DE NOVO CLASSIFICATION REQUEST FOR
PREVENA 125 AND PREVENA PLUS 125 THERAPY UNITS

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Negative pressure wound therapy device for reduction of wound complications.** A negative pressure wound therapy device for reduction of wound complications is a powered suction pump intended for wound management and reduction of wound complications via application of negative pressure to the wound, which removes fluids, including wound exudate, irrigation fluids, and infectious materials. This device type is intended for use with wound dressings classified under 21 CFR 878.4780. This classification does not include devices intended for organ space wounds.

NEW REGULATION NUMBER: 21 CFR 878.4783

CLASSIFICATION: Class II

PRODUCT CODE: QFC

BACKGROUND

DEVICE NAME: PREVENA 125 and PREVENA PLUS 125 Therapy Units

SUBMISSION NUMBER: DEN180013

DATE OF DE NOVO: March 15, 2018

CONTACT: KCI USA, Inc.
6203 Farinon Dr.
San Antonio, Tx 78249

INDICATIONS FOR USE

PREVENA 125 and PREVENA PLUS 125 Therapy Units manage the environment of closed surgical incisions and remove fluid away from the surgical incision via the application of -125mmHg continuous negative pressure. When used with legally marketed compatible dressings, PREVENA 125 and PREVENA PLUS 125 Therapy Units are intended to aid in reducing the incidence of seroma and, in patients at high risk for post-operative infections, aid in reducing the incidence of superficial surgical site infection in Class I and Class II wounds.

LIMITATIONS

The sale, distribution, and use of PREVENA 125 and PREVENA PLUS 125 Therapy Units are restricted to prescription use in accordance with 21 CFR 801.109.

The device is not intended to treat surgical site infection or seroma.

Safety and effectiveness in pediatric population (<22 years old) have not been evaluated.

Safety and effectiveness in Class III (Contaminated) and Class IV (Dirty/Infected) wounds have not been demonstrated. Furthermore, Class IV surgical wounds are not expected to be closed primarily, and the subject device should only be used on closed surgical incisions.

The device has not been demonstrated to reduce deep incisional and organ space surgical site infections.

The device has not been demonstrated to be effective in reducing the incidence of surgical site infection and seroma in all surgical procedures and patient populations; therefore, the device may not be recommended for routine use to reduce surgical site infection and seroma. Please refer to the '*Summary of Clinical Information*' section for the specific surgical procedures and patient populations included in the clinical studies. Surgeons should continue to follow the '*Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection*'[2] and the '*American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines*'[1] for best practices in preventing surgical site infection.

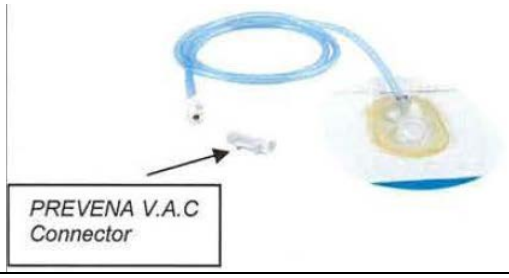
PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS, AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The PREVENA 125 and PREVENA PLUS 125 Therapy Units ("PREVENA pumps") are single-use, compact and portable powered suction pumps. The therapy units are packaged with compatible sterile canisters (45 ml for PREVENA 125 or 150 ml for PREVENA PLUS 125) and sterile tubing set. The therapy units can be used with compatible, legally marketed wound dressings classified under 21 CFR 878.4780, such as the PEEL & PLACE dressing and the CUSTOMIZABLE dressing, which, when combined are referred to as the PREVENA Incision Management Systems ("PREVENA systems"). The PREVENA Incision Management Systems deliver a pre-set, continuous negative pressure of 125 mmHg to the incision site. The systems are intended to be applied to incision sites immediately after surgery for a minimum of 2 days up to a maximum of 7 days depending on the surgeon's preference. The therapy units can be used up to 192 hours, after which they will automatically shut off.

The subject devices are identical to the currently marketed PREVENA pumps, except for the change in the intended use (reduction in the incidence of wound complications). The PREVENA 125 Therapy Unit was most recently cleared under K161897, and the PREVENA PLUS 125 Therapy Unit was most recently cleared under K173426. There is no change to the user interface, design, mechanisms of operation, and specifications for delivery of negative pressure therapy from the previously marketed PREVENA pumps.

Table 1. Device Description

	PREVENA 125	**PREVENA PLUS 125**
1x Disposable non-sterile therapy unit (including compatible non-sterile carrying case)	PREVENA 125 Therapy Unit  • Powered by 3 "AA" batteries • Visual and audible alarms: o Leak o Canister full o Low battery o Critical battery o System error	PREVENA PLUS 125 Therapy Unit  • Powered by rechargeable lithium battery or power cord • Visual and audible alarms: o Leak or canister missing o Blockage in tubing or canister full o Batteries need to be recharged o 8 hours of therapy time remain o System fault
1x Sterile canister	45 mL canister	150 mL canister
1x Sterile tubing set	PREVENA Tubing Set – single-lumen, integrated tubing set for direct connection to the PREVENA 125 Therapy unit. Comes with PREVENA V.A.C. Connector, which is necessary for connection to a V.A.C. Therapy Unit 	SENSAT.R.A.C. Tubing Set – multi-lumen, non-integrated tubing set for direct connection to the PREVENA PLUS 125 Therapy Unit and to a V.A.C. Therapy Unit 

SUMMARY OF NONCLINICAL/BENCH STUDIES

All non-clinical/bench test data were referenced from the following previously-cleared 510(k) submissions of the device: K100821, K141017, K150006, K153199, K161897, K173426. No new non-clinical/bench testing was provided in the De Novo request.

BIOCOMPATIBILITY/MATERIALS

The current De Novo request contains only the PREVENA 125 and PREVENA PLUS 125 therapy units, canisters and tubing sets, which do not have direct patient contact. The therapy units must be used with compatible, legally-marketed wound dressing kits classified under 21 CFR 878.4780.

SHELF LIFE/STERILITY

The PREVENA 125 and PREVENA PLUS 125 therapy units are provided non-sterile. All canisters and tubing sets are sterilized using gamma irradiation to achieve a sterility assurance level (SAL) of 10^{-6}. The sterilization method was validated per ISO 11137-1:2006 (*Sterilization of health care products – Radiation – Part 1: Requirements for development, validation and routine control of sterilization process for medical devices*).

The shelf life of the canisters and tubing sets was evaluated after accelerated aging equivalent to three years. The packaging was subject to testing per ASTM-F1980 (*Standard guide for accelerated aging of sterile barrier systems for medical devices*). Aged canisters and tubing sets were also subject to a series of functional testing, including leak test, canister to tubing bond strength test, and tubing to in-line connector bond strength test. The test articles met the acceptance criteria for each test.

ELECTRICAL SAFETY AND ELECTROMAGNETIC COMPATIBILITY

The following Electrical Safety and Electromagnetic Compatibility testing has been performed:

- AAMI/ANSI ES60601-1:2005 + A1 2012 Medical Electrical Equipment – Part 1: General requirements for basic safety and essential performance, amendments
- IEC 60601-1-2:2014 4th edition Medical Electrical Equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests

The PREVENA 125 and PREVENA PLUS 125 therapy units passed all relevant portions of the testing.

SOFTWARE

All components of the device are controlled/monitored by software, which is responsible for the functionality, user interface, safety checks and performance accuracy. The agency considers the software to be a moderate level of concern (LOC) because inadvertent software errors could result in injury or delayed wound healing to the patient.

All elements of software information corresponding to moderate LOC devices as outlined in FDA's guidance document *"Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices"* (issued May 11, 2005) were provided in previous 510(k) submissions (reference K150006 and K173426) and contain sufficient detail to provide reasonable assurance that the software will operate in a manner described in the specifications.

