DE NOVO CLASSIFICATION REQUEST FOR FETAL PILLOW

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Fetal head elevator: A fetal head elevator is a prescription device consisting of a mechanism that elevates the fetal head to facilitate delivery during a Caesarean section.

NEW REGULATION NUMBER: 21 CFR 884.4350

CLASSIFICATION: II

PRODUCT CODE: PWB

BACKGROUND

DEVICE NAME: Fetal Pillow

SUBMISSION NUMBER: DEN150053

DATE OF DE NOVO: November 18, 2015

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INDICATIONS FOR USE

Fetal Pillow is intended to elevate the fetal head and facilitate delivery of the fetus in women requiring a Caesarean Section at full dilation or those requiring a Caesarean Section after a failed instrumental vaginal delivery. Fetal Pillow is indicated for use at a gestational age ≥37 weeks.

LIMITATIONS

- The Fetal Pillow is a prescription device under 21 CFR Part 801.109.
- The Fetal Pillow should not be used in the presence of active genital infection, as it could increase the risk of ascending infection.
- The safety and effectiveness of Fetal Pillow has not been established in the following:
  - In women who have had a previous Caesarean Section
  - In women with a pregnancy less than 37 weeks
  - Multiple gestations

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

DEVICE DESCRIPTION

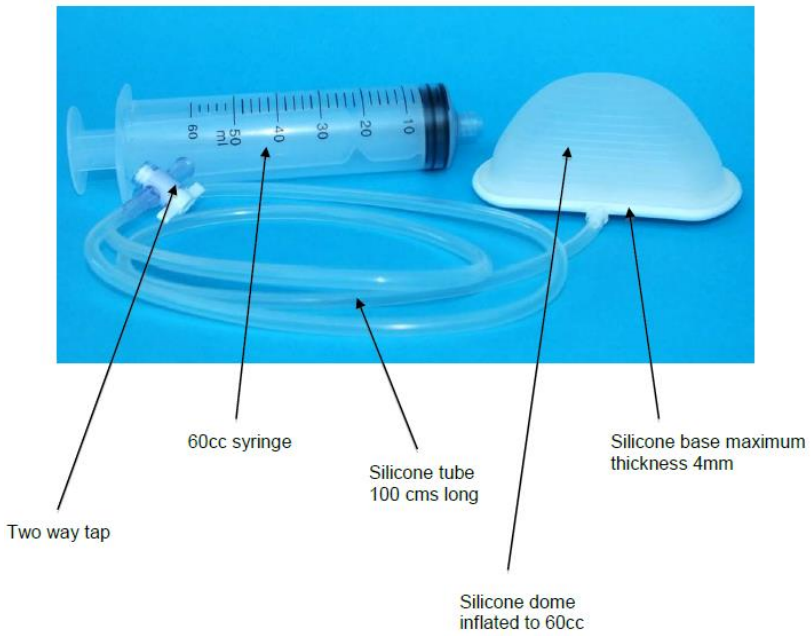
The Fetal Pillow is an inflatable balloon device which consists of the following components:

- **Silicone Balloon:** Dome shaped balloon attached to base plate, inflated to elevate fetal head.
- **Base plate:** Oval shaped silicone base plate (9.3cm x 5.0cm) with internal connecting channel to allow attachment to silicone tube.
- **Silicone Tube:** 4mm tube attaches to connecting channel of base plate for inflation.
- **Two-way tap:** Two-way stopcock at distal end of silicone tube, allows for inflation/deflation of balloon.
- **Syringe:** 60cc polypropylene syringe attached to distal end of silicon tube, used to inflate balloon with saline solution.

The Fetal Pillow is a single use, disposable, sterile device.

Figure 1 below is an image of the Fetal Pillow.

Figure 1. Fetal Pillow



SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Fetal Pillow 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 the FDA guidance document, Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process." The following tests were conducted to assess biocompatibility of the device:

- Cytotoxicity
- Sensitization
- Vaginal Irritation

The results demonstrated the Fetal Pillow is non-cytotoxic, non-sensitizing, and non-irritating.

