

## Technical Report of Flexsafe® 2D Bags in Shell Qualification

For Liquid Handling & Shipping



### Technical Note

**Scope** – This technical report describes the qualification of our liquid shipping solutions for 5 L, 10 L and 20 L Flexsafe® bags in shell in order to provide reliable and robust liquid handling & transportation.

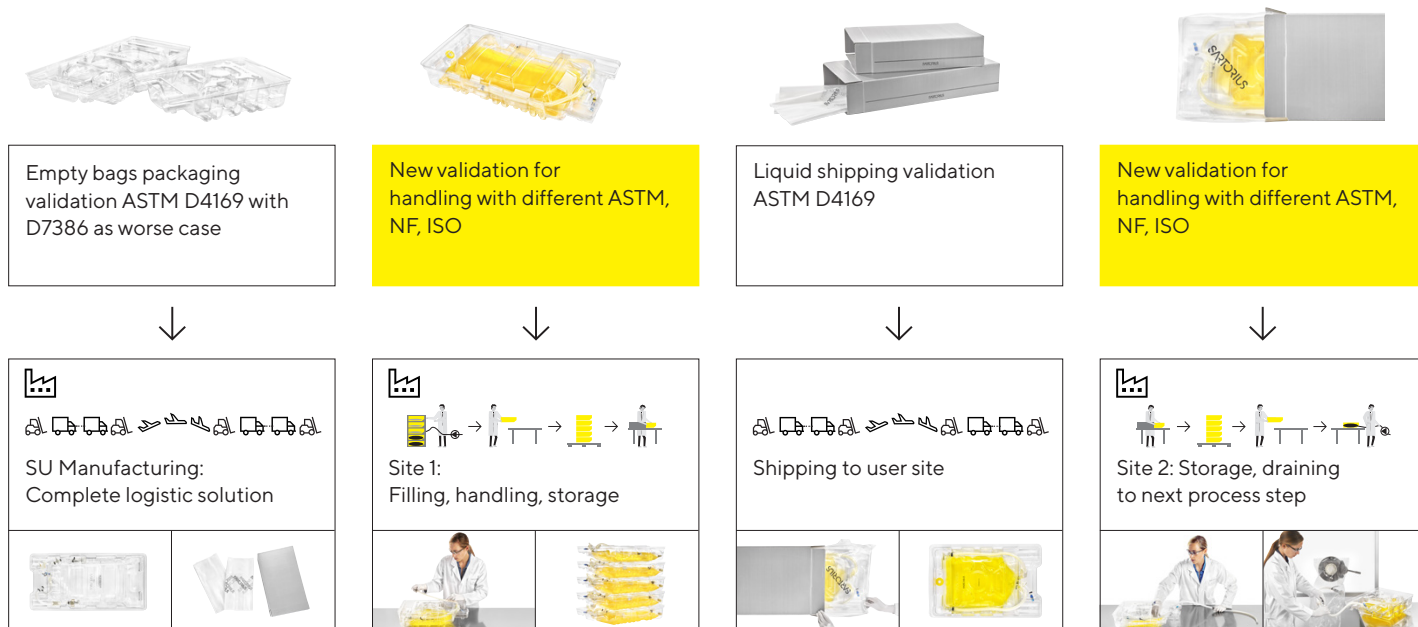
The Flexsafe® shipping systems have been extensively tested against the most stringent international standards (ASTM D4169 and D7386) and a mix of ISO, EN or NF norms for a range of temperature from 4°C (39.2°F) to 40°C (104°F).

### Executive Summary

Sartorius Stedim Biotech has qualified liquid handling & shipping for Flexsafe® 2D bags in shell and shippers in order to support end users for shipping biotech fluids, like media, buffer, intermediates, drug substances and drug products. The liquid handling & shipping qualification is designed to answer new challenges associated with the growing adoption of single-use technologies in more critical process steps of cGMP commercial production, and the increased need for transportation of valuable liquids all around the world.

Understanding the product life cycle and associated risks are prerequisites to establishing a suitable qualification testing approach. For truck or international transportation conditions and during manual handling, the shipping system must withstand various mechanical shocks and vibration levels to maintain container closure which have been evaluated during preliminary testing under real conditions and in laboratory.

Flexsafe® 2D Bags have been qualified via a 4-step qualification program providing an end-to-end logistic solution for liquid handling & transportation:



Flexsafe® 2D bags offer a robust and reliable end-to-end logistic solution for handling and shipping high critical fluids like bulk drug substances, and are extensively qualified for a range of volumes from 10% to 120% of their nominal volume for a range of temperature from 4°C (39.2°F) to 40°C (104°F).

## Qualification Approach

Regulatory agencies like FDA<sup>2</sup>, EMA<sup>3</sup> or EU<sup>4</sup> emphasize the need for end users to ensure that their drug processes produce consistent and reproducible results which meet the quality standard of the drug product. Validation is “Establishing documented evidence that provides a high degree of assurance that a specific process” including shipping “will consistently produce a product meeting its pre-determined specifications and quality attributes” (FDA<sup>2</sup>).

