

PANEL QUESTIONS

1. Infection

The safety evaluation included adverse events collected to 3 months post-operative. The overall rate of surgical wound infection in the DuraSeal clinical study was 9/111 (8.1%) with a 7.2% rate of deep surgical infection, all requiring repeat surgery. Please discuss whether this infection rate raises concern.

2. Post-operative CSF leaks

The primary efficacy endpoint of the study was the number of patients with continued CSF leak intra-op after DuraSeal application. The study design specified an >80% study success criteria. The sponsor achieved a success rate of 98.2%. The purpose of establishing a water-tight closure of the dura is to limit the post-operative CSF leak rate and associated morbidity. There were 5 cases (5/111, 4.5%) of protocol defined post-operative CSF leaks observed in the study. Three patients had a pseudomeningocele and the other two had incisional CSF leaks. There was one additional case of a CSF leak during re-operation for a deep wound infection. Including this event, the rate is 6/111 or 5.4%. Please discuss the observed post-operative CSF leak rate.

3. To be included for treatment, patients were assessed for CSF leaks after sutured dural closure. If CSF was observed leaking from the sutured incision either spontaneously or during an induced Valsalva maneuver (to 20 cm H₂O) the patient was included for treatment with DuraSeal. This selection process was intended to include a subset of patients a risk for post-operative CSF leak; however, all of the patients tested, leaked. The proposed instructions for use are for all patients with sutured dural closure.

- a. Do you believe the results of the study support an adequate risk/benefit ratio in spontaneous leakers?
- b. Do you believe the results of the study support an adequate risk/benefit ratio in patients who leaked only after Valsalva maneuver?

4. The proposed indication for use for DuraSeal is “The DuraSeal Dural Sealant system is intended for use as an adjunct to sutured dural repair during cranial surgery to provide watertight closure.” Please discuss the adequacy of the proposed indications for use.

5. 21 CFR 860.7(d)(1) states that there is a reasonable assurance that a device is safe when it can be determined that the probable benefits to health from use of the device for its intended uses, when accompanied by adequate instructions for use and warnings against unsafe use, outweigh any probable risks. Please discuss whether the data in the PMA provide a reasonable assurance of safety.

6. 21 CFR 860.7(e)(1) states that there is a reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warning against unsafe use, will provide clinically significant results. Please discuss whether the data in the PMA provide a reasonable assurance of effectiveness.

7. A reasonable assurance of safety and effectiveness as defined in questions 5 and 6 must be demonstrated for device approval. If you believe this has been demonstrated, but think there are specific focused questions regarding this device that still remain and can be addressed in a post-approval study, please identify those questions.