# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

**Device Generic Name:** Sealant, Dural

**Device Trade Name:** SpineSeal Spine Sealant

**FDA Product Code:** NQR

**Applicant's Name and Address:** Pramand, LLC
201 Burlington Road, Suite 210
Bedford, MA 02420

**Date(s) of Panel Recommendation:** None

**Premarket Approval Application (PMA) Number:** P240027

**Date of FDA Notice of Approval:** February 14, 2025

## II. INDICATIONS FOR USE

The SpineSeal Spine Sealant System is indicated for use as an adjunct to sutured dural repair during spinal surgery to provide watertight closure.

## III. CONTRAINDICATIONS

Do not apply the SpineSeal Spine Sealant to confined bony structures where nerves and spinal cord are present since neural compression may result due to hydrogel swelling. The hydrogel may swell up to 12% of its size in any direction.

## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the SpineSeal Spine Sealant labeling.

## V. DEVICE DESCRIPTION

The SpineSeal Spine Sealant consists of components for preparation and delivery of an absorbable polyethylene glycol (PEG) hydrogel sealant and an applicator (i.e. a Y connector and spray tips) packaged sterile for single patient use. The device is available in a 5mL configuration.

The SpineSeal Spine Sealant is composed of two solutions, a PEG ester solution and a Trilysine amine solution which are referred to as the “blue” and “clear” precursors, respectively. When mixed, the precursors rapidly polymerize *in-situ* to form the hydrogel sealant. The mixing of the precursors occurs in the applicator as the hydrogel material exits the spray tip. The applicator (i.e., Y-connector and spray tip) allows a conformal coating that adheres to the tissue surfaces. The mixing provided by the applicator also ensures a complete reaction of the precursors. The polymerization requires no external energy requirements, such as light or heat, and takes place by a nucleophilic substitution reaction. The PEG component contains hydrolysable ester bonds which enable the hydrogel to be degraded through hydrolysis after application. FD&C Blue no. 1 provides the color of the blue solution and enables the user to discern the thickness of the hydrogel layer and the area of hydrogel application. The gel swells, no more than 12% of its size in any direction. For a 2 mm thick hydrogel that isotropically swells 12%, the maximum linear dimensional change in any direction is <1 mm. minimal heat evolution occurs during the polymerization reaction.

The cross-linked solid hydrogel is more than 90% water at application. Due to this high-water content, the hydrogel has physical properties like tissue. The hydrogel implant is absorbed in approximately 9 to 12 weeks and the absorbed hydrogel components are excreted from the body. The SpineSeal Spine Sealant can be used for up to one hour following reconstitution. **Figure 1** provides an overview diagram of the SpineSeal Spine Sealant.

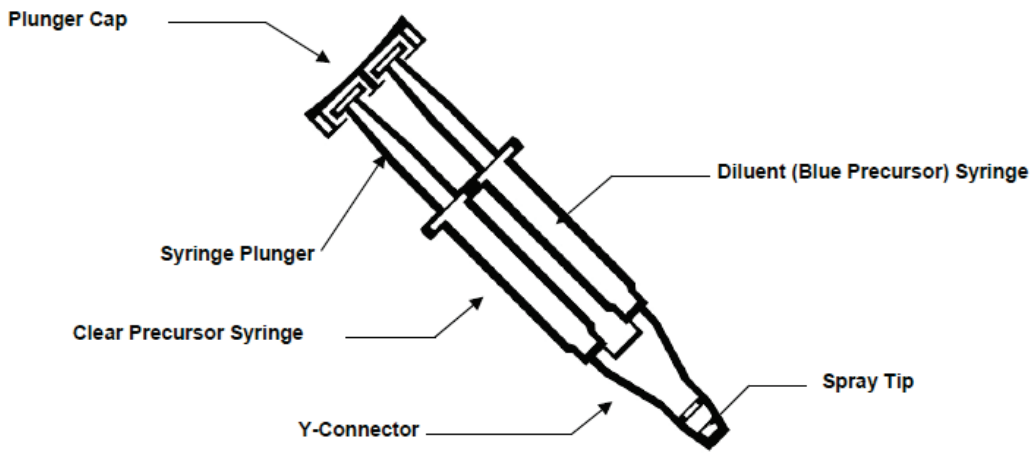


**Figure 1:** Assembled SpineSeal Spine Sealant

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of dural repair that consist of the direct application of sutures or the use of sutures with adjunctive dural repair materials such as commercially available dural sealants, fibrin glue/sealant, absorbable gelatin or collagen sponge, autologous muscle, temporalis fascia, fascia lata, pericranium, ligamentum nuchae or fat grafts. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

## VII. MARKETING HISTORY

The SpineSeal Spine Sealant has not been commercialized in the United States or any foreign country.

## VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device, but are not limited to the following:

- Allergic reaction
- Blood and lymphatic system disorders
- Cardiac disorders
- Dermatologic events
- Gastrointestinal disorders
    - Nausea and/or vomiting
- General disorders
    - Delayed healing
    - Wound dehiscence
- Hematologic abnormality
- Infections and infestations
    - Deep incisional surgical site infections
    - Superficial surgical site infections
    - Meningitis (aseptic or bacterial)
    - Late incisional surgical site infections
- Inflammatory reaction
- Musculoskeletal events
- Neoplasms benign and malignant, including cysts and polyps
- Nervous system disorders
    - Acute gait dysfunction
    - Epidural hematoma
    - Headache
    - Seizure
    - Cerebral hemorrhage
    - CSF leak

- Double vision
- Hydrocephalus
- Cerebral edema
- Brain tumor
- Severe neurological deficit post-op
- Respiratory and thoracic disorders
- Leakage of cerebrospinal fluid

- Renal compromise

## IX. SUMMARY OF PRECLINICAL STUDIES

### A. Laboratory Studies

1. Sterilization

The SpineSeal Spine Sealant is sterilized by E-beam sterilization, which was validated in accordance with ANSI/AAMI/ISO 11137, "Sterilization of health care products – Requirements for validation and routine control – Radiation sterilization," and EN552, "Sterilization of medical devices – Validation and routine control of sterilization by irradiation," to achieve a sterility assurance level of at least $10^{-6}$.

2. Shelf Life

A 15-month shelf life was established based on results from real-time (65 weeks) test evaluations for 105 SpineSeal Spine Sealants from 2 product lots. The real-time and accelerated age devices were tested for the following attributes: visual assessment, hydrogel performance, and packaging integrity.

3. Biocompatibility

Biocompatibility testing was performed on the SpineSeal Spine Sealant device as one system. All hydrogel samples evaluated in biocompatibility tests were prepared using the device components supplied, in accordance with the Instructions for Use labeling. Additional studies evaluated the SpineSeal delivery system (i.e., applicator, spray tips and plunger cap) for biocompatibility.

Biocompatibility testing (**Table 1**) of the formed SpineSeal Spine Sealant hydrogel has been performed consistent with the Good Laboratory Practices regulations (21 CFR §58) and the FDA guidance, "Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process"." The biocompatibility testing conducted is based on the SpineSeal Spine Sealant hydrogel defined as a tissue/bone contacting implant of permanent contact duration.

**Table 1: Summary of SpineSeal Spine Sealant System Biocompatibility Tests**

| Test Reference | Method Reference | Results |
|---|---|---|
| Cytotoxicity (ISO Elution Method) | International Organization for Standardization: (ISO) 10993-5, "Biological evaluation of medical devices, Part 5, Tests for in vitro cytotoxicity | Non-cytotoxic |
| ISO Modified Intracutaneous Study | ISO 10993-10, "Biological evaluation of medical devices - Part 10: Tests for skin sensitization | No evidence of significant irritation |
| ISO Maximization Sensitization Study (Guinea Pigs) | ISO 10993-10, "Biological evaluation of medical devices - Part 10: Tests for skin sensitization | Non-sensitizing |
| USP and ISO Modified Systemic Toxicity | ISO 10993-11, "Biological evaluation of medical devices - Part 11: Tests for systemic toxicity" | No mortality or systemic toxicity |
| USP Pyrogenicity<br>(Endotoxin Testing: <2.15 Endotoxin Units (EU)/Device Limit) | Guidance for Industry: Pyrogen and Endotoxins Testing: Questions and Answers | Non-pyrogenic |
| USP Pyrogenicity<br>(Material Mediated Pyrogenicity) | International Organization for Standardization: Biological Evaluation of Medical Devices, Part 11, 10993-11: *Tests for Systemic Toxicity* | Non-pyrogenic |
| Genotoxicity (Bacterial Reverse Mutation Assay) | ISO 10993-3: "Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity, and reproductive toxicity" | Non-mutagenic |
| Micronucleus Cytogenic Assay in Mice | ISO 10993-3: "Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity, and reproductive toxicity" | No clastogenic activity |
| ISO Muscle Implantation Study (4,8 and 13 weeks) | ISO 10993-6: Biological Evaluation of Medical Devices, Part 6: Tests for Local Effects after Implantation | Equivalent to DuraSeal Exact Sealant. Slight irritant compared to HDPE Control |
| | | Equivalent to DuraSeal Exact Sealant. |