A properly designed system will provide a high degree of assurance that every process step including shipping has been properly evaluated before its implementation. In the biopharmaceutical industry, qualification and validation are intended to demonstrate that the manufacturing process provides the desired level of compliance of the product and specifically its activity, sterility and potency. Qualification of the shipping system and equipment is part of the process validation.

According to the PDA technical report N°665, “Shipping systems must be qualified for their intended use through proper design and testing in consultation with a packaging engineer. The transportation routes must be defined for international shipment. A risk assessment for vibration, handling, delays and seasonal variation should be established.

ASTM D4169 is a well-known standard practice for simulating the possible hazards under worst-case conditions during various transportation phases. But what about manual handling during all the filling, storage, manipulation and draining steps that are necessary during the life cycle of the single-use system?

In order to qualify the system with the more relevant testing parameters and provide secure liquid handling & shipping systems, several preliminary tests have been performed before the final qualification testing program.

Since manual handling is not obviously covered by established standards, a first step consisted in identifying the different handling sequences. Secondly, acceleration of the filled Flexsafe® 2D bags in shell during these handling sequences have been measured under normal conditions and more severe conditions. Finally, this data was analysed in collaboration with a packaging engineer to provide the sequence of tests to be performed in order to qualify the system with a relevant margin.

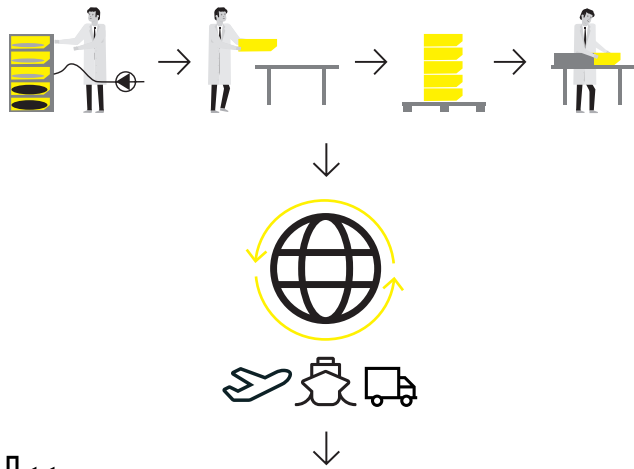
For shipping qualification, the ASTM D4169 testing standard contains well-known international methods to simulate the worst-case scenario of the hazards, shocks,

shakes and vibrations impacting a system during transportation. These standard practices have been used to qualify the packaging of empty bags in shell being shipped from Sartorius to the end user. They have also been used to qualify the transportation phases of filled Flexsafe® bags in shell packaged in their shippers and shipped from the filling site to the user site. This technical report provides the rationale, testing program and results for filled Flexsafe® 2D bags in shell considering all steps of their life cycle, including handling phases and shipping.

## Complete logistic solution for safe liquid handling & shipping



Site 1: Filling & Handling & Storage

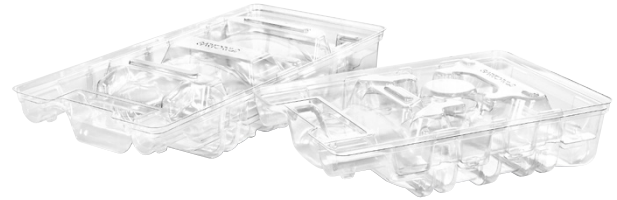


Site 2: Storage & Handling & Draining



## Material

The solution is composed of ready-to-use Flexsafe® 2D bags in a transparent protective shell to support all handling steps. After filling, the bag in shell is packaged into polyethylene overpouches and a plastic box which provides the appropriate shipping solution with optimized palletization.



Top & bottom 5 L shells



5 L & 10 L shippers with double polyethylene overpouches



Flexsafe® 2D 5 L bag in shell

### Dimensions of the shells









Volume	Length	Width	Height
5 L	562.5 mm	374.8 mm	143.5 mm
10 L	756 mm	375 mm	145.5 mm
20 L	766 mm	581 mm	218.5 mm

### Dimensions of the shippers

Volume	Length	Width	Height
5 L	600 mm	391 mm	160 mm
10 L	794 mm	391 mm	160 mm
20 L	797 mm	597 mm	227 mm

# Test Summary

This logistic solution has been extensively qualified according to the most stringent international standards in the industry for both manual handling and transportation cycle covering the entire life cycle:

	Step	Specimen	Norm	T=0	T=3y
 <p>SU Manufacturing: Complete logistic solution</p> 	1. Transportation to customer's site	2D bag in shell	ASTM D4169 D7386	h	NA
 <p>Site 1: Filling, handling, storage</p> 	2. Bag in shell Filling & Storage	2D bag in shell	Internal Specification	NA	h
	3. Bag in shell a) Handling & Packaging in shipper	2D bag in shell* & shipper	ISO, NF ASTM norms	NA	h
 <p>Shipping to user site</p> 	b) Transportation	2D bag in shell* & shipper	ASTM D4169 D7386	NA	h
 <p>Site 2: Storage, draining to next process step</p> 	c) Handling Storage & Draining	2D bag in shell*	ISO, NF ASTM norms	NA	h

\* Flexsafe® 2D bags in shell samples were the same samples that have been used and have been tested successively for the handling tests, the transportation and finally the second handling tests.