PERFORMANCE TESTING-BENCH

Bench testing was conducted to demonstrate that the PREVENA 125 and PREVENA PLUS 125 therapy units perform as expected under the anticipated conditions of use. This testing included evaluation of key device parameters such as maintenance of negative pressure at the wound site and system alarms. The following bench testing was conducted to demonstrate the device performance characteristics:

- Pressure manifold testing – The device was bench tested in a simulated wound model and under the worst-case scenarios of use (i.e., with substantial but non-alarming fluid leak and air leak). The device can maintain a continuous negative pressure of -125±25 mmHg across the entire compatible wound dressing for the labeled use life of 7 days.

- Exudate removal testing - The device was bench tested in a simulated wound model and under the worst-case scenarios of use (i.e., with substantial but non-alarming fluid leak and air leak). The device can remove simulated wound fluid as intended.

- The following system alarms were tested to ensure they function as intended: leak, blockage, low battery, 8-hour therapy time remaining, and system fault.

HUMAN FACTORS/USABILITY TESTING

Usability testing was performed to demonstrate that the device design and associated labeling are sufficient to enable intended operation of the device by each intended user populations (i.e., surgeons, operating room nurses, and patients). A list of critical user tasks was identified and prioritized in accordance with potential harm that would or could arise from users inadvertently performing tasks incorrectly or failing to perform the necessary tasks. Intended users were asked to perform the critical tasks under simulated use conditions. The usability data were reviewed in K141017 and found to be acceptable.

SUMMARY OF CLINICAL INFORMATION

The requester provided a systematic literature review and associated meta-analyses to support the safety and effectiveness of the PREVENA Incision Management Systems over closed incisions in reducing the incidence of surgical site infections (SSIs) and seromas versus conventional wound dressings. The systematic literature search was performed using PubMed, The Cochrane Library, OVID, EMBASE, ScienceDirect, and alternative resources such as Google searches and QUOSA. Search terms included: (“negative pressure wound therapy” OR “negative pressure” OR “negative pressure therapy” OR “NPWT”) AND (“PREVENA” OR “ciNPT” OR “prophylactic NPWT” OR “preventative NPWT” OR “incision management” OR “incisional management” OR “closed incision negative pressure wound therapy” OR “closed incision negative pressure therapy”).

Six (6) independent reviewers performed the study selection. Titles of manuscripts and abstracts that met the search criteria were logged and investigated for duplicates. The abstracts and manuscripts were assessed for inclusion and exclusion criteria (*Table 2*) by a subset of two (2) independent reviewers. When discordance was identified, the two reviewers deliberated until a consensus was reached.

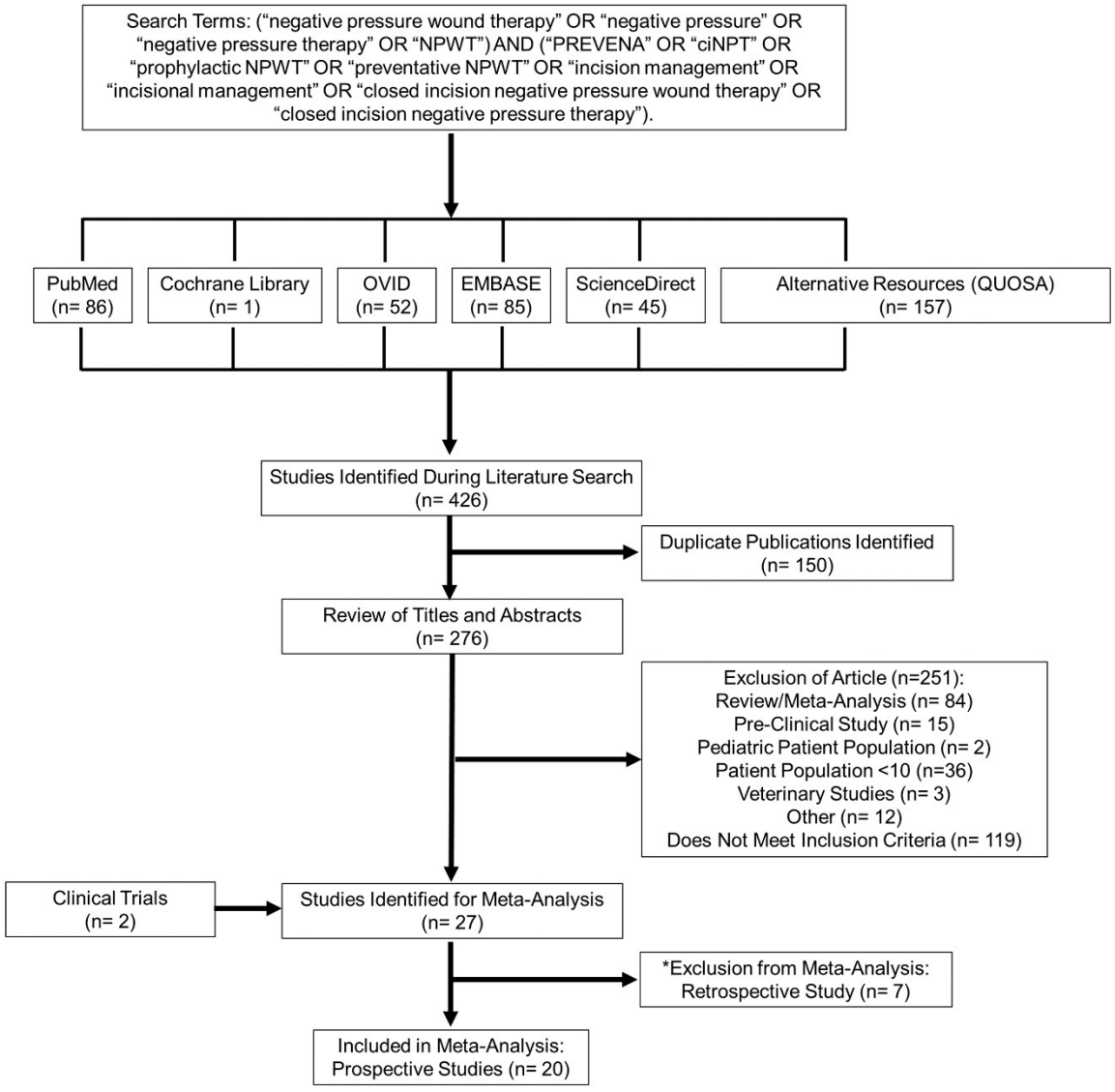
Table 2. Inclusion and exclusion criteria for the systematic literature review

Inclusion Criteria	Exclusion Criteria
• Abstract or manuscript written in English • Published or unpublished study • Studies that compare the use of PREVENA Incision Management Systems using -125 mmHg pressure with legally marketed compatible dressing over closed incisions to conventional wound dressings (e.g., occlusive gauze dressing) • Contained an endpoint/outcome of surgical site infection (SSI), dehiscence, seroma, hematoma, or post-operative pain • Studies that followed the subjects/patients for a minimum of 30 days for the SSI endpoint • Studies that followed the subjects/patients for a minimum of 10 days for the seroma endpoint	• Meta-analysis studies • Pre-clinical studies (i.e., animal or bench science assessments) • Studies on pediatric patients (age <18 years) • Studies with less than 10 patients • Veterinary studies

For abstracts and manuscripts that met all the inclusion criteria and none of the exclusion criteria, they were examined critically to: i) assess whether containing reference of any other articles that meet the inclusion criteria and ii) extract study characteristics by at least two additional independent reviewers. Registered studies at ClinicalTrials.gov were also reviewed using the same search criteria for completed and terminated studies. The Cochrane Collaboration tool was used for assessing risk of bias.

A total of 426 studies resulted from the initial search. After 150 duplicate publications were removed, a total of 276 unique studies were assessed for inclusion. An additional 251 articles were excluded based on the pre-specified inclusion/exclusion criteria (*Table 2*), which was comprised of 64 review/meta-analysis, 15 pre-clinical studies, 2 pediatric patient populations, 3 veterinary studies, 12 other (protocol, technical report, subsequent study included in the meta-analysis, and comment), and 119 that did not meet all inclusion criteria. Lastly, seven (7) articles identified as retrospective studies were removed to minimize bias and ensure only the highest level of evidence for the meta-analysis.