SHELF LIFE/STERILITY

The device is provided sterile in a Tyvek peel pouch by ethylene oxide (EtO) sterilization to achieve a sterility assurance level (SAL) of 10^{-6}. Sterilization validation was completed per ISO 11135-1:2014, Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices, using the EtO (b) (4) (b) (4) Testing was also performed to ensure the levels of ethylene oxide and ethylene chlorhydrin (ECH) sterilant residuals post degassing met the acceptance criteria in ISO 10993-7.

The device has a shelf life period of 2 years. To substantiate this shelf life, an accelerated aging study was completed to simulate 3 years of aging, and package integrity testing was conducted to confirm the sterile barrier properties are maintained throughout the duration of the shelf life. Aged samples were assessed via visual inspection of the aged Tyvek packaging and seal strength testing. The results demonstrated that the packaging is adequate to maintain the sterility of the device for the proposed shelf life.

Functional testing was conducted on real-time aged samples of two years. Real time aged devices were evaluated in the following tests (see Performance Testing below):

- Leakage
- Leakage under pressure
- Joint disconnection
- Stretching and distortion of balloon
- Maximum pressure resistance
- Deflation reliability

- Inflation pressure under force (Safe Pressures Test)

The results of the shelf life testing demonstrated that the subject device maintains its performance specifications throughout a shelf life of two years.

PERFORMANCE TESTING – BENCH

Bench testing was conducted to evaluate overall device functionality, mechanical performance, and material integrity. Table 1 provides a description of all bench testing conducted, acceptance criteria, results, and sample size.

Table 1. Fetal Pillow Bench Testing

Test Parameter	Test Method	Acceptance Criteria
Leakage	Device inflated to 300cc and evaluated for leakage	Device must not exhibit any fluid leakage after 2 min.
Leakage under pressure	Device inflated to 300cc and subjected to 43.5psi pressure for 10 min., then evaluated for leakage	Device must not exhibit any fluid leakage after 10 min.
Joint Disconnection Strength	2kg mass attached to the luer port and the device was suspended from the balloon for 2min. (tensile stress)	Device must be able to support 2 kg. of weight for 2 min. without any damage
Stretching/ Distortion of balloon	Device inflated to 300cc and measured internal balloon pressure every 15 second for 2min.	Device must inflate evenly without distension in any direction. Pressure must be maintained for 2min. period
Maximum Pressure resistance	Device attached to a pressure gun and inflated until balloon failure	Device must not exhibit leakage at a balloon pressure of 72.5psi
Deflation Reliability	Device inflated to 180cc or 300cc and tap was opened. Time taken for device to empty was recorded.	Time to taken to completely empty must be less than 2min.
Inflation pressure under force	The device was subjected to 80mmHg pressure and inflated from 60cc to 300cc. Inflation pressure was measured at 60, 120, 180, 240, and 300cc fill volume increments.	Device inflation pressure must remain below 142mmHg for all fill volumes.

All samples met the acceptance criteria for each test. The test results demonstrate the Fetal Pillow has adequate performance characteristics for its intended use.

SUMMARY OF CLINICAL INFORMATION

There were two primary clinical studies to support this application. The Indian randomized control trial was a prospective study of 240 patients carried out in West Bengal, India. The Australian retrospective cohort study was a retrospective study of 160 patients carried out in Brisbane, Australia. Differences between the patient populations in both studies, as well as

differences in standard of care clinical practices, necessitated additional information to support the safety and effectiveness of the Fetal Pillow in the US. In order to address concerns regarding differences in the study populations and standard of care clinical practices, the De Novo request included additional real-world data collected from a 75 patient study conducted at Wishaw Hospital in Scotland, as well as a reanalysis of the randomized controlled trial data.

Randomized control trial of elevation of fetal head with a fetal pillow during caesarean delivery at full cervical dilation (West Bengal, India)

This prospective randomized controlled trial was carried out in two teaching hospitals in India and compared the use of the Fetal Pillow with other methods of delivery in a second stage Caesarean Section (CS). A total of 240 patients who required a CS in second stage of labor were enrolled into the study. Thirteen patients were excluded from the study due to: lack of informed consent (n=4), previous caesarean (n=2), breech presentation (n=2) and suspected chorioamnionitis (n=5).

