University of Virginia Health System
Investigational Device Fact Sheet

Protocol Title: HSR 19530: Efficacy and Safety of LifeSeal kit for Staple Line Sealing in Colorectal and Coloanal Anastomoses: A Prospective Randomization Study (Protocol #: CLP-LS-0131, Rev 05)

NOTE: *THIS INFORMATION IS FOR CONFIDENTIAL REVIEW BY HOUSESTAFF AND NURSES ADMINISTERING INVESTIGATIONAL DRUGS*

DEVUCE NAME AND SYNONYMS: LifeSeal Surgical Sealant

DEVICE FORM(S) AND STRENGTH(S): LifeSealTM Kit is supplied as a single use system consisting of two separate packages:

- A cartridge that accommodates 2 prefilled syringes: porcine Gelatin solution (supplied in a capped Luer cone 5mL syringe) and microbial Transglutaminase stabilizer solution (supplied in a capped Luer cone 3mL syringe). The exterior surface of the syringes and the syringe carrying cartridge are provided non sterile.

USUAL DOSE RANGE, SCHEDULE AND ROUTES OF ADMINISTRATION: The maximum allowed dose of LifeSeal™ surgical sealant is up to two units of LifeSeal™ surgical sealant per study subject. The two units are for single patient use only. The safety profile of two units of LifeSeal™ Surgical Sealant has been comprehensively assessed and confirmed in animal studies. In addition, 3 out of the 35 subjects treated with LifeSeal™ Surgical Sealant in the pilot clinical study, were treated with 2 units of sealant and no adverse event that seem to be related to the use of the 2 units was noted. In terms of performance, two units are sufficient to cover both circular and linear staple lines.

OBJECTIVE: This study is designed to demonstrate superiority of LifeSeal to the control with respect to the leakage rate; the LifeSeal group leakage rate must be lower than standard of care group (without LifeSeal).

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STUDY COORDINATOR: Amy Harrigan, CRA

PROTOCOL DESIGN: Randomized, Single Blind

PROTOCOL DOSAGE RANGE: Subjects randomized to LifeSeal Kit will have it applied during surgery. The maximum allowed dose of LifeSeal Kit is up to two units per study subject. Units are for single patient use only.

PHARMACOLOGY: LifeSeal surgical sealant is delivered in a cartridge consisting of two prefilled syringes one with gelatin solution (5ml) and one with enzyme (PEGylated purified mTG) solution (2.7ml).
The Gelatin component is a liquid solution supplied in a syringe. Composed of medicalgrade type A porcine gelatin, and buffer excipients that keep the gelatin solution in a liquid state.
The Enzyme component is a liquid solution supplied in a pre-filled syringe. The solution is comprised of purified microbial Transglutaminase (mTG), along with buffer salts and stabilizing excipients.
The polymerization process starts when the two liquid solutions are mixed and this forms a clear, robust and flexible sealing gel.
Sealant Cartridge with the gelatin and enzyme components
Both the enzyme and the gelatin solutions are produced under aseptic conditions and supplied pre-packed in a cartridge to be loaded into the delivery system.

PROJECTED PLACE IN THERAPY: LifeSeal is intened to be used as an adjunct to stapled colorectal or coloanal anastomosis to provide reinforcement and help reduce leaks.

ADVERSE EFFECTS: Most commonly reported AEs reported for LifeSeal treatedand control subjects (occurring above 10%) are summarized below:

- Vomiting
- Abdominal Pain
- Pyrexia
- GI Stoma Complication
- Anastomotic leakage
- Post Opertive Ileus
- Nausea
- Diarrhea
- UTI

Potential Risks may include:

- Allergic reaction to porcine derived gelatin or collagen
- Allergic reaction to PEGylated microbial Transglutaminase
- Anaphylactic reation
- Infection
- Anastomotic Leakage
- Intra-abdominal abscess
- Adhesions
- Fistula
- Fecal Contamination
- Decreased Bowel motility (prolonged Ileus, bowel obstruction)
- Staple Line Bleeding
- Blood Coagulation abnormalities
- Dehydration and high output from stoma
- Strictures

CONTRAINDICATIONS: LifeSeal is contraindicated for subjects who have a history of hypersensitivity to porcine derived gelatin/collagen, microbial Transglutaminase, anyone who has been previously treated with LifeSeal Sealant, women who are pregnant, breastfeeding, or if of child bearing potential and is unwilling to practice birth control until 3 years following surgery. And should not be implanted in subjects with an active abdominal or pelvic infection at the operative site. Should not be used in subjects with known firinogenimeia, hypofibrinogenemia or dysfibrinogenemia, without preoperative correction of fibrinogen levels. See instructions for use for additional contraindications.

ADMINISTRATION AS PER STUDY: LifeSeal™ should be warmed to 24□C±1□C in an incubator for at least 8 hours prior to application. The time and date at which warming started should be noted on the package of the sealant. Two units of LifeSeal™ Surgical Sealant should be ready in a warm state prior to the initiation of a study operation on a new subject.

The first unit of LifeSeal™ Kit will be used to cover the circular staple line first and then the linear staple line (if applicable). The second unit of LifeSeal™ may be used in case of a positive intra-operative leak to cover the new anastomosis in case of anastomosis re-do or to cover the leak site (this is further described in the section " Intra-operative leak Test of Anastomotic Integrity" below). In case of a negative leak test, the second unit of LifeSeal™ Kit may be applied selectively, according to surgeon's discretion, if there are remaining uncovered staple lines.

Note: Only for side to end anastomosis in open procedures- the application should start with the linear staple line. If feasible, the same unit of LifeSeal™ Kit should be used to continue the application on the circular staple line. In case it is not feasible to use the first unit to cover the circular staple line after the linear staple lines have been covered (due to the limitation to use the sealant within 30 min after it has been taken from the warming conditions), then a second unit will be used for the application on the circular staple line. In such a case, no additional unit is available to treat a scenario of positive intra-operative leak test. Therefore, efforts should be made to cover both linear and circular staple-line with the first unit of LifeSeal™ Kit.

After sealant has been applied, it should be allowed to polymerize: 2 min after application sealant should be rinsed with saline and then another min is required for the sealant to complete the polymerization.

STORAGE AND STABILITY: Intact kits should be stored under refrigeration. LifeSeal™ Surgical Sealant should be warmed to 24±1 ^{0}C and held at that temperature for at least 8 hours and not more than 2 weeks before the surgical procedure (see product IFU for details). “Date of warming” and “Time” (time of warming) should be recorded on the designated label on the sealant’s box to confirm tracking and usage within two weeks. Unused product will be destroyed after surgery. Do not re-refrigerate. Do not microwave. Do not use after 2 weeks in the incubator.

COMPATABILITIES: Do not mix with other products

HAZARDOUS DRUG: No

DRUG INTERACTIONS, IF KNOWN: Do not use in subjects who have had Avastin in the previous 30 days.

PLEASE RETURN ALL UNUSED DOSES TO THE INVESTIGATIONAL PHARMACY

FOR QUESTIONS, CONTACT THE STUDY COORDINATOR, THE CLINICAL PHARMACIST, OR THE INVESTIGATIONAL DRUG PHARMACIST PIC 1925