DE NOVO CLASSIFICATION REQUEST FOR
HEM-AVERT® PERIANAL STABILIZER

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Pressure wedge for the reduction of cesarean delivery**. A pressure wedge for the reduction of cesarean delivery is a prescription device that provides external mechanical support to the perianal region during the labor and vaginal delivery process. External mechanical support of the perianal region is intended to help reduce the occurrence of cesarean delivery.

NEW REGULATION NUMBER: 21 CFR 884.5210

CLASSIFICATION: II

PRODUCT CODE: PNU

Background

DEVICE NAME: HEM-AVERT® PERIANAL STABILIZER

SUBMISSION NUMBER: DEN160005

DATE OF DE NOVO: JANUARY 29, 2016

CONTACT: STETRIX, INC.
70 CLAY ST
OAKLAND, TN 38060

INDICATIONS FOR USE

The Hem-Avert® Perianal Stabilizer provides counter-pressure to the anus during vaginal childbirth. This counter-pressure force, applied at 8-10 cm of dilation, is intended to help reduce the likelihood of cesarean delivery. Additionally, this counter-pressure force helps prevent the occurrence of external hemorrhoids during vaginal childbirth.

LIMITATIONS

- The Hem-Avert Perianal Stabilizer is a prescription device under 21 CFR Part 801.109.
- The Hem-Avert Perianal Stabilizer should be removed immediately if the physician feels the instrument in any way interferes with the childbirth process.
- Misuse or mishandling of the product may cause injury to the patient. Improper

handling can render the product unsuitable for its intended use. Other probable complications may include, but are not limited to:

- Infection - If the product sterility has been compromised.
- Pain, discomfort or abnormal sensation resulting from the presence of the instrument against the anus.
- Skin/tissue trauma.

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

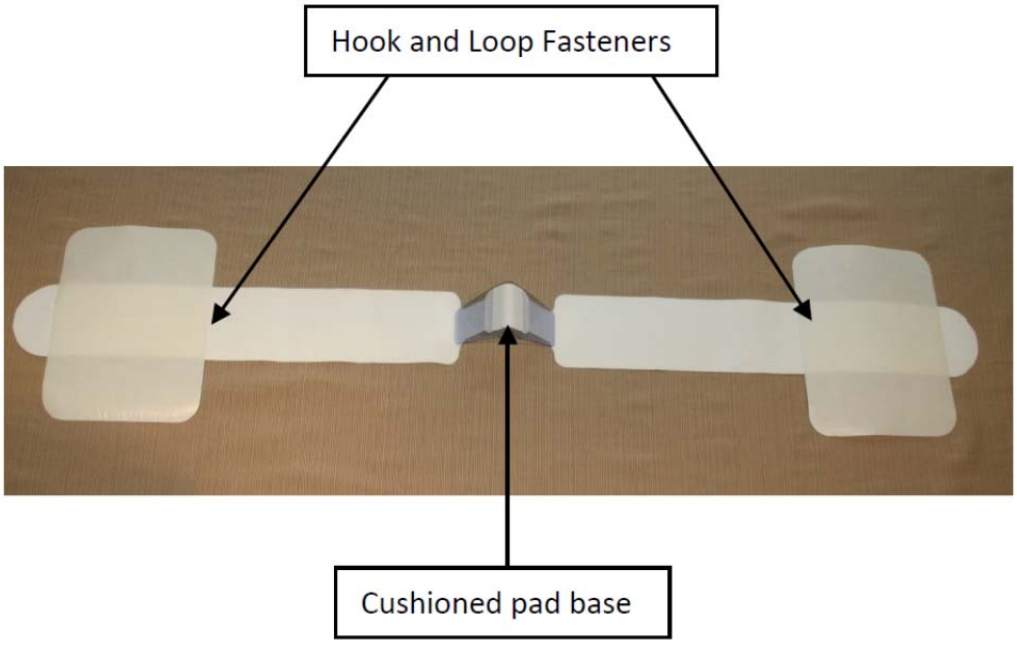
DEVICE DESCRIPTION

This is a single use, disposable, sterile device. The Hem-Avert Perianal Stabilizer (Hem-Avert) consists of three components:

1. Rigid polymer base manufactured from a polycarbonate
2. Centrally located cushioning pad composed of a laminate of polyester non- woven tape and polyethylene foam tape
3. Two lateral hook and loop adhesive strips (with liners) which provide the tension required to keep the device firmly in place during delivery.