| Test Reference | Method Reference | Results |
|---|---|---|
| | | Slightly irritant compared to HDPE Control |
| | | Equivalent to DuraSeal Exact<br><br>Non-Irritant |
| In Vitro Hemolysis (Modified ASTM-Direct Contact Method) | ISO 10993-4: "Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood | Slightly hemolytic* |

*The SpineSeal Spine Sealant and DuraSeal Exact Spine Sealant were evaluated for In Vitro Hemolysis via Modified ASTM – Direct Contact Method and found to be slightly hemolytic. The FD&C Blue #1 colorant found in both products was readily soluble in the centrifugation supernatant, potentially exacerbating the results from the absorbency reading and therefore affected the determination of the hemolytic response. Any impact from the blue coloring of the supernatant would have increased the absorbency of the supernatant during testing and increased the average blank corrected % hemolysis. For this reason, the results were determined to reflect a worse-case scenario, and the SpineSeal Spine Sealant tested with equivalent results to the existing commercial DuraSeal Exact Spine Sealant.

4. Bench Studies

A series of in vitro tests were performed on the components and materials of the SpineSeal Spine Sealant (final, sterilized devices). In addition to the studies identified in **Table 2**, environmental testing was performed to assure that the product is not affected by temperature extremes during storage and transport or a maximum irradiation dose.

**Table 2: Summary of In Vitro Product Testing – SpineSeal Spine Sealant**

| Design Characteristic | Test Description | Results |
|---|---|---|
| Gel Time and Pot Life | Test evaluates the time it takes for a hydrogel to form when the two precursor components are mixed (gel time), and 1 hour after reconstitution of the blue precursor with buffer (pot life). | Upon mixing precursors, a gel is formed in ≤ 3.5 seconds. |
| Swelling | Evaluates the percent weight gain resulting after a 24-hour immersion of the hydrogel in 37 °C phosphate buffered saline (PBS). | In-vitro gel swelling is ≤ 50% |
| In Vitro Absorption - Disappearance | Hydrogel time of dissolution when placed in PBS at 60.4 °C. | SpineSeal Spine Sealant hydrogel is visibly dissolved in 1.3 to 6 days after immersion into PBS, pH 7.4, at 60.4 °C. |
| Gel Application – Pressure Integrity | Test evaluates the mechanical joints of the applicator to ensure that the device is sufficiently robust to withstand anticipated use. | Applicators did not leak or fail when pressurized to 68 psi for a minimum of 4 seconds. |
| Uniform Gel Application | Evaluates proper function of the applicator and mixing of the precursors to the target area to assure uniform sealant application. | Applicator disperses gel in a pattern < 10 mm diameter when spray tip is 2-4 cm from target tissue. |
| Reconstitution | Upon mixing powder and diluent, the dissolution time shall not exceed 5.0 minutes. | The diluent syringe is mixed with PEG vial to create Blue Precursor and time of PEG dissolution is measured. |

## B. Animal Studies

Because the design and product specifications for the SpineSeal Spine Sealant are the same as for the commercialized DuraSeal Exact Spine Sealant approved under PMA P080013, the SpineSeal Spine Sealant in vivo testing plan did not repeat all animal studies conducted for the DuraSeal Exact Spine Sealant. A confirmatory ovine laminectomy with dural defect study to evaluate local tissue reaction and neurological effects of the SpineSeal Spine Sealant and the DuraSeal Exact Spine Sealant was completed. In this study, SpineSeal Spine Sealant is the test treatment and DuraSeal Exact Spine Sealant treatment serves as the control.

