Questions for Consideration
P040001

1. Patients who had the X STOP implanted had a higher incidence of musculoskeletal events, including lower back disorders, lower extremity disorders, hip disorders, upper back disorders, and neurological and neuropathological disorders, compared to the control group. Although these adverse events were considered by the sponsor to be not device related, changes in spinal biomechanical function that occur with the limits to extension could also be a potential source of pain. The sponsor provides a report of a pre-clinical study which characterizes the effects of the device in cadaveric specimens, showing an increase in canal and foraminal dimensions at the implanted level in the extended position, with no change in the dimensions at the adjacent levels. Please discuss the clinical significance of the musculoskeletal and other adverse events seen in the trial, and discuss whether the effects of the device on surrounding segments or on spinal biomechanics have been adequately addressed.

2. Based on your knowledge of the biomechanics of the spine and the nature of spinal stenosis, please discuss whether there is a clinical basis for pooling the outcomes of the one- and two-level patients.

3. The device labeling states that this device limits extension. In the pre-clinical cadaveric studies, ranges of flexion-extension were recorded under measured applied loads. The clinical radiographic measurements, however, were performed on static plain radiographs. Please discuss the interpretation of the measurements made on the clinical patients' radiographs, as it relates to device effectiveness.

4. Fewer than 50% in the X STOP treated group and fewer than 5% in the control group achieved overall successful outcome. These results are considerably lower than what had been predicted at the outset of the study. In this study, an operative treatment was compared to a nonoperative treatment in patients who had already failed conservative treatment, including epidural injections. A majority of patients had had symptom duration for more than 2 years prior to entering the study. Patients in both groups went on to have more than one epidural injection and/or laminectomies. In 10-15% of the X STOP treated patients who improved, symptoms returned during the course of the study. Moreover, there was a trend toward different results for use of this device at one vs two levels.
   (a) Based on the data from this study, please discuss the appropriate population who might benefit from this device.
   (b) Given the historical success rates for laminectomy, please discuss what impact the effectiveness results of this study have in relation to our interpretation of the risks and benefits of treatment with the X STOP device.

5. In this study, the protocol did not define what criteria were to be used in either group to determine when or whether patients proceeded to laminectomy; it also did not define whether to administer additional epidural injections to patients in the control group. Some patients in the investigational (X STOP) group received the control treatment

(epidural injection for pain) rather than proceeding to laminectomy, and it is not clear whether success in those patients was due to temporary relief from the injection or to the X STOP. Please describe the potential impact on the interpretation of the study result of these confounding factors.

6. Under CFR 860.7(d)(1) , safety is defined as reasonable assurance, based on valid scientific evidence, that the probable benefits to health under conditions of the intended use, when accompanied by adequate directions for use and warnings against unsafe use, outweigh any probable risks. Do the clinical data in the PMA provide reasonable assurance that the device is safe?

7. Under CFR 860.7(e)(1) effectiveness is defined as reasonable assurance that , in a significant portion of the population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results. Do the clinical data in the PMA provide reasonable assurance that the device is effective?