

Operating Instructions

SART System™

Gammasart™ ATD (Connector Device) and System Port

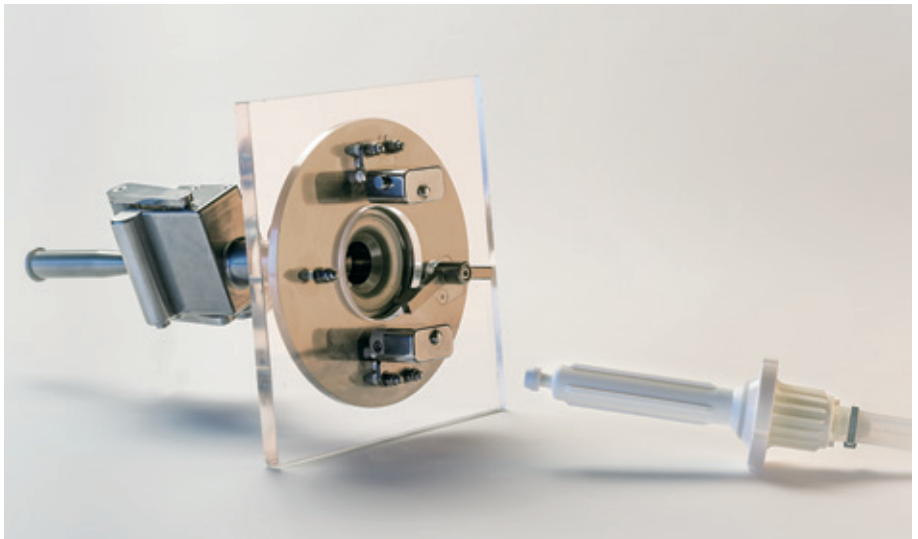


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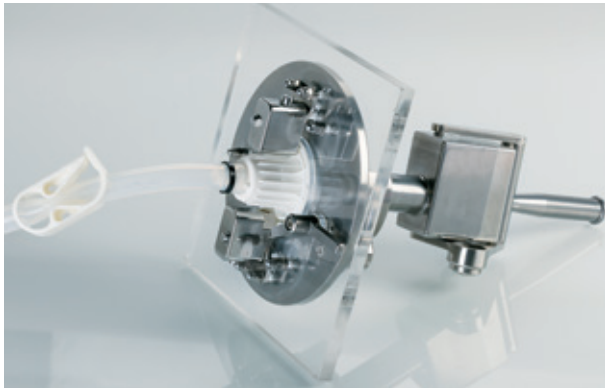
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1. The SART System™

1.1. Introduction

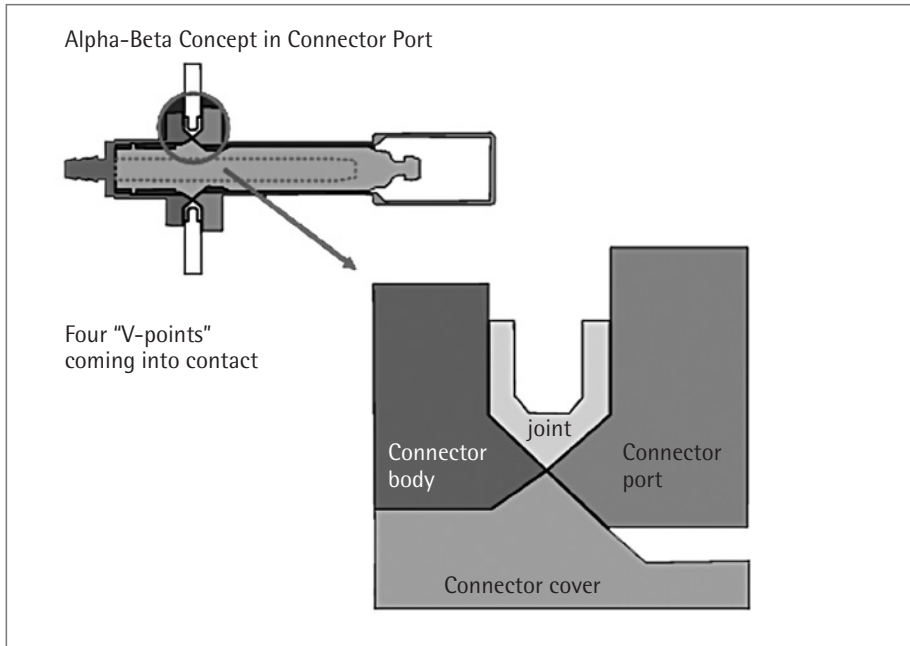
The SART System™ consists of an external port, an internal port and a disposable connection device (Gammasart™ ATD). It is designed to transfer liquids between two areas with different containment classifications. The most common applications include:

