

**DE NOVO CLASSIFICATION REQUEST FOR  
ESOPHAGEAL COOLING DEVICE**

**REGULATORY INFORMATION**

FDA identifies this generic type of device as:

**Esophageal thermal regulation device.** An esophageal thermal regulation device is a prescription device used to apply a specified temperature to the endoluminal surface of the esophagus via an external controller. This device may incorporate a mechanism for gastric decompression and suctioning. The device is used to regulate patient temperature.

**NEW REGULATION NUMBER:** 21 CFR 870.5910

**CLASSIFICATION:** II

**PRODUCT CODE:** PLA

**BACKGROUND**

**DEVICE NAME:** Esophageal Cooling Device

**DE NOVO REQUEST:** DEN140018

**DATE OF DE NOVO REQUEST:** May 9, 2014

**REQUESTOR CONTACT:** Advanced Cooling Therapy, LLC  
3440 S. Dearborn St. #215-South  
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**REQUESTOR'S RECOMMENDED CLASSIFICATION:** II

**INDICATIONS FOR USE**

The Esophageal Cooling Device is a thermal regulating device, intended to:

- connect to a Gaymar Medi-Therm III Conductive Hyper/Hypothermia System to control patient temperature, and
- provide gastric decompression and suctioning.

**LIMITATIONS**

Prescription use only: Federal (USA) law restricts this device to sale by or on the order of a physician.

The Esophageal Cooling Device may cause or exacerbate esophageal tissue damage in patients with esophageal deformity or evidence of esophageal trauma, or in patients who have ingested acidic or caustic poisons within the prior 24 hours.

The safety and effectiveness of the Esophageal Cooling Device have not been evaluated in patients with less than 40 kg of body mass.

The Esophageal Cooling Device should only be used by healthcare professionals with training in the use of orogastric tubes and the use of the Gaymar Medi-Therm III Conductive Hyper/Hypothermia System.

The Esophageal Cooling Device is intended for esophageal placement. Inserting the Esophageal Cooling Device in the trachea, bronchi or lungs can result in serious patient harm.

Attachment of the Esophageal Cooling Device to unapproved or unintended connections can result in serious patient harm.

The presence of the Esophageal Cooling Device may interfere with other devices in the esophagus or mouth. Dual placement of other devices in the esophagus with the Esophageal Cooling Device in place, such as an enteral feeding tube, may result in patient harm.

Large patients with a body mass greater than 120 kg may exhibit slower responses to intended temperature changes. Small patients with a body mass less than 60 kg may exhibit faster cooling than anticipated, and may exhibit slower rewarming than anticipated.

For a full list of warnings and precautions, refer to the Esophageal Cooling Device Instructions for Use.

## **DEVICE DESCRIPTION**

The Esophageal Cooling Device (ECD) is a silicone tube with three lumens that is placed in the esophagus (Figure 1). The intended function of the device is to control a patient's temperature, while simultaneously maintaining access to the stomach to allow gastric decompression and drainage. Modulation and control of patient temperature is intended to be achieved by connecting the ECD to an external heat exchanger and circulating temperature-controlled fluid (distilled water). Two lumens (the cooling lumens) connect to the external heat exchanger and are in contact with the esophageal tissues. A third central lumen connects to wall suction and is used for standard gastric decompression. A web supports the inner gastric lumen and separates the cooling lumens.



Figure 1: Esophageal Cooling Device

The ECD is made of standard medical-grade silicone. It is a single-use, disposable, non-implantable device with a stated intended duration of use of 36 hours or less.

The ECD is intended to be used in conjunction with the Gaymar Medi-Therm III Conductive Hyper/Hypothermia System (cleared under K100585) with the following operating specifications:

- Dead Head Pressure: Maximum 9 psi (62 kPa)
- Flow: Minimum 16 gallons/h (60.6 L/hr)
- Water Temperature Control Range: 4°C - 42°C

The Gaymar System supplies temperature-controlled water through a connector hose to the ECD. An accessory probe interfaces between the Gaymar System and the patient to sense patient temperature, which is displayed on the Gaymar System's control panel. The Gaymar device controls water temperature by mixing hot and cold water using hot and cold solenoid valves under microprocessor control and includes a circulating pump, heater, and refrigeration system.