Figure 1. Summary of study selection for the meta-analyses



Ultimately, twenty (20) prospective studies, including two (2) KCI USA, Inc.-sponsored, unpublished clinical studies from ClinicalTrials.gov, were included in the meta-analyses for SSI and seroma characterization. A total of up to 6,403 evaluable patients were included in these meta-analyses with 1,367 in the PREVENA Incision Management Systems therapy (treatment) group and 5,036 in the conventional wound dressing (control) group.

The two (2) KCI USA, Inc.-sponsored, unpublished clinical studies from ClinicalTrials.gov can be summarized as follows:

> **NCT01341444** was a randomized, single center, interventional trial evaluating the safety and effectiveness of PREVENA Incision Management Systems on closed surgical incisions in subjects who had undergone open renal transplant surgery. Subjects were randomized 1:1 to receive either the PREVENA therapy

(treatment group) or a silver-impregnated occlusive dressing (control group). The purpose of the study was to compare surgical site complications, which include incisional fluid accumulation, dehiscence, and surgical site infections, between the PREVENA therapy (treatment group) and conventional occlusive dressing (control group). The measurement outcome was the incidence of surgical site complications up to 30 days (+/- 2 days) post renal transplant surgery. Due to enrollment difficulties, KCI decided to terminate the study after enrolling 63 of 88 subjects. There were a total 28 subjects in the treatment group with 0 surgical site infections (0%) and 30 subjects in the control group with 2 surgical site infections (6.7%). Adverse events were reported: 25 subjects in the treatment group reported at least 1 adverse event and 24 subjects in the control group reported at least 1 adverse event. In the treatment group, 11 subjects reported at least 1 serious adverse event, and in the control group, 13 subjects reported at least one serious adverse event. None of the reported adverse events were related to the PREVENA therapy or conventional wound dressings used.

NCT02195310 was a randomized, multi-center, open label, interventional trial evaluating the safety and effectiveness of PREVENA Incision Management System (treatment group) on closed sternal midline incisions in patients at high risk for surgical site occurrences to a control group treated with conventional wound dressings, such as gauze with tape, pressure dressing with additional packing and tape, and silver-impregnated dressings. The purpose of the study was to assess the performance of PREVENA Incision Management System versus conventional wound dressings on closed median sternal incisions in subjects undergoing cardiac surgery. The primary endpoint was the incidence of surgical site infections (SSI) within 30 days postoperatively per CDC guidelines[21]. Five hundred twenty subjects were expected to be randomized 1:1. An interim data review was conducted on 257 subjects (128 PREVENA subjects, 129 control subjects). The conditional power from this analysis was below 60%. Since the calculated SSI rates from the interim data review were outside the ranges of the sample size assumptions, the study was terminated early due to the lack of evidence to support the objectives and assumptions of the study. A final analysis was conducted on 299 subjects; 145 subjects for the PREVENA arm and 154 subjects for the control arm. The incidence rate of SSI in the PREVENA arm was 9.0% (13 subjects) and in the SOC arm was 10.4% (16 subjects). There was a 1.5-fold higher rate of SSI in control subjects with a Body Mass Index (BMI) >35 kg/m^2. In the treatment group, 6/68 subjects with a BMI >35 kg/m^2 had an SSI (8.8%) and 10/75 control subjects with a BMI >35 kg/m^2 had an SSI (13.3%). Adverse events were reported. See '*Safety*' section below for more detail. There were 286 (83.6%) of subjects that experienced at least one adverse event. In the treatment group, 83.8% subjects experienced an adverse event, while 83.4% of the control group subjects experienced an adverse event. There were 18 subjects that experienced a treatment related adverse event. In the treatment group, 16 (9.2%) subjects experienced a treatment related adverse event, while 2 (1.2%) subjects in the control group experienced a treatment related adverse event. There were 118 serious adverse events. In the treatment group, 36.4% of subjects experienced a serious adverse event, while 32.5% of the control subjects experienced a serious adverse event. There were no device-related serious adverse events in either the treatment or control group.

Surgical Site Infection (SSI)

Sixteen (16) prospective studies were included in the meta-analyses for SSI, which are summarized in Table 3 below. Nine (9) studies are randomized controlled trials, which are considered level I evidence. The remaining seven (7) studies are considered level II evidence, which include five (5) prospective treatment and historical controls studies and two (2) prospective observational studies that alternated patient assignment into either the treatment or control group (i.e., not randomized).

Table 3. Characteristics of studies included in the SSI meta-analyses

Study/ Level of Evidence*	***Study Design***	***Surgical Procedure***	***Subjects' Risk Factors***	***Study Duration***	***Incisional Dressings Used***	***No. of Subjects***	***Treatment Duration (days)***
Cantero 2016[3] Level II	Prospective & Historical Controlled	Diverting loop ileostomy reversal	NR	30 days	PREVENA IMS	17	5-7
					Conventional Wound Dressing	43	1-2, then daily
DiMuzio 2017[4] Level I	RCT	Elective vascular surgery†	BMI> 30kg/m^2, pannus, immunosuppressant disorder, reoperation, prosthetic graft, HbA_{1c}>8	30 days	PREVENA IMS	59	NR
					Standard gauze dressing	60	NR
Grauhan 2013[6] Level II	Prospective Observational	Median sternotomy†	BMI Mean Treatment: 37 kg/m^2, Control: 36 kg/m^2; Diabetes; COPD; LVEF	90 days	PREVENA IMS	75	6-7
					Conventional wound dressings	75	1-2
Grauhan 2014[7] Level II	Prospective & Historical Controlled	Median sternotomy	NR	30 days	PREVENA IMS	237	6-7
					Conventional sterile wound tape dressing	3508	1-2
Gunatilake 2017[8] Level I	RCT	Cesarean delivery	BMI Mean Treatment: 46.3 kg/m^2, Control: 46.8 kg/m^2; Diabetes	42 ± 10 days	PREVENA IMS	39	5-7
					Steri-strips, sterile gauze, Tegaderm	43	1-2
Lavryk 2016[10] Level II	Prospective Observational	Reoperative colorectal surgery†	Diabetes; Hx of Smoking	30 days	PREVENA IMS	55	7±2
					Standard gauze dressing	101	NR
Lee AJ 2016[11] Level I	RCT	CABG with harvesting of GSV†	Diabetes; Smoking; COPD; HTN; CHF; LVD; Aortic Stenosis; AF; CVD; Dyslipidemia; CKF; PVD; Hypothyroidism; Arthritis; Gout; Asthma	42 days	PREVENA IMS	33	Up to 7
					Conventional dry dressing	27	NR

Lee K 2017[12] Level I	RCT	Femoral to distal artery bypass; femoral endarterectomy; femoral artery crossover; other†	BMI Mean Treatment: 29 kg/m^2, control: 29 kg/m^2; Diabetes; Hx of Smoking/ COPD; CAD; LVD; HTN; CKD; Anticoagulation; Ischemic tissue loss	30 days and 90 days	PREVENA IMS	53	First day of discharge up to 8 days
					Standard gauze dressing	49	2
Matatov 2013[13] Level II	Prospective & Historical Controlled	Femoral cutdown for vascular procedures	BMI Mean Treatment: 26 kg/m^2, Control: 27 kg/m^2; Diabetes; Hx of Smoking/; COPD; CAD; CHF; HTN; renal insufficiency, anemia	30 days	PREVENA IMS	41 (52 wounds)	5-7
					Primapore or Dermabond Adhesive	49 (63 wounds)	3
NCT01341444 Level I	RCT	Renal transplant†	BMI Mean Treatment: 29.05 kg/m^2, Control: 28.73; Diabetes; Tobacco Use;	30 days	PREVEANA IMS	28	5
					Standard incisional dressing	30	3
NCT02195310 Level I	RCT	Median sternotomy (elective cardiac surgery) †	BMI Mean Treatment: 35.64 kg/m^2, Control: 35.27 kg/m$^{2;}$ Diabetes; Immunosuppressant Disorder; Hx of Smoking; Dialysis; Planned Bilateral Mamery Artery; Chronic Lung Disease; CKD; Previous Chest Wall Radiotherapy; Breast Size D Age > 75 years; LVEF< 30%;	30 days	PREVENA IMS	145	4-7
					Traditional sterile wound dressings (included gauze with tape, pressure dressings and silver impregnated dressings)	154	2-3
Newman 2017[14] Level I	RCT	Total hip or knee arthroplasty (elective revision) †	Blood thinners other than aspirin postoperatively, BMI≥ 35 kg/m^2; PVD; diabetes mellitus; current smoker; hx of prior joint infection; current use of corticosteroids or immunomodulators; hx or current cancer/hematological malignancy; inflammatory arthritis; renal failure or dialysis; malnutrition, liver disease; transplant status; HIV infection	84 days	PREVENA IMS	80	≥2
					Silver impregnated occlusive dressing	80	7