- Transferral from a class ISO7/Grade C clean room inside an isolator or a RABS (class ISO5/Grade A). The isolator could be either a filling isolator, a formulation isolator or a glove box for research applications.
- Distribution of liquid into multiple containers (e.g., dividing a formulation batch into multiple sub-batches for storage).



1.2 The Alpha-Beta Concept

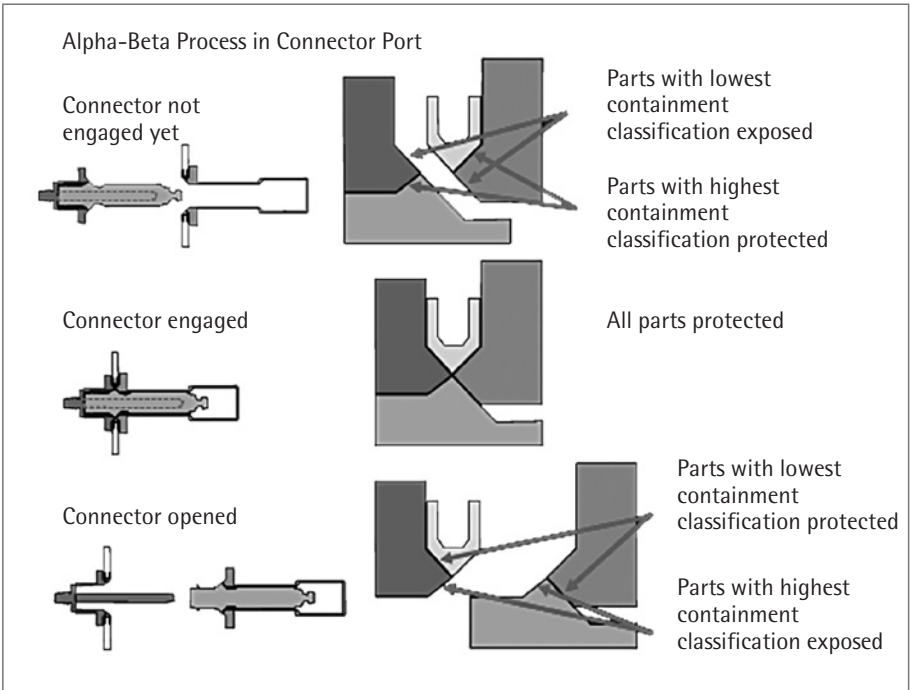
The alpha-beta concept is a well-accepted method for transferring liquids inside contained areas. The principle is illustrated in the figures below. It is based on the principle that four V points come into contact at their apexes and that each surface is in closed contact with another one at any moment in time. The extremities of each point create a line called the “line of confidence”. Close contact between surfaces is ensured by two opposing flexible joints, i.e., the thermoplastic elastomer joint on the connector cover and the silicone joint on the port.



The concept creates two different surfaces: one that is exposed to the lower containment classification and one that is exposed to the higher containment classification.

When the connector is not inserted in the port, the surfaces with the lower containment classifications are exposed and the surfaces with the higher containment are protected by their tight contact with each other.

Once the connector is opened, the surfaces with the higher containment classification are exposed to the air with the highest sterility assurance level (e.g., inside the isolator), while the other surfaces are protected by the tight contact. This ensures that the surfaces with the lower containment classification do not contaminate the area with the higher sterility assurance level.



