicochemical Tests

The purpose of these tests was to evaluate the physicochemical suitability of PD2 film. The purpose of the USP <661> test, of the European Pharmacopoeia Guidelines was to check that the PD2 film meets their requirements.

Test Type and General Description	Test Reference	Summary Description of Test Reference
B4.1. Tests on Plastic Materials and Components Used to Package Medical Articles Evaluates the physical and chemical properties of plastics and their extracts.	USP <661>	Material dependent: measures the properties of impurities extracted post gamma irradiation from plastics when leached with extraction medium over a specified period and temperature. Includes the following: heavy metals, buffer capacity and non-volatile residue.

B5. Functional Testing on Powder Handling Bag

The following tests were carried out on the powder handling bags to provide information on its functional performances.

Test Type and General Description	Test Reference	Summary Description of Test Reference
B5.1. Functional Weight Test Provides information how long the handle and bag can hold a certain mass of powder without a lot of bending of the handle and without damage to the bag.	N/A	A filled bag hangs on a round hook for 7 days. Peel of all seals will be measured.
B5.2. Powder Transfer Efficiency Provides information how much powder is remaining in a bag when the content of one bag is transferred.	N/A	A first bag is filled with powder (sucrose, salt, lactose, diatomaceous earth) and this powder is then transferred to a second bag. The first bag is weighed before filling and after being emptied.
B5.3. Functional Drop Test Gives information if a filled bag is intact after being dropped.	ASTM 5276-2009	A filled bag is dropped and then checked if it is intact. A hanging drop test and a flat drop test are performed.
B5.4. Burst Test This test will determine the maximum pressure that can be used in powder handling bags.	WI-01837	Bags are inflated until they burst. 5-100 L bags; 5 samples/volume; before and after gamma; 3 different film lots.
B5.5. Leakage Test Provides information on the peel behavior of the seals during leakage testing.	WI-01837	3 film lots, different powder handling bag sizes; 5 L up to 100 L; 30 non gamma sample/volume; Production leakage test settings will be used. Peel of all seals will be measured after test. Specification is equal to or smaller than 2 mm, no failure allowed.
B5.6. Vibration Test This test will establish that the bag is not losing the content during transport (1 h truck, 2 h air) and that there is no visual seal damage on the powder handling bag.	ASTM D4169-09	Vibration tests will be performed on flour and salt filled 15 L and 30 L non gamma and gamma irradiated powder handling bags.

B6. Overview Testing Results

B6.1. Mechanical Results

The following mechanical properties were investigated: flex crack resistance (Gelbo), thickness, tensile strength and elongation, film modulus, puncture resistance, dart impact and tear resistance. The tests were carried out before and after gamma irradiation. The gamma irradiation dose was minimum 50 kGy.

B6.1.1. Gelbo Test

		Before Gamma					
		MD[1] PD2 Lot Number			TD[2] PD2 Lot Number		
		4085137	4085236	4085239	4085137	4085236	4085239
Results After 900 Cycles / 45 cpm							
Average #pinholes	300 cm² (ASTM surface)	3	3	5	4	4	5

1 MD = machine direction, which is the direction that the films moves through the machine form start to finish.

2 TD = transverse direction, which is the direction perpendicular to the machine direction.

		After Gamma					
		MD PD2 Lot Number			TD PD2 Lot Number		
		4085137	4085236	4085239	4085137	4085236	4085239
Results After 900 Cycles / 45 cpm							
Average #pinholes	300 cm² (ASTM surface)	3	6	4	3	5	4

These results are the average of 4 measurements.