Redfern 2017[18] Level II	Prospective & Historical Controlled	Total hip or knee arthroplasty (elective primary)	BMI Mean Treatment: 30.5 kg/m^2, Control: 30.9 kg/m^2; Diabetes; HTN; Hx of Cancer/Tumor; Arthritis; Myocardial Infarction/Heart Disease; Tobacco use	60 days	PREVENA IMS	192	6-8
					Traditional gauze dressing	400	Standard
Ruhstaller 2017[19] Level I	RCT	Unscheduled cesarean delivery†	Gestational Diabetes; Tobacco Use; HTN;	28 days	PREVENA IMS	67	3
					Telfa bandage with gauze and surgical tape	69	1
Sabat 2016[20] Level I	RCT	Vascular surgery involving groin incision	NR	120 days	PREVENA IMS	30 wounds	5
					Gauze and Tegaderm	33 wounds	NR
Swift 2015[22] Level II	Prospective & Historical Controlled	Cesarean section†	BMI ≥ 30 kg/m^2; Diabetes; Chronic Hypertension; Preeclampsia; HELLP syndrome; rupture of membranes > 4 hours; chorioamnionitis, anticoagulation; multiple gestation	42 days	PREVENA IMS	110	3
					Standard sterile dressing	209	NR

†Population or Procedure identified as high-risk for wound complication
*Oxford Centre of Evidence-Based Medicine
RCT = Randomized Controlled Trial
NR= Not Reported
IMS= Incision Management System
ciNPWT= closed incision Negative Pressure Wound Therapy
BMI= Body Mass Index
HX= History
COPD= Chronic Obstructive Pulmonary Disorder
GERD= Gastroesophageal Reflux Disease
HTN= Hypertension
AF= Atrial Fibrillation
CVD= Cardiovascular disease
CKF= Chronic kidney failure
PVD= Peripheral vascular disease
LVD= Left ventricle dysfunction
CAD= Coronary artery disease
CKD= Chronic kidney disease
LVEF= Left ventricle ejection fraction
HIV= Human immunodeficiency virus
HELLP = Hemolysis, Elevated Liver enzymes, Low Platelet counts

Together, the sixteen (16) studies contained 1,264 evaluable patients receiving the PREVENA Incision Management Systems therapy (treatment group) and 4,923 patients receiving conventional wound dressings (control group). The conventional wound dressings used in each study can be found in Table 3 above and range from occlusive gauze dressings to silver-impregnated dressings. The primary endpoint in the studies was the incidence of surgical site infection in the treatment group compared to the control group for at least four weeks following surgery.

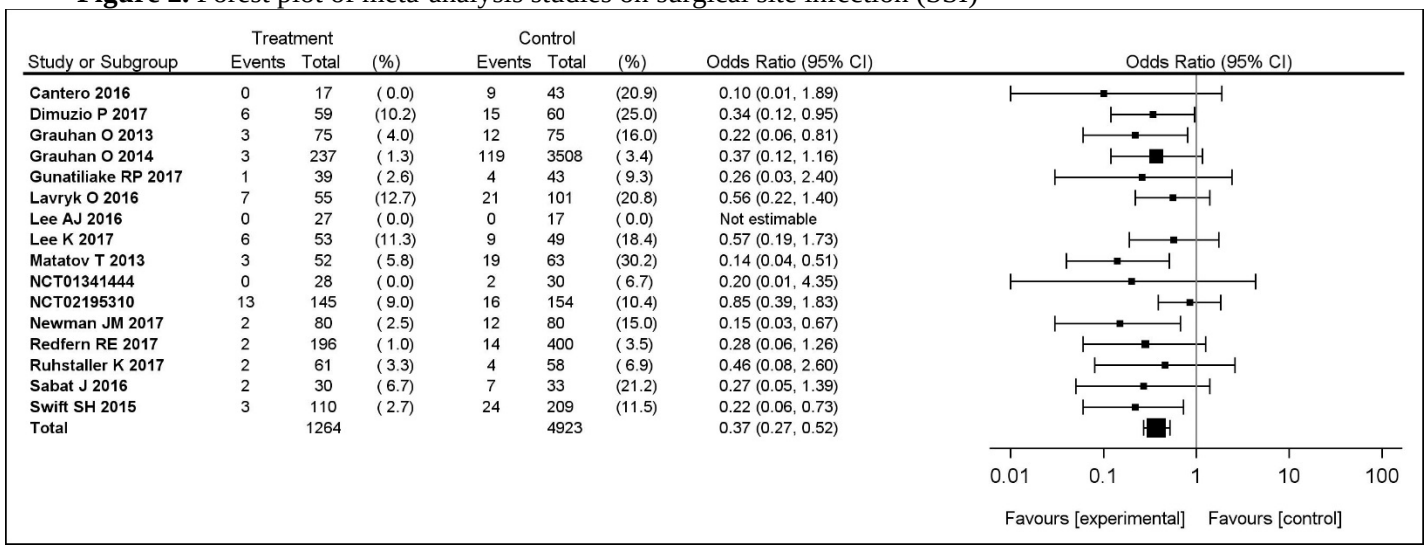
The treatment effect for each study was summarized using odds ratio (OR), which was calculated using the following formula:

OR = AD/BC, where

A = the number of subjects with SSI events for the treatment group
B = the number of subjects without SSI events for the treatment group
C = the number of subjects with SSI events for the control group
D = the number of subjects without SSI events for the control group

An OR of less than 1 suggests a favorable effect by the treatment in reducing SSI, whereas an OR greater than 1 suggests a favorable effect by the conventional wound dressings. The 95% confidence interval (95% CI) for the odds ratio is calculated based on the standard error of Log(OR). The individual study effects for SSI are summarized in Figure 2 below.

Figure 2. Forest plot of meta-analysis studies on surgical site infection (SSI)[a]



Overall, there is an observable trend supporting a favorable effect by the PREVENA system in reducing the incidence of SSI. The SSI rates ranged from 0% to 30.2% for the control group in the individual studies, and the SSI rates in the treatment group ranged from 0% to 12.7%. However, the benefit of the PREVENA systems varies considerably across different studies, possibly due to many confounding factors such as different surgical procedures and patient risk factors, which are further explored in subgroup analyses below. Additionally, there are many inherent limitations associated with meta-analyses and biases with each individual study, which are discussed in the '*Limitations of the Clinical Evidence*' section below. Because of these confounding factors and limitations of the studies, statistical significance cannot be reliably inferred for the treatment effect based on the combined results from the sixteen (16) studies.

[a] One (1) study (Lee AJ 2016[11]) had no events in either the treatment or control group, and an odds ratio cannot be estimated for this study.