Figure 1 below is an image of the Hem-Avert.

Figure 1. Hem-Avert Device



This De Novo request is for an expanded indication (new intended use) of providing counter-pressure to the anus during vaginal childbirth, applied at 8-10 cm of dilation, to help reduce the likelihood of cesarean delivery.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Hem-Avert includes materials that have direct patient contact for less than 24 hours. The complete device in its final, finished form was subjected to biocompatibility testing in accordance with ISO 10993-1: Biological evaluation of medical devices, Part 1: Evaluation and Testing. The following tests were conducted:

- Cytotoxicity
- Sensitization
- Irritation (Intracutaneous Reactivity)

The results demonstrated the Hem-Avert is non-cytotoxic, non-sensitizing, and non-irritating.

SHELF LIFE/STERILITY

The device is provided sterile in a b(4) CCI peel pouch by b(4) CCI to achieve a sterility assurance level (SAL) of 10 . Sterilization validation was completed per ISO 11137:2006 using 10 samples at b(4) CCI and 10 samples at b(4) CCI . Three samples had positive growth at b(4) CCI and none had positive growth at b(4) CCI .

The device has a shelf life period of 2 years. To substantiate this shelf life, accelerated aging studies were completed to simulate 1, 2, and 3 years of age, utilizing 60, 60, and 65 samples respectively. After the initial accelerated aging, 10 samples from the 1, 2, and 3 year studies were further aged to simulate 5 years and tested for package integrity via visual inspection to identify obvious signs of package degradation, dye penetration testing (per ASTM F1929-98 (Reapproved 2004)), and peel strength testing (per ASTM F88-07). The results of all tests were deemed acceptable.

PERFORMANCE TESTING – BENCH

To mitigate the risk of device breakage static compression three-point bending testing was conducted on 5 samples of the Hem-Avert. The Hem-Avert was found to endure a compressive load of 188N (to flattening without breaking). The device is designed to withstand the pushing force exerted by a woman in labor without breaking.

SUMMARY OF CLINICAL INFORMATION

There were two clinical studies supporting this application. The Niagara Falls Memorial Medical Center study was a prospective, randomized, single-site clinical study. This study provided the primary data supporting device effectiveness. The Dignity Health clinical study was an observational, single arm study; it provided supportive information regarding effectiveness. Both studies provided information about device safety.

Niagara Falls Memorial Medical Center Study

The clinical investigator performed a prospective, randomized, single-site clinical study comparing the rate of cesarean delivery in patients treated with the Hem-Avert Perianal Stabilizer to a control group of patients who did not receive the device. A total of 102 patients who presented for anticipated singleton vaginal delivery were enrolled in the study. Four patients were removed from the study secondary to protocol violations (one from the device group, three from the control group). Of the remaining 98 patients, 50 were assigned to the subject device arm and 48 to the control arm.

Primary Outcome:

- Difference in cesarean deliveries between the investigational and control groups

Additional Outcomes:

- Adverse events associated with delivery
- Duration of second-stage of labor
- Length of hospital stay

Inclusion Criteria:

Women were allowed to participate in the study if the following inclusion criteria were met:

- Patient scheduled for a vaginal delivery
- Patient exam indicated that delivery would be a singleton birth
- Able to provide Informed Consent

Exclusion Criteria:

Women were excluded if any of the following criteria were encountered during the course of the study:

- Patient's prenatal information indicated that delivery would not be a singleton birth
- Patient was scheduled for an elective cesarean delivery
- The patient was scheduled for a vaginal delivery with anticipated complications (i.e. breech presentation)

Study Methodology:

All patients treated by the investigator during the course of the study were approached to determine eligibility. Block randomization (1:1) was performed using a computer-generated randomization schedule. Patient consent was performed by a member of the research team while the patient was between 1 and 5 centimeters dilated. Patient randomization occurred when subjects were between 5 and 8 centimeters dilated. Management of labor and delivery for both groups was managed in accordance with American Congress of Obstetricians and Gynecologists (ACOG) standards.

Subjects assigned to both groups began delivery in the low lithotomy position. The Hem-Avert device was placed in the device group arm once the patients reached 8-10 cm in cervical dilation.