## **SUMMARY OF NONCLINICAL/BENCH STUDIES**

Non-clinical/bench studies conducted on the Esophageal Cooling Device to demonstrate a reasonable assurance of safety and effectiveness of the device are summarized in the sections below.

### **BIOCOMPATIBILITY/MATERIALS**

The Esophageal Cooling Device contacts the lining of the patient’s esophagus for up to 36 hours. The Esophageal Cooling Device is categorized as a surface-contacting device that is in contact with an intact mucosal membrane for a prolonged exposure time. In accordance with ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing within a Risk Management Process, the following biocompatibility testing was conducted on the Esophageal Cooling Device. The biocompatibility assessment was deemed adequate.

Table 1: Esophageal Cooling Device Biocompatibility Testing

Test	Purpose	Results
Cytotoxicity Evaluation – L929 MEM Elution Test/L929 Neutral Red Uptake Test	To assess the biological activity of L-929 mouse fibroblast cells (grown in culture) after exposure to extracts prepared from the completed Esophageal Cooling Device	Non-cytotoxic
Kligman Maximization Test	To estimate the potential for sensitization of the Esophageal Cooling Device extract using the guinea pig as an animal model	Sensitization rate = 0%, Sensitization grade = “Weak”
Intracutaneous Injection Test	To assess the irritating potential of extracts of the Esophageal Cooling Device to cause irritation to the exposed part of the body	No difference between mean test article score and mean control score

### **SHELF LIFE/STERILITY**

The Esophageal Cooling Device is provided non-sterile, is not intended to be sterilized, and is for single use. The Esophageal Cooling Device has a shelf life of one year, which was assessed by repeating bench performance testing after one year of accelerated aging.

### **PERFORMANCE TESTING – BENCH**

The Esophageal Cooling Device was subjected to a series of bench tests to assess its functional performance. These tests were performed on final manufactured product that had been pre-conditioned to simulate exposure to worst-case acidic gastric conditions. This conditioning consisted of exposure to simulated gastric contents (pH ≈ 1.2), water-based lubricants, and coolant containing the maximum recommended concentration of algacide/cleaner provided by the external heat exchanger manufacturer for at least 36 hours. Heated coolant (40°C) was circulated through the device to increase the reactivity of the chemicals.

Table 2: Esophageal Cooling Device Bench Testing

Test	Purpose	Results
Tensile force	To ensure all components and joints in the Esophageal Cooling Device assembly are capable of withstanding tensile forces experienced during insertion, use, and removal	Passed; $\geq 15$ N acceptance criteria
Burst strength	To ensure the Esophageal Cooling Device can withstand the operating pressures supplied by the external heat exchanger	Passed; $\geq 15$ psi
Ultimate material strength	To determine the ultimate strength of the material used to manufacture the Esophageal Cooling Device extruded tube and evaluate the device's ability to withstand pressures experienced during a worst-case scenario	Passed; $\geq 5$ MPa
Leakage	To ensure the Esophageal Cooling Device does not allow a potentially hazardous amount of coolant into the esophagus or stomach	Passed; no visible evidence of leakage
Flow rate	To ensure the thermal transfer capacity of the Esophageal Cooling Device is not adversely affected by an insufficient flow rate from the external heat exchanger	Passed; $\geq 31$ L/h
Resistance to vacuum	To ensure the Esophageal Cooling Device does not collapse and prevent suctioning when placed under vacuum	Passed; no visible evidence of occlusion
End cap axial deflection testing	To ensure the Esophageal Cooling Device does not puncture or irritate the esophageal mucosa during tube insertion	Passed; $\leq$ mean force required to cause end cap axial deflection for a currently marketed enteral feeding connector
Hardware verification (temperature control and safety)	To ensure the external heat exchanger can accurately monitor coolant temperature when connected to the Esophageal Cooling Device  To ensure the external heat exchanger can, adjust coolant temperature when connected to the Esophageal Cooling Device  To ensure the safety features of the external heat exchanger operate properly when connected to the Esophageal Cooling Device (high/low temperature alarms, coolant flow occlusion alarm)	Passed; temperature probe accurate to within $\pm 1.0^\circ\text{C}$  Passed; coolant temperature at lowest setting reached $4.5^\circ\text{C}$ within 30 minutes  Passed; all alarms and indicators sounded appropriately
Transportation simulation	To ensure the finished device packaging is capable of withstanding the rigors of shipping without damaging the product	Passed in accordance with ISTA 2A 2011
Packaging integrity	To ensure the finished device packaging is capable of preventing contamination of the device from outside sources	Passed in accordance with ASTM F2096-11

Compatibility with the Gaymar System was assessed via the burst strength, flow rate, and hardware verification testing described above.