B6.1.2. Thickness

	Before Gamma PD2 Lot Number		
	4085137	4085236	4085239
Thickness (µm)	204	208	202

These test results are the average of minimum 36 measurements.
Release specification: 200 ± 20 µm

B6.1.3. *Strength and Elongation*

	Before Gamma PD2 Lot Number			After Gamma PD2 Lot Number		
	4085137	**4085236**	**4085239**	**4085137**	**4085236**	**4085239**
Tensile and Elongation						
Max strength (MPa) – MD	33	31	32	29	29	28
Max strength (MPa) – TD	24	21	25	24	21	25
Elongation at break (%) - MD	1049	1061	1059	962	1028	932
Elongation at break (%) - TD	887	815	888	811	752	850
Young Mod (MPa) - MD	436	524	445	435	389	367
Young Mod (MPa) - TD	416	452	456	481	349	462

These results are the average of 5 measurements.

B6.1.4. *Puncture Resistance*

	Before Gamma PD2 Lot Number			After Gamma PD2 Lot Number		
	4085137	**4085236**	**4085239**	**4085137**	**4085236**	**4085239**
Puncture Resistance						
Max load (N)	78	90	86	79	76	83
Deflection at max load (mm)	33	35	35	32	31	32

These results are the average of 10 measurements.

B6.1.5. *Dart Impact*

	Before Gamma PD2 Lot Number			After Gamma PD2 Lot Number		
	4085137	**4085236**	**4085239**	**4085137**	**4085236**	**4085239**
Dart Impact (g)	729	685	703	822	720	754

B6.1.6. *Tear Resistance*

	Before Gamma PD2 Lot Number			After Gamma PD2 Lot Number		
	4085137	**4085236**	**4085239**	**4085137**	**4085236**	**4085239**
Tear Resistance						
Avg force (N) - MD	19	19	21	19	19	20
Avg force (N) - TD	29	31	30	27	28	27
Initial max load (N) - MD	20	20	22	20	20	21
Initial max load (N) - TD	30	33	32	28	30	28

These results are the average of 5 measurements.

B6.2. Physical Testing

B6.2.1. Surface Resistivity

	Before Gamma PD2 Lot Number			After Gamma PD2 Lot Number		
	4085137	4085236	4085239	4085137	4085236	4085239
Surface Resistivity (Ohm/square)						
Inside	10^{10}	10^{9}	10^{11}	10^{10}	10^{10}	10^{10}
Outside	10^{10}	10^{10}	10^{11}	10^{12}	10^{12}	10^{10}

These results are the highest results of 2 measurements.

Release Specification: Maximum 10^{12} Ohm/square

B6.3. Chemical and Biological Testing

B6.3.1. Biological Reactivity – In Vitro – ISO 10993-5 and USP <87> Elution Test

Description	Standard	PD2 Lot Number 4085137 (min 50 kGy gamma irradiated)
Biological reactivity	USP <87>	PASS
in vitro	ISO 10993-5	PASS

B6.3.2. Biological Reactivity – In Vivo – USP <88> Class VI Plastics Test

Description	Standard	PD2 Lot Number 4085137 (min 50 kGy gamma irradiated)
Biological reactivity *in vivo*	USP <88>	PASS, USP Class VI

B6.4. Physicochemical Test Results

B6.4.1. Tests on Plastic Materials and Components Used to Package Medical Articles USP <661>

Description	Standard	PD2 Lot Number 4085137 (min 50 kGy gamma irradiated)
Test on plastic materials and components used to package medical articles	USP <661>	PASS

B6.5. Functional Tests on Powder Handling Bag

B6.5.1. Functional Weight Test

Test method: Different non gamma and gamma (min 50 kGy) bags are filled with different weights. The test has been done with 5 samples per bag for non-gamma irradiated bags and 3 samples per bag for gamma irradiated bags. A filled bag hangs on a round hook for 7 days by its handle.

Weight Test			Non-Gamma	Gamma (min 50 kGy)
Volume	Connector	Weight	# of Samples	# of Samples
5 L	2 in.	5 kg	5	3
15 L	4 in.	15 kg	5	3
30 L	4 in.	30 kg	5	3
40 L	6 in.	40 kg	5	3
50 L	6 in.	50 kg	5	3
100 L	6 in.	100 kg	5	3

Result: The non-irradiated bags, as well as the irradiated bags can hold max 25 kg per handle. During the holding time there has been no bending of the handle, no peel or no visual seal elongation.