Primary Outcome Measure

- Major uterine incision extensions (grade 2-3)

Secondary Outcome Measures

- Total time taken for CS
- Incision to delivery interval
- Difficulty with delivery of fetal head
- Duration of hospital stay
- Blood loss >1000cc
- Need for blood transfusion
- 5 minute APGAR <3
- NICU stay >24 hours
- Neonatal sepsis
- Neonatal death

Inclusion Criteria

- Ability to give informed consent
- CS at full dilation
- CS after failed instrumental delivery

Exclusion Criteria

- Presence of active genital infection
- Chorioamnionitis
- Breech presentation
- Previous Caesarean Section

- Pregnancy less than 36 weeks
- Inability to give informed consent

Study Methodology

All patients were informed about the trial when admitted to the labor ward. Patients who were able to give informed consent if requiring a CS at full dilation were included in the study. Participants were randomized 1:1 into two parallel groups: the Fetal Pillow group (FP group) and the non-Fetal Pillow group (NFP group).

CS was carried out using the standard technique and the Fetal Pillow was inserted and inflated prior to performing the CS.

Results

The two groups were similar in terms of their baseline characteristics (Table 2).

Table 2. Baseline characteristics

Variable	FP Group N= 120	NFP Group N= 120
Maternal age, y (range)	22.1 ± 2.6 (18-28)	22.8 ± 2.0 (18-33)
Maternal weight, kg	55.6 ±4.6	54.8 ±4.9
Parity: n		
0	82 [68.3%]	84 [70%]
1	33 [27.5%]	27 [22.5%]
2	5 [4.2%]	7 [5.8%]
3	0	2 [1.7%]
1st Stage of Labor, hrs[a]	7.8 ±0.7	7.6 ±0.6
Augmentation of Labor	79 [65.8%]	80 [66.7%]
2nd Stage of Labor, hrs[b]	1.9 ±0.3	1.9 ±0.3
Pregnancy duration, wk	38.9 ±1.0	39.0 ±1.0
Indication for CS		
Failed progress	88 [73.3%]	82 [68.3%]
Failed instrumental	20 [16.7%]	21 [17.5%]
Fetal distress	12 [10.0%]	17 [14.2%]
Station of head		
0	2 [1.7%]	2 [1.7%]
1	46 [38.3%]	50 [41.7%]
2	72 [60.0%]	68 [56.7%]
Position of head		
Occipito Anterior	48 [40%]	60 [50%]
Occipito Transverse	33 [27.5%]	27 [22.5%]
Occipito Posterior	39 [32.5%]	33 [27.5%]
Birth weight, kg	2.85 ±0.26	2.87 ±0.31

[a]Data available for 89 patients in FP group and 92 in NFP group, because some were transferred from other hospitals already in labor

[b]Data available for 90 patients in FP group and 95 in NFP group, because some were transferred from other hospitals already in labor

There were no differences in characteristics between the two groups.

Major extensions of uterine incisions were significantly lower in the FP group (Table 3). Total time for CS, incision to delivery interval, need for blood transfusions and length of hospital stay were lower in the FP group. The intra-operative blood loss >1000cc was more common in the NFP group (Table 3).