# 1. Transportation to customer's site

The test program was chosen in order to test the packaged bags in worst-case conditions, and is relevant for pallet shipments (ASTM D4169 - Standard Practice for Performance Testing of Shipping Containers and Systems), and for single parcel shipments (ASTM D7386 - Performance Testing of Packages for Single Parcel Delivery Systems). Since the single parcel test program is more rigorous than the pallet tests, the Flexsafe® 2D bags in shell and the shells alone have been tested according to ASTM D7386.

After the test sequences, the boxes, over-pouches, shells, and bags are visually inspected. A functional test is performed by checking the bag and primary overpouch integrity via the dye penetration method.

## Sequence of tests for single parcel shipment (ASTM D7386, assurance level II)

Boxes of Flexsafe® 2D Bags in shell and shells alone (5 boxes per volume) have been tested according the following test sequence:

Tropical pre-conditioning	ASTM D4332	40°C (104°F)   90%humidity during 72 hours
Free fall drop test	ASTM D5276	4 drop tests 358 mm, 2 drop tests 508 mm
Vibration under compressive load	ASTM D4728	one side 60 min, two sides 30 min
Low pressure	ASTM D6653	40°C & 4°C 595.73 hPa 1 hour
Free fall drop test	ASTM D5276	4 drop tests 358 mm, 2 drop tests 508 mm
Vibration without compressive load	ASTM D4728	two times 30 min opposite side
Free fall drop test	ASTM D5276	2 drop tests 358 mm, 3 drop tests 508 mm, 3 drop tests 813 mm
Stacking - Box compression	DIN 55440	V= ±10 mm/min

## Test configurations

The tested configurations incorporated a complex tubing assembly, thus representing worst-case conditions as described in the table below:

	Type of finished product	Packaging configuration	Irradiation dose	Quantity of tested products
Flexsafe® 2D bags in shell	Standard Flexsafe® 5 L (shell, MPC, LT   MPC)	Single parcel	25 - 45 kGy	5
	Standard Flexsafe® 10 L (Shell, MPC, LT   MPC)	Single parcel	25 - 45 kGy	5
	Standard Flexsafe® 20 L (Shell, MPC, LT   MPC)	Single parcel	25 - 45 kGy	5
Shells alone	Standard Shell 5 L for Handling	Single parcel	Non irradiated	5
	Standard Shell 10 L for Handling	Single parcel	Non irradiated	5
	Standard Shell 20 L for Handling	Single parcel	Non irradiated	5

## Test results

### For each configuration, results are listed below:

Packaging of Flexsafe® 2D bags in shell 5 L, 10 L & 20 L – Single parcel – ASTM D7386 assurance level II

Inspected part	Test	Acceptance criteria	Results
Box for Flexsafe® 2D bags in shell 5 L, 10 L & 20 L	Visual inspection	No holes, no damage on glued   taped areas, no collapsed boxes	Pass
Primary overpouches	Visual inspection	No channel, no hole, no tear	Pass
Shells	Visual inspection	No breakage, no cracks	Pass
Flexsafe® 2D bags and components 5 L, 10 L & 20 L	Visual inspection	No damage, no leak on bags or connections	Pass
	Functional test	No leak	Pass

Packaging of shells alone 5 L, 10 L & 20 L – Single parcel – ASTM D7386 assurance level II

Inspected part	Test	Acceptance criteria	Results
Box for Shells 5 L, 10 L & 20 L	Visual inspection	No holes, no damage on glued   taped areas, no collapsed boxes	Pass
Shells	Visual inspection	No breakage, no cracks	Pass
	Functional test	Snapping possible	Pass

### Conclusion

Flexsafe® 2D bags in shell and shell alone are securely packaged and their packaging is designed to withstand the most commonly used distribution cycles on pallets or via single parcel shipments.

## 2. Bag in shell filling and storage

The purpose of this test was to demonstrate the compatibility of the bags and shell, and the ability to secure the tubing throughout the life cycle when used at minimum, nominal or maximum filling volumes.

A variety of designs representing the different possible configurations for this product range have been tested:

- Tubing lengths from 500 mm to 2,000 mm
- Various connectors, e.g. Opta®, MPC, TriClamp, STCII, GammaSart® ...
- Configurations with the leak test line

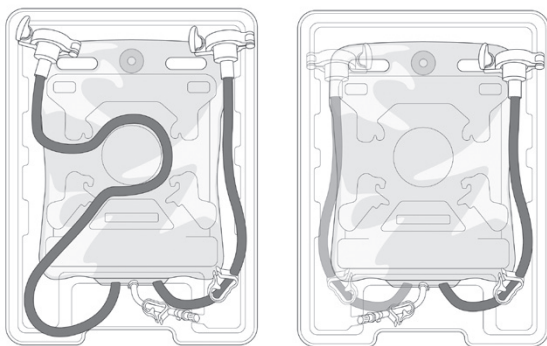
Samples were irradiated under worst-case conditions of 50 kGy and aging was accelerated up to an equivalent of 3 years of shelf life.