B6.5.2 Powder Transfer Efficiency

Test method: The empty bags with connector and the gasket, clamp and sanitary clamp are weighed. The bags are filled with powder: sucrose, salt, lactose and diatomaceous earth (Celite) (3 kg in 15 L bags and 6 kg in 30 L bags). The bag is first closed with a pinch and then with a gasket, cap and sanitary clamp. The bag is shaken so that the powder reaches all sides of the bag. The gasket, clamp and sanitary clamp are removed. The pinch is removed and the bag is emptied in another bag. The empty bag with connector and the closing system is weighed. The amount of powder that remained in the first bag and on the closing system is calculated. The test was performed on the 15 L and the 30 L bag.

Result: The % powder transfer for all types of powder is very high and ≥ 99.9%. Residue is mostly located on 60° seal next to the connector.

The % transfer data on the gamma irradiated bag are in line with the data measured on the non-gamma bags. The % transfer of all powders is again very high and above 99.9%.

The tests were performed with bags with an extended neck. This confirms that almost no powder remains in the extended neck.

B6.5.3 *Functional Drop Test*

Test method: A bag filled with NaCl is dropped from a hanging and from a vertical lying position and then checked if it is intact as described in ASTM 5276-2009 and 49 CFR (Code of Federal regulations) Chapter 1 part 178.

Result:

Before gamma irradiation

The drop test was carried out on 4 different volumes of bags (5 L, 15 L, 30 L and 50 L, respectively filled with 5 kg, 15 kg, 30 kg and 50 kg salt). Two types of tests were done: the flat drop test and the hanging drop test.

5 L bag	Bag 1	Bag 2	Bag 3	Bag 4	Bag 5
1.2 m flat drop	PASS	PASS	PASS	PASS	PASS
1.5 m flat drop	PASS	PASS	PASS	PASS	PASS
1.2 m hanging drop	PASS	PASS	PASS	PASS	PASS

15 L bag	Bag 2	Bag 2	Bag 2	Bag 3	Bag 4	Bag 5
1.2 m flat drop	PASS	PASS	PASS	PASS	PASS	PASS
1.5 m flat drop	PASS	PASS	PASS	PASS	PASS	PASS
1.1 m hanging drop	PASS	PASS	PASS	PASS	PASS	PASS

30 L bag	Bag 1	Bag 2	Bag 3	Bag 4	Bag 5
1.2 m flat drop	PASS	PASS	PASS	PASS	PASS
1.5 m flat drop	PASS	PASS	PASS	PASS	PASS
0.8 m hanging drop	PASS	Film break near the connector, pinch clamp keeps content	PASS	PASS	PASS

50 L bag	Bag 1	Bag 2	Bag 3
1.2 m flat drop	PASS	PASS	PASS
1.5 m flat drop	PASS	PASS	PASS
0.8 m hanging drop	Pinhole near the connector, pinch clamp keeps content	Film damage probably caused by pinch clamp	PASS

All bags passed the 1.2 m flat drop test up to 50 L bag (filled with 50 kg salt). This test was repeated on at least 3 different bags. All of these bags were tested again at 1.5 m. All bags passed again the test at 1.5 m flat drop.

The most critical test was the hanging drop test. Only the 5 L and 15 L bag passed this test. For the 30 L bags, this test failed for 20% of bags evaluated. The failure was due to a film break near the connector. For the 50 L bags, this test failed for 66% of bags evaluated. These failures were due to a pinhole near the connector and film damage caused by the pinch clamp.

Based on these results, it will be recommended to customers to transport the filled, higher weight bags in a flat position.

After gamma irradiation

The drop tests on gamma irradiated bags (min 50 kGy) were only performed on the highest weight bags: 30 L and 50 L, respectively filled with 30 kg and 50 kg salt.

