Package leaflet: Information for the user

VeraSeal solutions for sealant
human fibrinogen/human thrombin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What VeraSeal is and what it is used for

VeraSeal contains human fibrinogen and human thrombin, two proteins extracted from the blood that form a clot when they are mixed together.

VeraSeal is used as a sealant during surgical operations in patients. It is applied to the surface of bleeding tissue to reduce bleeding during and after the operation when standard surgical techniques are not sufficient.

VeraSeal is indicated in all age groups.

2. What you need to know before you are treated with VeraSeal

Your surgeon must not treat you with VeraSeal

- if you are allergic to human fibrinogen or human thrombin or any of the other ingredients of this medicine (listed in section 6).

VeraSeal must not be applied inside blood vessels.

VeraSeal must not be used to treat severe or rapid bleeding from an artery.

Warnings and precautions

Allergic reactions are possible. Signs of such reactions include hives, rash, tightness of the chest, wheezing, drop in blood pressure (e.g. light-headedness, fainting, blurred vision), and anaphylaxis (a severe reaction with a rapid onset). If these symptoms occur during surgery, the use of the medicine should be stopped immediately.

VeraSeal spray application should only be used if it is possible to accurately judge the spray distance. The spray device should not be used closer than the recommended distance.

Special safety warning

For medicines such as VeraSeal that are made from human blood or plasma, certain measures are taken to prevent infections being passed on to patients. These include carefully selecting blood and plasma donors to make sure those at risk of carrying infections are excluded, and testing each donation and pooled plasma for signs of virus/infections. Manufacturers also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (fetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).

It is strongly recommended that every time you are treated with VeraSeal, the name and batch number of the medicine are recorded in order to maintain a record of the batches used.

Children and adolescents

VeraSeal is recommended for use in children and adolescents under 18 years of age.

Other medicines and VeraSeal

The product may be affected after contacting solutions containing alcohol, iodine or heavy metals (e.g. antiseptic solutions).

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before being treated with this medicine. Your doctor will decide whether you should be treated with VeraSeal.

3. How VeraSeal is used

The use of VeraSeal is restricted to experienced surgeons who have been trained in the use of VeraSeal.

The surgeon will apply VeraSeal to the surface of blood vessels or to the tissue surface of internal organs using an application device during the course of the operation. This device allows equal amounts of the two components of VeraSeal to be administered at the same time, and ensures that they mix evenly, which is important for the sealant to work at its best.

The amount of VeraSeal that will be applied depends on a number of factors, including the type of surgery, the size of the area to be treated during your operation and the way VeraSeal is applied. The surgeon will decide how much is appropriate, and will apply just enough to form a thin, even layer. If it does not seem to be enough, a second layer can be applied.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

VeraSeal contains the component of fibrin sealant. Fibrin sealants may, in rare cases (up to 1 in 1,000 people), cause an allergic reaction. If you experience an allergic reaction you might have one or more of the following symptoms: swelling under skin (angioedema), skin rash, hives or wheals (nettle-rash), tightness of the chest, chills, flushing, headache, low blood pressure, lethargy, nausea, restlessness, heart rate increase, tingling, vomiting or wheezing. In isolated cases, these reactions may progress to a severe allergic reaction. Allergic reactions may especially be seen if the preparation is applied repeatedly, or administered to patients known to be allergic to constituents of the product. If you experience any of these symptoms after surgery, you should immediately consult your doctor or surgeon.

There is also a theoretical possibility that your immune system will produce proteins to attack VeraSeal and, that these may interfere with your blood clotting. The frequency of this type of event is not known.

If this product is accidentally placed inside a blood vessel, it can lead to blood clots, including disseminated intravascular coagulation (DIC) (when blood clots form throughout the blood vessels in the body). There is also a risk of a severe allergic reaction.