#### **PERFORMANCE TESTING – ANIMAL**

The following animal study was used to support the in vivo evaluation of the safety and effectiveness of the Esophageal Cooling Device:

Kulstad et al. “Induction, Maintenance, and Reversal of Therapeutic Hypothermia with an Esophageal Heat Transfer Device” (Resuscitation 2013; 8; p. 1619-1624).

The primary aim of this study conducted in five female domestic b(4) swine (range 61-70 kg) was to evaluate the integrity of esophageal mucosa tissue and adjacent organs after experimental temperature modification, as determined by gross pathological and histological analysis at necropsy.

#### **Study Protocol**

Thirty minutes after anesthesia and insertion of the Esophageal Cooling Device, the baseline body temperatures of the swine were monitored for 15-60 minutes and then reduced by b(4) Celsius and maintained for approximately 24 hours. b(4)

After the 24-hour period, the swine were rewarmed at a rate of approximately b(4) by setting the external heat exchanger (Gaymar Medi-Therm III) to warming mode. The swine were allowed to recover from anesthesia and kept under surveillance for 3 to 14 days prior to sacrifice and necropsy.

After device placement, low-intermittent wall suction was connected to the Esophageal Cooling Device gastric outlet to provide gastric decompression and suctioning for the full duration of treatment. The total gastric fluids suctioned for each swine were measured and recorded. Arterial blood pressure, heart rate, electrocardiograms, end tidal CO<sub>2</sub> and O<sub>2</sub> saturation were monitored and recorded every 30 minutes to 1 hour while the animals were anesthetized. Arterial blood gases were measured at intervals throughout the treatment duration.

#### **Study Outcomes**

All swine were recovered from anesthesia successfully and transferred to cages while spontaneously breathing. One animal expired approximately 4 hours after completion of the protocol. This death was determined by the veterinary pathologist to be due to tracheal edema and tissue damage induced by the prolonged pressure of the inflated endotracheal tube balloon and not the Esophageal Cooling Device. With the exception of that swine, all animals recovered successfully from anesthesia and returned to normal behavioral, eating, and drinking habits.

Multiple sections of each esophagus were taken (cranial, mid-cranial, mid, mid-caudal,

caudal, and gastroesophageal junction). As reported by the veterinary pathologist, no adverse effects from the Esophageal Cooling Device were identified in gross or histological (sections were stained with hematoxylin and eosin) analyses, demonstrating that the device did not cause harm to the esophageal lining following use.

Between 300 and 825 mL of gastric fluids were collected from each animal. All five swine were cooled successfully, with an average rate of temperature decrease of 1.3 °C/hour b(4) . Warming rates averaged 0.4°C/hour b(4) b(4) . The average deviation from goal temperature was 0.2°C during the maintenance phase of the study. Thermogenic shivering did not occur in any of the animals.

### **SUMMARY OF CLINICAL INFORMATION**

Clinical data summaries for 16 patients were supplied to support a determination of a reasonable assurance of the safety and effectiveness of the Esophageal Cooling Device. These data were obtained from centers outside the United States, from locations where the Esophageal Cooling Device is commercially available. All of the data summaries describe therapeutic cooling, maintenance of the target temperature, and eventual rewarming. Ten reports included a patient body temperature chart plotted over time. Target temperatures were set from 33°C – 36.5°C, and each of the ten temperature charts showed adequate device performance at achieving and maintaining goal temperatures.

In the majority of the clinical cases, the Esophageal Cooling Device was used to cool and eventually re-warm patients that had been resuscitated from cardiac arrest. Some of the patients had a fever at baseline, while others were at normal or below-normal body temperatures prior to placement of the device. The duration of temperature management ranged from 24 to 36 hours. No adverse events or device malfunctions were reported, and the gastric suctioning was reported by the centers to have worked as intended without the need for additional tube insertion.