Results:

- All subjects assigned to the device group were able to be fitted with the device
- Patients assigned to the device group had a lower cesarean section rate compared to the control group; these findings were statistically and clinically significant
- There was no statistically or clinically significant difference in the duration of the second stage of labor between groups (24.9 minutes for device group and 40.8 minutes for control)
- Skin/tissue trauma, pain, slippage, and obstruction to the treatment area were not reported among the adverse events in the clinical study
- Results are summarized in Tables 1 and 2.

Table 1. Patient Demographics, Niagara Falls Memorial Medical Center Study*

Summary	Hem-Avert Patients	Control Patients
Number of Patients	50	48
Mean Age (Time of Delivery) **Minimum and Maximum Age**	25.0 14 and 36 years	25.0 16 and 41 years
Mean Weight (Standard Deviation)	180.6 (44.46)	183.2 (43.79)
Number of Patients with Previous Cesareans	2 (4.0%)	2 (4.0%)
Number of Previous Vaginal Births		
0	20 (40.0%)	25 (52.1%)
1	15 (30.0%)	11 (22.9%)
2	6 (12.0%)	4 (8.3%)
3	6 (12.0%)	4 (8.3%)
4	2 (4.0%)	2 (4.2%)
5	1 (2.0%)	0
6	0	2 (4.2%)

* There were no statistically or clinically significant differences in patient demographics.

Table 2. Cesarean Delivery Rate by Treatment and Adverse Events

Summary	Hem-Avert Patients	Control Patients	p-value
Number of Patients	50	48	
Overall Number of Cesarean Deliveries	6 (12%)	19 (39.6%)	0.0017
Cesarean Rate for Patients Receiving an Epidural	4/28 (14.3%)	17/36 (47.2%)	0.0072
Cesarean Rate for Patients Not Receiving an Epidural	2/22 (9.1%)	2/12 (16.7%)	0.6015
Number of Primiparous Patients	20	25	
Number of Primiparous Cesarean Deliveries	3 (15%)	15 (60%)	0.0022
Cesarean Rate for Primiparous Patients Receiving Epidural	2/14 (14.3%)	14/23 (60.9%)	0.0073

Table 2. Cesarean Delivery Rate by Treatment and Adverse Events			
Summary	**Hem-Avert Patients**	**Control Patients**	**p-value**
Cesarean Rate for Primiparous Patients not Receiving Epidural	1/6 (16.7%)	1/2 (50.0%)	0.4643
Patients Experiencing Adverse Events/Complications	0	7 (14.6%)	0.0053
Specific Complications			
Fetal Bradycardia	0	1 (2.1%)	0.4898
Hemorrhoids	0	6 (12.5%)	0.0117
Right Sulcus Tear	0	1 (2.1%)	0.4898

Dignity Health Clinical Study

The clinical investigator performed a single-site, observational study following the phased introduction of the Hem-Avert device into routine clinical practice. Study participants were all women who presented for vaginal delivery at Dignity Health during the 3-month study period. The investigator extracted existing data from electronic health records (baseline retrospective chart review) to compare cesarean delivery rates between women who delivered prior to the introduction of the Hem-Avert device into clinical practice and those who delivered after device implementation into clinical practice.

Objective:

To assess whether the Hem-Avert device reduces cesarean delivery in women undergoing labor and delivery

Primary Outcome:

- Cesarean Section rate

Secondary Outcomes:

- Duration of second stage of labor
- Adverse events including episiotomies and lacerations

Inclusion Criteria:

- Patients who presented to labor and delivery for anticipated vaginal delivery during the study period

Exclusion Criteria:

- Patients scheduled for cesarean delivery prior to labor and delivery admission

- Failure to progress in labor prior to 8-10 cm in dilation
- Fetal indications
- Maternal indications
- Precipitous labor

Study Methodology:

The investigator performed a baseline retrospective chart review prior to the introduction of the Hem- Avert device into standard clinical practice at the study hospital. The baseline data collection and analysis were performed to identify the number of subjects who presented for planned vaginal delivery who ultimately delivered by cesarean section during a 3-month study period (January 1-March 30, 2015). After review of patient charts, it was determined that 521 subjects met the inclusion criteria (delivered during the 3-month time period). Subjects were excluded from the retrospective baseline review if 1) They were scheduled for cesarean delivery prior to admission to labor and delivery 2) There was evidence of fetal distress prior to reaching 8 cm in dilation or 3) There was failure to progress in labor prior to reaching 8 cm in dilation.