Side effects which were reported during clinical trials with VeraSeal included:

<u>Most serious side effects</u>

Uncommon (may affect up to 1 in 100 people):

- Abdominal (belly) abscess (swollen area in abdomen caused by infection)
- Abdominal (belly) wound dehiscence (wound breakdown due to incomplete healing)
- Leak of bile (a liquid produced by the liver) after the procedure
- Cellulitis (infection of the skin)
- Deep vein thrombosis (blood clots in the blood vessels)
- Liver abscess (swollen area in the liver caused by infection)
- Peritonitis (inflammation of the wall of the abdomen)
- Positive parvovirus B19 test (laboratory result showing infection with the virus)
- Postoperative wound infection
- Pulmonary embolism (blood clots in blood vessels in the lungs)
- Wound infection

<u>Other side effects</u>

Common (may affect up to 1 in 10 people):

- Nausea
- Pain caused by the surgery
- Pruritus (itching)

Uncommon (may affect up to 1 in 100 people):

- Anaemia (insufficiency of red blood cells)
- Anxiety
- Atrial fibrillation (irregular heartbeat)
- Back pain
- Bladder spasm
- Chills

- Conjunctival irritation (eye irritation)
- Constipation
- Contusion (bruise)
- Decreased urine output (reduced urine production)
- Dyspnoea (difficulty in breathing)
- Dysuria (pain or difficulty in urination)
- Ecchymosis (bruising)
- Erythema (reddening of the skin)
- Flatulence
- Headache
- High body temperature
- High or low blood pressure
- High or low levels of white cells in blood
- High potassium levels in blood
- Ileus (obstruction of the intestine)
- Impaired coagulation of blood
- Incision site erythema (reddening of the skin at the incision site)
- Incision site infection
- Increased blood bilirubin
- Increased levels of liver enzymes
- Increased or decreased glucose levels in blood
- Insomnia
- Low blood pressure due to the procedure
- Low calcium levels in blood
- Low magnesium levels in blood
- Low oxygen in blood
- Low potassium levels in blood
- Low protein levels in blood
- Low red blood cell levels caused by blood loss
- Low sodium levels in blood
- Oedema peripheral (accumulation of fluid)
- Pain, not specified
- Pain at the incision site
- Pain in extremity
- Plasma cell myeloma (cancer of blood cells)
- Pleural effusion (abnormal amount of fluid around the lung)
- Pleurisy (inflammation of lungs wall)
- Post procedural haemorrhage (bleeding after the procedure)
- Post procedural infection (infection after the procedure)
- Pulmonary oedema (excess of watery fluid in lungs)
- Retroperitoneal haematoma (accumulation of blood in the abdomen)
- Rhonchi (rattling lung sounds)
- Sleepiness
- Urinary retention
- Vascular graft complication (complication of vessel bypass)
- Vascular graft thrombosis (blood clots in blood vessel bypass)
- Ventricular tachycardia (rapid heartbeats)
- Vessel puncture site haematoma (bruising at site of vessel puncture)
- Vomiting
- Wheezing
- Wound secretion

Reporting of side effects
If you get any side effects, talk to your doctor or surgeon. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How VeraSeal is stored

VeraSeal must be kept out of the sight and reach of children.

This medicine must not be used after the expiry date which is stated on the label and carton after EXP.

It must be stored and transported frozen at -18 ºC or colder. The cold storage chain must not be interrupted until use. Keep the sterilized blister in the outer carton in order to protect from light. Thaw completely before use. Do not refreeze once thawed. After thawing, it can be maintained not more than 7 days at 2 ºC - 8 ºC or 24 hours not above 25 ºC before use.

Once the blister is opened, VeraSeal should be used immediately.

It must not be used if the solutions are cloudy or have deposits.

Discard if the package is damaged.