For each configuration, a variety of tests have been performed to simulate the use of the bags from initial handling and filling, up to draining and discarding.

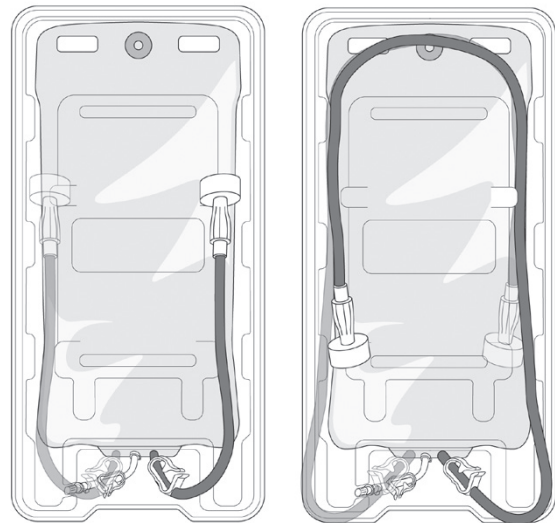
The results are summarized in the following table:

Test	Acceptance criteria	Results
Assembly   disassembly of the bags in shell system	No plastic deformation of the shell	Pass
	No damages   leak on the bag and tube line	Pass
Components and tubing positioning	No contact of the connector with the bag	Pass
	Draining and filling connector are accessible	Pass
Bags in shell filling by peristaltic pumping	No leakage of the bag nor plastic deformation of the shell	Pass
Shell transparency	Bag visible	Pass
Capability to read the label on tubing or bag	Label readable	Pass
Ensure the containment   leak proof of the liquid in case of bag leakage	The maximal liquid volume remain contained by the system	Pass
Disposal	System is dismountable	Pass
Stacking of bags in shell with up to 1.5 m tube lines	Shell design allows a tube line placement up to 1.5 m	Pass

The Flexsafe® 2D bag in shell system demonstrated the ability to secure the bags and tubing during handling under a combination of worst-case configurations. The shells accommodate multiple connectors and tubing lengths from 0.5 m to 2 m as described in the following drawings.



Examples: Flexsafe® 2D bags in shell for 5 L with 2 different configurations (500 mm or 1,000 mm tubing length)



Examples: Flexsafe® 2D bags in shell for 10 L with 2 different configurations (500 mm or 1,500 mm tubing length)

### 3. Handling, stacking & transportation qualification

The purpose of this test is to demonstrate the mechanical resistance of the shell and the integrity of the Flexsafe® 2D bags during handling, stacking and shipping operations.

The new testing protocol designed for this mechanical resistance testing is a combination of tests developed by packaging engineers and R&D experts. The aim was to take into account the complete life cycle of the product:

- Handling in cleanroom when filling the Flexsafe® 2D bags in shell
- Transportation for Flexsafe® 2D bags in shell, packaged into the shipper
- Handling in cleanroom for draining the Flexsafe® 2D bags in shell

Flexsafe® 2D bags in shell for handling and in shippers for transportation have been qualified for secure and robust liquid handling & shipping applications under the most stringent standards like ISO, NF EN, several ASTM norms including ASTM D4169 via the following qualification program.





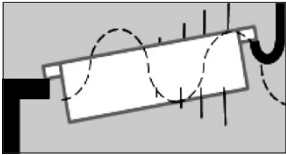

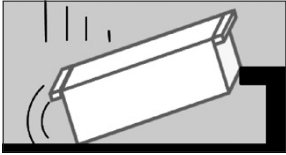

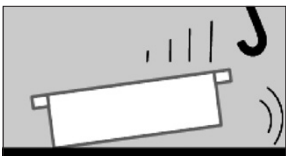

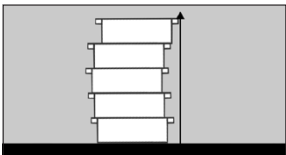

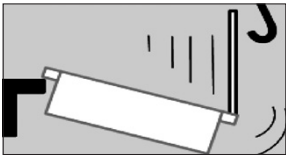

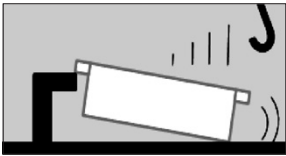

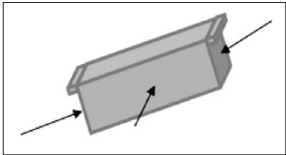

# Test Definition

The tests for handling have been defined by understanding how the product will be used in real conditions. Based on this life cycle analysis, each test has been assigned a risk classification of worst-case or accidental which are defined as follows:

- Worst-case tests simulate the most severe scenarios that could occur during normal usage of the product (i.e. normal handling, installation on a table, etc.) to ensure reliable product performance
- Accidental tests simulate use cases which are not normally expected to occur. These tests simulate accidents or mis-usage of the product such as bumping the corner of a table, or an unexpected fall. Performing this testing provides additional margin.