Subgroup analyses were performed to elucidate potential confounding factors contributing to the heterogeneity in the treatment effect. The subgroup analyses conducted were based on: i) Wound classification, ii) Infection depth (i.e., superficial, deep, organ space), iii) Risk factors for surgical site infection.

i. Wound classification

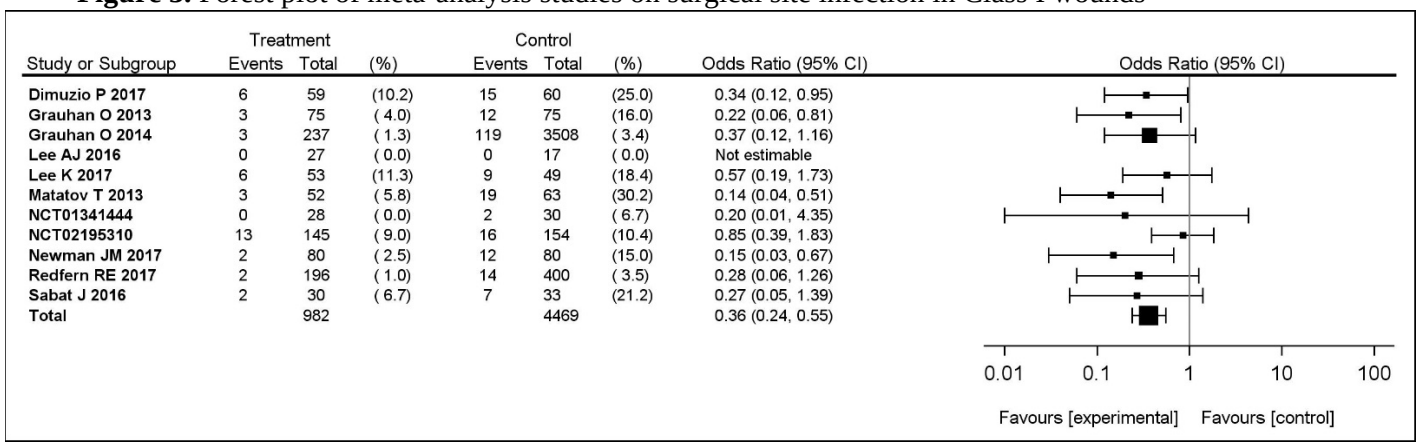
To analyze the effect of the PREVENA Incision Management Systems on SSI in wounds of different degrees of contamination, a wound classification designation following the Center for Disease Control and Prevention (CDC) guidelines (*Table 4*) was assigned to each study based on the surgical procedure performed and CDC wound classification definitions. Each study was reviewed, and a CDC wound classification was assigned by two individuals with appropriate medical and clinical trials background. All the same wound types in each study were treated the same unless the publication (e.g., Newman et. al.[14]) specifically gave guidance that some wounds were more severe in a particular subgroup (e.g., septic revisions). If the publication provided a CDC wound classification, the provided classification was utilized. One study (Lavryk et. al.[10]) was excluded as only patients with wound classifications of II, III and IV were enrolled and could not be separated into the individual wound classification groups.

Table 4. Surgical wound classifications and definitions[21]

Surgical Wound Classification	Definition
Class I/Clean	An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.
Class II/Clean-contaminated	An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.
Class III/Contaminated	Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered are included in this category.
Class IV/Dirty-infected	Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

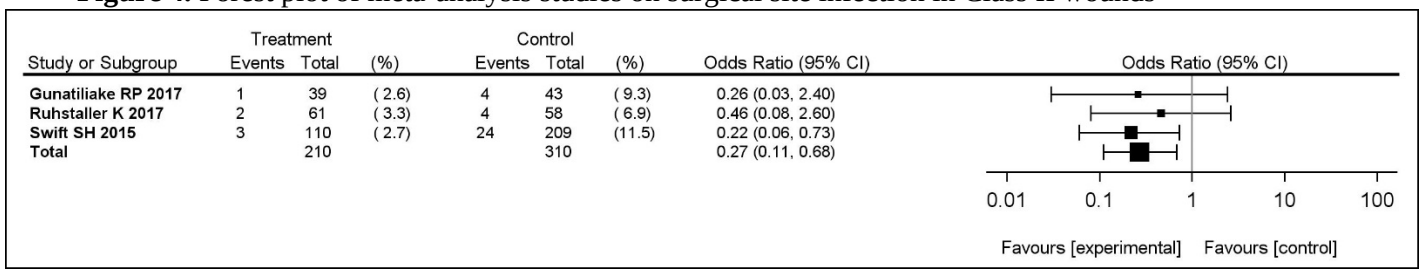
Eleven (11) of the sixteen (16) studies were determined to contain only Class I wounds, and these eleven (11) studies consist of approximately 88% of the total patient population for the overall SSI meta-analysis. The subgroup analysis results of Class I wounds (*Figure 3*) show a reduction in favor of the PREVENA Incision Management Systems therapy and are consistent with the overall reduction in SSI observed in Figure 2.

Figure 3. Forest plot of meta-analysis studies on surgical site infection in Class I wounds



Three (3) of the sixteen (16) studies were included in the subgroup analysis for Class II wounds, and these three (3) studies consist of approximately 8% of the total patient population for the overall SSI meta-analysis. The subgroup analysis results of Class II wounds (*Figure 4*) show a reduction in favor of the PREVENA Incision Management Systems therapy and are consistent with the overall reduction in SSI observed in Figure 2.

Figure 4. Forest plot of meta-analysis studies on surgical site infection in Class II wounds



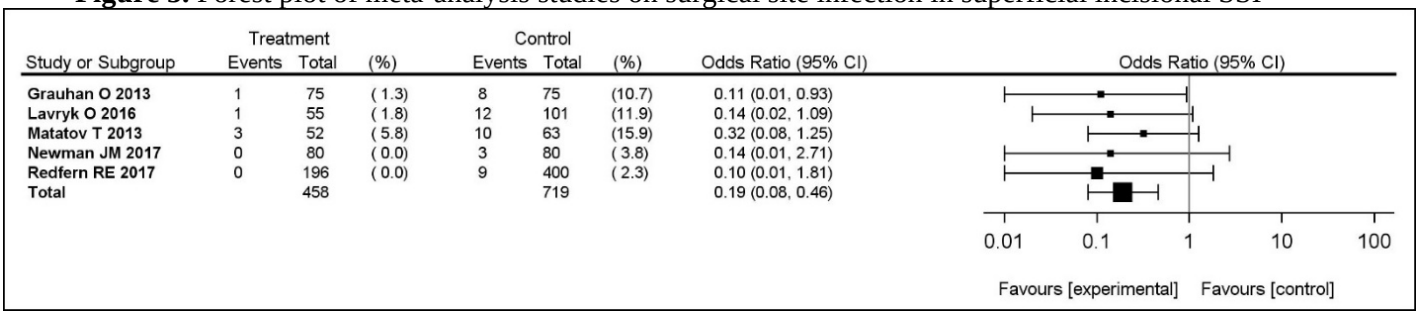
There was only one (1) study identified as having Class III wounds; therefore, a subgroup analysis for Class III wounds was not performed. In this study, no SSI events were reported for the treatment group (0 out of n=17) and nine (9) SSI events were reported for the control group (9 out of n=43). There were no studies containing Class IV wounds that could be isolated for analysis; therefore, a subgroup analysis was not performed for Class IV wounds. It should be noted that the PREVENA systems are intended to be used only on closed incisions. As Class IV wounds are generally not expected to be surgically closed primarily, the PREVENA systems should not be used on Class IV wounds.

ii.Infection depth

Surgical site infection (SSI) can be divided into three (3) subgroups: superficial incisional SSI, deep incisional SSI, and organ space SSI[9]. Superficial incisional SSI is infection that is limited to the skin or subcutaneous tissue of the surgical incision. Deep incisional SSI is infection that has spread to deep soft tissues such as fascial and muscle layers. Organ space SSI is deeper infection that involves any part of the anatomy that was opened or manipulated during the operation[9].

Five (5) of the sixteen (16) studies selected for SSI meta-analyses included information to stratify patient SSI events into superficial, deep, and organ space infections. Subgroup analyses examining the effect of the PREVENA systems on different SSI locations were conducted based on these five (5) studies. Among the three subgroups, the PREVENA systems demonstrated the greatest benefit in reducing superficial incisional SSIs (*Figure 5*). The reduction in superficial SSI appears to be greater than the SSI reduction in the overall data (*Figure 2*). There was little to no benefit of the PREVENA systems in reducing deep incisional SSIs and organ space SSIs when compared to the control group.