30 L bag	Bag 1	Bag 2	Bag 3	Bag 4	Bag 5
1.2 m flat drop	PASS	PASS	PASS	PASS	PASS
1.5 m flat drop	PASS	PASS	PASS	PASS	PASS
0.8 m hanging drop	PASS	Small pinhole in film probably by pinch clamp	Film break connector, pinch keeps content	PASS	PASS

50 L bag	Bag 1	Bag 2	Bag 3
1.2 m flat drop	PASS	PASS	PASS
1.5 m flat drop	PASS	PASS	PASS
0.8 m hanging drop	Small pinhole on connector, pinch keeps content	PASS	Small pinhole in film, probably caused by pinch clamp

The flat drop test was repeated for each volume on at least 3 bags. If the test at 1.2 m was positive, the same bag was tested at 1.5 m. All bags up to 50 L (filled with 50 kg) passed the flat drop test at 1.2 m and 1.5 m. Data is in line with the drop test results before gamma.

The hanging drop test on the 30 L bag passed the test for 60% of bags evaluated. The hanging drop test on the 50 L bag passed the test for 33% of bags evaluated. Based on these results, it will be recommended to customers to transport the filled, higher weight bags in a flat position.

B6.5.4 *Burst Test*

Test method: A variety of different powder handling bag volumes (5-100 L) have been inflated until they burst. 3 different film lots are used. The 30 L powder handling bag is tested with different connectors.

The purpose of this test is to establish the maximum pressure the bags can safely handle. The location of break and maximum pressure are reported.

The test results are based on 5 samples per bag before and after gamma irradiation.

Result:

		Average Max Pressure (mbar)	
Volume	Connector	Non-gamma	Gamma (min 50 kGy)
5 L	2 in.	371	406
15 L	4 in.	256	289
30 L	2 in.	206	No data available
30 L	4 in.	186	191
30 L	6 in.	181	No data available
40 L	6 in.	175	183
50 L	6 in.	153	158
100 L	6 in.	131	136

The film breaks film near the 60° weld or middle of the bag.

The safety specification for maximum pressure of all PD2 powder handling bag volumes is 100 mbar.

B6.5.5 *Leakage Test*

Test method: Different bags have been tested for leakage. This includes 3 film lots, different powder handling bag sizes (5 L up to 100 L) with 30 samples per volume. Production leak test settings will be used for the test.

The peel of all seals will be measured after the test and should be equal to or smaller than 2 mm.

Result: No peel occurred on any of the bags during the test.

B6.5.6 *Vibration Test*

Test method: Bags are tested on a big vibration table which will simulate 60 min inside of a truck and 120 min in an airplane (ASTM D4169-09). The bags have passed the test when they are not losing the content after the vibration test and if there is no visual seal damage.

15 L and 30 L powder handling bags with 4 in. extended neck, gamma irradiated and non-gamma irradiated, were tested. 16 bags have been tested in total. The bags were packed with (light) pressure. They were filled with 10 kg and 20 kg flour and 15 kg and 30 kg NaCL.

Result: All samples passed the vibration test with no visual seal peeling or losing content.

B6.5.7. *Conclusion*

Powder transfer bags may be lifted and supported by their integral handle alone, provided they contain no more than 25 kg of material per handle. If loads above 25 kg per handle are anticipated, Pall recommends using an external support device such as a tray, tank, support rod or overbag to avoid the risk of the handle becoming distorted. Loads above 50 kg are not recommended.

C. Aging Test Study – Accelerated Shelf Life Study

Shelf life studies will be performed on film properties, film on film weld properties and film on connector weld properties.

Shelf life studies are performed as accelerated aging tests.

Shelf Life Study	Part 1	Part 2
Film properties	Complete	Ongoing
Weld properties	Complete	Ongoing

C1. Accelerated Aging Tests on Film Properties

C1.1. Aim of the Study

An accelerated study has been performed in order to demonstrate that film has a minimum shelf life of 4 years on non-gamma irradiated and worst case gamma irradiated material (min 50 kGy).

