Brief Summary of the Gastroenterology and Urology Panel of the Medical Devices Advisory Committee Meeting – February 26, 2016

Introduction

On February 26, 2016, during session I, the committee discussed and made recommendations regarding the reclassification of urogynecologic surgical mesh instrumentation from class I to class II. The committee, during session II, discussed and made recommendations regarding the classification of three additional product codes: LKX for Thermal Hemorrhoids Devices; Hemorrhoids Cushions assigned to product code LRL; and the Automated Therapeutic Blood Cell and Plasma Separator Devices assigned to product code LKN. These devices are considered preamendments devices, since they were in commercial distribution prior to May 28, 1976, when the Medical Devices Amendments became effective. FDA sought committee input on the safety and effectiveness and the regulatory classification of Thermal Hemorrhoids Devices; Hemorrhoids Cushions; and Automated Therapeutic Blood Cell and Plasma Separator Devices.

Discussion

Reclassification of Urogynecologic Surgical Mesh Instrumentation

he Panel agreed with the inclusion of the following risks to health in the overall risk assessment of urogynecologic surgical mesh instrumentation:

- *Perioperative risks*. Organ perforation or injury and bleeding (including hemorrhage/hematoma).
- *Damage to blood vessels, nerves, connective tissue, and other structures*. This may be caused by improperly designed and/or misused surgical mesh instrumentation. Clinical sequelae include pelvic pain and neuromuscular problems.
- *Adverse tissue reaction*. This may be caused by non-biocompatible materials.
- *Infection*. This may be due to inadequate sterilization and/or reprocessing instructions or procedures.

One Panel member recommended including device fragmentation as an additional risk to health.

The Panel agreed with FDA that sufficient information exists to establish special controls for urogynecologic surgical mesh instrumentation. Accordingly, the Panel agreed with the FDA's proposed reclassification from class I to class II (special controls) for urogynecologic surgical mesh instrumentation.

The Panel agreed that the following special controls appropriately mitigated the identified risks to health for urogynecologic surgical mesh instrumentation:

- The device must be demonstrated to be biocompatible;
- The device must be demonstrated to be sterile, including adequate reprocessing for reusable devices;
- Performance data must support the shelf life of the device by demonstrating package integrity and device functionality over the requested shelf life;
- Non-clinical performance testing must demonstrate that the device meets all design specifications and performance requirements, and that the device performs as intended under anticipated conditions of use; and
- Labeling must include:

    - Information regarding the mesh design that may be used with the device;
    - Detailed summary of the clinical evaluations pertinent to use of the device;
    - Expiration date; and
    - Where components are intended to be sterilized by the user prior to initial use and/or are reusable, validated methods and instructions for sterilization and/or reprocessing of any reusable components.

The Panel did not recommend additional or different special controls for urogynecologic surgical mesh instrumentation. One Panel member suggested including clinical data as a special control for new devices.

Classification of Hemorrhoid Devices, LKX

The Panel agreed with the inclusion of all of the below risks in the overall risk assessment of the heating and cooling hemorrhoid devices and electrically powered hemorrhoid devices that deliver heat under product code "LKX" and that no additional risks should be included.

Heating and cooling hemorrhoid devices (LKX):

• Device Failure/Tissue Injury
• Operator Error
• Adverse Tissue Reaction
• Infection

Electrically powered hemorrhoid devices that deliver heat (LKX):

• Electrical Shock Hazard
• Adverse Tissue Reaction
• Device Failure/Tissue injury
• Operator Error
• Infection

The Panel agreed with FDA that sufficient information exists to establish general controls for heating and cooling hemorrhoid devices. The Panel also agreed with FDA that sufficient information exists to establish special controls for electrically powered hemorrhoid devices that deliver heat. Accordingly, the panelists agreed with FDA's proposed classifications of Class I (general controls) for heating and cooling hemorrhoid devices, and Class IIwith special controls for electrically powered hemorrhoid devices that deliver heat.

The Panel agreed that the following special controls appropriately mitigated the identified risks to health for electrically powered hemorrhoid devices that deliver heat:

- The patient contacting components of the device must be demonstrated to be biocompatible;
- Performance data must demonstrate that the device performs as intended under anticipated conditions of use. At a minimum, the following performance characteristics must be tested:
    - performance bench testing must demonstrate that the device is durable for repeated use;
    - performance testing must verify the maximum treatment temperature is not exceeded;
    - performance testing must evaluate the mechanical integrity of the device, including the structural strength;
    - appropriate analysis and non-clinical testing must be conducted to validate electrical safety and electromagnetic compatibility (EMC).

- Labeling must include the following:
    - a description of the device and operational parameters;
    - detailed instructions for the user to properly clean, disinfect and maintain the device over the intended use life;
    - a summary which describes the possible susceptibility to electrical hazards associated and to electromagnetic interference (EMI) with the use of the device.