1. Ovine Laminectomy Study Methods

The study was performed in 24 female sheep in which an approximate 1cm incision was made in the dura mater overlying the L2/3 intervertebral disc to expose the spinal cord. The dural defect was closed using absorbable suture material. The test material, SpineSeal, or commercial control, DuraSeal Exact Spine Sealant was formulated and applied directly to the suture line of the dura and the seal was assessed using a Valsalva maneuver. SpineSeal and DuraSeal Exact Spine Sealant resorption profiles were evaluated at necropsy, including the external surface of the body, all orifices, the oral, thoracic, abdominal, and pelvic cavities, and their contents was performed. Histology assessments were conducted at 2, 6, and 14 weeks and compared with those of the DuraSeal Exact Spine Sealant.

Histopathology assessments supported the safety of the SpineSeal Spine Sealant. The SpineSeal Spine Sealant was shown to have a biologically equivalent response to the commercially available, DuraSeal Exact Spine Sealant configuration in the dural defect ovine laminectomy model. At all-time points (2, 6 and 14 Weeks), there were no significant adverse findings associated with the test or control articles in the systemic tissues evaluated.

Results from the completed animal study indicate that the SpineSeal Spine Sealant device meets safety and performance specifications for absence of CSF leak at treatment site following dural defect with suturing. No difference was noted between the SpineSeal and DuraSeal Exact Spine Sealant products by the study surgeon.

## C. Additional Studies

1. Dye Toxicology Evaluations

The SpineSeal Spine Sealant, like the PMA approved DuraSeal Exact Spine Sealant (P080013), contains FD&C Blue #1 colorant for visualization of the hydrogel during application to the identical specification detailed in the SSED for the DuraSeal Exact Spine Sealant device. The colorant is a certified color listed in 21 CFR 82 and it has been approved for use in foods (21 CFR 74.101), drugs (21 CFR 74.1101) and cosmetics (21CFR 2101). The determination that the colorant is not present in the body for a significant amount of time is directly applicable to the SpineSeal Spine Sealant, because the same volume and concentration of FD&C Blue #1 is used in both the SpineSeal Spine Sealant and the DuraSeal Exact Spine Sealant, and the two devices have the same design and chemical specifications. Therefore, no new studies were performed related to the dye toxicological profile for the SpineSeal Spine Sealant as the prior studies conducted on the commercialized DuraSeal Exact Spine Sealant is applicable to the subject device.

FD&C Blue #1 is water soluble and has been evaluated in life-exposure animal studies in the PMA (P080013) of the DuraSeal Exact Spine Sealant that determined an acceptable daily intake (ADI) for the colorant of 12 mg/kg/day. Calculations comparing the amount of colorant absorbed by ingestion, and the amount of colorant a patient will be exposed to in one application of the DuraSeal Exact Spine Sealant, indicate that the absorbed amount of ingested colorant would be much greater. *In vitro and in vivo* determinations found low microgram/mL concentrations after 9 hours of elution from polymerized hydrogel in a saline bath or undetectable amounts (low microgram detection sensitivity) of the colorant at 7 – 8 days, post-implantation in a dog model. The colorant was determined to not be present in the body for a significant amount of time.

## X. SUMMARY OF CLINICAL STUDIES

The SpineSeal Spine Sealant has not been the subject of a published clinical study. Pramand, LLC is relying on the "six-year rule" as described in Section 216 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) and the FDA guidance, "Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997," to use the clinical data supporting a previous PMA application of the DuraSeal Exact Spine Sealant (P080013) approved on September 4, 2009. Following approval of PMA P080013, the hydrogel formulation for the DuraSeal Exact Spine Sealant System was modified and the name of the device was changed to DuraSeal Exact Spine Sealant, the current commercial configuration. In consideration of the PMA approval of DuraSeal Exact Spine Sealant, reasonable assurance of safety and effectiveness of the subject SpineSeal Spine Sealant is supported because the two devices have the same chemical specifications and design. The safety and effectiveness of the original DuraSeal Exact Spine Sealant (P080013) was primarily supported by one US pivotal study conducted in the United States (US). The details of the pivotal study are provided in the SSED for P080013 which is available on the CDRH website and incorporated here by reference. The safety and effectiveness of the DuraSeal Exact Spine Sealant was confirmed in a post-approval study (PAS) that was required as a condition of approval of the formulation change which was also considered in support of the SpineSeal Spine Sealant. A brief overview of this post-approval study is presented below.