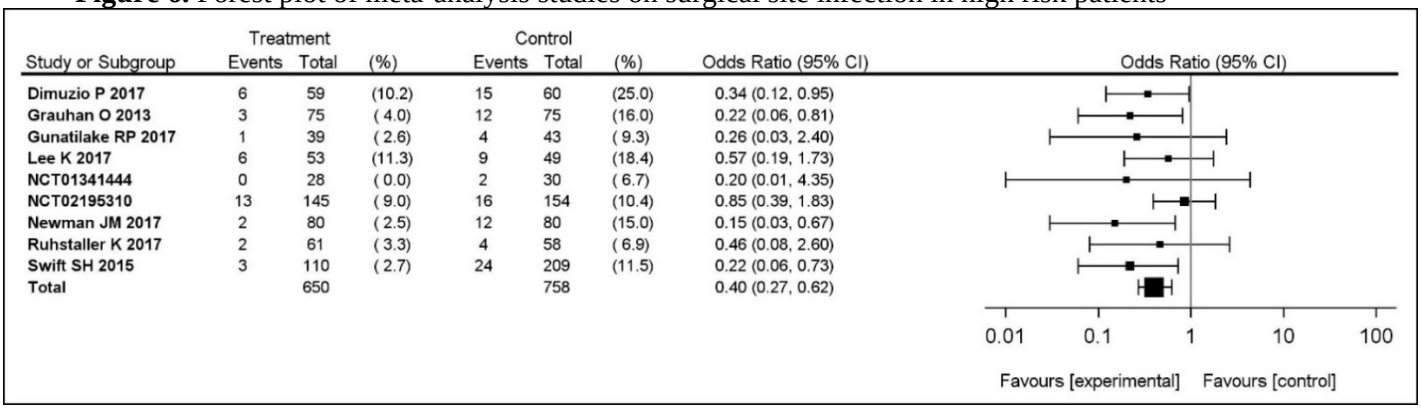
Figure 5. Forest plot of meta-analysis studies on surgical site infection in superficial incisional SSI



iii. Risk factors for surgical site infection

Patients having one or more co-morbidities are generally considered to be at higher risk for surgical site complications. High risk patients were defined in the selected studies as having one or more of the following co-morbidities: obesity (body mass index ≥30 kg/m^2); diabetes; history of smoking; immune suppression or receiving drugs that can cause immune suppression, such as steroids, chemotherapeutic medications, and/or antimetabolites; malnutrition with a hydrated serum albumin of less than 3.0 grams/deciliter; neutropenia; preeclampsia; patients who have cardiac, pulmonary, liver or renal disease; history of previous surgery or radiation in the treatment area. Subjects' risk factors for each of the sixteen (16) studies are described in Table 3; however, some of the studies contain all comers with only a portion being high-risk patients. Upon further examination, nine (9) studies were determined to contain only high-risk patients. A subgroup analysis was performed on these nine (9) studies (*Figure 6*). As expected, the incidence of SSI, in both the treatment and control groups, is higher in high-risk patients (5.5% and 12.9%, respectively) compared to the overall study population (4.2% and 5.8%, respectively). Additionally, there appears to be a greater overall percentage reduction in SSI in high risk patients. Thus, while the reduction in SSI, as measured by odds ratio, in high risk patients does not appear to be significantly different than the reduction observed in the overall data (*Figure 2*), there is a greater clinical benefit of the PREVENA systems in patients at high risk for surgical site infection based on a greater absolute percentage reduction in the incidence of SSI.

Figure 6. Forest plot of meta-analysis studies on surgical site infection in high risk patients



Together, the subgroup analyses on wound classification, infection depth, and patient risk factors for surgical site infection serve as the basis for granting the following Indications for Use:
PREVENA 125 and PREVENA PLUS 125 Therapy Units manage the environment of closed surgical incisions and remove fluid away from the surgical incision via the application of -125mmHg continuous negative pressure. When used with legally marketed compatible dressings, PREVENA 125 and PREVENA PLUS 125 Therapy Units are intended to aid in reducing the incidence of seroma and, in patients at high risk for post-operative infections, aid in reducing the incidence of superficial surgical site infection in Class I and Class II wounds.

Additional subgroup analyses for surgical site infection were performed based on surgical procedure risk factor, combination of surgical procedure and patient risk factors, and incision location. While the results from these subgroup analyses were reviewed, they did not serve as the basis for granting this De Novo request.

Seroma
Seven (7) prospective studies were included in the meta-analysis for seroma, which are summarized in Table 5 below. Five (5) studies are randomized controlled trials, which are level I evidence. The remaining two (2) studies are considered level II evidence, which include one (1) prospective treatment and historical controls study and one (1) prospective observational study that alternated patient assignment into either the treatment or control group (i.e., not randomized).

Table 5. Characteristics of studies included in the Seroma meta-analysis

Study/ Level of Evidence*	***Study Design***	***Surgical Procedure***	***Subjects' Risk Factors***	***Study Duration***	***Incisional Dressings Used***	***No. of Subjects***	***Treatment Duration (days)***
Ferrando 2017[5] Level II	Prospective Observational	Breast conserving surgery, oncoplastic surgery, tissue sparing, simple mastectomies[†]	BMI mean Treatment: 27 kg/m^2; Control: 29.5 kg/m^2; Diabetes; Hx of Smoking; HTN; Use of Corticosteroids; Artery and Liver	1 year	PREVENA PLUS™ CUSTOMIZABLE ™	17 (25 wounds)	7
					Steri-strip skin adhesive closure	20 (22 wounds)	14

			Disease; Chemotherapy; Radiation; Previous Surgery; Invasive surgery				
Gunatilake 2017[8] Level I	RCT	Cesarean delivery	BMI Mean Treatment: 46.3 kg/m^2, Control: 46.8 kg/m^2; Diabetes	42 ± 10 days	PREVENA IMS	39	5-7
					Steri-strips, sterile gauze, Tegaderm	43	1-2
NCT01341444 Level I	RCT	Renal transplant†	BMI Mean Treatment: 29.05 kg/m^2, Control: 28.73; Diabetes; Tobacco Use;	30 days	PREVEANA IMS	28	5
					Standard incisional dressing	30	3
Pachowsky 2012[15] Level I	RCT	Total hip arthroplasty	NR	10 days	PREVENA IMS	9	5 days
					Standard wound dressing	10	NR
Pauser 2016[16] Level I	RCT	Hip hemiarthroplasty†	NR	10 days	PREVENA IMS	11	5
					Standard wound dressing consisting of dry wound coverage	10	NR
Pleger 2017[17] Level I	RCT	Vascular procedures with access in common femoral artery†	BMI Mean Treatment: 26.7 kg/m^2, Control: 27.8 kg/m^2; Diabetes; HX of Smoking/; COPD; Renal Insufficiency; Malnutrition; Age > 50 years; Overweight	30 days	PREVENA IMS	43 (58 wounds)	5-7
					Conventional adhesive plaster	57 (71 wounds)	1
Redfern 2017[18] Level II	Prospective & Historical Controlled	Total hip or knee arthroplasty (elective primary)	BMI Mean Treatment: 30.5 kg/m^2, Control: 30.9 kg/m^2; Diabetes; HTN; Hx of Cancer/Tumor; Arthritis; Myocardial Infarction/Heart Disease; Tobacco use	60 days	PREVENA IMS	192	6-8
					Traditional gauze dressing	400	Standard

†Population or Procedure identified as high-risk for wound complication
*Oxford Centre of Evidence-Based Medicine
NR= Not Reported
RCT = Randomized Controlled Trial
IMS= Incision Management System
ciNPWT= closed incision Negative Pressure Wound Therapy
BMI= Body Mass Index
HX= History
COPD= Chronic Obstructive Pulmonary Disorder
GERD= Gastroesophageal Reflux Disease
HTN= Hypertension
AF= Atrial Fibrillation
CVD= Cardiovascular disease
CKF= Chronic kidney failure

PVD= Peripheral vascular disease
LVD= Left ventricle dysfunction
CAD= Coronary artery disease
CKD= Chronic kidney disease
LVEF= Left ventricle ejection fraction
HIV= Human immunodeficiency virus

Together, the seven (7) studies contained 366 evaluable patients receiving PREVENA Incision Management Systems therapy (treatment group) and 586 patients receiving conventional wound dressings (control group). The conventional wound dressings used in each study can be found in Table 5 above and mostly consist of gauze and occlusive dressings. The primary endpoint in the studies was the incidence of seroma in the treatment group compared to the control group for at least 10 days following surgery.