Note:
 Lower containment classification and one that is exposed to the higher containment classification.

1.3. Description of the Gammasart™ ATD Connection Device (P/N AN-CON-101025 and AN-CON-102025)

The Gammasart™ ATD is made of two elements, the connector body and the connector cover. The materials used are PBT Celanex grade 2404 MT supplied by Ticona and a thermoplastic elastomer for the joint (Santoprene Grade 281-64 from Advanced Elastomer System or Thermolast TM6MED from Kraiburg).

The connector body has two important functions:

- Allow the liquid flow to pass through its tubing
- Be inserted into the port and secured with the port closing system.

The connector cover protects the inside part of the connector body until it is released in the area with the higher containment classification when the port is open (see Chapter 4). The end of the cover is designed for clamping inside the internal port (see Chapter 3.1). The connector cover is equipped with a thermoplastic elastomer joint which is crucial to the alpha-beta concept.

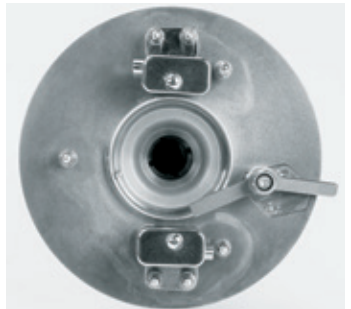


Connector device (top), connector body (bottom left) and connector cover (bottom right)

1.4. Description of the SART System™ Connector Port (P/N AN-CON-305025)

The connector port is made of 4 elements:

- 1. An external port, which is fastened on the wall. Its two functions are, first, to secure the connector body with the closing systems and, second, to secure the docking of the internal port with the interlock in the absence of the connector device
- 2. An internal port, which can be unscrewed and separated from the external port. Its functions are to secure the connector cover by clamping its end down and for unscrewing the connector device to enable release the tubing inside the area with the higher containment classification
- 3. An internal port stopper, which is designed to protect the internal port mechanism during cleaning and sanitization
- 4. An external port cover, which is designed to close the transfer port during cleaning and sanitization



Left: View of internal port (bottom), external port cover (top left) and internal port cover (top right); Right: overview of the external port

2. Preparation and Installation

2.1. Preparing the Gammasart™ ATD Connection Device

2.1.1. Gamma Irradiation

Gammasart™ ATD devices are supplied in two packaging formats: the blister packaging is used for connectors that have undergone gamma-irradiation and the shrink-band packaging is used for assemblies that will undergo irradiation process later when equipped to single-use bag or tubing assemblies.

Since one-time gamma-irradiation is mandatory, it is important that each type of packaging be used for its intended purpose. Gamma-irradiation ensures complete sterilization of all parts of the connector.

It is also critical that an irradiated Gammasart™ ATD connector device is not subjected to any additional irradiation procedures that have not been validated. The maximum validated irradiation dose is 45 kGray.

2.1.2. Assembling onto Containers

The connector device is designed to allow liquid transfer from an area with a low containment classification to an area with a higher containment classification, or vice-versa. To protect the liquid, the connector device should be connected to the container located in the lowest containment area, with the final connection done inside the area with the higher containment classification.

The following recommendations should be observed to ensure optimal assembly of the Gammasart™ ATD connection device:

- Always assemble before the last sterilization step (for non presterilized connectors only)
- Perform the assembly in the higher classified environment to avoid particle contamination or introduction of viable particles
- Verify that the blue mark located on the joint is still complete. Any small separation of the mark should be considered an accidental opening of the connector device and means that the device should not be used.
- Install tubing with an internal size of 3/8 inch (9.52 mm) or 5/16 inch (7.92 mm)
- Once the connector is connected to tubing, attach clamping devices to the tubing to prevent any accidental transfer of liquid inside the connector before opened (e.g., during transportation)
- After assembly, secure the assembly with a tightening device to avoid accidental dismantling during operations (e.g., cable tie tightening).



