Classification of Ultrasonic Surgical Devices Under Product Codes “LFL”, “NLQ”, and “LBK”

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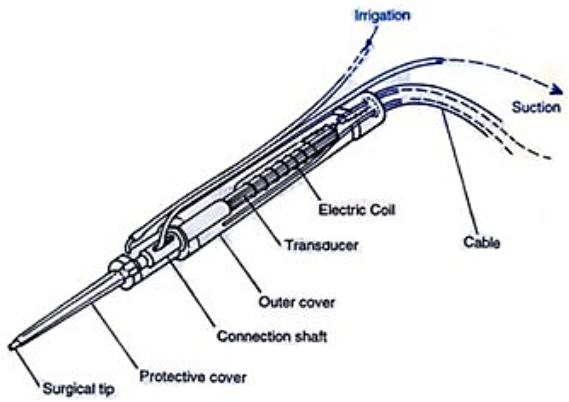
Device Description

- Ultrasonic surgical devices are hand-held tools indicated for use in a wide variety of open and minimally invasive surgical specialties
- Ultrasonic surgical devices utilize rapid vibrations in the ultrasonic frequency range, which in turn develops heat at the active site.
- They generally employ a handpiece containing a metal tip oscillating at a frequency of at least 20kHz.
- Device power generation is supplied from a console.
- These devices fragment, emulsify and remove unwanted soft and hard tissues in combination with irrigation and aspiration.
- Some devices may be used for bleeding control or ligation of vessels.
- LFL: Ultrasonic surgical instruments
- NLQ: Single-use reprocessed versions of “LFL” devices
- LBK: Ultrasonic surgical instruments specifically indicated for neurosurgical uses



Indications for Use

- All devices currently cleared under “LFL”, “NLQ”, and “LBK” are for prescription use only.
- Most devices are indicated for use in the fragmentation, emulsification, and aspiration of both soft and hard tissue.
  - Some devices may also be indicated for bleeding control or ligation of vessels.

Indications for Use

- Some IFU statements reference these additional surgery types:
  - Neurosurgery
  - Gastrointestinal and affiliated organ surgery
  - Gastroenterology
  - General Surgery
  - Gynecological Surgery
  - Laparoscopic Surgery
  - Orthopedic Surgery
  - Plastic and Reconstructive Surgery
  - Thoracic Surgery
  - Thoracoscopic Surgery
  - Urological Surgery
  - Wound Care

Regulatory History

- Pre-amendment, i.e., marketed prior to May 1976
- Unclassified when marketed
- Currently these devices are being regulated through the 510(k) pathway.
- These devices are cleared for marketing if their intended use and technological characteristics are “substantially equivalent” to a legally marketed predicate device.
- There is no regulation associated with the product codes.

Clinical Background: Surgical Outcomes

- LFL/NLQ devices provide patient benefit as surgical tools employed to treat various conditions within each surgical subspecialty.
- LBK devices are commonly used in intracranial and intraspinal tumor resection.
- There are risks both inherent with each specific procedure and with the anesthetic employed to complete the operation.
- Surgical outcomes following the use of LBK devices are based on a combination of parameters
- Potential intra-surgical and post-surgical adverse events for intracranial and intraspinal tumor resection using LBK devices include:
  - Infection, neurological deficits, seizure, hydrocephalus, thermal injury, leptomeningeal seeding (LMS)
- The effectiveness of intracranial and intraspinal tumor resection using LBK devices is measured by post-surgery tumor recurrence or progression (PSTRP), overall and progression free survival, gross tumor resection, length of surgery and hospital stay, and post-surgical improvement

Clinical Background: Currently Available Treatment

- Hand-held, hand-powered sharp instruments are commonly employed by surgeons to divide tissues.
- Ultrasonic surgical devices can perform both tissue division and hemostasis, thus preserving and promoting economy of motion and can shorten operative times.
- LBK devices are considered part of clinical usual care in the United States (US) when fragmentation and aspiration of neurological tissues is desired.
- Surgical hemostasis can be achieved by other electrosurgical devices capable of tissue coagulation, as well as suture ligation methods.
- Staplers can be employed for the control and division of larger blood vessels and/or vascular pedicles.