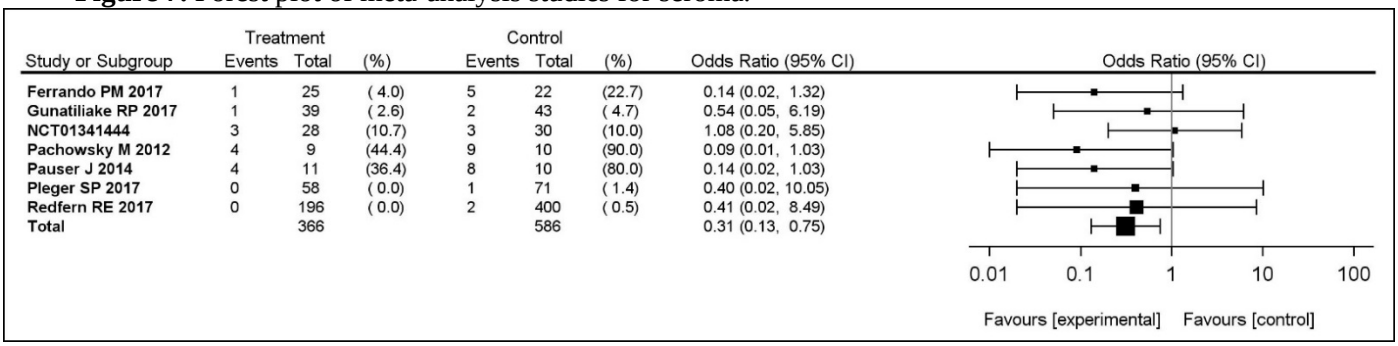
The treatment effect for each study was summarized using odds ratio (OR), which was calculated using the following formula:

OR = AD/BC, where

A = the number of subjects with seroma events for the treatment group
B = the number of subjects without seroma events for the treatment group
C = the number of subjects with seroma events for the control group
D = the number of subjects without seroma events for the control group

An OR of less than 1 suggests a favorable effect by the treatment in reducing seroma, whereas an OR greater than 1 suggests a favorable effect by the standard of care in reducing seroma. The 95% confidence interval (95% CI) for the odds ratio is calculated based on the standard error of Log(OR). The individual study effects are summarized in Figure 7 below.

Figure 7. Forest plot of meta-analysis studies for seroma.



Overall, there is an observable trend supporting a favorable effect by the PREVENA systems in reducing the incidence of seroma formation. The seroma rates ranged from 0.5 % to 90 % for the control group in the selected studies, and the seroma rates in the treatment group ranged from 0 % to 44.4 %. However, the benefit of the PREVENA systems in reducing the incidence of seroma formation varies broadly across different studies, possibly due to many confounding factors such as different surgical procedures and patient risk factors. Subgroup analyses for seroma were not conducted as there are only seven (7) studies total and dividing them into subgroups would not result in meaningful analyses. Additionally, there are many inherent limitations associated with meta-analyses and biases with each individual study, which are discussed in the '*Limitations of the Clinical Evidence*' section below. Because of these

confounding factors and limitations, statistical significance cannot be reliably inferred for the treatment effect on seroma rates based on the combined results from the seven (7) studies.

Limitations of the Clinical Evidence

There are many inherent limitations to meta-analyses, such as publication bias and selection bias. In addition, surgical site infection (SSI) and seroma are complex post-operative outcomes that have many potential causes. While efforts were made in the study identification and selection process to ameliorate biases by including both published and unpublished studies and only the highest quality studies, not all aspects of each selected meta-analysis study are identical. First, even though only prospective studies were included in the meta-analyses, these studies often had many potential sources of bias. Bias assessment was conducted using the Cochrane guidelines and focused on randomization, allocation concealment, differences in baseline patient and risk characteristics, blinded assessments, loss to follow up, comparing purpose of study to outcomes reported, and when possible, comparing outcomes to those listed on ClinicalTrials.gov, when available. Fourteen (14) of the twenty (20) meta-analysis studies were identified as high-risk for bias (Cantero 2016[3], DiMuzio 2017[4], Ferrando 2017[5], Gunatilake 2017[8], Lavryk 2016[10], Lee AJ 2016[11], Matatov 2013[13], NCT013471444, Newman 2017[14], Pleger 2017[17], Redfern 2017[18], Sabat 2016[20], Swift 2015[22]). One (1) study was assessed as low risk for bias (Lee K 2017[12]). Risk for bias was unclear in the remaining five (5) studies due to the lack of information reported in the studies. Second, the unit of the analysis is not consistent in all studies. Some studies used the wound as the unit of analysis and others used the patient as the unit of analysis. As a result, some of the data used in these analyses were based on wounds and some patients contributed more than one (1) wound to the analyses. Third, the timing of the outcome assessments was not consistent across each of the different studies. For example, although all the SSI studies evaluated SSI events for at least four weeks post-surgery, the duration of some of the studies was much longer. Similarly, although all the seroma studies evaluated the incidence of seroma for at least ten days after surgery, the duration of some of the studies was much longer. Fourth, the reported SSI rates in the meta-analysis studies varied broadly across different studies. It should be noted that the following SSI rates based on wound classification and types of SSI (*Table 6*) have recently been reported based on a retrospective review of the 2011 American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database[9]:

Table 6. Surgical Site Infection (SSI) rates based on ACS NSQIP database[9].

30-d postoperative outcomes	Total	Wound Classification			
		Class I	Class II	Class III	Class IV
Surgical Site Infection (SSI)	3.4%	1.8%	4.8%	5.6%	8.5%
Superficial incisional SSI	1.9%	1.2%	2.6%	2.8%	2.7%
Deep incisional SSI	0.6%	0.4%	0.6%	0.8%	1.5%
Organ space SSI	1.1%	0.3%	1.6%	2.2%	4.4%

The SSI rates reported in the studies selected for the meta-analysis, even for the control groups, are generally higher than those reported in the literature. Factors contributing to this discrepancy may be surgeon-, procedure-, or patient-dependent, but nevertheless cannot be pinpointed based on the information provided in the studies. Fifth, five (5) of the seven (7) prospective studies included in the meta-analysis for SSI and one (1) prospective study included in the meta-analysis for seroma compared the PREVENA systems to historical

controls. There have been significant evidence-based changes in patient care to define and reduce the risk for post-operative complications, including surgical site infections. Additionally, surgical site infection reduction measures vary among surgeons, hospitals, and countries. Changes in disease definitions, interventions, and treatment effectiveness over time contribute to non-contemporaneous bias. Results of studies using historical controls should be evaluated with caution.

These limitations should be considered when examining the results from these meta-analyses.

Conclusion
Overall, there appears to be a small but consistent trend supporting the benefit of the PREVENA systems in reducing surgical site infection (SSI) and seroma. However, due to the many limitations of the selected studies in the meta-analyses described above, any statistical inferences based on the combined results of these studies are inherently unreliable. The benefit of the PREVENA systems in reducing SSI and seroma appears to be small in general and varies potentially based on several factors, including wound classification, infection depth, and patient risk factors for post-operative wound complication. Subgroup analyses demonstrated that while the trend observed in the overall data continues to be observed in most subgroup studies, the greatest benefit of the PREVENA system appears to be in reducing superficial SSI in Class I and Class II wounds. Additionally, there is a greater absolute percentage reduction in the incidence of SSI in patients at high risk for post-operative infections, likely because of the higher incidence of SSI in this patient population. Therefore, taken as a whole, the data may not be supportive of routine use of the PREVENA systems for the sole purpose of reducing surgical site infection and seroma; however, as an adjunct therapy to good clinical practice, the PREVENA system has demonstrated to aid in reducing the incidence of seroma and, in patients at high risk for post-operative infections, aid in reducing the incidence of superficial surgical site infection in Class I and Class II wounds. Surgeons should continue to follow the '*Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection*'[2] and the '*American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines*'[1] for best practices in preventing surgical site infection.

