

**DE NOVO CLASSIFICATION REQUEST FOR
cNEP AIRWAY MANAGEMENT SYSTEM**

REGULATORY INFORMATION

FDA identifies this generic type of device as:

External Negative Pressure Airway Aid. An external negative pressure airway aid is a prescription device that applies negative pressure to a patient's neck to aid in providing a patent airway during procedures requiring anesthesia.

NEW REGULATION NUMBER: 21 CFR 868.5105

CLASSIFICATION: CLASS II

PRODUCT CODE: PMB

BACKGROUND

DEVICE NAME: cNEP AIRWAY MANAGEMENT SYSTEM

SUBMISSION NUMBER: DEN140024

DATE OF DE NOVO: AUGUST 18, 2014

CONTACT: PROMEDIC

REQUESTER'S RECOMMENDED CLASSIFICATION: CLASS I EXEMPT

In DEN140024, the sponsor requested Class I exempt. However, in DEN140024 we indicated that the device should more appropriately be classified as Class II with special controls given the identified risks. The sponsor agreed upon the Class II classification.

INDICATIONS FOR USE

The cNEP Airway Management System is to be used as an aid for maintaining the patency of the upper airway in spontaneously breathing adults undergoing medical procedures less than 2 hours in duration, where the patient is intended to have mild to moderate sedation with non-propofol containing medications.

LIMITATIONS

The sale, distribution, and use of the cNEP Airway Management System is limited to prescription use only.

Use is limited to 2 hours duration, based on the maximal time of exposure to the cNEP Airway Management System in clinical studies that focused on carotid blood flow.

Contraindications

- Exclude patients with cutaneous hypersensitivity to the silicone rubber materials in the cNEP collar.

Warnings

- This device should not be used during medical procedures involving propofol.
- The device is intended for external use only on intact skin.
- Do not use the cNEP Airway Management System on any patient where an airtight seal cannot be obtained with the collar on the patient's neck, e.g., patients with hyperhidrosis or excessive sweating, if the collar flanges extend over the ears, or patient has excessive facial hair.
- Excessive filling of collar with loose neck tissue may reduce effectiveness of the device in opening a patient's airway. A larger collar size may ameliorate this condition.
- Ensure that the reference mark on the cNEP Airway Management System is aligned with the chin and mandible as indicated
- Only connect cNEP Airway Management System to a regulated source of vacuum that can be set to provide a nominal value of -45 cmH₂O
- Use of the cNEP Airway Management System is not a substitute for continuously monitoring the patient's respiratory status.
- Airway obstruction and respiratory distress may occur while the cNEP Airway Management System is in use.
- Exclude patients with known or suspected carotid vascular disease
- Exclude patients who are an aspiration risk
- Exclude patients with anatomical abnormalities in the pharyngeal region such as enlarged tonsils or pharyngeal malignancy
- Exclude patients with anatomical abnormalities of the cervical region which prevent adequate collar fit or function such as current or previous neck surgery/injury, previous radiation therapy, tracheal deviation, tracheostomy, scleroderma and CREST syndrome.
- Screen patients for unknown carotid vascular disease, which includes the following:
 - A history of CVA or TIA of uncertain etiology
 - Carotid bruit on physical examination
 - Diminished carotid pulse on physical examination

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

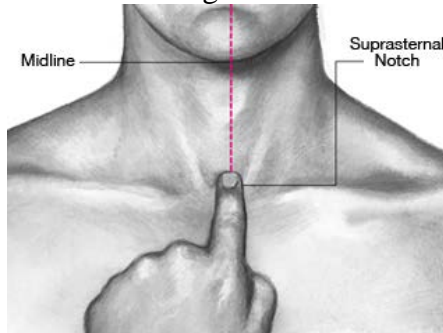
The cNEP Airway Management System is a silicone rubber collar that is attached to the neck by a hydrogel and provides negative suction through a regulated vacuum source (see Figure 1). The vacuum suction allows the device to provide a patent airway during mild to moderate sedation.

Figure 1



The patient is placed in a supine position before beginning the sedation procedure. Within the labeling information provided, the user is instructed to grasp lateral ends of the collar and hold away from patient's skin while rotating the bottom edge of the collar toward the suprasternal notch as shown in Figure 2 below.