Assembled connector device with tubing secured and tubing clamp

2.1.3. Sterilization

- Gammasart™ ATD devices attached to containers supporting irradiation (e.g., pouches) are submitted to gamma irradiation on the condition that the connector device has undergone previous irradiation treatment

Note: Sterilization of Gammasart™ ATD Connectors, supplied sterile in a blister packed with 5 units for on-site connection, has been validated according to the AAMI TIR 27:2001 VD MAX method.

- If Gammasart™ ATD devices are connected to containers not designed for gamma irradiation (e.g., stainless steel vessels), they may undergo a steam sterilization process. The steam sterilization of the assembly should be validated to meet GMP requirement. If long tubing is used to connect the container to the connector device, the sterilization procedure should be adapted to ensure that steam spreads throughout the entire tubing, for example, by the following procedures:
 - Installing a vent filter close to the connector with a closing device
 - Performing pressure cycles to force the vapor into the tubing

IMPORTANT:

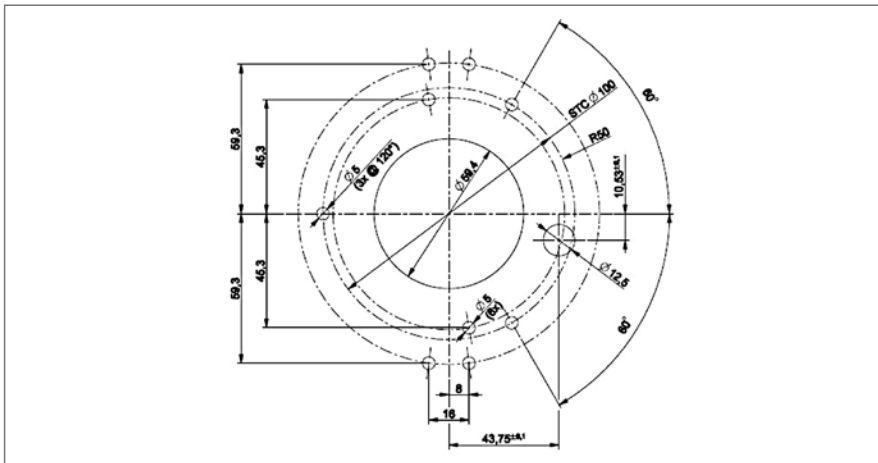
Never hold the connector by the cover once it is connected to a container. Gravity, weight or resistance to movement could cause it to become unscrewed. Operators should be trained to always handle the connector by the connector body.

2.2. Installing the Port

The port must be installed on a flat surface made of either stainless steel or Plexiglas. It is recommended that the port is installed with the clamping devices in vertical position and with flexibility for movement of the interlock. The thickness of the wall should be 8.0 mm (precisely). If the thickness is lower, a plate made of stainless steel or other acceptable material should be added. Wall thickness is critical to ensure optimal compression of the connector by the rotating parts. A critical dimension is the distance

between the flat surface of the rotating part, and the supporting face of the silicone joint. The distance should be $10.3 +0.0/-0.3$ mm (the dimensions CD8* should be measured for both closing systems after installation).

The port comes supplied with a Plexiglas plate which can be used as a gauge to identify the area to be pierced. The dimension of the holes and the operating space required are shown on the following drawings.



Sanitizing the Port

The objective of sanitization is to treat all parts which will be in contact with the higher containment area, in particular, the V points of the equipment.

