Confluent Surgical, Inc.

PMA P040034 Condition of Approval Study Summary
DuraSeal® Dural Sealant System

Company Overview

Confluent Surgical, Inc., a wholly owned subsidiary of United States Surgical, a division of Tyco Healthcare, is a medical device company specifically focused on developing *in-situ* polymerized biomaterials to address unmet or underserved clinical needs. Specifically, Confluent Surgical has developed the DuraSeal® Dural Sealant System, a synthetic, absorbable hydrogel intended for use an adjunct to sutured dural repair during cranial surgery to provide watertight closure.

Device Description

The DuraSeal Dural Sealant System consists of components for preparation of a synthetic absorbable polyethylene glycol (PEG) hydrogel sealant and an applicator for delivery of the sealant to the target site. The 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 together, the precusors rapidly polymerize *in-situ* to form a biocompatible, absorbable hydrogel suitable for sealing the dura mater. The mixing of the precursors is accomplished as the materials exit the tip of the applicator. The applicator allows a conformal coating that adheres to the tissue surfaces. The mixing provided by the applicator also ensures a complete reaction of the precursors. No external energy requirements, such as light or heat source, are required to initiate the reaction. The polymerization reaction occurs within 2 seconds 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 cross linked solid hydrogel is more than 90% water at application. Due to this high water content, the hydrogel has physical properties similar to tissue. The hydrogel implant is absorbed in approximately 4 to 8 weeks, sufficient time to allow for healing. The absorbed hydrogel components are excreted from the body.

Condition of Approval Study

Confluent Surgical's DuraSeal Dural Sealant System was granted premarket approval by FDA under PMA P040034 on April 7, 2005. This PMA included results from a prospective, multi-center, non-randomized single arm clinical investigation. The then current standard of care for prevention of CSF leaks following surgeries involving incision of the dura included a variety of approaches. There was no approved dural sealant that could be included in the clinical study design as a control. The study involved 10 investigational sites within the United States and 1 site in Europe. A total of 111 subjects were treated with the DuraSeal Sealant. The primary endpoint for this study was the percent (%) success in the treatment of intraoperative CSF leakage following DuraSeal Sealant application defined as no CSF leakage from dural repair intraoperatively after up to two DuraSeal applications during Valsalva maneuver up to 20 cm H_20 for 5 to 10 seconds. Safety was assessed based on evaluation of wound healing, and adverse device-related adverse events diagnosed by physical examination,

protocol-specified diagnostic laboratory tests, neurological assessments, and CT imaging assessment performed by independent radiologists for evaluation of extradural collections and adverse findings.

All 111 subjects treated with the DuraSeal Sealant showed no leakage during the intraoperative assessment. One hundred and nine (109) of the 111 (98.2%) met the criteria for primary endpoint success; i.e., intraoperative sealing. Two subjects were tested intraoperatively at a pressure of only 10 cm H_20, and although no leak was seen, these subjects could not technically be classified as successes.

The incidence of post-op CSF leaks in this study was 4.5%. Of these leaks 1.8% were incisional and 2.7% were pseudomeningoceles. There were 9/111 wound infections (8.1%) with 7.2% identified as deep wound infections.

Based on the data obtained in this clinical study, the dural sealant was demonstrated to prevent intraoperative CSF leaks and reduce the incidence of post-operative CSF leaks when used as an adjunct to standard methods of dural repair, such as sutures, to provide watertight closure. The incidence and nature of adverse events observed in the subjects studied were consistent with the type and complexity of the surgery performed and the co-morbid state of the treated subjects. No device-related adverse events were reported during the course of the study.

As a condition of PMA approval, a post-market study to further evaluate the incidence of wound related complications, including infection and CSF leak rates associated with the use of the device was to be conducted. The study was to be initiated within 6 months of PMA approval.

Confluent Surgical has agreed to conduct a prospective, single blind, multi-center, post-market study to further characterize the DuraSeal Sealant as compared to “standard of care” in subjects scheduled for cranial surgery that entails a dural incision. An estimated 250 subjects will be randomized to either a standard of care group or DuraSeal Sealant group. Subjects will be followed for 30 days after treatment. The primary study endpoint is the incidence of neurosurgical complications related to unplanned intervention (i.e., minimally invasive procedures) or return to the operating room.

The study will involve up to 25 sites within the United States. The expected duration of this post-market study is approximately 24 months.

Study Progress

Enrollment

The condition of approval study was initiated on September 12, 2005, approximately five months after PMA approval. As of January 1, 2007, one hundred and one (101) subjects have been randomized at eight (8) clinical sites. Of the 101 subjects, 50 have been randomized to DuraSeal Sealant treatment and 51 have been randomized to the standard of care control group. Study follow-up (30 days after treatment) has been completed for 78 subjects. A summary of subject demographic information is provided in **Table 1**.