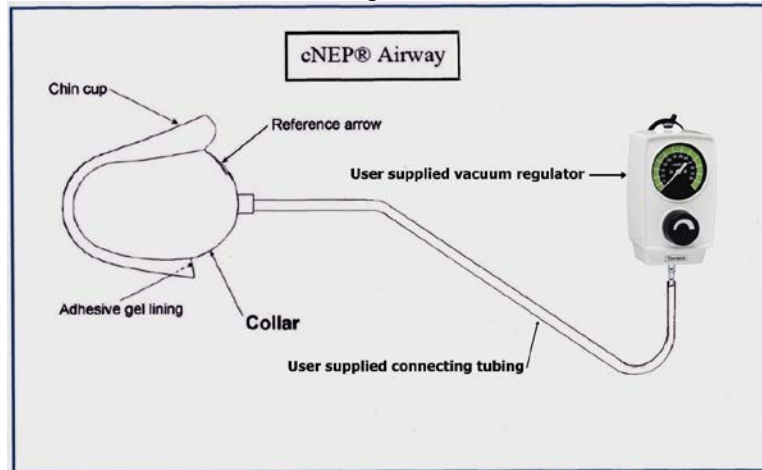
Figure 2



When the bottom of the collar is resting on the patient's skin, the user is directed to release the lateral ends, allowing the collar to contact the patient's skin, below the ears.

The collar is placed on the surface of the mandible and neck overlying the upper airway. A connector for attachment to suction tubing is connected to a regulated vacuum source and then used to deliver continuous negative external pressure and when placed correctly, prompts the device to suction the neck. By suctioning or pulling on the neck and the soft tissue below, the device is intended to open the upper airway of adults during mild to moderate sedation. A gauge on the vacuum source is used keep the vacuum within the operating range. Figure 3 illustrates how the cNEP Airway Management System is connected to a regulated vacuum source.

Figure 3



The device is made up of a silicone material which seals the collar across the patient’s skin. The following specifications were provided in the submission:

- Collar sizes: small, medium, large
- Nominal collar weight (medium): 100 g
- Maximum operating period: 2 hours
- Operational vacuum level: -44 ± 4 cmH₂O
- Maximum vacuum level: -50 cmH₂O
- Operating temperature range – collar: 15°C to 37°C
- Operating atmospheric conditions: sea level to 8000 feet
- Storage and transportation temperature range: -20°C to 40°C

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The cNEP Airway Management System contacts the skin for a limited duration of ≤ 24 hours. Therefore, the device is classified as a surface device with a limited duration of contact. In accordance with the guidance document “G95-1 Memorandum: Initial Evaluation Tests for Consideration” and ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing within a Risk Management Process, the following tests were conducted on the cNEP Airway Management System: *In Vitro* Cytotoxicity, Sensitization, and Intracutaneous Reactivity (or Irritation). A summary of these tests is provided in Table 1.

Table 1 – Summary of Biocompatibility Testing

Test	Purpose	Results
<i>In Vitro</i> Cytotoxicity	To assess the biological reactivity of device extracts	Non-cytotoxic
Sensitization	To assess the sensitization potential of device extracts	Non-sensitizing
Irritation	To assess the irritation potential device extracts	Non-irritating

The results indicated that the device is non-cytotoxic, non-sensitizing and non-irritating, and were found to be acceptable.

SHELF LIFE/STERILITY

The cNEP Airway Management System is to be marketed non-sterile. It is for single patient use only and does not have a shelf life. This is appropriate for this type of technology.

PERFORMANCE TESTING – BENCH

Performance testing was conducted on the cNEP Airway Management System to ensure the device does not lose collar seal or vacuum while the patient is in various positions, is able to operate under various operational temperature and storage conditions, and no leakage occurs while the device maintains vacuum. The performance tests conducted on the cNEP Airway Management System and results are outlined in Table 2.

