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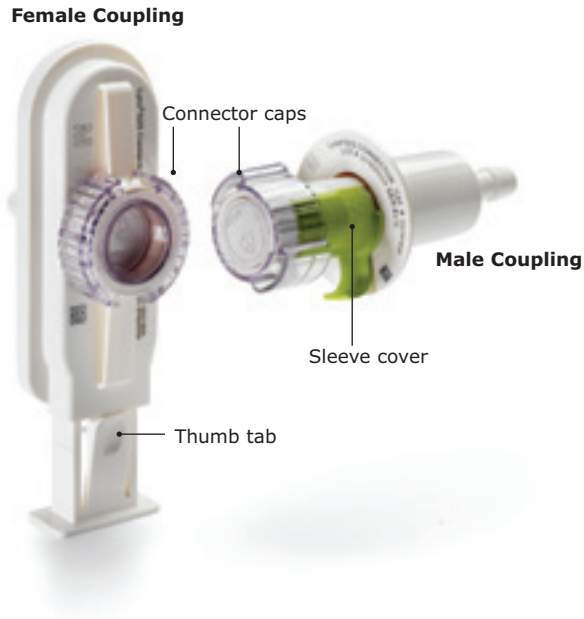
Technical Brief

# Lynx® S2S Connector Capability and Integrity after Three Autoclave Sterilization Cycles

The demand for increased quality assurance and product safety continues to rise for biopharmaceutical manufacturing processes, and with it the need for a reliable and sterile connector that ensures sterile fluid transfer between processes even at the worst-case environmental conditions. The Lynx® S2S connector is a single-use, single-actuation, gamma and autoclave-compatible connector. It enables the sterile connection of pre-assembled, pre-sterilized filters, tubing, and process containers in biopharmaceutical processes, in both non-classified and classified environments.

The Lynx® S2S connector comprises a female and male coupling, and utilizes solid plugs with O-ring seals to ensure that the flow path of the single-use assembly remains closed, before, during and after the connection. The process contact materials are high temperature and gamma-stable polysulfone with an over-molded silicone gasket, which have temperature stability above 130°C.

This technical brief summarizes data demonstrating the integrity and functionality of Lynx® S2S connectors after exposure to aggressive autoclave sterilization conditions.




## Purpose of Study

The purpose of this study was to demonstrate 1) physical integrity of both the individual Lynx® S2S couplings (integrity testing) and the actuated Lynx® S2S connection (burst testing) and 2) microbial integrity of the Lynx® S2S connection/flow path following an aerosol bacterial challenge of the separate male and female connector couplings, after the male and female couplings have been subjected to three autoclave sterilization cycles of 130°C/30 min. Typical autoclave cycles are at 121°C, 123°C or possibly as high as 126°C for a duration of 30 minutes. This testing was done at 130°C to represent a worse-case customer process.

## Test Methodology and Experimental Design

### Preparation

All Lynx® S2S female and male coupling were pre-sterilized by gamma-irradiation at a minimum of 45 kGy.

### Autoclave Sterilization

Lynx® S2S female and male couplings were autoclave sterilized as follows. Connector couplings were assembled onto a test manifold and the assemblies were then autoclaved using a validated equipment cycle in a validated autoclave. The test assemblies were autoclaved three times at a minimum temperature of 130°C for 30 minutes.

### Physical Integrity Testing

Testing was performed according to manufacturing release and product testing requirements documented at the third-party manufacturer.  A total of 21 female couplings and 21 male couplings were individually integrity tested. Next, the same devices were connected and actuated in random combinations of male and female couplings and burst testing was performed on the actuated connectors.

### Microbial Integrity Testing

An aerosolized bacterial challenge test was used to simulate worst-case environmental conditions. This test challenges the Lynx® S2S male and female couplings prior to actuation with a minimum of $10^6$ bacteria (in colony forming units (CFU)) per device, assuring that sterile connection can be made in a non-classified environment. In this test, 12 coupling sets were challenged with an aerosolized suspension of *Brevundimonas diminuta* (ATCC® 19146™) at a minimum of $10^6$ CFU per coupling set. They were connected and actuated after application of the aerosol challenge. Sterile media was then flowed through the actuated connectors into sterile receiving vessels and assayed to determine the presence or absence of growth. Negative control devices comprised a coupling set that was connected and actuated without application of bacterial challenge in the test environment. Positive control devices, demonstrating test system suitability, comprised a coupling set from which the device plugs were removed prior to application of the challenge, allowing penetration of microorganisms into the flow path.

### Results

All unconnected devices, which were gamma-irradiated at a minimum of 45 kGy and then autoclaved three times at 130°C/30 min, passed the manufacturing release integrity test. After connection of the male and female devices, which were gamma-irradiated, autoclaved and integrity tested, the connected devices were burst tested and passed the acceptance criteria. Connected devices, which were microbial challenge tested while unconnected, demonstrated a sterile flow path upon actuation.

## Physical Integrity Test

| Coupling Gender | Lot | # of Devices Tested | Results | |
|---|---|---|---|---|
| | | | Pre-autoclave | Post-autoclave |
| Female | 1 | 7 | Pass | Pass |
| | 2 | 7 | Pass | Pass |
| | 3 | 7 | Pass | Pass |
| Male | 1 | 7 | Pass | Pass |
| | 2 | 7 | Pass | Pass |
| | 3 | 7 | Pass | Pass |

## Physical Burst Test

| Female Lot | Male Lot | # of Device Pairs Tested | Results |
|---|---|---|---|
| 1 | 1 | 7 | Pass |
| 2 | 2 | 7 | Pass |
| 3 | 3 | 7 | Pass |

## Microbial Integrity Test

| Female Lot | Male Lot | Control or Test Article | Results |
|---|---|---|---|
| 4 | 1 | Negative Control | No Growth |
| | | Test Article | No Growth |
| | | Test Article | No Growth |
| | | Test Article | No Growth |
| | | Positive Control | Growth |
| 2 | 2 | Negative Control | No Growth |
| | | Test Article | No Growth |
| | | Test Article | No Growth |
| | | Test Article | No Growth |
| | | Positive Control | Growth |
| 3 | 3 | Negative Control | No Growth |
| | | Test Article | No Growth |
| | | Test Article | No Growth |
| | | Test Article | No Growth |
| | | Positive Control | Growth |
| 1 | 1 | Negative Control | No Growth |
| | | Test Article | No Growth |
| | | Test Article | No Growth |
| | | Test Article | No Growth |
| | | Positive Control | Growth |

## Summary

The design of the Lynx® S2S connector has demonstrated quality and performance robustness that provides significant benefit to the industry by facilitating sterile transfer of fluids with the highest degree of assurance and process safety. This study demonstrated device integrity after three autoclave cycles of 30 minutes at 130°C for physical strength by the physical integrity burst test and microbial integrity by the aerosol bacterial challenge test:

- All male and female devices are integral per the manufacturing release test after being autoclaved three times for 30 minutes at 130°C.
- All actuated devices resisted burst after pressurization > 100 psi
- The flow path of the actuated connector device is integral to microbial ingress, demonstrated by aerosolized challenge at >1 x $10^6$ CFU onto the unconnected device couplings.

As a key component of Mobius® flexible bioprocessing solutions, the Lynx® S2S connector provides a safe and robust connection that ensures sterile transfer of liquids between unit operations within a biopharmaceutical manufacturing process.

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