6. Contents of the pack and other information

What VeraSeal contains

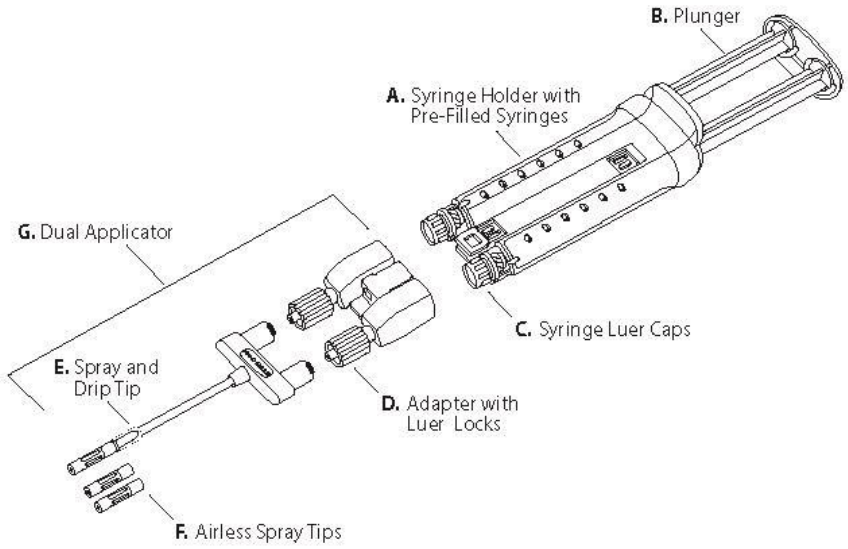
The active substances are:
- Component 1: Human fibrinogen
- Component 2: Human thrombin

The other ingredients are:
- Component 1: Sodium citrate dihydrated, sodium chloride, arginine, isoleucine, glutamic acid monosodium, water for injections.
- Component 2: Calcium chloride, human albumin, sodium chloride, glycine, water for injections.

What VeraSeal looks like and contents of the pack

VeraSeal is presented as solutions for sealant. It is supplied as a single-use kit containing two pre-filled syringes assembled in a syringe holder. Frozen solutions. After thawing the solutions are clear or slightly opalescent and colourless or pale yellow.

One Dual Applicator with two additional Airless Spray Tips is supplied with the product, for application by spraying or dripping. The Airless Spray Tips are radiopaque. See scheme below.



VeraSeal is available in the following pack sizes:
- VeraSeal 2 ml (containing 1 ml of human fibrinogen and 1 ml of human thrombin)
- VeraSeal 4 ml (containing 2 ml of human fibrinogen and 2 ml of human thrombin)
- VeraSeal 6 ml (containing 3 ml of human fibrinogen and 3 ml of human thrombin)
- VeraSeal 10 ml (containing 5 ml of human fibrinogen and 5 ml of human thrombin)

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing authorisation holder and manufacturer:
Instituto Grifols, S.A.
Can Guasc, 2 - Parets del Vallès
08150 Barcelona – Spain

This leaflet was last revised in 06/2024

The following information is intended for healthcare professionals only:

Posology and method of administration

The use of VeraSeal is restricted to experienced surgeons who have been trained in the use of this medicinal product.

The volume of VeraSeal to be applied and the frequency of application should always be oriented towards the underlying clinical needs for the patient.

The dose to be applied is governed by variables including, but not limited to, the type of surgical intervention, the size of the area and the mode of intended application, and the number of applications.

Application of the product must be individualised by the treating physician. In clinical trials, the individual doses have typically ranged from 0.3 to 12 ml. For other procedures, larger volumes may be required.

The initial volume of the product to be applied at a chosen anatomic site or target surface area should be sufficient to entirely cover the intended application area. VeraSeal should be applied as a thin layer. The application can be repeated, if necessary.

Incompatibilities

This medicinal product must not be mixed with other medicinal products.

Special precautions

For epilesional use only. Do not apply intravascularly.

Life threatening thromboembolic complications may occur if the preparation is unintentionally applied intravascularly.

When using accessory tips, the instructions for use of the tips should be followed.

Before administration of VeraSeal, care must be taken that the parts of the body outside the desired application area are sufficiently protected (covered) to prevent tissue adhesion at undesired sites.

VeraSeal should be applied as a thin layer. Excessive clot thickness may negatively interfere with the product's efficacy and the wound healing process.

Instructions for use

Read this leaflet before you open the package. Please see pictograms at the end of this leaflet.

Handling of VeraSeal

VeraSeal comes ready to use in sterilized packages and must be handled using sterile technique in aseptic conditions. Discard damaged packages as re-sterilisation is not possible.

An overview of thawing methods and storage after thawing is provided in Table 1.