The observational study began on April 1, 2015, after completion of the baseline chart review, and was completed on June 30, 2015. All patients who presented to labor and delivery for anticipated vaginal delivery were given the opportunity to receive the Hem-Avert device (patients were not randomized into either the device or control group). All patients and physicians were given the opportunity to accept or reject the use of the device. Eligible patients had the device placed when they reached 8-10 cm of dilation. Informed consent was not obtained (nor required by IRB), as the Hem-Avert device was being used as indicated. (It was already indicated for preventing the occurrence of external hemorrhoids during vaginal childbirth.) During the 3-month study period, a total of 799 consecutive patients delivered; 790 patients presented with complete demographic data (228 patients treated with the Hem-Avert device, and 562 patients who did not receive the device). Of the 799 patients who delivered, 500 met the inclusion criteria; 227 subjects received the Hem-Avert device, and 273 subjects were placed in the control arm (no device). Duration of the second stage of labor could not be documented because of inconsistencies in documentation related to second stage onset.

Results:

- There were no significant differences in demographics between the populations in the two study arms.
- Among patients who reached 8-10 cm of cervical dilation, 1.76% of Hem-Avert patients had a cesarean delivery compared to 13.55% of control patients. Accordingly, the Hem-Avert patients had a statistically significantly lower incidence rate of cesarean delivery compared to the control patients ($p < 0.0001$).
- Eighty patients (35.24%) who received the Hem-Avert device experienced perineal lacerations compared to 60 (21.98%) of the control patients. As the rate of perineal lacerations was a secondary endpoint, this result was not evaluated for statistical significance.
- Skin/tissue trauma, pain, slippage, and obstruction to the treatment area were not reported among the adverse events in the clinical study.

- Results are summarized in Tables 3 through 6.

Table 3. Summary of Demographic Data at Time of Delivery		
Characteristics	**Hem-Avert® Patients**	**"No Device" Patients**
Age (Years) – Number with Information	228	562
Mean Age	28.1	29.4
Minimum Age	16	16
Maximum Age	44	45
Race (Number, Percentage)	230	569
Caucasian	131 (57.0%)	307 (54.0%)
African American	15 (6.5%)	57 (10.0%)
Hispanic	40 (17.4%)	111 (19.5%)
Asian	28 (12.2%)	57 (10.0%)
Missing	14 (6.1%)	37 (6.6%)
Other	2 (0.9%)	0 (0.0)
Weight (lbs)	209	535
Mean Weight	179	188
Minimum	77	101
Maximum	440	480
Primiparous Patients	99 (43.3%)	222 (39.0%)
Multiparous Patients	131 (56.7%)	347 (61.0%)

Note: Of the 799 consecutive patients who delivered, demographic data were only available for 790 patients; 9 patients were excluded for incomplete demographic data.

Table 4. Primary Endpoint: Cesarean Delivery Rate			
Cesarean Delivery Rate: Overall Patient Population Baseline (No Device) – Control (No Device) - Investigational (Hem-Avert®)			
Summary	**Baseline Patients**	**Control (Study Patients)**	**Hem-Avert® (Study Patients)**
Number of Patients	521	273	227
Cesarean Deliveries	46 (8.83%)	37 (13.55%)	4 (1.76%)*
Vaginal Deliveries	475 (91.17%)	236 (86.45%)	223 (98.24%)

* The Hem-Avert patients had a statistically significantly lower incidence rate of cesarean delivery compared to the control patients ($p < 0.0001$).

Note: Baseline (No Device) patients delivered prior to the introduction of the Hem-Avert device into clinical practice. Control (No Device) patients delivered after Hem-Avert implementation into clinical practice.

Table 5. Cesarean Delivery Rate (Primiparous Patients) Baseline (No Device) – Control (No Device) – Investigational (Hem-Avert®)			
Summary	**Baseline Patients**	**Control (Study Patients)**	**Hem-Avert® (Study Patients)**
Number of Patients	237	106	97
Cesarean Deliveries	17 (7.17%)	28 (26.42%)	4 (4.12%)
Vaginal Deliveries	220 (92.83%)	78 (73.58%)	93 (95.88%)

Note: Baseline (No Device) patients delivered prior to the introduction of the Hem-Avert device into clinical practice. Control (No Device) patients delivered after Hem-Avert implementation into clinical practice.