To sanitize the port, perform the following steps:

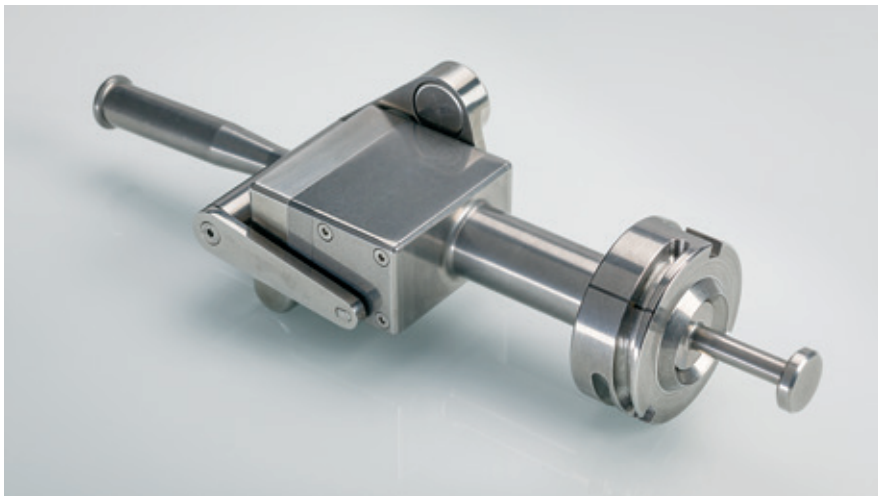
- Close the connector port hole with the external port cover and secure it with the closing systems. To attach the cover, lift the interlock, place the interlock and secure it with the two closing systems (safety pins engaged).



External port with cover placed

* Definition of CD8: distance between the flat surface of the clamping device up to the external stainless steel surface where the silicone joint is placed (without the joint)

- Close the tubing with the internal port cover. The objective is to make sure that aggressive sanitization products (e.g., bleach) do not penetrate any of the port's precision mechanisms and do not pose any risk of deterioration. It is important to note that the cover part will never be exposed to the area with the higher containment classifications.



Stopper placed in the internal port

- Place the external port in classical unscrewed position
- Perform cleaning and sanitization (wiping with bleach and/or alcohol, VHP cycle in an isolator, ...)
- After sanitization, connect the internal port to the external port (as described in Chapter 4.2) without changing the position of either the internal port stopper or the external port cover

- Remove the external port cover



- Remove the internal port stopper



Once the internal port cover is withdrawn through the external port, the port is ready for operation.

2.3. Special Assemblies

Some special cases are illustrated in this section:

2.3.1. Loading a Container

It is possible to load a container through the connector. In that case, the liquid is coming from an area with high containment classification (e.g., class ISO 5/Grade A formulation clean room to the container in the corridor). For that application, the connector device must be connected to the container and the flow goes in the opposite direction than normal (e.g., for transferral inside an isolator).

2.3.2. Loading and Unloading a Container

It is not only possible to load a container through a connector (see Chapter 2.3.1.), but also to transfer its liquid to another area with a higher containment classification (e.g., from a formulation clean room to container to a filling isolator). In that case, we strongly recommend using a container with two completely separate tubing systems and connector devices. The authorities will usually not accept a double pass (in and out) through the same tubing unless this procedure has been validated.

2.3.3. Circulation Loop

For products precipitation (e.g., suspensions), a circulation loop may be necessary. In that case, two connector ports should be installed and two connector devices connected. One is used to transfer the product inside the area with the higher containment classification and the second to return the non-processed liquid back to the container. The path to go to the process area can then be located very close to it. That minimizes the risk of sedimentation.

3. Connector & Port Operation

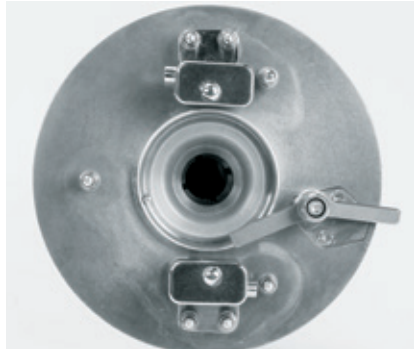
3.1. Installing the Internal Port and Gammasart™ ATD Connector

Follow the procedure described below for optimal use of the connector port and device:
The operator inside the area with the highest containment classification should:

- Install the port in its starting position after sanitization is completed and two covers have been removed (see Chapter 3.3). This is done by moving the internal port until the line of the internal port is aligned with the START position marked on the external port. Once the internal port is in the right position, the interlock moves up until it is definitively engaged.



