charles river

Summary
The approach to histological processing and microscopic evaluation of a novel device can mean the difference between success and having to rerun a study. Every device is unique, but there are important considerations to factor into every histopathology plan that greatly improve conditions for success. Having evaluated a vast array of medical devices, our experienced scientists have assembled their informed recommendations for a well-designed plan.

SAFETY ASSESSMENT

Histopathology for Medical Devices

Key considerations for study design

The following is a list of items that are essential to understand ahead of time for most medical device studies. If a study plan/protocol is already available that addresses these points, we advise sharing those documents directly (where possible) with the team working on the project.

Overall goal of this project

1. Publication vs. presentation vs. regulatory submission vs. internal use by sponsor for product development vs. marketing images/information?
2. Relevant specific guidance/regulation you are going to use this report for submission (e.g., ISO 10993 series)
3. Can a copy of the current protocol be shared?

Medical device details

1. Implant size
2. Implant composition
3. Is any component and/or the entire article expected to be degradable? Is anything known about the rate of degradation?

Model details

1. Species and age range for animal models
2. Are there control/sham articles? Will additional clinical interventions be performed (e.g., indwelling catheter)?
3. Will only the device/implant site be processed and evaluated, or will there be other tissues (e.g., regional draining lymph nodes, systemic tissues)?

Histology parameters

1. Has this article been processed histologically prior to the current study? If previous methods worked well, can the methods be shared?
2. If ideal histology methods have not been identified, is an un-implanted section for the histology available to use for method optimization?
3. Is standard fixative (neutral buffered formalin) or special fixatives used (e.g., glutaraldehyde)?
4. How much sampling is needed to fully evaluate the device (e.g., one section shows the entire device or there are multiple components that should be evaluated)?

5. Does orientation matter for the device when it is embedded (e.g., longitudinal vs. cross section through an implant site)?
6. For samples containing bone/mineral: is decalcification required or contraindicated (e.g., will it dissolve/ destroy the article)?
7. How should samples be processed (e.g., paraffin, frozen sections, hard plastic, plastic)?
8. Are standard paraffin processing chemicals acceptable or are alternatives needed (e.g., non-xylene alternatives)?
9. Are stains other than H&E needed?

Microscopic evaluation and reporting

1. What are the report expectations (e.g., memo style, standard reporting style)?
2. Is initial masked pathology evaluation requested? Please note that this is not always possible if different devices are microscopically distinct (e.g., different color).
3. Are there scoring systems that have been used before or a specific parameter that is most important? If so, is the scheme or a relevant paper available?
4. What type of evaluation is expected in the report (e.g., descriptive, semi-quantitative, quantitative)?

Microscopic images (if applicable)

1. Will slides be scanned (digital slides that can be viewed using a computer program as if one is looking through a microscope at the glass/plastic slide)?
2. Are images required? Representative vs. album with each implant site photographed?
3. How should images be labeled/described in a figure legend?

Additional considerations

1. Is IHC planned?
2. Is electron microscopy planned (scanning or transmission)?
3. Is image analysis required? Manual easy analysis (e.g., linear measurements of the thickness of s a structure) or computer-aided evaluation (e.g., algorithms)?
4. Is there any auxiliary data expected to be interpreted and integrated by the pathologist (e.g., clinical signs, macroscopic findings, clinical pathology data, biochemical evaluations)?
5. Is there any additional important information that has not yet been covered?