Safety
Adverse events (AEs) and Serious Adverse Events (SAEs) were reported in three (3) of the twenty (20) studies included in the meta-analyses [Gunatilake (Cesarean section) 2017[8], NCT01341444 (Renal transplant), NCT02195310 (Sternotomy)]. There were no treatment related AEs or SAEs reported in the Cesarean section study (Gunatilake 2017[8]). In the two studies conducted by KCI (NCT01341444 (Renal transplant), NCT02195310 (Sternotomy)), there were no SAEs, and the twenty one (21) reported AEs related or possibly related to the device including pain (5), blisters (4), dehiscence (4), draining/wound secretion (2), erythema (2), skin irritation (2), ecchymosis (1), and hematoma (1), which are known adverse events that may be seen with the use of the device on surgical incisions.

No significant differences were reported in AEs or SAEs between the PREVENA systems (treatment group) and conventional wound dressings (control group). No adverse device events, serious adverse device events, or device failures were reported. These results suggest that the

PREVENA systems have a similar safety profile as conventional wound dressing for closed surgical incisions.

Post Market Data

PREVENA 125 and PREVENA PLUS 125 Therapy Units first received 510(k) clearance in 2010 and have been legally marketed globally. Since 2010, there have been (b) (4) units shipped with (b) (4) complaints. The complaint total includes data from both "Non-Harm" and "Alleging Harm" complaints. Post market surveillance data, from Medical Device Reporting (MDR) and Manufacturer and User Facility Device (MAUDE) databases, have been reviewed against the device risk profile and have been determined to be within acceptable limits. Additionally, the post market reports are consistent with the adverse events reported in the meta-analysis studies.

Although Medical Device Reporting (MDR) is a valuable source of information, this passive surveillance system has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to potential under-reporting of events and lack of information about frequency of device use. MDR data alone cannot be used to establish rates of events, evaluate a change in event rates over time, or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices.

Pediatric Extrapolation

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

LABELING

Device labeling includes a clinician guide and patient labeling. The clinician guide includes a description of the sterile and non-sterile device components, instructions for use, relevant clinical evidence, electromagnetic compatibility information, shelf life, and device disposal instructions.

Patient labeling includes instructions for use and information regarding when the treating physician should be contacted.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a negative pressure wound therapy system for reduction of wound complications and the measures necessary to mitigate these risks.

Table 7. Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Adverse tissue reaction	Biocompatibility evaluation
Infection	Sterilization validation Shelf life testing Labeling
Electrical shock or electromagnetic interference with other devices	Electromagnetic compatibility testing Electrical safety testing Labeling
Damage to underlying tissue (e.g., wound maceration, uncontrolled bleeding) due to • Mechanical failure • Software malfunction • Use error	Clinical data Non-clinical performance testing Usability testing Shelf life testing Software verification, validation, and hazard analysis Labeling
Increase in wound complications due to use error	Clinical data Usability testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the negative pressure wound therapy system for reduction of wound complications is subject to the following special controls:

(1) Clinical data must demonstrate that the device performs as intended under anticipated conditions of use and evaluate the following:
   (a) Wound complication rates; and
   (b) All adverse events.

(2) The patient-contacting components of the device must be demonstrated to be biocompatible.

(3) Performance data must demonstrate the sterility of the patient-contacting components of the device.

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

(5) Usability testing must demonstrate that intended users can correctly use the device, based solely on reading the instructions for use.

(6) Non-clinical performance data must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested in a worst-case scenario for the intended use life:
   (a) Ability to maintain pressure levels at the wound site under a worst-case scenario for the intended use life;

(b) Fluid removal rate consistent with the wound types specified in the indications for use; and
(c) Timely triggering of all alarms.

(7) Performance data must demonstrate the electrical safety and electromagnetic compatibility (EMC) of the device.

(8) Software verification, validation, and hazard analysis must be performed.

(9) Labeling must include the following:
(a) Instructions for use;
(b) A summary of the device technical specifications, including pressure settings, modes (e.g., continuous or intermittent), alarms, and safety features;
(c) Compatible components and devices;
(d) A summary of the clinical evidence for the indications for use;
(e) A shelf life for sterile components; and
(f) Use life and intended use environments.

(10) For devices intended for use outside of a healthcare facility, patient labeling must include the following:
(a) Information on how to operate the device and its components and the typical course of treatment;
(b) Information on when to contact a healthcare professional; and
(c) Use life.

BENEFIT/RISK DETERMINATION

Risks

The risks of the device are based on nonclinical laboratory studies, data collected in clinical studies, and post-market surveillance data described above. Adverse events (AEs) and Serious Adverse Events (SAEs) were reported in three (3) of the twenty (20) studies included in the meta-analyses (Gunatilake (Cesarean section) 2017[8], NCT01341444 (Renal transplant), NCT02195310 (Sternotomy)). There were no treatment related AEs or SAEs reported in the Cesarean section study (Gunatilake 2017[8]). In the two studies conducted by KCI USA, Inc. (NCT01341444 (Renal transplant), NCT02195310 (Sternotomy)), there were no SAEs, and the twenty-one (21) reported AEs related or possibly related to the device included skin irritation, blisters, erythema, ecchymosis, pain, drainage, hematoma, and dehiscence, which are known adverse events that are anticipated with the use of the device on surgical incisions. Post-market surveillance (PMS) data of seven years also demonstrate the safety of the PREVENA systems. Overall, the risk of the PREVENA systems is low when used on closed surgical incisions. The risks associated with the PREVENA systems have been appropriately mitigated using the identified special controls. Device labeling will help ensure that the end users clearly understand the system description, indications, contraindications, precautions, warnings, and instructions for use.

Benefits

The probable benefits of the device are based on nonclinical laboratory studies and clinical evidence based on meta-analyses described above. The proposed intended use is supported by a meta-analysis from twenty (20) clinical studies, seven (7) years of post-market surveillance (PMS) data, and preclinical testing; all of which contribute to a favorable benefit risk profile. Overall, the collective clinical evidence demonstrates a small but consistent trend supporting the benefit of the PREVENA systems in reducing surgical site infection (SSI) and seroma. However, due to the many limitations of the selected studies in the meta-analyses, any statistical inferences based on the combined results of these studies are inherently unreliable. The benefit of the PREVENA systems in reducing the incidence of SSI and seroma appears to be small in general and varies potentially based on several factors, including wound classification, infection depth, and patient risk factors for post-operative wound complication. Subgroup analyses demonstrated that while the trend observed in the overall data continues to be observed in most subgroup studies, the greatest benefit of the PREVENA system appears to be in reducing superficial SSI in Class I and Class II wounds. Additionally, there is a greater absolute percentage reduction in the incidence of SSI in patients at high risk for post-operative infections, likely because of the higher incidence of SSI in this patient population. The data, however, do not support the use of the PREVENA systems in reducing surgical site infection and seroma for all surgical procedures and patient populations. Therefore, taken as a whole, the data may not be supportive of routine use of the PREVENA systems for the sole purpose of reducing surgical site infection and seroma; however, as an adjunct therapy to good clinical practice, the PREVENA system has demonstrated to aid in reducing the incidence of seroma and, in patients at high risk for post-operative infections, aid in reducing the incidence of superficial surgical site infection in Class I and Class II wounds. Surgeons should continue to follow the '*Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection*'[2] and the '*American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines*'[1] for best practices in preventing surgical site infection.

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, for the following indication statement:

> When used with legally marketed compatible dressings, PREVENA 125 and PREVENA PLUS 125 Therapy Units are intended to aid in reducing the incidence of seroma and, in patients at high risk for post-operative infections, aid in reducing the incidence of superficial surgical site infection in Class I and Class II wounds .

The probable benefits outweigh the probable risks for the PREVENA systems. The device provides benefits and the risk can be mitigated using general controls and the identified special controls.

CONCLUSION

The De Novo request for the PREVENA 125 and PREVENA PLUS 125 Therapy Units is granted, and the device is classified under the following:

Product Code: QFC
Device Type: Negative pressure wound therapy device for reduction of wound complications
Class: II
Regulation: 21 CFR 878.4783

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