FDA Questions

May 30, 2019 meeting of the
General Surgery Devices Panel of the Medical Devices Advisory Committee
Internal Surgical Stapler Classification

Please refer to the Regulatory Reference Sheet for additional information regarding classification procedures and definitions.

1. In the April proposed reclassification order, FDA has identified the following risks to health for surgical staplers for internal use based on FDA's literature review and MDR analysis:

   - *Complications associated with device failure/malfunction.* Device failures or malfunctions may result in prolonged surgical procedures, unplanned surgical interventions, and other complications such as bleeding, sepsis, fistula formation, tearing of internal tissues and organs, increased risk of cancer recurrence, and death.

   - *Complications associated with use error/improper device selection and use.* Use error may result from a device design that is difficult to operate and/or labeling that is difficult to comprehend. For example, user difficulty in firing the stapler may result in staples not being fully deployed, and misfiring may result in staples being inadvertently applied to the wrong tissue. Inadequate instructions for use may result in selection of incorrectly sized staples for the target tissue. When staples are applied to the wrong tissue or when incorrectly sized staples are applied, staples are unable to properly approximate the underlying tissue, resulting in tissue damage, anastomotic leakage, and bleeding. This in turn, may lead to more severe complications, such as abscess, sepsis, peritonitis, hemorrhage, or death.

   - *Adverse tissue reaction.* If the patient-contacting materials of the device are not biocompatible, local tissue irritation and sensitization, cytotoxicity, or systemic toxicity may occur when the device contacts sterile tissue.

   - *Infection.* If the device is not adequately reprocessed or sterilized, the device may introduce pathogenic organisms into sterile tissue and may cause an infection in a patient.

a. **Please comment on whether you believe FDA has identified a complete and accurate list of the risks to health presented by surgical staplers for internal use. Since the publication of the proposed reclassification order in April, FDA has identified the potential for additional risks specifically associated with powered surgical staplers for internal use. Please include the consideration of the risks posed by powered staplers in your comments.**

b. **Please comment on whether you disagree with inclusion of any of these risks or whether you believe any other risk should be included in the overall risk assessment of surgical staplers for internal use.**

2. As defined in 21 CFR 860.7(d)(1), "there is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury association with the use of the device for its intended uses and conditions of use." As defined in 21 CFR 860.7(e)(1), "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 warnings against unsafe use, will provide clinically significant results."

   Please comment on whether, based on the available scientific evidence, there is a reasonable assurance of safety and effectiveness for surgical staplers for internal use.

3. In the April proposed reclassification order, FDA proposed that the following special controls would adequately mitigate the risks to health and provide reasonable assurance of safety and effectiveness for surgical staplers for internal use:

   - Performance testing must demonstrate that the stapler, when used with compatible staples, performs as intended under anticipated conditions of use.

Performance testing must include the following:

- Evaluation of staple formation characteristics in the maximum and minimum tissue thicknesses for each staple type;
- Measurement of the worst-case deployment pressures on stapler firing force;
- Measurement of staple line strength;
- Confirmation of staple line integrity; and
- In vivo confirmation of staple line hemostasis.

- Usability testing and a labeling comprehension study must demonstrate that the clinician can correctly select and use the device, as identified in the labeling, based on reading the directions for use.
- The elements of the device that may contact the patient must be demonstrated to be biocompatible.
- Performance data must demonstrate the sterility of the device.
- Validation of cleaning and sterilization instructions must demonstrate that any reusable device components can be safely and effectively reprocessed per the recommended cleaning and sterilization protocol in the labeling.
- Performance data must support the shelf life of the device by demonstrating continued device functionality, sterility, and package integrity over the identified shelf life.
- Labeling of the device must include the following:
  - Unless data demonstrates the safety of doing so, contraindications must be identified regarding use of the device on tissues for which the risk of stapling outweighs any reasonably foreseeable benefit due to known complications, including the stapling of necrotic or ischemic tissues and tissues outside of the labeled limits of tissue thickness.
  - Unless available information indicates that the specific warnings do not apply, the labeling must provide appropriate warnings regarding how to avoid known hazards associated with device use including:
    - Avoidance of obstructions to the creation of the staple line and the unintended stapling of other anatomic structures;
    - Avoidance of clamping and unclamping of delicate tissue structures to prevent tissue damage;
    - Avoidance of use of the stapler on large blood vessels, such as the aorta;

        - Establishing and maintaining proximal control of blood vessels prior to stapling;
        - Appropriate measures to take if a stapler malfunction occurs while applying staples across a blood vessel, such as clamping or ligating the vessel before releasing the stapler, while the stapler is still closed on the tissue; and
        - Ensuring stapler compatibility with staples.
    - Specific user instructions for proper device use including measures associated with the prevention of device malfunction, evaluation of the appropriateness of the target tissue for stapling, and evaluation of the resultant staple line.
    - List of staples with which the stapler has been demonstrated to be compatible.
    - Identification of key performance parameters and technical characteristics of the stapler and the compatible staples needed for safe use of the device.
    - Information regarding tissues on which the stapler is intended be used.
    - Identification of safety mechanisms of the stapler.
    - Validated methods and instructions for reprocessing of any reusable device components.
    - An expiration date/shelf life.
- Package labels must include critical information and technical characteristics necessary for proper device selection.

Please comment on whether you believe any other special controls are necessary to mitigate the risks to health and provide reasonable assurance of device safety and effectiveness or whether you disagree with inclusion of any of these special controls. Also, please specifically comment on if you believe that additional special controls may be necessary for powered surgical staplers such as electrical safety and electromagnetic compatibility testing and software verification and validation.

4. Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:

- insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls would provide such assurance, AND

- if, in addition, the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

A device should be Class II if:

- general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, AND

- there is sufficient information to establish special controls to provide such assurance.

A device should be Class I if:

- general controls are sufficient to provide reasonable assurance of the safety and effectiveness

OR

- insufficient information exists to:
  - determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness or
  - establish special controls to provide such assurance

BUT

- is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and
- does not present a potential unreasonable risk of illness or injury.

Please discuss the following questions:

a. Please comment on whether the general controls, required for all medical devices, are insufficient to provide a reasonable assurance of safety and effectiveness for surgical staplers for internal use.

b. Please comment on whether you agree or disagree with FDA's view that the application of general controls and special controls, are sufficient to

provide reasonable assurance of safety and effectiveness for surgical staplers for internal use when intended to deliver compatible staples to internal tissues during surgery for resection, transection, and creating anastomoses.

c. FDA believes that surgical staplers for internal use are for a use which is of substantial importance in preventing impairment of human health, but does not present a potential unreasonable risk of illness or injury when intended to deliver compatible staples to internal tissues during surgery for resection, transection, and creating anastomoses. Do you agree with these assessments? If not, please explain why.

5. Based upon the available scientific evidence and special controls proposed in Question 3, do you recommend Class I (general controls) or Class II (special controls) for surgical staplers for internal use when intended to deliver compatible staples to internal tissues during surgery for resection, transection, and creating anastomoses. Please provide a rationale for your final classification recommendation, taking into account the available scientific evidence and your responses to Question 4 above.