There is no existing standard dedicated to handling in the biotech industry. Nevertheless, there are standards in other industries with comparable applications that have been used to develop the test methods.

The test description, rationale, risk classification, and existing similar standard are summarized in the following table.

Description	Risk	Rationale	Existing Similar Standard
Vibration 	Worst-case	<ul style="list-style-type: none"> <li>▪ Operator walking and carrying the bag in shell (asynchronous walk)</li> <li>▪ Fatigue of the gripping system</li> </ul>	 NFH 34-010
Drop on corner 	Worst-case	<ul style="list-style-type: none"> <li>▪ Bag in shell being dropped on a bench. Because the product is heavy, the operator tends to first place the corner of the system on the bench</li> </ul>	 ISO 7965
Rotational flat drop 	Worst-case	<ul style="list-style-type: none"> <li>▪ Bag in shell being dropped on a bench</li> </ul>	 ISO 7965
Stacking 	Worst-case	<ul style="list-style-type: none"> <li>▪ Vertical deflection measurement to qualify stack-ability</li> </ul>	 NA
Hangman 	Accidental	<ul style="list-style-type: none"> <li>▪ Rough gripping of the bag in shell by its handle</li> <li>▪ Bag in shell in semi-free fall and held firmly by the operator's hand</li> </ul>	 NFH 34-010
Rotational edge drop 	Accidental	<ul style="list-style-type: none"> <li>▪ Accidental fall</li> </ul>	 ISO 7965
Impact test 	Accidental	<ul style="list-style-type: none"> <li>▪ Accidental shock of the bag in shell on a corner of bench</li> </ul>	 NFH 060

Tests performed on 10%, 100% and 120% filled volume

Transportation protocol has been defined using well-known ASTM D4169 standards.

# Test Protocol

A detailed analysis of the realistic product usage allows the test protocol to be defined in terms of the number and type of tests to be performed during the qualification.

Samples were irradiated under worst-case conditions of 50 kGy and aging was accelerated up to an equivalent of 3 years of shelf life.

The following tables summarize the rationale for this handling qualification:

## 1. First handling from filling to packaging

Life cycle analysis				Testing protocol	
Step	Event   Risk	Type	Maximum Length or Quantity of Events	Test	Quantity
Before filling, empty shell and bag in shell	Stacking	Normal	Few hours	Worst-case	24 hours
	Hangman	Accidental*	0	Accidental	1
After filling, handling of the system to intermediate storage area	Vibration	Normal	Few seconds	Worst-case	1 min
	Rotational edge drop	Accidental*	0	Accidental	1
From the storage to the packaging area	Rotational flat drop	Normal	4	Worst-case	5
	Dropt test on corner	Normal	4	Worst-case	5
From packaging to the cleanroom exit area	Impact test	Accidental*	0	Accidental	1
	Stacking	Normal	Few hours	Worst-case	24 hours

\* Accidental should not occur under normal conditions.

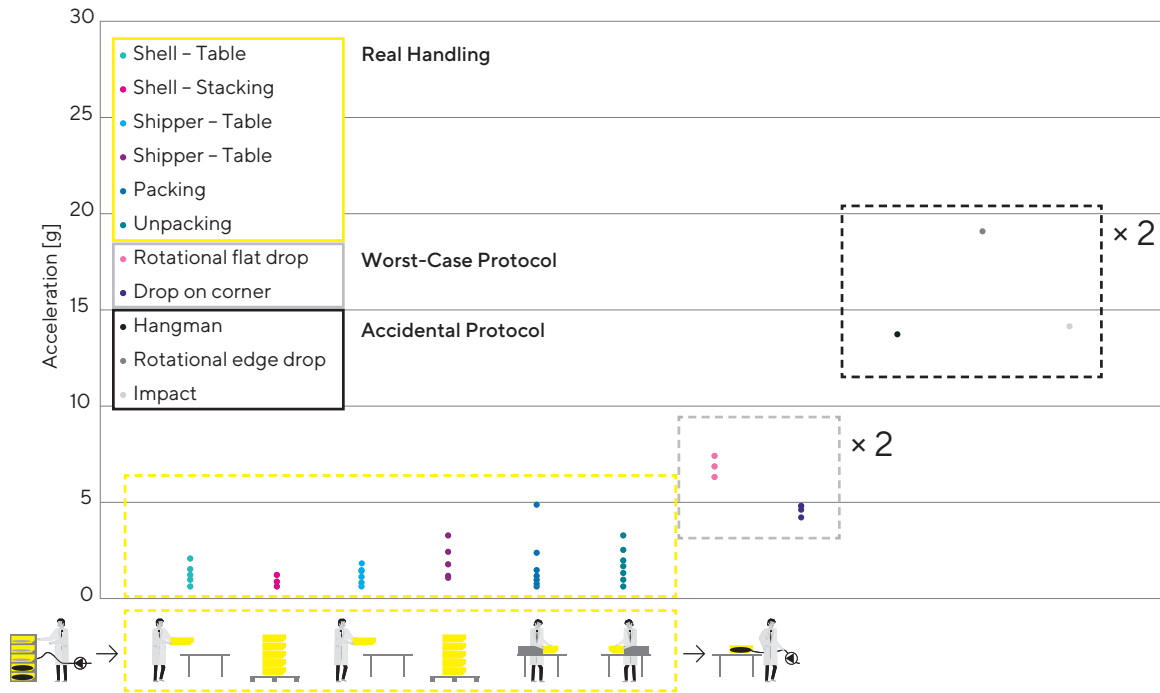
Measurement of acceleration on filled Flexsafe® 2D bags in shell during handling in real-world conditions with 3 different operators & on filled Flexsafe® 2D bags in shell & in their shipper during testing in laboratory according to the newly defined handling protocol.