A shelf life of two years will apply to intermediates, resulting in 2 years shelf life for finished goods starting from their manufacturing date, both for gamma and non-gamma irradiated goods.

Part 1

The purpose of this study is to document a shelf life up to 4 years on PD2 film for tensile strength (incl. elongation at break) and surface resistivity. Three lots of PD2 will get tested. The tests will be performed on non-gamma irradiated and worst case gamma irradiated material (min 50 kGy).

Part 2

To simulate normal use conditions, the PD2 film will be stored until 2 years accelerated aging. Then the film will get worst case gamma irradiated (min 50 kGy). Further accelerated aging tests will be performed up to 2 year after gamma irradiation.
One lot of PD2 will be tested.

C1.2. Storage Conditions

Part 1

Non-gamma and gamma irradiated (min 50 kGy worst case) non-aged PD2 material will get tested and afterwards stored in the incubator at 55 °C for accelerated aging.

Part 2

Non-gamma treated PD2 material will get aged accelerated in an incubator at 55 °C. After an equivalent of 2 years, the film will be sent for gamma irradiation (min 50 kGy worst case condition). “Time 0 after gamma” tests will be performed. Afterwards the material will be stored again in the incubator at 55 °C for accelerated aging up to 2 years and tests will be repeated.

C1.3. Testing Frequency

The accelerated aging time was calculated on the basis of the Arrhenius reaction rate function. This function states that 10 °C increase or decrease in temperature of a homogeneous process results in approximately a 2 times or ½ times change in the rate of a chemical reaction.

Accelerated aging time = Real life time/AAF

AAF= Accelerated aging factor= 11.3 following ASTM F1980-02 (if stored at 55 °C and ambient temperature = 20 °C).

This means that 1 year at 20 °C is equivalent to 32.3 days at 55 °C.

C1.4. Analytical Method and Specifications:

Test	Standard/Method	Specifications
Tensile strength	ASTM D882	For information only
Elongation at break	ASTM D882	For information only
Surface resistivity	ASTM D257	NMT 10^{12} Ohm/sq

C1.5. Results

Part 1

Non-gamma irradiated PD2 film

Lot Number 4085137 (lot 1)

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Max.tensile strength (MPa)	MD: To generate data	Average	33	33	31	28	31	28	33
	TD: To generate data	Average	24	26	24	23	23	25	27
Elongation at break (%)	MD: To generate data	Average	1049	1056	1052	971	1044	1015	1035
	TD: To generate data	Average	887	905	874	822	816	977	918
Surface resistivity inside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{10}	1^{11}	1^{10}	1^{10}	1^{9}	1^{9}	1^{9}
Surface resistivity outside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{10}	1^{11}	1^{10}	1^{10}	1^{10}	1^{9}	1^{9}

Lot Number 4085236 (lot 2)

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Max.tensile strength (MPa)	MD: To generate data	Average	31	29	28	31	33	31	31
	TD: To generate data	Average	21	23	22	22	22	25	24
Elongation at break (%)	MD: To generate data	Average	1061	1046	993	1056	1044	977	1055
	TD: To generate data	Average	815	960	822	840	787	862	873
Surface resistivity inside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{9}	1^{11}	1^{10}	1^{11}	1^{11}	1^{9}	1^{9}
Surface resistivity outside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{10}	1^{11}	1^{10}	1^{11}	1^{11}	1^{9}	1^{9}

Lot Number 4085239 (lot 3)

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Max.tensile strength (MPa)	MD: To generate data	Average	32	28	32	32	32	32	31
	TD: To generate data	Average	25	26	25	24	24	25	26
Elongation at break (%)	MD: To generate data	Average	1059	1040	1048	1057	1051	998	1051
	TD: To generate data	Average	888	884	850	908	872	854	907
Surface resistivity inside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{11}	1^{10}	1^{10}	1^{10}	1^{10}	1^{9}	1^{9}
Surface resistivity outside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{11}	1^{10}	1^{10}	1^{10}	1^{10}	1^{8}	1^{9}