Secondary Endpoint: Occurrence of Perineal Lacerations

Table 6: Perineal Lacerations Related to Delivery and Severity Baseline (No Device) – Control (No Device) – Investigational (Hem-Avert®) All Patient Groups Reached 8-10cm of Dilation			
Categories	**Baseline Period**	**Control (Study Patients)**	**Hem-Avert® (Study Patients)**
Number of Patients	521	273	227
Patients Without Lacerations	268 (51.43%)	209 (76.55%)	144 (63.43%)
Grade I Lacerations	25 (4.79%)	31 (11.35%)	34 (14.975)
Grade II Lacerations	49 (9.40%)	27 (9.89%)	42 (18.50%)
Grade III Lacerations	1 (0.19%)	1 (0.19%)	3 (1.32%)
Grade IV Lacerations	1 (0.19%)	1 (0.19%)	1 (0.19%)
Total Lacerations	76 (14.58%)	60 (21.98%)	80 (35.24%)
No Laceration Data Available	177 (33.97%)	4 (1.46%)	3 (1.32%)

Note: Baseline (No Device) patients delivered prior to the introduction of the Hem-Avert device into clinical practice. Control (No Device) patients delivered after Hem-Avert implementation into clinical practice.

The data from the clinical studies indicate that the Hem-Avert can assist in reducing the occurrence of cesarean delivery.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The Hem-Avert Perianal Stabilizer complies with the labeling requirements under 21 CFR § 801.109 for prescription devices. The labeling must include specific instructions regarding the proper placement and use of the device to mitigate the risks of skin/issue trauma, device failure, pain, and use error. The labeling must also identify the validated shelf life of the device. Additionally, the labeling should indicate that if the sterile barrier has been compromised, the device must not be used.

RISKS TO HEALTH

Table 7 identifies the risks to health that may be associated with use of the Pressure wedge for the reduction of cesarean delivery and the measures necessary to mitigate these risks.

Table 7. Identified Risks to Health and Mitigation Measures

Identified Risk	Mitigation Method
Skin/tissue trauma	Nonclinical performance data Clinical performance data Labeling
Device failure ▪ breakage ▪ slippage	Nonclinical performance data Labeling
Infection	Sterilization validation Shelf life testing Labeling
Adverse tissue reaction	Biocompatibility evaluation
Pain	Labeling
Use error	Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the Pressure wedge for the reduction of cesarean delivery is subject to the following special controls:

1) The patient contacting materials must be evaluated to be biocompatible.

2) Nonclinical performance data must demonstrate that the device will not break when subjected to the forces it will be exposed to during labor.

3) Performance data must validate the sterility of the device.

4) Performance data must support the shelf life of the device by demonstrating continued sterility and package integrity over the labeled shelf life.

5) Clinical performance data must be provided that characterizes the rate of skin/tissue trauma.

6) The labeling must include:

    a) specific instructions regarding the proper placement and use of the device
    b) a shelf life.

BENEFIT/RISK DETERMINATION

The benefits and risks of the Hem-Avert Perianal Stabilizer are based on two clinical studies.

The probable benefits are based primarily on the Niagara Falls randomized, controlled clinical study, in which the overall rate of cesarean deliveries was 12% in the Hem-Avert patients, compared to 39.6% in the control patients. Supportive information was also provided by the Dignity Health observational study, in which 1.76% of Hem-Avert patients had cesarean deliveries, compared to 13.55% of control patients.

The Digital Health observational clinical study identified the probable risk of perineal lacerations after delivery. In the Hem-Avert device group, 80/227 (35.24%) experienced perineal lacerations after delivery (34/80 were grade I, 42/80 were grade II, 3/80 were grade III and 1/80 was grade IV), compared to 60/273 (21.98%) in the control group (31/60 were grade I, 27/60 were grade II, 1/60 were grade III and 1/60 was grade IV). In the Niagara Falls study, no patients reported adverse events.

Additional factors to be considered in determining probable risks and benefits for the Hem-Avert include:

- Infection (as a consequence of compromise to device sterility)
- Pain/discomfort
- Skin/tissue trauma

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, the data support that for the reduction of cesarean delivery, the probable benefits outweigh the probable risks for the Hem-Avert Perianal Stabilizer. 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 Hem-Avert Perianal Stabilizer is granted and the device is classified under the following:

Product Code: PNU
Device Type: Pressure wedge for the reduction of cesarean delivery
Class: II
Regulation: 21 CFR 884.5210