### ***DuraSeal Exact Spine Sealant Post-Approval Study***

#### A. Study Design

A prospective, multi-center, non-randomized, two-arm, post-approval study was performed to evaluate the safety and efficacy of the DuraSeal Exact Spine Sealant for spinal dural repair, when used as an adjunct to suture dural repair, as

compared to current methodologies (Control) for producing a watertight dural closure reflecting a real-world practice. This literature was published in 2019 (Kim KD, Ramanathan D, Highsmith J, et al. DuraSeal Exact Is a Safe Adjunctive Treatment for Durotomy in Spine: Post approval Study. Global Spine Journal. 2019;9(3):272-278. doi:10.1177/2192568218791150). This study was designed to evaluate incidence of postoperative CSF leak and adverse events in patients receiving DuraSeal Exact Spine Sealant for treatment of intentional or incidental durotomies, and to compare that to the corresponding rates of alternative dural repair adjuncts. The study involved 36 sites within the United States. A total of 924 subjects were enrolled, including 489 subjects treated with the DuraSeal Exact Spine Sealant, and 435 subjects treated with all other modalities in the control arm. The subjects meeting study criteria were enrolled either prospectively or retrospectively in the control arm. Sites were not required to enroll in both study arms. The number of subjects completing the study was 429 in the DuraSeal Exact Spine Sealant treatment arm and 406 in the control arm.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment from the DuraSeal Exact Spine Sealant post-approval study was limited to patients who met the following inclusion criteria:

   Inclusion Criteria

   - Patient is 18 years of age or older.
   - Patient had a spinal procedure where a dural opening (either intentional or incidental) occurred and was treated with either:
   - DuraSeal Exact Spine Sealant (DuraSeal Sealant group only) or
   - Any other method of sealing the dura with the exception of DuraSeal Sealant - either spinal or cranial. (Control group only)
   - Subject, or authorized representative, has been informed of the nature of the study and has provided written informed consent approved by the appropriate Institutional Review Board (IRB) of the respective clinical site prior to the collection of study data.
   - Prospective subjects: Consent must be obtained within 24 hours of surgery stop time.
   - Retrospective subjects (Control group specific): IRB approval may be granted to individual sites to waive requirement for informed consent.

   Exclusion Criteria

   - The investigator determines that the subject will not be able to comply with the required follow-up visits (not required if subject is being enrolled retrospectively- control group ONLY)
   - Pregnant or breastfeeding females (as documented in the medical records; no testing beyond the site's standard of care is required)

2. Follow-Up Schedule

The DuraSeal Exact Spine Sealant treatment arm consisted of subjects who underwent a spinal procedure where DuraSeal Exact Spine Sealant was administered, in addition to any other methods of dural closure. Eligible subjects were enrolled prospectively within 24 hours after completion of the spine surgery. The control arm consisted of subjects who underwent a spinal procedure where the standard of care other than DuraSeal Exact Spine Sealant was administered. The subjects meeting study criteria were enrolled either prospectively or retrospectively in this arm. Sites were not required to enroll in both study arms.

The study consisted of 2 study visits: a screening visit/baseline data collection and a 90-day postoperative follow-up visit (±30 days). The follow-up included a physical examination, complete neurologic examination, and wound healing evaluation. Any reported adverse events were documented.

3. Clinical Endpoints

The primary endpoint of the study was the occurrence of postoperative CSF leak within 90 days after spine surgical procedure. A CSF leak was defined as a CSF fistula or a pseudomeningocele confirmed by clinical examination or diagnostic testing (i.e., magnetic resonance imaging (MRI) or computed tomography (CT)), whether treatment such as surgical repair or drainage was required. The secondary endpoints of the study were the occurrence of deep surgical site infection (DSSI) and neurological serious adverse event (SAE) within 90 days after the surgical procedure. Serious adverse events included, but were not limited to, those leading to a life-threatening illness or injury or those that required inpatient hospitalization.