Table 3. Maternal outcomes

Variable	Fetal Pillow Group N= 120	Non-Pillow Group N= 120
Total Time taken for Lower Segment Caesarean Section, min	32.7 ±4.3	53.9 ±10.3
Incision to delivery interval, sec	176.5 ±14.0	297.2 ±27.1
Difficulty with delivery of fetal head		
Very difficult	2 [1.7%]	26 [21.7%]
Difficult	5 [4.2%]	21 [17.5%]
Moderately easy	11 [9.2%]	3 [2.5%]
Easy	57 [47.5%]	31 [25.8%]
Very easy	45 [37.5%]	39 [32.5%]
Pre-operation Hemoglobin, g/dL	10.3 ±0.6	10.3 ±0.5
Post-operation Hemoglobin, g/dL	9.6 ±0.5	9.0 ±0.8
Uterine extensions*	12 [10%]	43 [35.8%]
Grade of uterine extensions		
I	6 [50%]	4 [9.3%]
II	3 [25%]	12 [27.9%]
III	3 [25%]	27 [62.7%]
Major uterine extensions (Grade 2-3)**	6 [5%]	39 [32.5%]
Blood loss > 1000 mL: n [%]	5 [4.2%]	26 [21.7%]
Blood transfusions: n [%]	4 [3.3%]	22 [18.3%]
Hospital stay in days: mean [s.d.]	3.9 ±0.80	5.0 ±1.2
Re-laparotomy: n [%]	0	4 [3.3%]

*RR 0.37 (0.22 to 0.63), **RR 0.23 (0.11 to 0.48)

Table 4. Neonatal outcomes

Variable	Fetal Pillow Group N= 120	Non-Pillow Group N= 120
5 minutes APGAR score ≤ 3	1 [0.8%]	8 [6.7%]
Admission to NICU	13 [10.8%]	21 [17.5%]
Duration of NICU stay >24 hours	3 [23.1%]	12 [57.1%]
Neonatal sepsis	0	4 [3.3%]
Neonatal death	0	3 [2.5%]

Reanalysis of the randomized controlled trial data

Randomized Control Trial data was reanalyzed to study the maternal and fetal outcomes in the hand push group from the Non Fetal Pillow group vs. the Fetal Pillow group. The patients in the

control group were delivered using three different methods, depending on the preference of the surgeon and difficulty encountered during delivery. These methods were: the normal abdominal delivery method, hand push from below method, and reverse breech extraction method.

Results

Mode of delivery in the Non Fetal Pillow group (n=120)

1. 40 women were delivered using the hand push method
2. 12 women were delivered using a reverse breech extraction method
3. 68 women were delivered using the normal abdominal delivery method

Table 5. RCT reanalysis: Fetal Pillow Group vs. Non Fetal Pillow Group with Hand Push Method (Controls n=40) for Maternal outcomes

	Fetal Pillow Group N= 120	**Non Fetal Pillow, Hand Push Method Group N= 40**
Mean Incision to Delivery time (sec.)	176.5	278.0
Extension of uterine incision*		
Yes	10 (8.3%)	23 (57.5%)
No	110 (91.7%)	17 (42.5%)
Total Time taken for Caesarean Section (min.)	32.7	55.3
Blood loss >1000 mL	1 (0.8%)	15 (37.5%)
Mean Length of stay in Hospital (days)	3.93	5.30

*Chi-squared Test p-value P< 0.0001

Extensions of uterine incisions were significantly less common in the FP group. The observed values for incision to delivery interval, total time for CS, intra-operative blood loss and length of hospital stay were also lower in the FP group when compared with the hand push method of delivery.

Retrospective cohort study of maternal and neonatal outcomes from full-dilatation caesarean deliveries using the Fetal Pillow or hand-push method (Brisbane, Australia)

A retrospective cohort study was conducted to compare maternal and neonatal outcomes of full-dilatation Caesarean deliveries using the Fetal Pillow or hand- push method. A total of 160 patients were identified from all women who underwent full-dilatation Caesarean deliveries at term that involved the use of the Fetal Pillow or the hand-push method at Mater Mothers' Hospital, Brisbane, Australia between May 1, 2013 and March 31, 2015.

Outcome Measures

Maternal Outcomes

- Estimated blood loss

- Need for blood transfusion
- Uterine angle extension
- Duration of stay in hospital following delivery

Neonatal Outcomes

- 5-minute Apgar score below 7
- Cord arterial pH
- Admission to neonatal intensive care unit
- Need for endotracheal intubation.