Comparison of both measurements in order to confirm the right set up parameters of the testing program used to qualify handling conditions with a relevant margin:

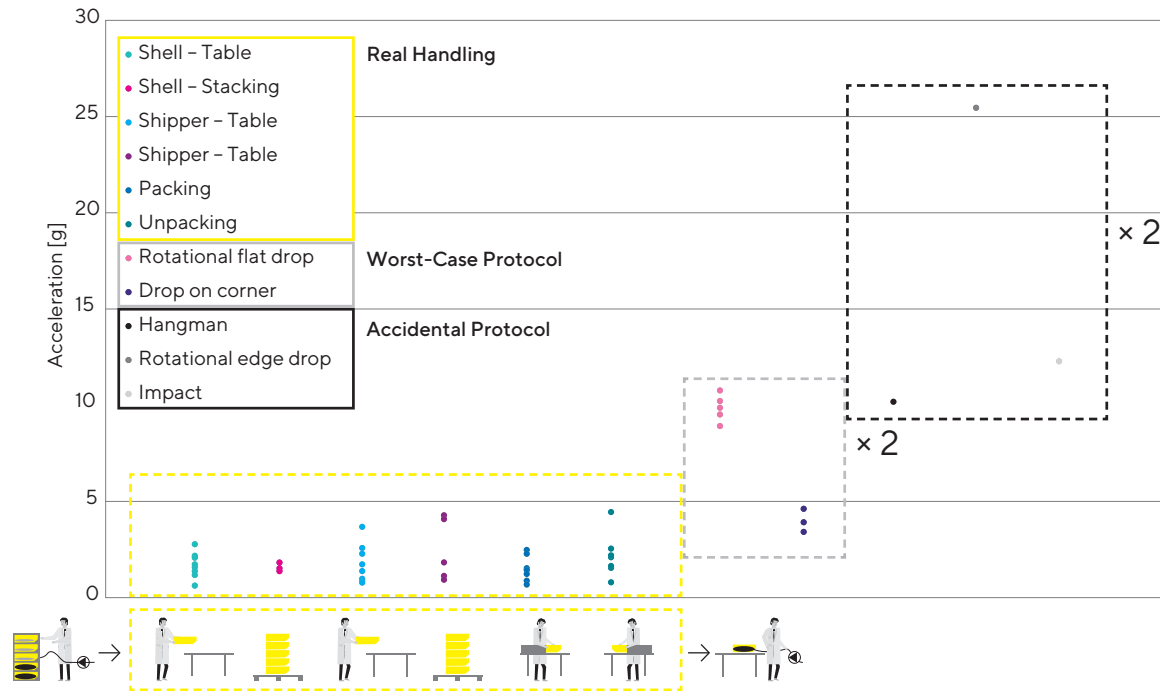
- Worst case laboratory solicitations for normal usage are more stringent than real testing conditions in level and number of solicitations.
- Accidental solicitation in laboratory exceed between 2 and 5 times real solicitations. Real accidental event are in reality really rare. According to protocol, it has been decided to be as safe as possible to apply 2 times per product the 3 types of accidental solicitations.

Applying the worst-case conditions twice and the 3 accidental testing conditions to each product during the qualification will ensure a sufficient margin to confirm that the solution is sufficiently robust.

Flexsafe® 2D bags in shell for laboratory use are validated according to this handling protocol.