## B. Accountability of Post-Approval Study Cohort

Between October 5, 2011, and June 7, 2016, a total of 924 subjects underwent a spinal procedure during which 489 subjects received DuraSeal Exact Spine Sealant and 435 subjects received other products and/or treatments (control arm) to close the dura.

## C. Study Population Demographics and Baseline Parameters

The demographics of the DuraSeal Exact Spine Sealant post-approval study population are presented in the following publication: (Kim KD, Ramanathan D, Highsmith J, et al. DuraSeal Exact Is a Safe Adjunctive Treatment for Durotomy in Spine: Post approval Study. Global Spine Journal. 2019;9(3):272-278. doi:10.1177/2192568218791150).

## D. Summary of Safety and Effectiveness Results

Of the 886 subjects for whom data is available, 30 (6.6%) of subjects receiving the DuraSeal Exact Spine Sealant and 6.5% of subjects in the control arm experienced the primary endpoint event of a CSF leak within 90 days after the spine surgical procedure.

There was no statistically significant difference in the proportion of subjects with Deep Surgical Site Infections between DuraSeal Exact Spine Sealant treatment and Control arms (1.6% DuraSeal vs 2.1% control). Nor was there any statistically significant difference in the proportion of subjects with a neurological SAE between DuraSeal Exact Spine Sealant treatment and control arms as shown in **Table 3** below. Ninety-two subjects experienced at least 1 adverse event (AE) (DuraSeal Exact Spine Sealant treatment arm, 51 [10.4%] subjects; control arm, 41 [9.4%] subjects). There was no statistically significant difference in the proportion of subjects with at least 1 AE between the DuraSeal Exact Spine Sealant treatment arm and control arm.

**Table 3: Adverse Events**

| | Spine Sealant, n (%) | Control, n (%) | *P* |
|---|---|---|---|
| Subjects with any surgical site infections, n | 463 | 426 | 0.2295 |
| No | 443 (95.7) | 414 (97.2) | |
| Yes | 20 (4.3) | 12 (2.8) | |
| Type of surgical site infection | | | |
| Deep | 7 (1.6) | 9 (2.1) | 0.6160 |
| Superficial | 13 (2.8) | 2 (0.5) | 0.0076 |
| Organ space | 0 (0.0) | 1 (0.2) | 0.4792 |

There was no statistically significant difference in the proportion of subjects with a neurological SAE between DuraSeal Exact Spine Sealant and the control. A total of 75 SAEs were reported during the study, with no unanticipated adverse device effects (DuraSeal Exact Spine Sealant treatment arm, 42 [8.6%] subjects; control arm, 33 [7.6%] subjects) and no statistically significant difference in the proportion of subjects with at least 1 SAE between the DuraSeal Exact Spine Sealant treatment arm and the control arm (8.6% vs 7.6%; $P = 0.5755$). There was no statistically significant difference in the proportion of subjects between the

treatment groups in terms of AE relatedness to the study device ($P = 0.5370$) and AE severity ($P = 0.5979$).

1. Pediatric Extrapolation

In this premarket application, existing clinical data was leveraged to support the reasonable assurance of safety and effectiveness of the proposed device in adolescent pediatric patients ≥ 18 years of age. This adolescent patient population is also included in the indications for use of the commercialized DuraSeal Exact Spine Sealant. Since the PAS data from the DuraSeal Exact Spine Sealant PMA was used to support the safety and effectiveness of the SpineSeal Spine Sealant based on the "six-year rule" as described in Section 216 of FDAMA and the FDA guidance, "Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997," the same patient population indicated for use with the DuraSeal Exact Spine Sealant is also applicable to the subject device.

## XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The SpineSeal Spine Sealant has not been the subject of a published clinical study. Pramand, LLC is relying on the "six-year rule" as described in Section 216 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) and the FDA guidance, "Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997," to use the clinical data supporting a previous PMA application of the DuraSeal Exact Spine Sealant (P080013) and results from a post-approval study conducted on a modified version of DuraSeal Exact Spine Sealant support the reasonable assurance of safety and effectiveness of the subject SpineSeal Spine Sealant.

## XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A comprehensive literature review using PubMed was performed on the clinical use of the commercialized DuraSeal Exact Spine Sealant from January 1, 2005, through January 1, 2023, to further support the safety and effectiveness of the SpineSeal Spine Sealant that has the same chemical specifications and design as the DuraSeal Exact Spine Sealant. The literature review focused on publications related to the clinical application of the DuraSeal Exact Spine Sealant in human patients as an adjunct to sutured dural repair during spine surgery. The results of the literature review did not

identify any new or increased risks of use of the DuraSeal Exact Spine Sealant or issues with effectiveness.

## XIII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Neurological Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel. There was a prior FDA advisory committee meeting of the Neurological Devices Panel on May 14, 2009, for the review of the DuraSeal Exact Spine Sealant PMA P080013.

## XIV. CONCLUSIONS DRAWN FROM PRECLINCAL AND CLINICAL STUDIES

### A. Effectiveness Conclusions

The effectiveness of the SpineSeal Spine Sealant was assessed in a direct comparison to the FDA approved, commercially available DuraSeal Exact Spine Sealant in an ovine dural defect model and nonclinical in vitro performance evaluations. In the sheep animal study, each animal had a laminectomy incision created exposing the spinal cord. The dural defect sites were repaired with suture and either the SpineSeal Spine Sealant hydrogel or the DuraSeal Exact Spine Sealant hydrogel was applied as an adjunct to the sutures. Valsalva maneuver was performed following sealant application for both devices to confirm the absence of CSF leakage prior to closure. All treatment sites were reported to be sealed with the appropriate thickness of hydrogel prior to wound closure. The treated defect sites were examined macroscopically, histologically processed, and microscopically evaluated by a blinded pathologist for a final report assessment. The results confirm the effectiveness of the SpineSeal Spine Sealant is comparable or equivalent to the commercialized DuraSeal Exact Spine Sealant as an adjunct to sutured dural repair in achieving a successful watertight seal in the ovine study. The nonclinical in vitro performance evaluations further support this conclusion that the SpineSeal Spine Sealant has a comparable effectiveness to the DuraSeal Exact Spine Sealant because both devices are designed the same with the same chemical specifications.

## B. Safety Conclusions

The risks of the SpineSeal Spine Sealant are based on nonclinical laboratory and animal studies as well as data collected in clinical studies assessing the safety and effectiveness of the commercialized DuraSeal Exact Spine Sealant (P080013). Pramand, LLC is relying on the "six-year rule" as described in Section 216 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) and the FDA guidance, "Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997." In doing so, clinical data provided in the DuraSeal Exact Spine Sealant PMA (P080013), was used to support the reasonable assurance of safety and effectiveness of the subject SpineSeal Spine Sealant because the two devices have the same chemical specifications and design.

The nonclinical laboratory and animal studies demonstrate that the SpineSeal Spine Sealant is biocompatible and does not cause any toxic effects because it has an equivalent chemical formulation and specifications as the commercialized DuraSeal Exact Spine Sealant. The responses observed during the in-life assessments in the ovine study for animals treated with SpineSeal Spine Sealant were equivalent to those observed from animals treated with the DuraSeal Exact Spine Sealant commercial control. At 2-, 6- and 14- weeks post implantation on the dura of the sheep, the SpineSeal Spine Sealant was considered to elicit no adverse effects on surgical intraoperative observations, clinical observations, body weights, neurological observations, macroscopic and microscopic observations when compared to the DuraSeal Exact Spine Sealant control.

## C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a pivotal clinical study conducted to support PMA approval of the DuraSeal Exact Spine Sealant (P080013). As discussed in the P080013 SSED of the DuraSeal Exact Spine Sealant, 93 subjects (91.2%) had a watertight closure upon Valsalva within the DuraSeal Exact Spinal Sealant arm, following the first application. The 9 subjects with a non-watertight closure were treated with a second application of the hydrogel Sealant and all had a watertight closure upon second post-treatment Valsalva. All 102 subjects (100%) treated with the hydrogel Sealant met the criteria for primary endpoint success, i.e. intra-operative sealing.