Internal port cover aligned in START position



Interlock in blocking position

The operator in the area with the lower containment classification should:

- Wipe both confidence lines located on the port and on the connector with alcohol to minimize presence of viable particles on the critical area
- Open the two closing systems on the external port
- Lift the interlock and insert the connector device



Interlock lifted during connector device insertion

- Secure the holding by pressing the pin to unlock the closing system and start rotation. The same pin is used for connector release when rotated backward.



Connector device secured in the port with the closing system.

- The operator inside the area with the higher containment classification should:
- Rotate the handle to 90° of the internal port tubing to clamp the connector cover inside the internal port



Handle in clamping position

- Rotate the internal port counter-clockwise until it does not move further. It is preferable to hold the internal port by the central part rather than by the handle. This minimizes stainless steel to stainless steel friction during rotation. Nevertheless, if rotating this way poses resistance (e.g., difficult access), try using the handle.



Port rotated and being opened

- Remove the internal port and place it in a designated location (designated location to be defined by user). This action frees the connector device tubing and makes it available for connection inside the area with the higher containment classification.



Open port with connector device tube exposed for connection

- Install the tubing by simply pushing it on the connector device tubing until it reaches at least the last rip (may go over it). The tubing should have an internal size of 3/8 inch (9.52 mm). Securing the tubing holder is not required. The connection is now ready for operation and all the safety clamps installed on tubing can be removed or released.



Tubing installation

3.2 Dismantling the Internal Port and Removing the Gammasart™ ATD Connector

After production, the connector device can be closed and released without creating any opening. For that purpose, follow the procedure described below:

- Empty all tubing and the connector e.g., by using the pump in reverse order or by clamping all tubing. This is done to prevent any liquid still present inside the connector from leaking out.
- Operation inside the area with the higher containment classification:
 - Withdraw the tubing by pulling it away

IMPORTANT:

Pull the tubing away from the connector with a movement in line with the tubing and not perpendicular to it.

- Bring the internal port to the front of the connector device tubing with the handle at approximately 30° in the top left quarter, turn it around until it reaches the end



Insertion of the internal port prior to the rotation step

- Rotate the internal port clockwise until it reaches the “STOP” position, i.e., the line on the internal port is aligned with the stop position. Rotating past the “START” position allows the operator to achieve a slightly longer screw path and thereby over-compress the connector cover joint on the connector body. This over-compression prevents the closure integrity from being affected by potential joint deformation due to longer compression before initial use.



Line in STOP position after closing

- Push on the large button to allow the handle movement and release the handle by aligning it with the rest of the internal port

Handle release:

- The operator in the area with the lower containment classification should:
 - Unlock the closing systems
 - Take the connector device out of the port

IMPORTANT:

Pull out the connector without any rotation as it can open the connector.

3.3. Special Operation: Re-use of the Gammasart™ ATD Connection Device

The connector device can be re-used. For example, an assembly is set up in isolator on a filling line and the filling line breakdowns suddenly. Repairs will take a long time and the isolator connection is interrupted. In this case, the Gammasart™ ATD connection device can be reused. This enables the connector to be closed and the formulated batch safely returned to storage area. Once the line is repaired, the connector can be opened again.

IMPORTANT:

This operation should be performed in strict observance of the following:

- 1. Never disconnect the connector from the initial container and connect it to another
- 2. The opening and closure has been validated as follows:
 - A maximum of 3 series of opening and closure cycles were
 - The last opening and closure should happen within one week of the initial opening
- 3. To operate the connector, follow the instructions below:
 - For the second and third openings, observe the instructions in Chapter 4.1 with the following modifications:
- Align the line on the internal port not in the “START” position, but in the “STOP” position, as the connector has already undergone one closing process with over-compression. If the “START” position is selected, there is a risk that the external clamps will not fit properly and that the connector body and the connector cover will disengage during closing and be damaged
- Start rotation of the internal port from the STOP position, but reach the same release point
- All other operations are identical to Chapter 4.1

For the second and third closings, the process is identical to Chapter 4.2. Nevertheless, it is important to note that there will be no more over-compression after closing. Therefore, an open and re-closed connector device should never be stored for long periods, otherwise the closure integrity cannot be guaranteed once the joint has been deformed by over compression.