Literature Review

- For ultrasonic surgical devices under product codes LFL and NLQ, two electronic databases (Embase and PubMed/MEDLINE) were searched for
  - Studies published from 1/1/07 to 1/1/22
  - Search terms Ultrasonic Surgical Instruments (LFL), Ultrasonic Surgical Aspirators (LFL), and Reprocessed Ultrasonic Surgical Instruments (NLQ).
- In total, 632 unique records were identified and screened at the title/abstract level.
  - Excluded 583 records that were not relevant to the review at the title/abstract level,
  - 49 full-text records assessed for eligibility. 46 records were retrieved and screened full-text.
    - Three records were not available for full-text screening.
  - After a comprehensive literature review, 18 articles were identified that addressed incidence of adverse events with the use of ultrasonic instruments.

Literature Review

- For ultrasonic surgical devices under product codes LBK, two electronic databases (Embase and PubMed/MEDLINE) were searched for
  - Studies published from 1/1/10 to 9/1/20, with a follow-up review for literature published between 9/1/20 to 5/13/20.
  - Search terms: ultrasonic or ultrasound devices in the neurological field/neurosurgery.
- A total of 534 references were identified and screened at the title/abstract level.
  - 514 references remaining after removing duplicates
  - 476 articles were excluded following a review of titles and abstracts and full-text articles
  - 16 published literature references determined to be relevant to the safety and/or effectiveness
  - Additional 22 articles identified on devices that appear used for neurological indications, but not identified as a device cleared under LBK
  - Following the supplemental search (September 1, 2020, to May 13, 2022), yielded two additional publications were considered.

Literature Review – Safety Assessment

- For LFL and NLQ devices, pain was the most commonly reported safety outcome (reported in 14/18 studies)
  - Results were mixed; some studies report statistically significant pain difference comparing ultrasonic surgical devices to other surgical cutting devices, others do not
- Infection was reported in 9/18 studies
  - Incidence ranged from 0.7% to 6.5% among the 9 studies.
  - No statistical difference in incidence rates between ultrasonic and other surgical cutting devices.
- Tissue injury was reported in three studies
- Hematoma reported in one study
- Mortality reported in one study
- No reports of device malfunction or device-related injuries to the user or patients

Literature Review – Safety Assessment

- For the LBK related search, there was a great variation of device-related adverse events across studies.
- The adverse events included:
  - mortality
  - leptomeningeal seeding (LMS)
  - thermal injury
  - neurological deterioration
  - complications
- Aside from complications specific to neurological surgery, the potentially device-related adverse events appear to be consistent with those identified under the more general search of products associated with product codes LFL and NLQ.

Literature Review – Effectiveness Assessment

- LFL and NLQ encompass a wide variety of surgical procedures, and therefore effectiveness outcomes were not assessed.
- Given that these devices are generally surgical tools, the outcomes related to specific surgeries are not particularly influential in the classification decision making for these products.
- Given the specificity of the LBK product code to neurological surgical uses, only the literature associated with LBK was also assessed for effectiveness outcomes.
- The evidence suggests that overall, these devices are reported to be effective for the removal of soft or hard tissue in the brain and spine.

Literature Review – Summation

- LFL and NLQ devices are
  - Used in a wide variety of surgical procedures
  - Effectiveness was not assessed due to the nature of use
  - Risks include pain, infection, tissue injury, and hematoma.
- LBK devices are
  - Primarily used for the resection of brain and spinal tumors.
  - Effective for the removal of soft and hard tissues in the brain and spine.
  - Risks include death, LMS, thermal injury, meningitis, bleeding, pneumonia, and neurologic deterioration with transient or permanent deficits.