Table 2 – Summary of Bench Testing

Test	Purpose	Acceptance Criteria	Results
Collar Seal Maintenance	Demonstrate that the collar seal is not lost and maintained a seal during the procedure	Un-occluded reading gauge reading should equal occluded gauge reading	Pass
Patient Repositioning	Demonstrate the ability to reposition a patient while wearing the device	Device must remain on subject at operating vacuum.	Pass
Jaw Thrust	Demonstrate the ability for a caregiver to execute mandibular advancement (jaw thrust) while the device is applied	Ability to displace mandible forward.	Pass
Ability to Talk	Demonstrate the patient can talk with medical professionals while wearing the device	The subject must be able to speak during use.	Pass
Mouth Accessibility	Demonstrate medical professional can have full access to the patient’s mouth while wearing the device	Device remains in place when patient opens their mouth.	Pass
Device Application on Side	Demonstrate the ability for a caregiver to apply the device to a patient while he/she is lying on their side	Device can be applied to subject.	Pass
Operational Testing at High and Low Temperature	Demonstrate accuracy of the operational vacuum zone cutoff boundary	Vacuum level within 40 ± 2 cm H ₂ O	Pass

Test	Purpose	Acceptance Criteria	Results
Drop Test	Demonstrate the device's ability to resist damage associated with inadvertent dropping	Device does not have damage and pass functional test	Pass
Low and High Temperature Storage	Demonstrate the device's ability to function properly after being stored in a hot/cold environment	No visual damage and pass functional test	Pass
Device Leakage	Demonstrate the device maintains vacuum	Vacuum level to be greater than 40 cmH ₂ O	Pass

SUMMARY OF CLINICAL INFORMATION

The applicant provided clinical test reports for three clinical studies conducted.

- 5iS-009: Effectiveness and safety of continuous negative external pressure in preventing sedation-related respiratory impairment in adults undergoing colonoscopy
- 5iS-010: Exploratory study to determine the effect of the application of continuous external negative pressure (cNEP Airway Management System) by a cervical collar on carotid blood flow in adults
- 5iS-10B: Similar study protocols as 5iS-010 but patients were exposed to -45 cm H₂O for 120 mins instead of -50 cm H₂O for 10 mins

Study 5iS-009 – Proof of Concept and Safety Study

Protocol:

Fifty-four (54) subjects were recruited to undergo routine colonoscopy and were monitored for the presence of apneas and impaired oxygenation. The control group containing 24 subjects received standard care at the study site. The treatment group containing 30 subjects received standard care with cNEP Airway Management System at a pressure of -45 cmH₂O.

Primary Endpoint

- The frequency of respiratory impairment (RI) events in the treatment (cNEP) group compared to the control group, where RI is defined by the occurrence of either of the following:
 - A decline in oxygenation as determined by pulse oximetry (SpO₂) by at least 4 % from baseline for at least 20 seconds
 - Presence of apneas as defined by the American Academy of Sleep Medicine (AASM Scoring Manual, 2007), lasting longer than 15 seconds

Secondary Endpoints

- The safety of cNEP Airway Management System as determined by adverse events reported by the investigators.
- The incidence of subjects with one or more RI in the treatment group compared to the control group.
- The frequency of interventions to alleviate RI in the treatment group compared to the control group. Such interventions include reduction or reversal of sedation; increased oxygen administration; jaw thrust; placement of an oral, nasal oropharyngeal airway; intubation and early termination of the colonoscopy.

Inclusion Criteria

- Male or female subjects 18-80 years of age undergoing routine colonoscopy at the study site.

Exclusion Criteria

- Presence of severe cardiopulmonary or neurologic disease as determined by the investigator.
- History of vascular fragility associated with cutaneous pressure.
- History of hypersensitivity to silicone.
- Inability to properly fit the cNEP Airway Management System collar to the subject.
- The presence of excessive facial hair in the region where the cNEP Airway Management System collar is positioned.
- Known carotid vascular disease, previous major neck surgery or radiation therapy to the cervical region.
- Presence of anatomical abnormalities in the neck or pharyngeal region (such as enlarged tonsils).
- Inability to provide informed consent.

