Robustness Study:

Aggressive Drop Conditions for Secondary Containment

INTRODUCTION

In the ever-changing world of biopharma, maintaining and ensuring the integrity of drug products, especially during handling, remains a priority. Entegris has designed secondary blast and plate shell containers to ensure single use bags are less susceptible to damage during use. This application note explores the robustness of Entegris' secondary containers, more commonly referred to as Entegris shells, used in conjunction with the Aramus bag which is known for its superior robustness in handling and storage, Entegris freezing shells have successfully been validated for simulated stresses like drops and have been proven to be robust in protecting Aramus bags as detailed in our Entegris freezing shell validation guides. The shells not only ensure the integrity of drug products; they are designed to protect the most vulnerable components of single use bags, such as tubing which becomes brittle at low temperatures. The focus of this study is to assess the performance of these shells post exposure to aggressive conditioning, evaluating their efficacy in protecting valuable Aramus bag-contained drug products. Due to the high probability of accidents occurring in busy labs and manufacturing spaces, this study is crucial to determine the shells' ability to withstand such unexpected accidents.

MATERIALS AND METHODS

The Entegris freezing shells have previously demonstrated capability to protect Aramus bag assemblies when rotationally dropped from all four sides at greater than 95/90% confidence reliability interval, during validation.

To ensure the shells were capable beyond those criteria, a minimum drop height was selected as a base drop height. This value was obtained from a screen of publicly available data, and a minimum drop height of 1.5 ft. was selected. Bags used during this study were subject to prior testing. All bags and shells were inspected for integrity before testing.

Bag acceptance criteria (Pass/Fail): No visual damage to bag assemblies, No cracks, tears or leaks observed.

Liquid Shell Drops

Bags were filled with room temperature DI water to the required fill volumes and then subjected to drop testing to evaluate their performance under liquid handling conditions.

Frozen Shell Drops

Bags were filled and frozen to -80°C for at least 24 hours before undergoing drop testing immediately after removal from the freezer, simulating handling conditions of frozen products.

1. Blast Shells

The Entegris blast freezing shell (Figure 1) has been designed to fit into both static and controlled rate blast freezers. In this study, Aramus 2 L and 5 L bag assemblies were used with Entegris 2 L and 5 L blast freezing shells. Varying bag samples were used, and this study was limited to one drop per test due to the aggressive conditions.

- Bags were filled to the maximum (100%) volume with DI water
- Bags were assembled in shell
- Bags were transferred to a -80°C conventional freezer and frozen for 24 hours
- Frozen shells were dropped as per test parameters

Liquid only drop tests were performed directly after being filled with DI water.

2. Plate Shells

The Entegris plate freezing shell (Figure 2) has been designed for use with plate freezing systems. In this study, Aramus 9.5 L and 11.5 L bag assemblies were used with Entegris 9.5 L and 11.5 L plate freezing shells.

- Each bag was filled with DI water to the maximum (100%) fill volume
- Bags were assembled in shells
- Bags were transferred to a -80°C conventional freezer and frozen for 24 hours
- Shells were removed from the freezer
- Frozen shells were subjected to drop testing.

Bag acceptance criteria of Pass/Fail: No visual damage to bag assemblies, no cracks, tears or leaks observed.

Figure 1.

Figure 2.

RESULTS

For the initial frozen drops, each shell was taken out of the freezer and immediately subjected to one flat drop test at a height of 1.5 ft. Subsequent shells were dropped once with incremental heights of 0.5 ft. until the established maximum drop height of 5 ft. was reached.

Entegris Blast Freezing Shells

Per pass criteria, the 2 L shells saw a 100% pass rate up to 2.5 ft., and an 80% pass rate at 3 ft. The 5 L shells saw a 100% pass rate at 1.5 ft. and 2.5 ft., however saw a 60% pass rate at 2 ft.

Table 1. Frozen Drop Tests

Shell size	Fill volume	Test notes	Drop height	# Drop pass	# Drop fail	Pass %
2 L	2 L	Frozen, flat in shell	1.5 ft.	4	0	100
2 L	2 L	Frozen, flat in shell	2.0 ft.	5	0	100
2 L	2 L	Frozen, flat in shell	2.5 ft.	5	0	100
2 L	2 L	Frozen, flat in shell	3.0 ft.	4	1	80
2 L	2 L	Frozen, flat in shell	3.5 ft.	3	1	75
2 L	2 L	Frozen, flat in shell	4.0 ft.	5	0	100
2 L	2 L	Frozen, flat in shell	5.0 ft.	4	1	80
5 L	5 L	Frozen, flat in shell	1.5 ft.	5	0	100
5 L	5 L	Frozen, flat in shell	2.0 ft.	3	2	60
5 L	5 L	Frozen, flat in shell	2.5 ft.	5	0	100
5 L	5 L	Frozen, flat in shell	3.0 ft.	3	1	75
5 L	5 L	Frozen, flat in shell	3.5 ft.	4	1	80
5 L	5 L	Frozen, flat in shell	4.0 ft.	3	2	60