The probable risks of the device are also based on data collected in a post-approval study to support DuraSeal Exact Spine Sealant (P080013). In this post-approval study, 30 (6.6%) subjects of DuraSeal Exact Spine Sealant arm and 28 (6.5%) control arm experienced a CSF leak within 90 days after the spine surgical procedure.

Outcomes from the post-approval study indicated that there was no statistically significant difference in the proportion of subjects with Deep Surgical Site Infections between DuraSeal Exact Spine Sealant treatment and Control arms (1.6% vs 2.1%; P=0.6160). Nor was there any statistically significant difference in the proportion of subjects with a neurological SAE between DuraSeal Exact Spine Sealant treatment and control arms. A total of 75 SAEs were reported during the study, with no unanticipated adverse device effects (DuraSeal Exact Spine Sealant treatment arm, 42 [8.6%] subjects; control arm, 33 [7.6%] subjects) and no statistically significant difference in the proportion of subjects with at least 1 SAE between the DuraSeal Exact Spine Sealant treatment arm and the control arm (8.6% vs 7.6%; P = .5755). There was no statistically significant difference in the proportion of subjects between the treatment groups in terms of AE relatedness to the study device (P=0.5370) and AE severity (P=0.5979).

1. Patient Perspective

This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the indication for use as an adjunct to sutured dural repair during spinal surgery to provide watertight closure; the probable benefits outweigh the probable risks.

## D. Overall Conclusion

The data in this application support the reasonable assurance of safety and effectiveness of the SpineSeal Spine Sealant when used in accordance with the indications for use. The SpineSeal Spine Sealant has demonstrated to have the same design and chemical specifications as the commercialized DuraSeal Exact Spine Sealant for the same intended use. Therefore, Pramand, LLC is relying on the "six-year rule" as described in Section 216 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) and the FDA guidance, "Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997," to use the clinical data supporting a previous PMA application of the DuraSeal Exact Spine Sealant (P080013) and data from a post-approval study conducted on a modified version of the DuraSeal Exact Spine Sealant, to support the reasonable assurance of safety and effectiveness of the subject SpineSeal Spine Sealant.

Results from nonclinical studies indicate that the SpineSeal Spine Sealant is functionally the same as the commercially available DuraSeal Exact Spine Sealant and has a comparable safety and effectiveness profile. Furthermore, the pivotal clinical study used to support PMA approval of the DuraSeal Exact Spine Sealant

(P080013), the PAS conducted on the modified version of the DuraSeal Exact Spine Sealant, and a comprehensive literature review of the DuraSeal Exact Spine Sealant did not identify any safety or effectiveness concerns and continue to support the reasonable assurance of safety and effectiveness of the DuraSeal Exact Spine Sealant for its proposed indications for use. These conclusions also apply to the SpineSeal Spine Sealant due to similarities between the SpineSeal Spine Sealant and the DuraSeal Exact Spine Sealant.

## XV. CDRH DECISION

CDRH issued an approval order on February 14, 2025.

The final clinical conditions of approval cited in the approval order are described below.

The post-approval study, "SpineSeal Spine Sealant Post-Approval Study" is a new enrollment cohort post-approval study (PAS) that will be initiated within a clearly defined timeline in agreement with FDA after PMA approval of the SpineSeal Spine Sealant. This prospective, multicenter, non-randomized, 2-arm, PAS will collect and compare CSF leak rates in consecutive subjects who received SpineSeal Spine Sealant and control subjects who receive DuraSeal Exact Spine Sealant. The PAS should enroll a statistically justified number of subjects indicated for spinal surgical procedures with the indications for surgery clearly specified in the selection criteria. The primary effectiveness outcome of the PAS will evaluate the incidence of cerebrospinal fluid (CSF) leakage or pseudomeningocele at 90-days post-operative as confirmed by neurodiagnostic imaging [i.e., computed tomography (CT) or magnetic resonance imaging (MRI)]. The PAS will evaluate the incidence of post-operative surgical site infections as a secondary outcome. The safety outcome of the PAS will be evaluated by the collection of all new and ongoing adverse events within 90-days post-procedure.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

## XVI. APPROVAL SPECIFICATIONS

Directions for Use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.