Classification of Vapocoolant Devices Under Product Code "MLY"

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Device Description

- Vapocoolant devices encompass a family of devices used to apply a chemical to induce rapid topical cooling.

- The mechanism for chemical ejection and the formulation of these chemicals varies between specific products and includes both manual and powered devices.
  - Many of the devices utilize a metal aerosol can for delivery of coolant.

- Vapocoolant devices are commonly used as a form of local anesthetic.

Indications for Use

- Vapocoolant devices are intended for the following uses:
  - Temporary relief and reduction of minor topical pain and swelling
  - Pain reduction associated with hypodermic injections and for minor surgical procedures
  - Reduce pain by topical application to intact mucous membranes in the oral cavity, the lips and to minor open wounds.
  - Management of myofascial pain, restricted motion and muscle tension

Most, but not all, of these devices are cleared for prescription use.

Regulatory History

- Vapocoolant devices are currently a pre-amendment, unclassified device type
  - This means that this device type was marketed prior to the Medical Device Amendments of 1976 but was not classified by the original classification panels.

- These devices are being regulated through the 510(k) pathway

- Since these devices are unclassified, there is no regulation associated with the product code

- To date, the FDA has cleared 25 devices under the MLY product code.

Clinical Background

- Mechanical and thermal stimuli activate nociceptors in the skin and subcutaneous tissues that stimulate A delta and C neural fibers that transmit neural signals via multiple pathways to the central nervous system

- These stimuli are further processed and perceived as pain.

- Vapocoolant sprays rapidly reduce the temperature of the skin and impede the stimulation of nociceptors to temporarily reduce the perception of painful stimuli.

Clinical Background

- Currently Available Treatment:
  - Pain from minor injuries, injections, minor surgical procedures, minor wounds and myofascial pain can be mitigated with ice, cool compresses and topical analgesics.
  - Oral medication options include non-steroidal anti-inflammatory medications and acetaminophen.
  - Pain secondary to myofascial and mild muscle pathology can be managed with heat-conveying modalities, injection of local anesthetics, active or passive stretching, therapeutic exercise, and the application of direct or indirect pressure via manual techniques.

Literature Review

- A systematic literature review was conducted in an effort to gather any published information regarding the safety and effectiveness of vapocoolant devices under product code “MLY”.
- Literature searches were conducted to identify any relevant articles published between January 1, 2010 and December 31, 2020.
- The searches were limited to publications in English and excluded conference proceeding and abstracts.
- Limited to randomized controlled trials (RCTs) where at least one treatment arm used a vapocoolant device.
- A total of 35 published literature references were determined to be relevant to the safety and/or effectiveness of vapocoolant devices.

Literature Review – Safety Assessment

- The majority (71.4%) of publications reported no complications or did not report on adverse events or safety risks with the use of the device

- Reported Adverse Events Include:
  - Mild pruritus
  - Transient erythema
  - Swelling
  - Bruising
  - Blanching
  - Minor local skin reactions
  - Discomfort and pain

Literature Review – Effectiveness Assessment

- Overall, 22 out of 32 studies reported effective decreases in pain with the administration of vapocoolant devices prior to the needlestick procedure. ($p < 0.05$).
- 10 RCTs did not show effectiveness of topical refrigerants

Literature Review – Summation

- There is no evidence of a mortality risk from the use of the device. The adverse events were transient or temporary, and resolved soon after the cooling effect expired without the need for additional treatments.

- Clinical evidence from the published literature shows mixed results for the effectiveness of vapocoolant devices in the reduction of pain from routine procedures involving needlesticks such as vaccination, cannulation, and venipuncture.

- Based on the peer-reviewed medical literature, vapocoolant device use for the reduction of pain from routine procedures involving needlesticks is favorable, with no severe adverse events and only minor transient skin reactions occurring.

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)

Medical Device Reports

- 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:
    - rare, serious, or unexpected adverse events
    - adverse events that occur during long-term device use
    - adverse events associated with vulnerable populations
    - off-label use
    - user error

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 (Manufacturer And User Facility Device Experience) Database reviewed for product code “MLY” from November 1, 1989 through December 31, 2020:

- The search identified 15 relevant MDRs:
  - Malfunctions (n=4)
  - Injuries (n=10)
  - Deaths (n =1)

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

- A review of the database found two recalls for devices under MLY product code:
  - The first recall was initiated on April 17, 2007 for six prescription-only vapocoolant device due to Aspergillus fumigatus mold contamination identified during internal quality control sampling, specifically, during the six month stability testing of the microbial limits for total aerobic count. The recall was completed February 2, 2008.
  - The second recall was initiated on September 3, 2008 in response to a customer complaint which led to a Corrective and Preventive Actions (CAPA) investigation (CAPA (b)(4)) that revealed some lots of Gebauer's Fluro-Ethyl had a defective gasket. No injury was reported as a result of the malfunctioning unit. The recalled product was discontinued because the valve supplier was unable to correct the issue without a major re-design of the valve, which the Gebauer Company contended was not feasible from a business standpoint.