For the liquid drop tests, ten 2 L Aramus bag assemblies were tested at 3 ft. in 2 L Entegris blast freezing shells immediately after being filled to the maximum fill volume. To demonstrate use case for customers whose products exist solely in the liquid state at room temperature, bags filled with DI water were tested in the liquid state at room temperature. All bags and shells demonstrated robustness.

In the liquid drops, 5 L Aramus bag assemblies experienced large breaks at the S-weld above 1.5 ft., but observed a 100% pass rate at a drop height of 1.5 ft.

Table 2. Liquid Drop Tests

Shell size	Fill volume	Test notes	Drop height	# Drop pass	# Drop fail	Pass %
2 L	2 L	Liquid shell drop, flat	3.0 ft.	10	0	100
5 L	5 L	Liquid shell drop, flat	3.0 ft.	2	2	50
5 L	5 L	Liquid shell drop, flat	2.0 ft.	0	1	0
5 L	5 L	Liquid shell drop, flat	1.5 ft.	5	0	100

Entegris Plate Freezing Shells

Entegris 9.5 L bags were filled and placed in the Entegris plate freezing shell. Shells were frozen overnight in a HOF Plate Freezer and flat drop tested from 1 ft. in increments of 0.5 ft. up to 3 ft., and all shells demonstrated robustness. Bags were thawed to room temperature and visually inspected for leaks.

The next set of 9.5 L bags tested were a combination of bags that were pushed off from the benchtop at 3 ft., 90° drop on the side at 3 ft. and 90° drops at 1 ft., all of which survived the drop.

The final set of plate freezing tests were 11.5 L bags filled to 11.5 L fill volume, and these were dropped in the frozen state from 1.5 ft. in 0.5 ft. increments up to 2.5 ft. successfully. All Entegris plate freezing shells survived all tested drop heights.

Table 3. Frozen Drop Tests

Shell size	Fill volume	Test notes	Drop height	# Drop pass	# Drop fail	Pass %
9.5 L	9.5 L	Frozen drop, flat	1.0 ft.	5	0	100
9.5 L	9.5 L	Frozen drop, flat	1.5 ft.	5	0	100
9.5 L	9.5 L	Frozen drop, flat	2.0 ft.	5	0	100
9.5 L	9.5 L	Frozen drop, flat	2.5 ft.	5	0	100
9.5 L	9.5 L	Frozen drop, flat	3.0 ft.	5	0	100
9.5 L	9.5 L	Benchtop slide-off handle first	3.0 ft.	2	0	100
9.5 L	9.5 L	90° drop on side	2.0 ft.	1	0	100
9.5 L	9.5 L	90° drop on handle	1.0 ft.	1	0	100
9.5 L	9.5 L	90° drop on handle	2.0 ft.	1	0	100
11.5 L	11.5 L	Frozen drop, flat	1.5 ft.	5	0	100
11.5 L	11.5 L	Frozen drop, flat	2.0 ft.	5	0	100
11.5 L	11.5 L	Frozen drop, flat	2.5 ft.	5	0	100

CONCLUSION

In conclusion, this study clearly shows the effectiveness of Entegris freezing shells in protecting Aramus bags under aggressive conditions representative of accidents occurring in busy labs and manufacturing spaces. Our tests prove that these shells, with their robust design, are key in preventing damage to drug products during handling, storage, and transportation.

Our study findings show that Entegris plate freezing shells are particularly resilient, capable of withstanding drops from up to three feet without observed damages to the bag assemblies. The blast freezing shells similarly performed well, maintaining their integrity in 80% of our drop tests. These results confirm that Entegris freezing shells not only meet but surpass the usual industry standards and provide a safety factor to the claims in the published validation guides, offering a reliable solution for protecting sensitive drug products.

By effectively protecting the most vulnerable components of single-use systems, even under severe conditions, Entegris shells prove to be an essential asset in any biopharma setting where accidents might occur. Ultimately, this study highlights the essential role that these secondary container solutions play in ensuring the ongoing safety and integrity of drug products during handling, boosting confidence in their use across the biopharmaceutical industry.

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