Note that the connector can be inserted in different ports should its re-use become necessary (e.g., filling is started on line 1 and re-started on line 2).

4. QA/QC Release

4.1 SART System™ Port

The port can be released after completion of the following tests:

- Checking the stainless steel certificates provided by the suppliers
- Measuring the critical dimensions as CD8*
- Finishing quality controls
 - Presence of all joints
 - Roughness of the major surfaces of the port facing the area with the higher containment classification (Ra below 1.2 µm)
 - Absence of cutting edges
- Leak test all ports: test for leakage of the internal port at 350 mbar and a maximum allowable pressure loss of 15 mbar/min. Correct any ports that fail the test until they pass or are rejected.
- Check port function (insert and open the connector, check interlock function, ensure that the connector is a tight secured in the port and the rotation marks are located properly)

4.2. Gammasart™ ATD Connection Device

Various quality controls should be performed:

Inspect the molded connectors for critical dimension, any defects affecting closure integrity, any defects affecting operation and any cosmetic defects as defined in the table below.

Perform the tests on a randomly selected sample of connectors (random selection based on ISO 3951, previously called Military Standard 414).

* Definition of CD8: distance between the flat surface of the clamping device up to the external stainless steel surface where the silicone joint is placed (without the joint)

5. Service and Maintenance of the SART System™

This section only refers to the internal and external port of the SART System™. The Gammasart™ ATD connection device is a disposable component requiring no maintenance.

5.1. Maintenance

The port requires little maintenance. To facilitate operation, some silicone could be added to the pins used for rotating the internal port. The joint in the external port needs to be inspected during each preparation of the equipment. In case of damage, the joint must be changed.

IMPORTANT:

For closure integrity, it is critical that the face of the joint with the two edges is located in the area where it is in contact with the internal port. If not, rotation of the internal port may be very difficult.

For greater safety, inspect the joints on rotating clamps every two years under normal use (500–1000 openings/year).

5.2. Servicing

If the port is damaged, return it to Sartorius Stedim Biotech and receive a replacement so that operation can continue during the repair period. The following types of damages are critical and must be repaired immediately:

- Damage to the “V point” of the internal port based on the alpha-beta concept. If not repaired, there is a significant risk that viable particles could be introduced inside the area with the higher containment classification
- Damage or torsion to the internal mechanism to clamp the connector cover in the internal port. If not repaired, this could expose the contaminated surface of the connector cover inside the area with the higher containment classification
- Damage or torsion to the interlock. The interlock function is necessary to prevent accidental release of the internal port when the connector body disengaged
- Damage to the silicone joint. If not repaired, it could create a leak into the area with the higher containment classification

5.3. Maintenance of the port

The following spare parts are available

- Complete Port (P/N AN-CON-305025)
- External Port Complete (P/N AN-CON-306025)
- Internal Port Complete (P/N AN-CON-204025)
- Internal Port Plug (P/N AN-CON-205025)
- External Port Plug (P/N AN-CON-206025)
- External Port Seal (P/N AN-CON-207025)
- Internal Port long clamp shaft (P/N AN-CON-208025)
- Internal Port Short Clamp Shaft (P/N AN-CON-209025)
- Interlock assembly (P/N AN-CON-210025)

We must expressly draw your attention to the fact that replacement parts and accessories not supplied by Sartorius Stedim Biotech GmbH have also not been tested and approved by Sartorius Stedim Biotech GmbH. The installation of and | or use of such products can therefore have a negative effect on the system properties as constructed.

Sartorius Stedim Biotech GmbH is not liable for any damages resulting from the use of non-original parts or non-original accessory parts. Moreover, Sartorius Stedim Biotech can not assume liability if the entire SART System™ and the Gammasart™ ATD connector are used improperly.

We reserve the right to make changes in the interest of product development.

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