Inclusion criteria

- Singleton pregnancies
- Caesarean section at full dilation
- Pregnancy ≥37 weeks

Exclusion criteria

- Multiple pregnancies
- Intrauterine fetal death
- Major congenital abnormalities

Results

Of 361 Caesarean deliveries performed at full dilation during the study period, clinicians documented the use of a Fetal Pillow in 91 deliveries and use of the hand-push method in 69. The observed values for the Fetal Pillow group show lower mean intra- operative blood loss, a shorter duration of postpartum hospital admission, and higher mean cord arterial pH (Table 7). There were no clinically meaningful differences observed for 5-min Apgar score <7, neonate intubation, neonate ICU admission, blood transfusions, or uterine angle extension.

Table 6. Patient characteristics

Baseline characteristics	**Fetal Pillow Method (n=91)**	**Hand-push Method (n=69)**
Maternal age, y	29.94 ± 4.5	31.0 ± 4.9
Duration of pregnancy at delivery, wk	39.7 ± 1.1	39.8 ± 1.1
Nulliparous	75 (82%)	45 (65%)
BMI	24.7 ± 6.1	24.0 ± 4.5
Previous failed instrumental delivery	6 (7%)	3 (4%)
Category I caesarean section	45 (49%)	36 (52%)

Abbreviations: BMI, Body mass index

Table 7. Maternal and neonatal outcomes

Outcome	**Fetal Pillow Method**	**Hand-push Method**

	(n=91)	(n=69)
5-min Apgar score <7	3 (3%)	4 (6%)
Neonate required intubation	0	2 (3%)
Neonatal ICU admission	14 (15%)	17 (25%)
Cord arterial pH	7.24 ± 0.06	7.19 ± 0.09
Estimated blood loss	273 ± 145	403 ± 199
Blood transfusion required	3 (3%)	2 (3%)
Uterine angle extension	18 (20%)	24 (35%)
Duration of hospital stay, hr.	77.9 ± 19.6	97.8 ± 27.6

Analysis of real-world data collected from 75 patient study conducted at Wishaw Hospital (Scotland)

This was a retrospective audit carried out by Wishaw Hospital in UK of 75 consecutive patients with Fetal Pillow use. The data were analyzed to see the effect of high BMI, fetal weight and epidural use on the outcomes in patients when Fetal Pillow was used in second stage Caesarean Sections.

Inclusion criteria

All patients having CS at full dilation or after a failed instrumental delivery where the Fetal Pillow was used.

Maternal outcomes studied

- Mean incision to delivery time
- Extension of uterine incision
- Blood loss >1000 mL
- Need for blood transfusion
- Length of post-operative hospital stay

Results

There was no difference observed in outcomes of interest with the Fetal Pillow use in this analysis when maternal BMI, fetal weight, and use of epidural in labor were taken into account.

Table 8. Maternal BMI & Distribution of Maternal Outcomes in Women Treated with the Fetal Pillow

	Maternal BMI >=30 N = 38	**Maternal BMI < 30 N = 37**
Mean Incision to Delivery time (mins)	4.63	5.43
Extension of uterine incision		
Yes	13 (34.2%)	11 (29.7%)
No	25 (65.8%)	26 (70.3%)

Blood loss **>1000 mL**	4 (10.5%)	5 (13.5%)
Blood transfusion **Yes** **No**	1 (2.6%) 37 (97.4%)	1 (2.7%) 36 (97.3%)
Mean Length of stay in Hospital (days)	3.18	3.02

Table 9. Fetal Weight and Distribution of Maternal Outcomes in Women Treated with the Fetal Pillow

	Fetal weight ≥ 3500g **N = 53**	**Fetal weight <3500g** **N = 22**
Mean Incision to Delivery time (mins)	5.11	4.81
Extension of uterine incision **Yes** **No**	17 (32.1%) 36 (67.9%)	7 (31.8%) 15 (68.2%)
Blood loss **>1000 mL**	8 (15.1%)	1 (4.5%)
Blood transfusion **Yes**	2 (3.8%)	0
Mean Length of stay in Hospital (days)	3.15	3.00

Table 10. Epidural Use and Distribution of Maternal Outcomes in Women Treated with the Fetal Pillow