5 L handling acquisition real versus protocol



10 L handling acquisition real versus protocol

## 2. Shipping phase:

Transportation validation performed according to ASTM D4169 level I for pallet shipment and ASTM D7386 level II for the single parcel

The pallet testing program is used for the Flexsafe® 2D bags in shell packaged in their shipper within a range of temperatures: 4°C (39.2°F) and 40°C (104°F)

### **The validation protocol has been defined as follows:**

Test sequence test reference based on ASTM D4169-16, assurance level I for airplane spectrum, assurance levels I, II & II for truck spectrum – distribution cycle 12

- 1 Pre-conditioning 4°C (39.2°F) and 40°C (104°F) during 72 hours
- 2 Mechanical handling SCHEDULE A
  - 2.1 Truck handling ASTM D6055 Method A | 8 cycles round trip
  - 2.2 Horizontal impact ASTM D880 Method B | each side 1 shock (total 4)
  - 2.3 Rotational flat drop test ASTM D6179 Method C | 2 drop tests (short and long edge)
- 3 Vehicle vibration SCHEDULE E
  - 3.1 Vibration Truck spectrum ASTM D4169 60 minutes truck spectrum (40 min level III, 15 min level II, 5 min level I)
  - 3.2 Low pressure SCHEDULE I  
ASTM D6653 595.73 hPa – 60 min
  - 3.3 Truck & Air spectrum ASTM D4728 Method A | 60 minutes truck spectrum (40 min level III, 15 min level II, 5 min level I) + 120 minutes airplane spectrum level I
- 4 Mechanical handling SCHEDULE A
  - 4.1 Truck handling ASTM D6055 Method A | 8 cycles round trip
  - 4.2 Horizontal impact ASTM D880 Method B | each side 1 shock (total 4)
  - 4.3 Rotational flat drop test ASTM D6179 Method C | 2 drop tests (short and long edge)



The single parcel testing program is used for the Flexsafe® 2D bags in shell packaged in their shipper within a range of temperatures: 4°C (39.2°F) and 40°C (104°F)

**The validation protocol has been defined as follows:**

Test sequence test reference based on ASTM D4169-16, section ASTM D7386, assurance level II for airplane spectrum, assurance levels I, II & II for truck spectrum - distribution cycle 13

- 1 Pre-conditioning 4°C (39.2°F) and 40°C (104°F) during 72 hours
- 2 Handling SCHEDULE A ASTM D6179-07 | 6 drop tests (2 faces, 2 edges, 2 corners)
- 3 Vehicle stacking Schedule C  
Compression test ASTM D642
- 4 Loose Load vibration Schedule F  
ASTM D999-08 - 60 min
- 5 Low pressure SCHEDULE I  
ASTM D6653 - 595.73 hPa - 60 min
- 6 Vibration Truck & Air spectrum  
ASTM D4169-16 - 20 minutes truck spectrum (13 min, 20 s, Level III, 5 min level II, 1 min 40s level I) + 120 min airplane spectrum Level I; 3 faces



### 3. Final handling from clean room entry to draining area

**Life cycle analysis**

**Testing protocol**

Step	Event   Risk	Type	Maximum Length or Quantity of Events	Test	Quantity
From the cleanroom entry to intermediate storage area	Hangman	Accidental*	0	Accidental	1
	Vibration	Normal	Few seconds	Worst-case	1 min
From the storage to the operational area	Rotational edge drop	Accidental*	0	Accidental	1
	Rotational flat drop	Normal	4	Worst-case	5
To the draining area	Dropt test on corner	Normal	4	Worst-case	5
	Impact test	Accidental*	0	Accidental	1
	Stacking	Normal	Few hours	Worst-case	24 hours

\* Accidental should not occur under normal conditions.

This handling step is covered by the same protocol as item 1 since handling at the user's site is similar to handling at the first filling site.

# Test Results

Following the complete life cycle, the same samples of Flexsafe® 2D bags in shell were tested for handling, then tested for transportation (either on a pallet or for single parcel), and finally tested again for handling.