Risks

Identified Risk	Description/Examples
Pain or discomfort	This can result from burns and/or blistering.
Skin irritation	This can result from burns and/or blistering.
Thermal injury	This can result from frostbite or burns particularly when used in combination with electrical cautery leading to ignition, leading to redness, blistering and edema.
Electrical shock or burn	This can result from electrical failure or malfunction.
Interference with other devices	Electromagnetic disturbances that may cause unacceptable degradation in device performance, leading to delayed or ineffective treatment.

Risks

Identified Risk	Description/Examples
Device failure/malfunction leading to ineffective treatment	Device malfunction can cause spray to contact unintended areas of the body which can lead to burns and minor injury.
Asthma	This can result from an allergic response to the product or aerosol delivery system.
Hallucination	This can result from improper use of the device and subsequent inhalation toxicity.

Risks and Mitigations

Identified Risk	Recommended Mitigation Measure
Pain or discomfort	Labeling
Skin irritation, including: • Bruising • Numbness • Erythema • Swelling	Labeling
Thermal injury, including: • Skin blanching • Sores • Frostbite • Burns	Non-clinical performance testing Labeling

Risks and Mitigations

Identified Risk	Recommended Mitigation Measure
Electrical shock or burn	Electrical safety testing
Interference with other devices	Electromagnetic compatibility (EMC) testing
Device failure/malfunction leading to ineffective treatment	Non-clinical performance testing Labeling
Asthma	Labeling
Hallucination	Labeling

Proposed Classification

890.5871 Vapocoolant device.

(a) *Identification.*

A vapocoolant device is a cold therapy device intended for the temporary relief and reduction of minor topical pain and swelling. The device consists of a compressed low-vapor pressure liquid, which is rapidly sprayed onto the skin, whereupon the contacted skin is transiently cooled through rapid evaporation.

(b) *Classification.*

Class II (special controls)

Proposed Special Controls

We propose the following Special Controls for these devices:

1. Non-clinical performance testing must characterize the change in skin surface temperature control when the device is used as intended.

2. Non-clinical performance testing must demonstrate electrical safety and electromagnetic compatibility for powered devices.

3. Healthcare provider and patient labeling must include:
   a) Information on how the device operates and the typical course of treatment.
   b) A warning that the device should not be used near an open flame, high heat or electric cautery devices.
   c) A warning regarding the risk of frostbite or burns if device is not used as directed.
   d) A warning that if skin irritation persists, discontinue use of the product.
   e) A warning that the device should not be used by individuals with known allergies to product ingredients, as use by such individuals may lead to an allergic response including difficulty breathing
   f) A warning that the device should not be directly inhaled, as this may be harmful or fatal

U.S. FOOD & DRUG ADMINISTRATION

Thank You

End of Panel Questions for Product Code “MLY”

Question 1 to Panel

FDA has identified the following risks to health for vapocoolant devices:

Identified Risk	**Description/Examples**
Pain of Discomfort	This can result from burns and/or blistering.
Skin irritation	This can result from burns and/or blistering.
Thermal injury	This can result from frostbite or burns particularly when used in combination with electrical cautery leading to ignition, leading to redness, blistering and edema.

Question 1 to Panel

FDA has identified the following risks to health for vapocoolant devices:

Identified Risk	**Description/Examples**
Electrical Shock or Burn	This can result from electrical failure or malfunction.
Interference with other devices	Electromagnetic disturbances that may cause unacceptable degradation in device performance, leading to delayed or ineffective treatment.
Device failure/malfunction leading to ineffective treatment	Device malfunction can cause spray to contact unintended areas of the body which can lead to burns and minor injury.

Question 1 to Panel

FDA has identified the following risks to health for vapocoolant devices:

Identified Risk	Description/Examples
Asthma	This can result from an allergic response to the product or aerosol delivery system
Hallucination	This can result from improper use of the device and subsequent inhalation toxicity

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of vapocoolant devices under product code "MLY". In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these vapocoolant 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 controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls would provide such assurance, AND
- 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.

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 vapocoolant devices. 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
Pain or discomfort	Labeling
Skin irritation, including: • Bruising • Numbness • Erythema • Swelling	Labeling
Thermal injury, including: • Skin blanching • Sores • Frostbite • Burns	Non-clinical performance testing Labeling

Question 2 to Panel

Identified Risk	**Recommended Mitigation Measure**
Electrical shock or burn	Electrical safety testing
Interference with other devices	Electromagnetic compatibility (EMC) testing
Device failure/malfunction leading to ineffective treatment	Non-clinical performance testing Labeling
Asthma	Labeling
Hallucination	Labeling

Question 2 to Panel

Please discuss whether the identified special controls for vapocoolant devices 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 characterize the change in skin surface temperature control when the device is used as intended.

2. Non-clinical performance testing must demonstrate electrical safety and electromagnetic compatibility for powered devices.

3. Healthcare provider and patient labeling must include
   a) Information on how the device operates and the typical course of treatment.
   b) A warning that the device should not be used near an open flame, high heat or electric cautery devices.
   c) A warning regarding the risk of frostbite or burns if device is not used as directed.
   d) A warning that if skin irritation persists, discontinue use of the product.
   e) A warning that the device should not be used by individuals with known allergies to product ingredients, as use by such individuals may lead to an allergic response including difficulty breathing.
   f) A warning that the device should not be directly inhaled, as this may be harmful or fatal.

Question 3 to Panel

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for vapocoolant devices. 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 Code “MLY”