Gamma irradiated PD2 film

Lot Number 4085137 (lot 1)

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Max.tensile strength (MPa)	MD: To generate data	Average	26	28	28	26	25	27	27
	TD: To generate data	Average	21	22	24	19	19	22	21
Elongation at break (%)	MD: To generate data	Average	964	1041	999	995	967	949	988
	TD: To generate data	Average	766	819	818	788	750	816	770
Surface resistivity inside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{10}	1^{10}	1^{10}	1^{10}	1^{9}	1^{09}	1^{9}
Surface resistivity outside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{12}	1^{10}	1^{10}	1^{10}	1^{9}	1^{10}	1^{9}

Lot Number 4085236 (lot 2)

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Max.tensile strength (MPa)	MD: To generate data	Average	29	27	29	30	26	31	31
	TD: To generate data	Average	21	21	22	21	25	27	27
Elongation at break (%)	MD: To generate data	Average	1028	992	1023	1046	1066	1008	1027
	TD: To generate data	Average	752	802	801	845	1038	869	904
Surface resistivity inside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{11}	1^{10}	1^{11}	1^{11}	1^{9}	1^{9}	1^{9}
Surface resistivity outside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{11}	1^{10}	1^{10}	1^{11}	1^{10}	1^{9}	1^{9}

Lot Number 4085239 (lot 3)

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Max.tensile strength (MPa)	MD: To generate data	Average	26	28	28	26	25	27	27
	TD: To generate data	Average	21	22	21	19	19	22	21
Elongation at break (%)	MD: To generate data	Average	964	1041	999	995	967	949	988
	TD: To generate data	Average	766	819	818	788	750	816	770
Surface resistivity inside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{10}	1^{10}	1^{10}	1^{10}	1^{9}	1^{10}	1^{10}
Surface resistivity outside sleeve	$\leq 10^{12}$ Ohms/square	Highest of 2 measurements	1^{10}	1^{10}	1^{11}	1^{10}	1^{10}	1^{10}	1^{10}

Part 2

Gamma irradiated PD2 film

Lot Number 4085236

Test	Specification		T0 (+2Y)	1Y (+2Y)	2Y (+2Y)	3Y (+2Y)	4Y (+2Y)
Max.tensile strength (MPa)	MD: To generate data	Average	29.7	27.0	25.9	26.8	27.1
	CD[1]: To generate data	Average	21.6	21.1	21.0	20.7	22.2
Chord modulus (MPa)	MD: To generate data	Average	372.7	363.3	363.1	358.3	369.8
	CD: To generate data	Average	421.8	426.0	422.8	423.0	446.5
Elongation at break (%)	MD: To generate data	Average	966.8	1072.1	1015.2	1064.6	1062.9
	CD: To generate data	Average	751.6	886.7	893.7	851.7	1009.1
Surface resistivity antistatic inside sleeve	$\leq 10^{12}$	Highest of 2 measurements	1^{11}	1^{11}	1^{10}	1^{11}	1^{11}
Surface resistivity antistatic outside sleeve	$\leq 10^{12}$	Highest of 2 measurements	1^{10}	1^{10}	1^{10}	1^{10}	1^{11}

1 CD: Cross-direction, which is the direction perpendicular to the machine direction

C1.6. Conclusion

Part 1 results from all three lots for PD2 film as well as part 2 results for lot 4085236 are within specification and stable over the different time points for mechanical and antistatic properties.

With these results we can claim 2 years shelf life on intermediates and 4 years shelf life on finished goods.

C2. Accelerated Aging Tests on Film Weld Properties

C2.1. Aim of the Study

The purpose of this study is to prove a minimum shelf life of 4 years on PD2 film for welding behavior (incl. peeling effect).

A shelf life of two years will apply to intermediates (film and subassemblies), resulting in 2 years shelf life for finished goods (commercial products) starting from their manufacturing date, both for gamma and non-gamma irradiated goods.