Classification of Hemorrhoid Devices, LRL

The Panel agreed with the inclusion of the below risks in the overall risk assessment of the hemorrhoid cushion devices under product code "LRL" and that no additional risks should be included.
• Device Failure/Tissue Injury
• Operator Error

• Adverse Tissue Reaction

The Panel agreed with FDA that sufficient information exists to establish general controls for hemorrhoid cushions. Accordingly, the Panel agreed with FDA's proposed classification of Class I with general controls for hemorrhoid cushion devices.

Classification of Centrifuge-Type Therapeutic Apheresis Devices

The panelists agreed with the inclusion of all of the below risks in the overall risk assessment of centrifuge-type therapeutic apheresis devices under product code "LKN" and that no additional risks should be included.

- *Thrombosis in patient and device.* This can include clotting of the extracorporeal circuit, vascular access clotting, or clotting of other blood vessels.
- *Adverse tissue reaction.* This can result from the use of device components that are not biocompatible. This risk also includes allergic reactions, which can be reactions to device materials (e.g., reaction to ethylene oxide sterilant) or reactions to blood products used with the device.
- *Infection and pyrogen reactions.* This risk includes febrile reactions, inflammatory response syndromes, infection, sepsis, and microbial contamination.
- *Device failure / Disposable failure.* This risk includes injury resulting from failure (e.g., electrical, mechanical, software) of one or more of the device components (e.g., reservoir leak/rupture, tubing separation/breakage).
- *Air embolism.* This risk occurs if air enters the circuit and subsequently the bloodstream, which can result in occlusion of small blood vessels resulting in stroke, myocardial infarction, etc.
- *Hemolysis.* This risk includes damage to red blood cells with subsequent release of cellular contents resulting from the mechanical processing of blood.
- *Blood loss/Anemia.* This risk includes blood leaks from the circuit, loss of blood from a discarded extracorporeal circuit after clotting, or increased risk of bleeding from anticoagulation medications or removal of clotting factors during therapy.
- *Toxic reaction to anticoagulant.* This can include citrate toxicity, which is typically manifested by hypocalcemia (paresthesia, tetany, seizures, and cardiac arrhythmias) and alkalosis.
- *Electrical shock hazard.* This risk can include electrical burns and cardiac arrhythmias.
- *Fluid imbalance.* This risk can result in hypovolemia (e.g., hypotension, headache, nausea/vomiting, syncope) or fluid overload (e.g., hypertension, pulmonary congestion).
- *Inadequate separation of blood components.* This risk involves the unintended removal of blood components (e.g., loss of immunoglobulins, drugs, electrolytes, coagulation factors, etc.).
- *Operator error.* Incorrect use of the device can lead to additional clinical risks (e.g., data entry error that causes the system to incorrectly calculate patient total blood volume).

The Panel agreed with FDA that sufficient information exists to establish special controls for centrifuge-type therapeutic apheresis devices. Accordingly, the Panel agreed with the FDA's proposed classification of class II (special controls) for centrifuge-type therapeutic apheresis devices.

The Panel agreed that the following special controls appropriately mitigated the identified risks to health for Centrifuge-type Therapeutic Apheresis Devices:

- The patient-contacting components of the device must be demonstrated to be biocompatible;
- Performance data must demonstrate that the device performs as intended under anticipated conditions of use as follows:
    - functional testing must demonstrate:
        - mechanical integrity of the device and disposable;
        - device functionality in terms of separation and removal of blood components;
        - device functionality in terms of fluid and anticoagulation management when the device is used according to its labeling;
        - proper functionality of device safeguards and alarms;
    - mechanical hemolysis testing must be conducted;
    - a system-level hazard analysis must confirm that the device does not perform in an unexpected and/or unsafe manner;
    - software verification and validation testing must be performed;
    - appropriate analysis and non-clinical testing must be conducted to validate electrical safety;
    - appropriate analysis and non-clinical testing must be conducted to validate electromagnetic compatibility (EMC);
    - performance data must demonstrate sterility of the device;
    - performance data must support the shelf life of the device for continued sterility, package integrity, and functionality over the requested shelf life;
- Labeling must include the following:
    - a description of the device and individual device components; accessories that need to be used with the system, operational parameters, and software version;
    - a description of the pre-treatment, performance, and post-treatment steps needed to safely perform each therapy mode (if more than one may be performed);
    - a description of the alarms included in the system, the alarm format (e.g., visual, audible alarm), the suspected cause of the alarm condition, and how the user must respond to the alarm;
    - detailed instructions for the user to properly clean, disinfect, and maintain the device.
    - a detailed summary of the device-related and procedure-related complications pertinent to the use of the device;

    - a summary which describes the possible susceptibility to electromagnetic interference and possible electrical hazards associated with the use of the device; and
    - a troubleshooting guide for users to reference if problems are encountered
- Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use and document any adverse events observed during clinical use.

The Panel did not recommend additional or different special controls for centrifuge-type therapeutic apheresis devices. One Panel member recommended including performance testing which demonstrated the durability of the non-disposable component of the device. Another Panel member indicated that the long-term performance of the device is typically supported through maintenance contracts with the manufacturer.

Public Speakers

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