Results: The primary effectiveness endpoint was defined as 2 types of respiratory impairment events: a decline in oxygenation determined by pulse oximetry and a presence of apneas defined by the American Academy of Sleep Medicine. In the analysis of this endpoint, the mean number of RI events in the control group was 3.5 and in the treatment group 1.92. For the primary safety endpoints for study 5i-009, a statistically significant difference was observed ($p=0.01$) as increased oxygen supplementation was administered in 42% of the no-cNEP group and 10% in the cNEP group. In terms of apnea events, a statistically significant difference was seen in the two groups ($p=0.0006$). 74% of the no-cNEP group experience apnea compared to 28% of the cNEP group. In twelve of the twenty-nine subjects (41.3%) who used the AMS device during colonoscopy, cutaneous erythema at the site of contact of the cNEP collar with the neck was noted but was resolved within 20 minutes.

Secondary endpoints were defined as: the safety of cNEP Airway Management System as determined by adverse events reported by investigators, incidence of subjects with one or more RI in the control vs treatment group and frequency of interventions to alleviate RI in the control

vs treatment group. One (3%) intervention was required to relieve airway obstruction (jaw thrust) and three (10%) interventions to increase the amount of supplemental oxygen to the subjects in the treatment group. In the control group, 10 subjects (42%) were given increased oxygen administration. During sedation there was no effect of the cNEP Airway Management System on the heart rate or respiration as indicated in the study.

Study 5iS-10

Protocol:

Eight (8) subjects were evaluated for common and internal carotid artery blood flow by Doppler ultrasound for a period of 10 minutes. Carotid blood flow measurements were taken using Doppler ultrasound measurements before and after the duration of use.

Primary Endpoint

- The change in common carotid blood flow measured at baseline and at the end of a timed exposure to -50 cm H₂O cNEP.

Secondary Endpoints

- The safety of cNEP Airway Management System as determined by adverse events observed by the investigators.
- The safety of cNEP Airway Management System as determined by assessing any change in vital signs measured at baseline and compared to vital signs measured while on -45 cm H₂O cNEP Airway Management System.

Inclusion Criteria

- Male or female subjects 18-80 years of age with no active health problems

Exclusion Criteria

- Presence of severe cardiopulmonary or neurologic disease as determined by the investigator
- History of skin capillary fragility associated with cutaneous pressure
- History of hypersensitivity to silicone.
- Inability to properly fit the cNEP Airway Management System collar to the subject.
- The presence of excessive facial hair in the region where the cNEP Airway Management System collar is positioned.
- Known carotid vascular disease, previous major neck surgery or radiation therapy to the cervical region.
- Presence of anatomical abnormalities in the neck or pharyngeal region (such as enlarged tonsils).
- Inability to provide informed consent.

Study 5iS-10B

Protocol:

Nine (9) subjects were evaluated for common and internal carotid artery blood flow by Doppler ultrasound for a period of 2 hours. Carotid blood flow measurements were taken using Doppler ultrasound measurements before and after the duration of use.

Primary Endpoint

- The change in common carotid blood flow measured at baseline and at the end of a timed exposure to -45 cm H₂O cNEP Airway Management System.

Secondary Endpoints

- The safety of cNEP Airway Management System as determined by adverse events observed by the investigators.
- The safety of cNEP Airway Management System as determined by assessing any change in vital signs measured at baseline and compared to vital signs measured while on -45 cm H₂O cNEP Airway Management System.

Inclusion and Exclusion criteria were the same for this study as 5iS-10.

Summary of Results from 5iS-10 and 5iS-10B:

The age range of subjects studied was 57-74 years old in study 5iS-10, and 59-67 years old in 5iS-10B. There was no statistically significant difference in blood flow between the control group and the cNEP treatment arm. In the 2 hour study (5iS-10B), mean common carotid blood flow in the baseline group was 27.74 ml/min, while it was 28.37 ml/min in the cNEP treatment arm. Increased common carotid blood flow related to the device was observed overall but the effect was trivial. Vital signs (systolic blood pressure, diastolic blood pressure, heart rate and respiratory rate) were measured at baseline and after 2 hours with the cNEP device. There was no statistically significant difference between the groups. Based on the results, the study demonstrates the benefits outweigh the risks of the device.