Table 1

	DuraSeal (n=39)	**Standard of Care (n=39)**
Female n(%) Male n(%)	26 (66.7%) 13 (33.3%)	28 (71.8%) 11 (28.2%)
Age (yrs) (Average, Range)	(49.9, 19 – 73)	(47.8, 21 – 75)
Weight (lb) (Average, Range)	(166.5, 102.5 – 279)	(178.1, 110 – 277.4)
Height (in) (Average, Range)	(66.0, 59 – 74)	(65.9, 59 – 74)

Primary Endpoint Results

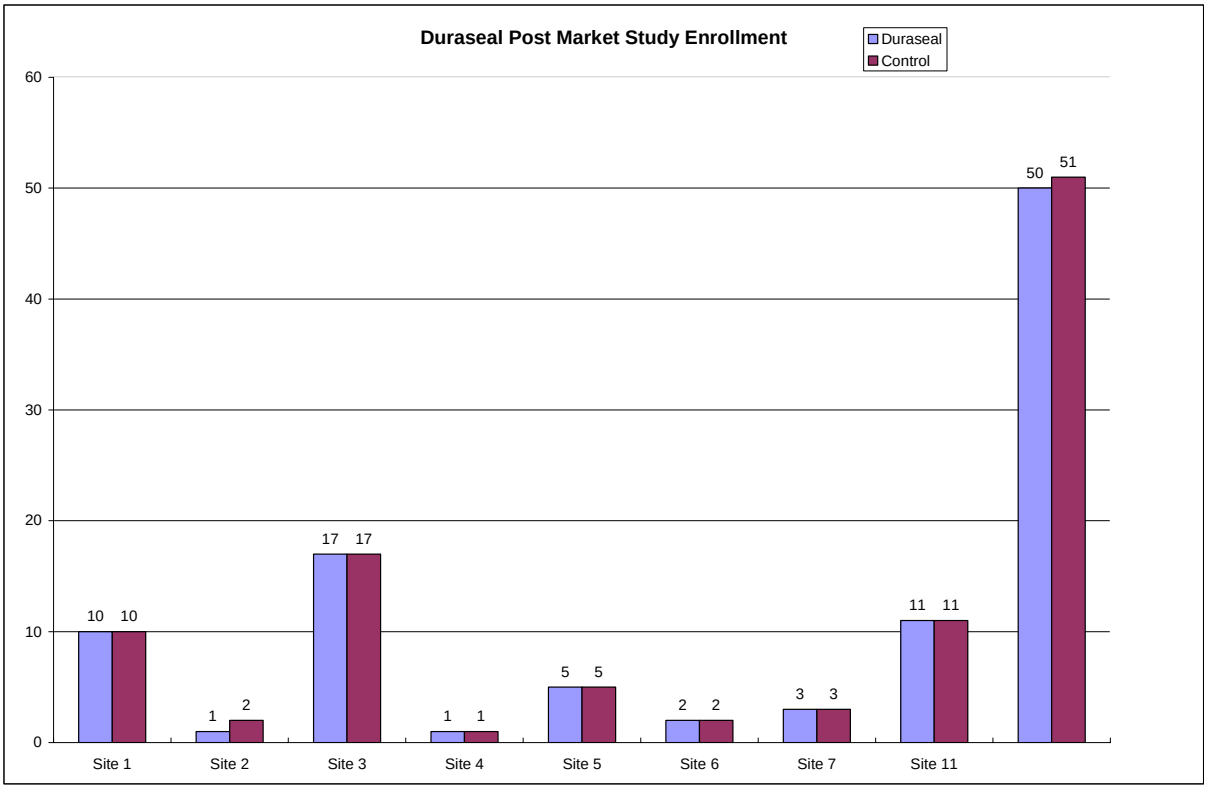
As of January 1, 2007, none of the DuraSeal treated subjects have experienced a device related complication. A summary of all primary endpoint complications is provided in **Table 2**.

Table 2

Complication Name	**Number of Subjects**	
	DuraSeal	**Standard of Care**
CSF Leak	0	2
Superficial SSI	1	1
Poor Wound healing	1	0
Neurosurgical complication with return to operating room Epidural hematoma	1	0

Details of subject enrollment as of January 1, 2007, are provided below in **Table 3**.

Table 3



Confluent Surgical continues to actively enroll subjects in the DuraSeal Sealant PMA condition of approval study, with a targeted completion in 2007. To date, sixteen (16) clinical sites have been qualified for participation in the study. Two (2) clinical sites have recently withdrawn from the study citing reasons including a lack of interest in randomizing subjects as the commercial DuraSeal Sealant has become widely used in the institution. Despite this and other challenges encountered in implementing post-market studies, Confluent Surgical remains committed to fulfilling this condition of approval for the DuraSeal Sealant PMA.