	Epidural Used **N = 54**	**No Epidural Used** **N = 21**
Mean Incision to Delivery time (mins)	5.22	4.52
Extension of uterine incision **Yes** **No**	14 (25.9%) 40 (74.1%)	10 (47.6%) 11 (52.4%)
Blood loss **>1000 mL**	5 (9.3%)	4 (19.0%)
Blood transfusion **Yes**	0	2 (9.5%)
Mean Length of stay in Hospital (days)	3.11	3.10

In summary, the data from the clinical studies indicate that use of the Fetal Pillow results in a reduction in clinically significant uterine incision extensions, as well as fewer observed cases of blood loss > 1000 mL and less need for blood transfusions.

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 Fetal Pillow complies with the labeling requirements under 21 CFR 807.87(e) and prescription device requirements under 21 CFR § 801.109. The device labeling includes physician labeling, Instructions for Use, and package labeling and bears the following: "Caution: Federal law restricts the use of this device by or on the order of a physician." The labeling also includes pertinent information regarding instructions for proper placement and use of the device, a contraindication for use in the presence of active genital infection, and a shelf life.

RISKS TO HEALTH

Table 11 below identifies the risks to health that may be associated with use of the Fetal Head Elevator and the measures necessary to mitigate these risks.

Table 11. Identified Risks to Health and Mitigation Measures

Identified Risk	Mitigation Measures
Adverse tissue reaction	Biocompatibility evaluation
Infection	Sterilization validation Shelf life testing Labeling
Fetal injury due to device failure	Non-clinical performance testing Shelf life testing Labeling
Maternal injury due to device failure	Non-clinical performance testing Shelf life testing Labeling
Use error	Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the fetal head elevator is subject to the following special controls:

1. The patient-contacting components of the device must be demonstrated to be biocompatible.
2. Performance data must demonstrate the sterility of patient-contacting components of the device.
3. Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.
4. Non-clinical performance data must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:

a. Reliability testing of device deployment and retrieval under relevant use conditions must be conducted.
b. Testing of the maximum force applied to the fetal head in an anatomic model must be conducted.
c. Testing of uniform application of the elevator mechanism on the fetal head must be conducted.

5. Labeling must include the following:
    a. Contraindication for use in the presence of active genital infection;
    b. Specific instructions regarding the proper placement and use of the device; and
    c. A shelf life.

BENEFIT/RISK DETERMINATION

The risks of the device are based on nonclinical bench testing, as well as data collected in the clinical studies described above. There were no fetal or maternal injuries attributed to Fetal Pillow use in either the randomized controlled trial or retrospective cohort study. In the supplemental data, one subject experienced a small second degree laceration during insertion of the Fetal Pillow, where the physician found it difficult to insert the device due to a very low fetal head (+3 station).

The probable benefits of the device are also based on data collected in the clinical studies described above. The probable benefit of Fetal Pillow is a reduction in clinically significant uterine incision extensions. In the Indian randomized control trial, major uterine incision extensions occurred in 6 (5.0%) women in the Fetal Pillow group and 39 (32.5%) in the control group. Other clinically relevant benefits include fewer cases of blood loss > 1000 mL and less need for a blood transfusion. Additionally, newborns in the Fetal Pillow group were less likely to be admitted to the NICU or require admission for more than 24 hours.

Additional factors to be considered in determining probable risks and benefits for the Fetal Pillow include: Supplemental data suggest that maternal BMI, fetal weight, and epidural use do not impact the performance of the Fetal Pillow. In addition, reanalysis of the RCT data using a comparator delivery group consistent with US practice standards supports the benefits of the Fetal Pillow.

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 elevation of the fetal head and facilitation of delivery of the fetus in women requiring a Caesarean Section at full dilation, or those requiring a Caesarean Section after a failed instrumental vaginal delivery at a gestational age ≥37 weeks, the probable benefits outweigh the probable risks for the Fetal Pillow. The device provides benefits and the risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The De Novo request for the Fetal Pillow is granted and the device is classified under the following:

Product Code: PWB
Device Type: Fetal head elevator
Class: II
Regulation: 21 CFR 884.4350