While the majority of the submitted clinical data was obtained from post-cardiac arrest patients, the Esophageal Cooling Device was only evaluated according to its ability to modulate patient temperature. No evaluation of whether hypothermia improved cardiac arrest outcomes was performed.

### **LABELING**

The Esophageal Cooling Device labeling consists of Instructions for Use and packaging labels. The Instructions for Use include the indications for use, warnings, precautions, and instructions for the safe use of the device. The labeling satisfies the requirements of 21 CFR 801.109.

Please see the Limitations section above for important warnings and precautions presented in the device labeling.

## **RISKS TO HEALTH**

The table below identifies the risks to health that may be associated with use of esophageal thermal regulation devices and the measures necessary to mitigate these risks.

<b>Identified Risk</b>	<b>Mitigation Measures</b>
Adverse Tissue Reaction	Biocompatibility Testing
Gastric Distension	Non-clinical Performance Evaluation Labeling
Injury to the Esophagus	Non-clinical Performance Evaluation Animal Testing Labeling
Harmful Hypo/Hyperthermia	Non-clinical Performance Evaluation Animal Testing Labeling
Injury to the Trachea	Labeling

## **SPECIAL CONTROLS:**

In combination with the general controls of the FD&C Act, the Esophageal Cooling Device is subject to the following special controls:

1. The patient contacting materials must be demonstrated to be biocompatible.
2. Non-clinical performance evaluation must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
  - a. Mechanical integrity testing
  - b. Testing to determine temperature change rate(s)
  - c. Testing to demonstrate compatibility with indicated external controller
  - d. Shelf life testing
3. Animal testing must demonstrate that the device does not cause esophageal injury and that body temperature remains within appropriate boundaries under anticipated conditions of use.
4. Labeling must include the following:
  - a. Detailed insertion instructions
  - b. Warning against attaching device to unintended connections, such as external controllers for which the device is not indicated or pressurized air outlets instead of vacuum outlets for those devices including gastric suction
  - c. The operating parameters, name, and model number of the indicated external controller
  - d. The intended duration of use.

## **BENEFIT/RISK DETERMINATION**

While 16 clinical use summaries were provided, no formal clinical study was provided, requested, or deemed necessary for the Esophageal Cooling Device based on the risks. The



probable risks of the device are based on the nonclinical data and the animal study described above. Potential device-related adverse events include adverse tissue reactions, gastric distension, injury to the esophagus, injury to the trachea, and inappropriate patient temperature. Based on the nonclinical information provided, the probability of each of these potential adverse events is low.

The probable benefits of the device are also based on nonclinical data and the animal study, as well as the clinical data summaries and clinical literature surrounding patient temperature management. The Esophageal Cooling Device lowers, maintains, or raises patient temperature as desired by the physician. The gastric suctioning feature precludes the need for additional gastric tube insertion. It should be noted that the clinical data were only reviewed in the context of the indications for use; that is, the device's ability to control patient temperature and provide gastric suctioning. Consequently, a demonstration of an improvement in clinical outcomes was not required.

Additional factors considered in determining probable risks and benefits for the Esophageal Cooling Device include:

- alternative methods of patient temperature management have different risks and difficulties associated with their use; intravascular cooling carries risk of vascular injury and infection, surface methods may be slower, and gastric lavage has risks of volume overload and electrolyte imbalance
- in some clinical case reports, the device more effectively lowered patient temperature after conventional methods had failed to achieve the target temperature
- the clinical data is limited for all temperature management methods and devices
- feedback from centers using the device outside of the United States has been positive in terms of ease of use and degree of temperature control

In conclusion, given the available information above, the data support that for controlling patient temperature the probable benefits outweigh the probable risks for the Esophageal Cooling Device. The device provides benefits and the risks can be mitigated by the use of general and the identified special controls.

## **CONCLUSION**

The *de novo* for the Esophageal Cooling Device is granted and the device is classified under the following:

Product Code: PLA  
Device Type: Esophageal thermal regulation device  
Class: II  
Regulation: 21 CFR 870.5910