Table 1. Thawing and storage after thawing

Thawing method	**Thawing time per package size**		**Storage after thawing**
	For 2 ml and 4 ml	**For 6 ml and 10 ml**	
Refrigerator (2 – 8 °C)	Minimum 7 hours	Minimum 10 hours	7 days at 2 - 8 °C (refrigerator) in original package OR 24 hours not above 25 °C in original package
Thawing at 20 - 25 °C	Minimum 70 minutes	Minimum 90 minutes	
Sterile water bath (37 °C) inside sterile field	Minimum 5 minutes. Do not exceed 10 minutes.	Minimum 5 minutes. Do not exceed 10 minutes.	Use immediately during the surgery

- **Preferred thawing methods**

  <u>Refrigerator thawing</u>

  1. Remove carton from freezer and place it in the refrigerator for thawing at 2 – 8 °C a minimum of 7 hours for the 2 ml and the 4 ml package sizes

a minimum of 10 hours for the 6 ml and the 10 ml package sizes

After thawing, it is not necessary to warm the product for its use.

After thawing, the solutions must be clear to slightly opalescent and colourless to pale yellow. Do not use solutions that are cloudy or have deposits.

Thawing at 20 ºC - 25 ºC
Remove carton from freezer, open it and take out the two blisters.
Place the blister containing the Dual Applicator on a surface at 20 ºC - 25 ºC until the fibrin sealant is ready to use.

Thaw blister with VeraSeal pre-filled syringes at 20 ºC - 25 ºC using the following steps:

1. Place the blister containing the syringe holder with pre-filled syringes on a surface at 20 ºC – 25 ºC
   a minimum of 70 minutes for the 2 ml and the 4 ml package sizes
   a minimum of 90 minutes for the 6 ml and the 10 ml package sizes

After thawing, it is not necessary to warm the product for its use.

After thawing the solutions must be clear to slightly opalescent and colourless to pale yellow. Solutions that are cloudy or have deposits should not be used.

Post-thawing storage

After thawing, the kit containing the VeraSeal syringe holder with pre-filled syringes and Dual Applicator can be stored before use for not more than 7 days in the refrigerator at 2 – 8 ºC or 24 hours not above 25 °C if it remains sealed in the original packaging. Once the blisters are opened, use VeraSeal immediately and discard any unused contents.

Once thawed, do not refreeze.

Transferring instructions

1. After thawing, remove the blister from the surface at 20 ºC - 25 ºC or from the refrigerator at 2 °C - 8 °C.
2. Open the blister and confirm that the VeraSeal pre-filled syringes are completely thawed. Make the VeraSeal syringe holder with pre-filled syringes available to a second person for transfer to the sterile field. The outside of the blister should not come in contact with the sterile field. See Figure 1.

- **Sterile Water Bath (Quick Thawing)**

Remove carton from freezer, open it and take out the two blisters.
Place the blister containing the Dual Applicator on a surface at 20 ºC - 25 ºC until the fibrin sealant is ready to use.

Thaw VeraSeal pre-filled syringes inside the sterile field in a sterile thermostatic water bath at a temperature of 37±2 ºC using the following steps:

NOTE: Once the VeraSeal blisters are opened, use the product immediately. Use sterile technique to avoid the possibility of contamination due to improper handling, and follow the steps below accurately. Do not remove the syringe luer cap until thawing is complete and the Dual Applicator is ready to be attached.

1. Open the blister and make the VeraSeal syringe holder with pre-filled syringes available to a second person for transfer to the sterile field. The outside of the blister should not come in contact with the sterile field. See Figure 1.
2. Place the syringe holder with pre-filled syringes directly into the sterile water bath ensuring that it is completely immersed in the water. See Figure 2.
3. At 37 ºC, the time needed is approximately 5 minutes for the 2 ml, 4 ml, 6 ml, and 10 ml package sizes, but must not be left at this temperature for longer than 10 minutes. The temperature of the water bath must not exceed 39 ºC.
4. Dry the syringe holder with pre-filled syringes after thawing, using a sterile surgical gauze.

Confirm that the VeraSeal pre-filled syringes are completely thawed. After thawing, the solutions must be clear to slightly opalescent and colorless to pale yellow. Do not use solutions that are cloudy or have deposits.

