U.S. FOOD & DRUG ADMINISTRATION

FDA Perspective:

When do fractures matter with respect to PMA submission?

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Always

Sometimes more than Others

FAQs

- Why do we worry about fractures that have been reported during the clinical study, even if there haven't been clinical sequelae?
- What do we ask of sponsors under the PMA when fractures have been reported?
- Have we approved PMAs when there have been fractures reported?
- When do we take PMAs to our Advisory Panel?

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Considerations Regarding Fractures

- All fractures are not equal, depending on the potential for:
  - Propagation
  - Loss of fixation
  - Damage to surrounding materials or tissues
- Studies may underestimate the rate and significance of fractures
  - IDE study subjects tend to be carefully selected compared to postmarket patients
  - Duration of follow-up is limited compared to the expected life of patients

- It’s not unreasonable to assume that the problem could be bigger once the product is on the market.

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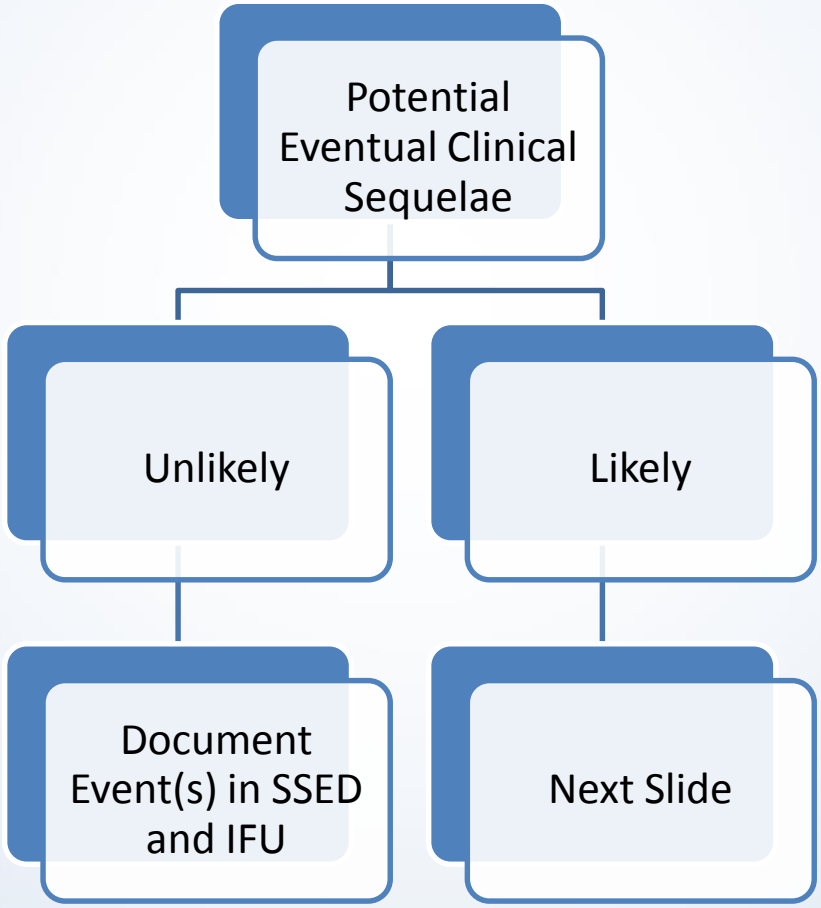
Characterize the Problem

- Identify the location of fracture(s)
  - Address if likely to propagate, affect fixation or seal, or poke holes in the graft
- Indicate the timing of the fracture(s)
- Report the number of study subjects with confirmed fractures
- Propose potential contributing factors

PMA Reporting of Fractures



Reporting if Potential for Clinical Sequelae

- Current data on all patients
  - Usually involves a re-review of imaging to determine the true rate and timing of fractures
  - A comparison of relevant event rates (e.g., migration, endoleaks) between subjects with and without fractures
- Root cause analysis
  - Potential contributing factors
  - Verified contributing factors
  - Erroneous assumptions, if applicable
  - Benchtop evaluation
  - Number of subjects at risk based on root cause
- Approaches to minimize the risk of fracture and the risk of clinical sequelae

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Yes

- Isolated cases
- Unlikely to happen again
- Unlikely to result in clinical sequelae

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When don't we?

- In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

When do we?

- The information in the PMA does not substantially duplicate information previously reviewed by this panel
  - Higher rate of events than they have considered
  - Different types of events or failures
  - Novel technology

Take Home Message

- Necessary to always disclose and discuss losses of device integrity
- Not all fractures are ‘fatal flaws’ with respect to PMA approval
- Most efficient to work with FDA from the time the first event is identified