LABELING

Labeling provided for the cNEP Airway Management System includes Instructions for Use and a Quick User Guide, which summarizes information from the Instructions for Use. The labeling provided is adequate and includes the appropriate information regarding specifications, instructions for use, contraindications, warnings, and cautions, as well as an appropriate prescription statement as required by 21 CFR 801.109.

Important components of the labeling include:

- Warnings and instructions to exclude patients with carotid artery disease, due to the potential risk of the device to dislodge arterial plaques in the carotid artery.
- Warning against use of the device during medical procedures involving medications that contain propofol.
- Warnings against use of the device in patients with anatomical abnormalities, which may negatively impact the safety and effectiveness of the device.
- Technical specifications to ensure proper use, including adequate collar fit, appropriate

- applied negative pressure, and duration of use.
- A summary of the safety and effectiveness results from clinical testing.

RISKS TO HEALTH

Table 3 below identifies the risks to health that may be associated with use of the External Negative Pressure Airway Aid and the measures necessary to mitigate these risks.

Table 3 – Identified Risks to Health and Mitigation Measures

Identified Risk	Mitigation Measure
Impaired blood flow	• Clinical Performance Testing
Failure of device or negative pressure mechanism	• Non-clinical Performance Testing
Adverse tissue reaction	• Biocompatibility
Dislodging of plaque, leading to possible stroke	• Labeling
Inadequate collar fit	• Labeling
Use error	• Labeling

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the External Negative Pressure Airway Aid is subject to the following special controls:

1. Clinical performance testing must document any adverse events observed during clinical use, including impaired blood flow, and demonstrate that the device performs as intended under anticipated conditions.
2. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated patient positions, does not fail during use and does not lose negative pressure capability. The following testing should be performed:
 - a. Ability of the device to maintain a seal during various patient positions
 - b. Device leakage testing to demonstrate the device maintains vacuum
 - c. Drop testing to ensure the device does not incur functional damage after dropping the device
 - d. Functional testing after high and low storage temperature.
3. All patient contacting components must be demonstrated to be biocompatible.
4. Labeling must include:
 - a. A summary of clinical testing results, including any adverse events and evidence that effectiveness has been achieved.
 - b. Technical specifications of the device, including collar sizes, maximum duration of use, operating temperature and storage temperature range.

- c. Technical specifications of the vacuum source, including maximum vacuum level and operational vacuum level.
- d. Instructions for use that includes how to place the device, determination of size, verification of suction, reference to training materials and information on troubleshooting the device if it does not attach properly.
- e. A warning to screen patients for carotid artery disease due to the probable risk of the device to dislodge arterial plaques in the carotid artery.
- f. A warning to exclude patients with anatomical abnormalities.
- g. A warning not to use the device during medical procedures involving medications that contain propofol.

BENEFIT/RISK DETERMINATION

The risks of the device are based on data collected in the studies described above. Device related serious adverse events were not observed. The most serious adverse event that was observed during the study was respiratory impairment events such as a decline in oxygenation. A potential risk of the device to dislodge arterial plaques in the carotid artery has been mitigated by a warning to screen patients for this disease in labeling. A less serious adverse event of redness or erythema occurred in 12 patients and resolved itself in 20 minutes.

The probable benefits of the device are also based on data collected in a clinical study as described above. The 5iS-009 study demonstrated that the treatment group (with cNEP Airway Management System) had fewer instances of providing supplemental oxygen (10%) when compared to supplemental oxygen (43%) provided to the control group (no cNEP). This demonstrated the benefit of the cNEP Airway Management System during a 2-hour procedure when compared to sedation procedures that have airway devices only intended for emergency scenarios involving oxygen desaturation and a closing airway.

In conclusion, given the available information above, the data support that for the device to be used as an aid for maintaining the patency of the upper airway in spontaneously breathing adults undergoing medical procedures where the patient is intended to have mild to moderate sedation with non-propofol containing medications, the probable benefits outweigh the probable risks for the cNEP Airway Management System. The device provides substantial benefits and the risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The De Novo request for the cNEP Airway Management System is granted and the device is classified under the following:

Product Code: PMB
Device Type: External Negative Pressure Airway Aid
Class: II
Regulation: 21 CFR 868.5105