Part 1

Welding of non-aged material, afterwards accelerated aging on seals (both non-gamma and gamma irradiated (min 50 kGy) seals). This study will include 3 different lots of PD2 film. Part 1 will only include the 60° film/film weld.

Part 2
Welding of non-aged material followed by accelerated aging on seals (both non-gamma and gamma irradiated (min 50 kGy) seals). This seal study will be performed to simulate aging of the PD2 film before welding of the PD2 film. For this study 1 lot of PD2 material will be used. Part 2 will include 60° film/film weld, double bottom film/film weld and film/connector welds.

C2.2. Storage Conditions:

Part 1
Non-aged PD2 material will get welded (half of the material will be gamma irradiated at minimum 50 kGy after welding) and afterwards stored in the incubator at 55 °C for accelerated seal aging.

Part 2
PD2 material is aged accelerated in an incubator at 55 °C. After an equivalent of 2 years aging of the film, seals (film-film and film-connector) will be made from the aged film. One part of those seals will be sent for gamma irradiation at 50 kGy (worst case condition) and afterwards stored again in the incubator at 55 °C. Another part of the seals (film-film and film-connector) will be stored directly (without gamma irradiation) in the incubator at 55 °C.

C2.3. Testing Frequency

The accelerated aging time was calculated on the basis of the Arrhenius reaction rate function. This function states that 10 °C increase or decrease in temperature of a homogeneous process results in approximately a 2 times or ½ times change in the rate of a chemical reaction.

Accelerated aging time = Real life time/AAF

AAF= Accelerated aging factor= 11.3 following ASTM F1980-02 (if stored at 55 °C and ambient temperature = 20 °C).

This means that 1 year at 20 °C is equivalent to 32.3 days at 55 °C.

C2.4. Analytical Method and Specifications:

Evaluation of the results

Welding

- Film-film 60° weld: ≥25 N/15 mm
- Film-film double bottom weld: ≥25 N/15 mm (Part 2 only)
- All powder connectors: ≥20 N/15 mm (Part 2 only)
- Passed leak test (Part 2 only)

C2.5. Results

Part 1

Non-gamma irradiated PD2 weld

Lot Number 4085137

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	46	47	47	46	47	47	47

Lot Number 4085236

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	46	47	47	49	46	47	46

Lot Number 4085239

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	43	46	48	48	45	48	46

Gamma irradiated PD2 weld

Lot Number 4085137

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	48	48	47	49	50	49	50

Part 2

Lot Number 4085236

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	49	48	48	47	48	48	47

Lot Number 4085239

Test	Specification		T0	3M	6M	1Y	2Y	3Y	4Y
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	47	47	45	46	49	48	47

Part 2

Non-gamma irradiated PD2 weld

Lot Number 4085236

Test	Specification		T0 (+2Y)	1Y (+2Y)	2Y (+2Y)	3Y (+2Y)	4Y (+2Y)
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	48.9	47.9	47.4	47.8	48.3
Film-film double bottom seal	≥25 N/15 mm	Avg Fmax (N)	49.6	50.2	49.8	50.6	51.2
2 inch fitment 700182C	≥20 N/15 mm	Avg Fmax (N)	45.1	44.1	46.4	43.4	44.9
4 inch fitment 701451C	≥20 N/15 mm	Avg Fmax (N)	74.7	63.8	55.5	64.8	71.6
Leak test	To pass		PASS	PASS	PASS	PASS	PASS

Gamma irradiated PD2 weld

Lot Number 4085236

Test	Specification		T0 (+2Y)	1Y (+2Y)	2Y (+2Y)	3Y (+2Y)	4Y (+2Y)
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	49.4	48.4	49.5	48.6	49.3
Film-film double bottom seal	≥25 N/15 mm	Avg Fmax (N)	51.3	52.3	52.4	52.9	53.3
2 inch fitment 700182C	≥20 N/15 mm	Avg Fmax (N)	45.9	45.7	45.9	48.1	55.2
4 inch fitment 701451C	≥20 N/15 mm	Avg Fmax (N)	66.7	61.8	57.0	66.2	64.6
Leak test	To pass		PASS	PASS	PASS	PASS	PASS

C2.6. Conclusion

Part 1 results from all three lots on PD2 film for welding behavior on film-film 60° welds are within specification and stable over the different time points.