Medical Device Reports

- Medical Device Reporting (MDR): the mechanism for the FDA to receive significant medical device adverse events from:
  - mandatory reporters (manufacturers, importers and user facilities)
  - voluntary reporters (health care professionals, patients, consumers)
- MDR reports can be used effectively to:
  - Establish a qualitative snapshot of adverse events for a specific device or device type
  - Detect actual or potential device problems used in a “real world” setting/environment, including

Medical Device Reports

- Limitations
  - Under reporting of events
  - Potential submission of incomplete, inaccurate, untimely, unverified, or biased data
  - Incidence or prevalence of an event cannot be determined from this reporting system alone
  - Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report
  - MAUDE data does not represent all known safety information for a reported medical device

Medical Device Reports

- MAUDE Database reviewed for product code “LFL” from 1/1/02 to 12/31/21:
  - 46,673 relevant MDRs were identified: Malfunction (N = 44,354), Serious Injury (N = 2,263), Death (N = 56).
    - Death reports were further assessed to examine possible risks
      - 34 did not implicate the device in death of the patient
      - 9 initiated from literature review
      - 13 identified as potentially device related
    - Malfunction reports noted unknown device problem, break, overheating, and device leak.
    - Injury reports noted bleeding, thermal burns, and foreign body in patient.
- MAUDE Database specific query for “NLQ” was not conducted
  - Adverse events are most commonly entered under the product code of the original single-use device a query for NLQ specific devices may be duplicative and result in skewed data

Medical Device Reports

- MAUDE Database reviewed for product code “LBK” through 7/12/22:
  - 57 relevant MDRs were identified: Malfunction (N = 39), Injury (N = 17), and Death (N = 1).
    - The injury reports noted delayed, prolonged or additional procedures, device fragments left in the patient, tissue damage (e.g., dural tears, burns, swelling), CSF leaks, wound healing issues, and pseudomeningocele.
    - The malfunction report noted unknown device problem, break, overheating, and device leak.
    - The death narrative indicated that the device was not in contact with the patient and that death was not device related.

Recall History

- The Medical Device Recall database contains Medical Device Recalls classified since November 2002.
- Since January 2017, it may also include correction or removal actions initiated by a firm prior to review by the FDA.
- The status is updated if the FDA identifies a violation and classifies the action as a recall and again when the recall is terminated.
- FDA recall classification (resulting in the posting date) may occur after the firm recalling the medical device product conducts and communicates with its customers about the recall.

Recall History

- 27 recalls for “LFL”
  - Related to device design, component integrity, and packaging and sterile barrier integrity
- 4 recalls for “NLQ”
  - Two recalls related to packaging of the devices, one related to lack of a regulatory clearance, and one was a technical issue.
- 1 recall “LBK”
  - Related to an accessory of a device that is used for electrocautery with or without ultrasonics.
- These recalls do not suggest that there are general safety concerns related to the class of ultrasonic surgical devices
  - except for the lack of regulatory clearance, these are risks that can be mitigated through the proposed special controls.

Risks

Identified Risk	Description/Examples
Infection	This can result from the use of devices that are not adequately sterilized or reusable device components that are not adequately cleaned and sterilized.
Adverse Tissue Reaction	This can result from the use of device materials that are not biocompatible and may also result from non-resorbable material fragments from the device left in the body due to device mechanical failure.
Bleeding/Hemorrhaging/Blood Loss	This can result from unintended damage to surrounding blood vessels or device malfunction/failure leading toa failure to seal or cauterize.
Tissue Injury (Thermal, Mechanical, Electrical)	Tissue injury can result due to excessive energy or heat applied to tissues causing burns or thermal injury, or mechanical injury due to the power of the device from fragmentation, emulsification, and aspiration. Tissue injury can occur from electric shock resulting from malfunction or failure of the electrical components of the device. Tissue injury can also result in: • Neurological Deterioration (neurological indications) • Prolonged surgical procedure • Death
Interference with other devices	Device electromagnetic (EM) emissions may affect other nearby surgical equipment. Device may be susceptible to EM interference from emissions from other nearby surgical equipment.

