Nerve FAQ Sheet

Product Specific

1. What exactly is it that allows NeuraGen® Nerve Guide to be compression resistant and maintain its shape, even after being hydrated? (This also answers questions regarding kink resistance and elasticity).
   The wall of the tube is spun out of a collagen dispersion to create counter helical windings of collagen fibers that emulate the structure of the perineurium. These fibers are heavily cross-linked with formaldehyde that creates elastic properties similar to those found in artery walls.

2. What is the thickness of Integra wraps/conduits?
   The exact thicknesses are controlled in manufacturing, but are approximately 0.5 mm.

3. When hydrating NeuraGen, what temperature should the saline be? Is there a suture recommendation?
   Room temperature sterile saline or Lactated Ringer’s solution should be used. Depending on the size of the nerve and surgeon preference, atraumatic 8-0, 9-0, 10-0 and 11-0 sutures should be used.

4. What is the reasoning behind the smooth inner lumen and is this where the fibrin clot forms?
   The inner lumen is where the fibrin clot forms. NeuraGen is spun out of a collagen dispersion onto a mandrel. The mandrel surface is smooth and that is what makes the inner lumen of the conduit smooth. The smoother inner wall of the NeuraGen Nerve Guide prevents escape of larger molecules, such as nerve growth factors, which are sequestered within the tube to support an optimal environment for natural nerve regeneration.

Procedure Specific

1. What is the overlap on the wraps? 1 or 2 mm? If you only have tubes and the nerve is 3 mm, do you use a 4 mm tube only to turn into a wrap or could you use the 4 mm to 6 mm?
   Oversized tubes can be used to wrap the nerve. Either size would be sufficient.

2. If a longer wrap is needed, such that you need 2 side by side on a nerve, do you suture them together? And if so, with an absorbable suture then?
   The two wraps should not be sutured together but implanted individually end to end.

3. How far (mm) do you pull each nerve stump into the conduit when there is a gap?
   The instructions for how to suture the nerve stumps into the tubes are illustrated in the package insert. The insert states that the suture should pass through the conduit at least 1 mm from the end of the nerve guide and transversely through the epineurium of one nerve stump at a distance from the cut nerve face at least equal to the diameter of the nerve.

4. If the conduit is hydrated in saline for more than 10 minutes, will it damage the conduit?
   No, NeuraGen is cross-linked, allowing the conduit to maintain its structure, even when hydrated for longer than 10 minutes. It is recommended that the conduit be hydrated as close to the time of implantation as possible.

5. Do I have to suture the wrap to the epineurium? Do I have to put a running stitch down the wrap? Will the epineurium try to close on its own and stay in place?
   You can suture it, but it is not entirely necessary. The preference is to use as little suture material as possible to avoid formation of scar tissue and lack of migration. Wrapping the epineurium may give all the benefits of protection however, there have not been any clinical or animal studies on nerve wrap effectiveness with sutures.
Competition Based

1. **Axogen® is promoting that the conduit becomes the mesoneurium. Is this true?**
   Mesoneurium is a correct term but is not used very often. It consists of very loose tissue that make up the outer layers of the connective tissue of the epineurium and allows for gliding of the nerve trunk in its bed.

2. **How does your conduit’s data compare to your competitor(s)?**
   NeuraGen Nerve Guide is the first collagen nerve guide to be introduced and is the result of 17 years of research and development aimed at creating an optimized Schwann cell regeneration chamber that would become a living conduit after implantation. No other conduit is composed of Ultra Pure Collagen™. There is extensive rodent, primate and clinical data showing that NeuraGen Nerve Guides perform to the same level as direct suture.

3. **How is Integra’s conduit different from Axogen AxoGuard™?**
   NeuraGen is composed of Integra’s Ultra Pure Collagen material, comes in more sizes than any other conduit on the market, and has extensive supporting published data.

4. **Why is NeuraGen produced in a cylindrical shape and not an hourglass shape?**
   NeuraGen is made of Ultra Pure Collagen and is cross-linked, allowing it to maintain its structure as the nerve regenerates.

5. **How does the environment our conduit “produces” within the chamber differ from the environment within Axoguard?**
   NeuraGen is designed to keep the pro-NGF in the tube and also allow smaller molecules (other growth factors in the wound bed) to freely exchange.

Scientific Processes

1. **Does the epineurium regeneration occur within the normal regeneration process within the conduit or does a portion of the conduit “create” a new epineurium?**
   The new perineurium and epineurium form within the conduit. The conduit allows for revascularization during the regenerative process but is completely resorbed. Some residual tissue may contribute to the diffuse outer layers of the epineurium, but we do not have a specific study on this.

2. **Is there a nerve density drop-off as nerves regenerate within the conduit? Either in human or animal testing, is there a “critical length” where we see a drop-off that would have a negative clinical impact on the outcome for the patient?**
   The “critical gap” is controlled by the time it takes for the fibrin clot to break down within the nerve guide. If the nerve gap has not been bridged before fibrinolysis (10-15 days in humans), then there is a significant reduction in the number of axons bridging the defect. However, this gap is somewhere between 2 cm and 5 cm in humans. NeuraGen Nerve Guides are deliberately designed for nerve repair in short gap repairs.

3. **What is the purpose of performing a saline flush? (ie, removing any dry blood particles or debris? Hydrating the inner lumen?)**
   The purpose of performing a saline flush is to remove any air bubbles in the tube lumen.

4. **Why do Schwann cells bind to walls of our tubes and not other tubes? Or do they bind to other tubes?**
   The fibrin clot that binds to the wall of a Type 1 Collagen tube allows the Schwann cells to migrate along the inner lumen of the collagen tube.
Evidence

1. Do we have any images of nerves repaired with NeuraGen, (in either rat, primate, or human) that show the nerve once regeneration has occurred and the collagen is resorbed?
   The best pictures we have of a regenerated nerve trunk are from the NeuraGen 3D rat study completed a few years ago. The primate studies were not photographed; however, at about 4 years post repair, the nerve looked completely normal in the 5 mm and 20 mm gap repairs. Obtaining photos of regenerated nerves in patients is nearly impossible, as the only time we would be able to obtain photos is during care of an adverse event that we have been made aware of. If there are no complications following the repair, there is no need to reopen the repair site.

2. Is there any evidence of our conduit/wrap sticking around for the 9-12 months that we advertise?
   We do not currently have any studies that demonstrate this specifically. However, the 9-12 months is based on anecdotal evidence from surgeons who have re-explored the repair and found that the conduit was no longer there by this time.

3. Are there any plans to do any competitive studies in humans?
   No, not currently.

NeuraGen® Nerve Guide
Indications For Use
NeuraGen Nerve Guide is indicated for the repair of peripheral nerve discontinuities where gap closure can be achieved by flexion of the extremity.

Contraindications
NeuraGen is not designed, sold or intended for use except as described in the indications for use and are contraindicated for patients with a known history of hypersensitivity to bovine-derived materials.