	Ageing	Irradiation dose	Number of samples	Standards	Acceptance criteria	Results
<b>Flexsafe® 2D Bags in shell 5 L</b>						
At 4°C (39.2°F)	3 years	50 kGy	3 batches, 8 units per batch = 24 units	Handling protocol: mix of ISO, EN NF & ASTM standards (§1, 2)	<ul style="list-style-type: none"> <li>▪ No leak in the bag</li> <li>▪ No break in the shell</li> </ul>	Pass
At 40°C (104°F)	3 years	50 kGy				Pass
<b>Flexsafe® 2D Bags in Shell &amp; in Shipper 5 L</b>						
Pallet At 4°C (39.2°F)	3 years	50 kGy	3 batches, 24 units per batch = 72 units	ASTM D4169-16, Assurance Level I for airplane spectrum, Assurance levels I, II & II for truck spectrum - DC 12		Pass
Pallet At 40°C (104°F)	3 years	50 kGy				Pass
Single parcel At 4°C (39.2°F)	3 years	50 kGy	3 boxes, 1 per batch	ASTM D4169-16, section ASTM D7386, Assurance Level II for airplane spectrum, Assurance levels I, II & III for truck spectrum - DC 13	<ul style="list-style-type: none"> <li>▪ No leak in the bag</li> <li>▪ No break in the shell</li> </ul>	Pass
Single parcel At 40°C (104°F)	3 years	50 kGy	3 boxes, 1 per batch			Pass
<b>Flexsafe® 2D Bags in shell 10 L</b>						
At 4°C (39.2°F)	3 years	50 kGy	3 batches, 8 units per batch = 24 units	Handling protocol: mix of ISO, EN NF & ASTM standards (§1, 2)	<ul style="list-style-type: none"> <li>▪ No leak in the bag</li> <li>▪ No break in the shell</li> </ul>	Pass
At 40°C (104°F)	3 years	50 kGy				Pass
<b>Flexsafe® 2D Bags in shell &amp; in shipper 10 L</b>						
Pallet At 4°C (39.2°F)	3 years	50 kGy	3 batches, 18 units per batch = 54 units	ASTM D4169-16, Assurance Level I for airplane spectrum, Assurance levels I, II & II for truck spectrum - DC 12	<ul style="list-style-type: none"> <li>▪ No leak in the bag</li> <li>▪ No break in the shell</li> </ul>	Pass
Pallet At 40°C (104°F)	3 years	50 kGy				Pass
Single parcel At 4°C (39.2°F)	3 years	50 kGy	3 boxes, 1 per batch	ASTM D4169-16, section ASTM D7386, Assurance Level II for airplane spectrum, Assurance levels I, II & II for truck spectrum - DC 13	<ul style="list-style-type: none"> <li>▪ No leak in the bag</li> <li>▪ No break in the shell</li> </ul>	Pass
Single parcel At 40°C (104°F)	3 years	50 kGy	3 boxes, 1 per batch			Pass

	Ageing	Irradiation dose	Number of samples	Standards	Acceptance criteria	Results
<b>Flexsafe® 2D Bags in shell 20 L</b>						
At 4°C (39.2°F)	3 years	50 kGy	3 batches, 8 units per batch = 24 units	Handling protocol: mix of ISO, EN NF & ASTM standards (§1, 2)	<ul style="list-style-type: none"> <li>▪ No leak in the bag</li> <li>▪ No break in the shell</li> </ul>	Pass
At 40°C (104°F)	3 years	50 kGy				Pass
<b>Flexsafe® 2D Bags in shell &amp; in shipper 20 L</b>						
Pallet At 4°C (39.2°F)	3 years	50 kGy	3 batches, 18 units per batch = 54 units	ASTM D4169-16, Assurance Level I for airplane spectrum, Assurance levels I, II & II for truck spectrum - DC 12	<ul style="list-style-type: none"> <li>▪ No leak in the bag</li> <li>▪ No break in the shell</li> </ul>	Pass
Pallet At 40°C (104°F)	3 years	50 kGy				Pass
Single parcel At 4°C (39.2°F)	3 years	50 kGy	3 boxes, 1 per batch	ASTM D4169-16, section ASTM D7386, Assurance Level II for airplane spectrum, Assurance levels I, II & II for truck spectrum - DC 13	<ul style="list-style-type: none"> <li>▪ No leak in the bag</li> <li>▪ No break in the shell</li> </ul>	Pass
Single parcel At 40°C (104°F)	3 years	50 kGy	3 boxes, 1 per batch			Pass

## Conclusion

Flexsafe® 2D bags in shell and in shipper have been extensively qualified for each step of the life cycle according to very stringent standards (ASTM, ISO, NF EN). The results demonstrate the robustness of Flexsafe® 2D systems for secure and reliable liquid handling and shipping, thereby securing the transportation of bulk drug substances starting at 4°C.



## Conclusion

The selection of proven and robust single-use solutions provides end users with reliable and easy-to-use handling systems to minimize the risk of product loss. Long-term product integrity and stability is maintained and secure international shipments are ensured.

Flexsafe® 2D bags in shell from Sartorius Stedim Biotech are qualified for liquid shipping at nominal volume under the international norm ASTM D4169-14 level I,II, III for cycle 12 & 13 at 4°C (39.2°F) and at 40°C (104°F) and provide secure liquid shipping for all biotech fluids.

## References


1. ASTM D4169: Standard Practice for Performance testing of Shipping Containers and Systems, 2014
2. FDA, Guidance for Industry Process Validation: General Principles and Practices, January, 2011
3. EMA, Guideline on Process Validation for the Manufacture of Biotechnology derived Active Substances and Data to be provided in the Regulatory Submission, London, April, 2014
4. EU, European Commission, EU guidelines for Good Manufacturing Practice (Brussels, February 2014)
5. PDA, Technical Report N°66, Application of Single-Use Systems to Pharmaceutical Manufacturing, 2014

### Germany

Sartorius Stedim Biotech GmbH  
August-Spindler-Strasse 11  
37079 Goettingen  
Phone +49 551 308 0

### USA

Sartorius Stedim North America Inc.  
565 Johnson Avenue  
Bohemia, NY 11716  
Toll-Free +1 800 368 7178

 For further contacts, visit  
[www.sartorius.com](http://www.sartorius.com)