Use VeraSeal immediately and discard any unused contents.

- **Connection instructions**

1. Open the blister and make the VeraSeal Dual Applicator and two additional Airless Spray Tips available to a second person for transfer to the sterile field. The outside of the blister should not come in contact with the sterile field.
2. Hold the VeraSeal syringe holder with syringe luer caps pointed upward. See Figure 3.
3. Unscrew and discard the syringe luer cap of both fibrinogen and thrombin syringes. See Figure 3.
4. Hold the syringe holder with the luers pointed upward. To remove air bubbles from syringes, strike gently the side of the syringe holder one or two times while keeping the syringe holder in an upright position and lightly depress the plunger to eject air. See Figure 4.
5. Attach the Dual Applicator. See Figure 5.
   NOTE: Do not depress plunger during attachment or prior to intended use because the two biologic components will pre-mix in the Airless Spray Tip, forming a fibrin clot that prevents dispensing. See Figure 6.
6. Tighten luer locks and ensure the Dual Applicator is firmly attached. The device is now ready to use.

- **Administration**

Apply VeraSeal using the syringe holder and plunger supplied.

Apply VeraSeal using the Dual Applicator provided with the product. Other CE-marked applicator tips (including open surgery and laparoscopic use devices) intended for specific use with VeraSeal may also be used. When using the provided Dual Applicator, follow the connection instructions described above. When using other applicator tips, follow the instructions for use that are provided with the applicator tips.

<u>Application by spraying</u>

1. Grasp and bend the Dual Applicator to the desired position. Tip will retain its shape.
2. Position the Airless Spray Tip at least 2 cm away from the target tissue. Apply firm even pressure to the plunger to spray the fibrin sealant. Increase distance accordingly to achieve desired coverage of the target area.
3. If expression is stopped for any reason, change the Airless Spray Tip prior to resuming application since a clot may form inside the Airless Spray Tip. To change the Airless Spray Tip, remove the device from the patient and unscrew the used Airless Spray Tip. See Figure 7. Place the used Airless Spray Tip away from the spare Airless Spray Tips.

Wipe the end of the applicator using dry or moist sterile surgical gauze. Then, connect a new Airless Spray Tip provided in the package and ensure it is firmly connected before use.
NOTE: Red indicator will not be visible if Airless Spray Tip is properly connected. See Figure 8.
NOTE: Do not continue pushing the plunger in an attempt to clear the fibrin clot within the Airless Spray Tip; otherwise the applicator may become unusable.
NOTE: Do not trim the Dual Applicator to avoid exposing internal wire.

Application by dripping

1. Remove the Airless Spray Tip portion of the spray and drip tip by unscrewing the Airless Spray Tip. See Figure 7.
2. Grasp and bend the drip tip to the desired position. Tip will retain its shape.
3. During dripping, keep the end of the drip tip as close to the tissue surface as possible without touching the tissue during application.
4. Apply individual drops to the surface area to be treated. To prevent uncontrolled clotting, allow the drops to separate from each other and from the end of the drip tip.
   NOTE: Do not reconnect a used drip tip after it has been removed from the adapter; otherwise a clot may form inside the drip tip and the applicator may become unusable.

