FDA NON-Voting Questions

11.1 Panel Non-Voting Questions

1. Patient Population:
   Based on the modified MERCURY dataset subgroup analysis, the sponsor has identified a target population that includes patients with mild or greater pain, mild to moderate arthritis, and previous meniscectomy, and meeting inclusion/exclusion criteria, specifically the exclusion of patients with meniscal extrusion ≥5mm and tibial spine height <11mm.
   - Please comment on what patient population(s) would benefit from this device, in consideration of available alternative non-surgical and surgical treatments.
   - Please comment on the clinical relevance of the sponsor's modified target population.
2. Clinical Success Criteria and Secondary Surgical Interventions:
   Overall clinical success for the modified MERCURY dataset was defined as improved $KOOS^{overall}$ and $KOOS^{pain}$, positive MRI, and no Automatic Study Failure (ASF). The Statistical Analysis Plan for the modified MERCURY dataset predefined Automatic Study Failures (ASF) as secondary surgical interventions (SSI) to permanently remove the device and revisions to reposition or replace the device. 17% (12/72) of NUsurface subjects experienced a device-related SSI and 25% (3/12) of those subjects had more than one SSI.
   - Please discuss the adequacy of the overall clinical success criteria and the clinical significance of the SSIs related to the device.
   - Please comment on the classification of these SSIs as ASFs.

3. Sub-group Analysis:
   The sponsor provided a subgroup analysis intended to identify a modified target population with a reduced rate of SSIs from the unmodified MERCURY dataset. The modified MERCURY dataset involves the exclusion of meniscal extrusion ≥5mm and tibial spine height <11mm. Please comment on the overall success rate of the modified MERCURY dataset.

   - Please comment on whether the modified MERCURY dataset provides sufficient information to understand whether the device improves pain and function in the medial compartment of a knee in which the medial meniscus has been resected.
   - Please comment on the study design characteristics as different datasets were utilized compared to a non-surgical control for the MERCURY trial, modified MERCURY dataset, and MCT study.
   - Please comment on the benefit-risk profile for use of the NUsurface Meniscus Implant in alternative subgroups.
   - Are there any additional subgroups in which the NUsurface Meniscus Implant would have a favorable benefit-risk profile?

4. Patient Preference Information:
   Multiple patient preference information (PPI) datasets have been provided to support benefit-risk determination.

- Please comment on the design and execution of the current PPI study (Study 7).
- Please discuss the contribution of the PPI studies to the final benefit-risk determination.

5. Risk Mitigation:
   The sponsor has identified several key considerations in risk mitigation, including the appropriate selection of patients (e.g., exclusion of meniscal extrusion >5mm and tibial spine height <11mm) and a more detailed surgical technique (e.g., the ability to precisely identify the appropriate device size and implant the device). The sponsor reported inter-rater disagreements over the meniscal extrusion and tibial spine height exclusion criterion.
   - How might these factors impact the clinical reproducibility, particularly the clinician's ability to identify patients that would benefit from the device?