Part 2 results show that the film-film and film-connector welds do not deteriorate over time after use with film aged up to two years.

With these results we can claim 2 years shelf life on intermediates and 4 years shelf life on finished goods.

D. Aging Test Study – Refrigerator Conditions

D1. Aim of the Study

This study is performed in order to prove that the quality of the product is not affected by storage at low temperatures for several weeks.

D2. Storage Conditions

Material is stored at low temperature (between 4 °C and 6 °C). The tests will be performed on non-gamma and gamma irradiated (min 50 kGy) material. Only the storage is carried out at this low temperature.

D3. Analytical Method and Specifications:

Test	Standard/Method	Specifications
Tensile strength	ASTM D882-02	For information only
Sealing strength film-film	ASTM F88-06	NLT 25 N/15mm
Sealing strength film-connector	ASTM F88-06	NLT 20 N/15 mm
Elongation at break	ASTM D882-02	For information only
Surface resistivity	ASTM D257 -78	NMT 10^{12} Ohm/sq

D4. Results

Non-gamma irradiated PD2 bag

Test	Specification		T0	1W	2W	6W	Conclusion
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	49	50	46	50	Conform
4 inch powder connector weld	≥20 N/15 mm	Avg Fmax (N)	38	45	44	43	Conform
Surface resistivity antistatic inside sleeve	≤10^{12} Ohms/square	Highest value of 3 samples	1^{10}	1^{9}	1^{10}	1^{10}	Conform
Surface resistivity antistatic outside sleeve	≤10^{12} Ohms/square	Highest value of 3 samples	1^{10}	1^{9}	1^{11}	1^{10}	Conform
Max. tensile strength (MPa)	MD: for information	Average	30	32	–	33	–
	CD: for information	Average	22	25	–	22	–
Elongation at break (%)	MD: for information	Average	1035	1052	–	428	–
	TD: for information	Average	786	914	–	545	–

Gamma irradiated PD2 bag

Test	Specification		T0	1W	2W	6W	Conclusion
Film-film 60° weld	≥25 N/15 mm	Avg Fmax (N)	49	50	48	51	Conform
4 inch powder connector weld	≥20 N/15 mm	Avg Fmax (N)	47	44	45	44	Conform
Surface resistivity antistatic inside sleeve	≤10^{12} Ohms/square	Highest value of 3 samples	1^{9}	1^{10}	1^{9}	1^{10}	Conform
Surface resistivity antistatic outside sleeve	≤10^{12} Ohms/square	Highest value of 3 samples	1^{12}	1^{11}	1^{11}	1^{11}	Conform
Max. tensile strength (MPa)	MD: for information	Average	28	27	30	26	–
	CD: for information	Average	20	19	21	20	–
Elongation at break (%)	MD: for information	Average	1031	951	1000	459	–
	TD: for information	Average	750	745	851	419	–

D5. Conclusion

After 6 week storage at 4 °C – 6 °C, all properties conform to the specifications. Overall, it can be seen that there is no trend of degradation with time.

E. Statement on TSE/BSE and Animal Derived Components

Some of the resins contain additive(s)/substance(s) synthesized from animal extracts, i..e. hydrolysis etc. of animal fats (tallow) into fatty acids. Therefore the PD2 film is not animal derived component free. However, the manufacturing process of these fatty acids includes a multi-step chemical treatment involving high temperatures, high pressures and long residence times. The processing conditions greatly exceed the requirements as specified in the “Note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products” and TSE transmissions (EMA/410/01 rev 3 July 2011). Therefore the PD2 film is safe to use in respect with BSE.

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