- **Disposal**

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Figure 1

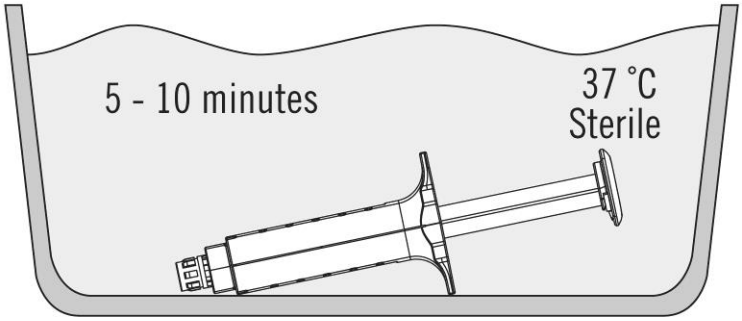


Figure 2

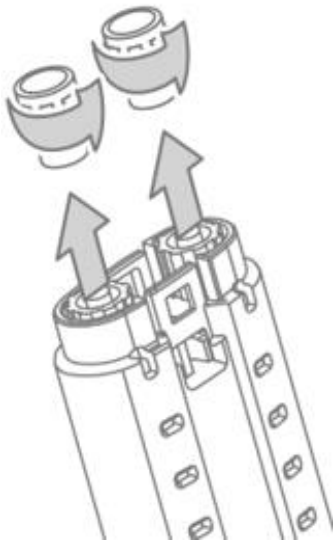


Figure 3

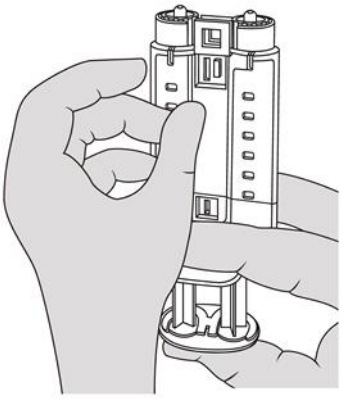


Figure 4

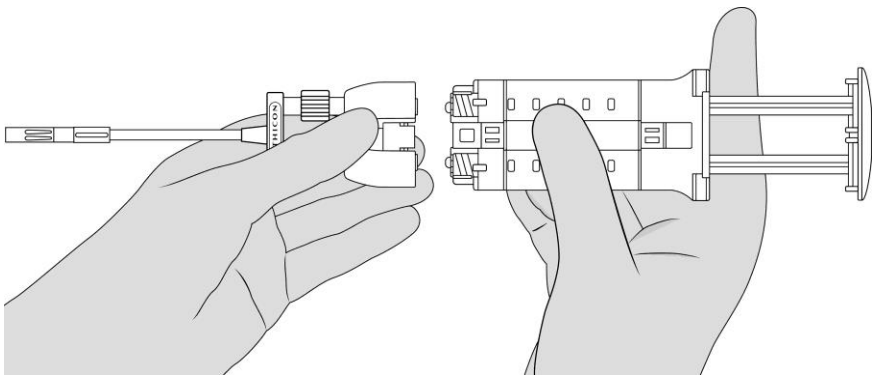


Figure 5

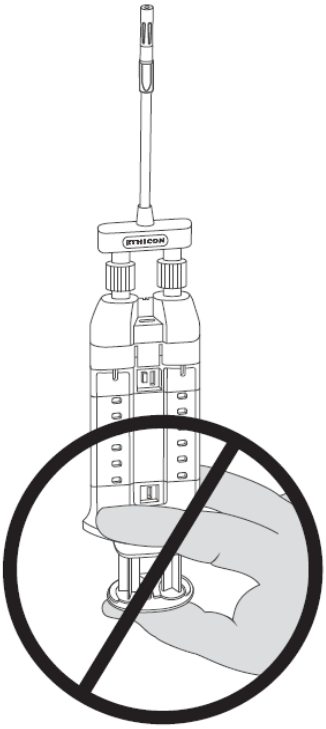


Figure 6

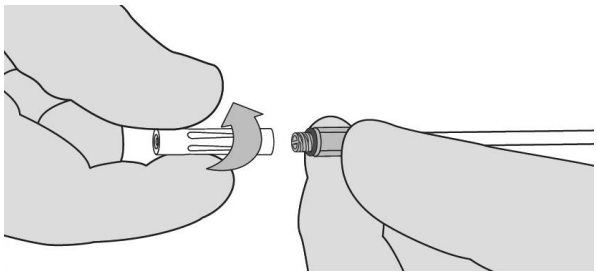


Figure 7

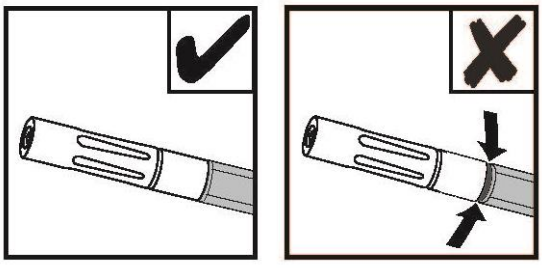


Figure 8