Risk and Mitigations

Identified Risk	Recommended Mitigation Measure
Infection	Sterilization Validation Reprocessing Validation Pyrogenicity Evaluation (neurosurgical devices only) Shelf-life Testing Packaging Validation Labeling
Adverse Tissue Reaction	Biocompatibility Evaluation Shelf-life testing
Bleeding, Hemorrhaging, Blood Loss	Non-clinical Performance Testing Bench Testing Animal Performance Testing
Tissue injury resulting from: Thermal effects, burns Mechanical failure, device breakage Electrical hazards, shock Software malfunction Use error	Labeling Non-clinical Performance Testing Bench Testing Device Reliability Testing Electrical Safety Testing Electromagnetic compatibility (EMC) testing Software Verification, Validation, and Hazard Analysis Animal Testing Shelf-Life Testing Use-Life Testing
Interference with other Devices	Electromagnetic Compatibility (EMC) Testing Labeling

Proposed Classification

878.4XXX Ultrasonic Surgical Device.

(a) *Identification.* An ultrasonic surgical device is a prescription device intended to heat, fragment, emulsify, or remove tissue by use of ultrasound frequency displacement and vacuum suction. This type of device may include ultrasonic scalpels, ultrasonic vessel sealers, ultrasonic surgical aspirators, and accessories such as assembly tools (wrenches), footswitches, and end effector tips.

(b) *Classification.* Class II (special controls).

Proposed Special Controls

1. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including the following:
    a. Characterization of the ultrasonic and power parameters (e.g., sonication frequency and displacement, irrigation rate, suction (negative) pressure).
    b. Bench testing of material strength to demonstrate the device will withstand forces encountered during use and maintain device integrity over the labeled shelf-life and use-life, including repeated cleaning/use cycles if reprocessed.
2. Software used to operate the device hardware must be described in detail in the software requirements specification (SRS) and software design specification (SDS). Software verification, validation, and hazard analysis must be performed.
3. Electrical safety, thermal safety, mechanical safety, and electromagnetic compatibility (EMC) testing must be performed.
4. Performance data must demonstrate the sterility of the tissue-contacting components of the device and must evaluate pyrogenicity (if intended for neurosurgical use).
5. Performance data must support the shelf-life and use-life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf-life and use-life.

Proposed Special Controls

6. The tissue-contacting components of the device must be demonstrated to be biocompatible.
7. Animal performance data must demonstrate that the device performs as intended and will not result in unintended tissue injury, including mechanical and thermal damage to surrounding tissue structures.
8. The labeling must include:
    a. Qualifications needed for the safe use of the device.
    b. A detailed summary of the device technical parameters.
    c. A detailed summary of the device- and procedure-related complications pertinent to use of the device.
    d. Information on how the device operates.
    e. A shelf-life for sterile components.
    f. The use-life of the device for reusable components.
    g. Validated methods and instructions for reprocessing of any reusable components.
    h. Information on the electrical safety and electromagnetic compatibility of the device.
    i. Prominent labeling adjacent to original equipment manufacturer (OEM) identifying the reprocessor for single-use reprocessed ultrasonic surgical instruments.

U.S. FOOD & DRUG ADMINISTRATION

Thank You

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Questions to Panel

Question 1 to Panel

- FDA has identified the following risks to health for ultrasonic surgical devices:

Identified Risk	Description/Examples
Infection	This can result from the use of devices that are not adequately sterilized or reusable device components that are not adequately cleaned and sterilized.
Adverse Tissue Reaction	This can result from the use of device materials that are not biocompatible and may also result from non-resorbable material fragments from the device left in the body due to device mechanical failure.
Bleeding/Hemorrhaging/Blood Loss	This can result from unintended damage to surrounding blood vessels or device malfunction/failure leading to a failure to seal or cauterize.
Tissue Injury (Thermal, Mechanical, Electrical)	Tissue injury can result due to excessive energy or heat applied to tissues causing burns or thermal injury, or mechanical injury due to the power of the device from fragmentation, emulsification, and aspiration. Tissue injury can occur from electric shock resulting from malfunction or failure of the electrical components of the device. Tissue injury can also result in: • Neurological Deterioration (neurological indications) • Prolonged surgical procedure • Death
Interference with other devices	Device electromagnetic (EM) emissions may affect other nearby surgical equipment. Device may be susceptible to EM interference from emissions from other nearby surgical equipment

Question 1 to Panel

- Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of ultrasonic surgical devices under product codes “LFL”, “NLQ”, and “LBK”.

- In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these ultrasonic surgical devices.

Question 2 to Panel

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

- insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of its safety and effectiveness, AND
- if, the device is purported or represented to be for use in supporting or sustaining human life, 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.

Question 2 to Panel

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.

Question 2 to Panel

FDA believes general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness and sufficient information exists to establish special controls to adequately mitigate the risks to health and provide reasonable assurance of device safety and effectiveness for this device type.

As such, FDA believes that Class II is the appropriate classification for ultrasonic surgical devices under product codes LFL, NLQ, and LBK. Following is a risk/mitigation table which outlines the identified risks to health for this device type and the recommended controls to mitigate the identified risks.

Question 2 to Panel

Identified Risk	Recommended Mitigation Measure
Infection	Sterilization Validation Reprocessing Validation Pyrogenicity Evaluation (neurosurgical devices only) Shelf-life Testing Packaging Validation Labeling
Adverse Tissue Reaction	Biocompatibility Evaluation Shelf-life testing
Bleeding, Hemorrhaging, Blood Loss	Non-clinical Performance Testing Bench Testing Animal Performance Testing
Tissue injury resulting from: Thermal effects, burns Mechanical failure, device breakage Electrical hazards, shock Software malfunction Use error	Labeling Non-clinical Performance Testing Bench Testing Device Reliability Testing Electrical Safety Testing Electromagnetic compatibility (EMC) testing Software Verification, Validation, and Hazard Analysis Animal Testing Shelf-Life Testing Use-Life Testing
Interference with other Devices	Electromagnetic Compatibility (EMC) Testing Labeling

Question 2 to Panel

Please discuss whether the identified special controls for ultrasonic surgical devices under product codes LFL, NLQ, and LBK appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

Proposed Special Controls:

1. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including the following:
    a. Characterization of the ultrasonic and power parameters (i.e., sonication frequency, irrigation rate, suction (negative) pressure).
    b. Bench testing of material strength to demonstrate the device will withstand forces encountered during use and maintain device integrity over the labeled shelf-life and use-life, including repeated cleaning/use cycles if reprocessed.
2. Software used to operate the device hardware must be described in detail in the software requirements specification (SRS) and software design specification (SDS). Software verification, validation, and hazard analysis must be performed.
3. Electrical safety, thermal safety, mechanical safety, and electromagnetic compatibility (EMC) testing must be performed.
4. Performance data must demonstrate the sterility of the tissue-contacting components of the device and must evaluate pyrogenicity (if intended for neurosurgical use).
5. Performance data must support the shelf-life and use-life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf-life and use-life.

Question 2 to Panel

6. The tissue-contacting components of the device must be demonstrated to be biocompatible.
7. Animal performance data must demonstrate that the device performs as intended and will not result in unintended tissue injury, including mechanical and thermal damage to surrounding tissue structures.
8. The labeling must include:
    a. Qualifications needed for the safe use of the device.
    b. A detailed summary of the device technical parameters.
    c. A detailed summary of the device- and procedure-related complications pertinent to use of the device.
    d. Information on how the device operates.
    e. A shelf-life for sterile components.
    f. The use-life of the device for reusable components.
    g. Validated methods and instructions for reprocessing of any reusable components.
    h. Information on the electrical safety and electromagnetic compatibility of the device.
    i. Prominent labeling adjacent to original equipment manufacturer (OEM) identifying the reprocessor for single-use reprocessed ultrasonic surgical instruments.

Question 3 to Panel

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for ultrasonic surgical devices under product codes "LFL," "NLQ," and "LBK". If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

End of Panel Questions for Product Codes “LFL”, “NLQ”, “LBK”

Thank you.