DE NOVO CLASSIFICATION REQUEST FOR ECLIPSE SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> Rectal Control System: A rectal control system is a prescription device intended to treat fecal incontinence by controlling the size of the rectal lumen. The device is inserted in the vagina and includes a portion that expands to reduce the rectal lumen to prevent stool leakage and retracts to allow normal passage of stool. The device includes an external regulator to control the state of expansion.

NEW REGULATION NUMBER: 876.5930

CLASSIFICATION: II

PRODUCT CODE: PJH

BACKGROUND

DEVICE NAME: Eclipse System

SUBMISSION NUMBER: DEN140020

DATE OF DE NOVO: June 25, 2014

REQUESTOR CONTACT: Pelvalon, Inc.
923 Thompson Pl.
Sunnyvale, CA 94085

REQUESTER'S RECOMMENDED CLASSIFICATION: II

INDICATIONS FOR USE

The Eclipse System is indicated for the treatment of fecal incontinence in adult women. It is intended for prescription use.

LIMITATIONS

The sale, distribution, and use of the Eclipse System are limited to prescription use only.

Limitations on device use are also achieved through the following statements included in the Physician Instructions:

Contraindications

- Presence of vaginal infection
- Presence of open vaginal wound

Warnings

- This product contains metal and so must be removed before undergoing an MRI, in order to prevent any potential adverse events that may occur due to heating or movement of the Insert during the MRI.
- Before obtaining a pelvic X-ray, patients should consult their physician about whether or not to remove the Eclipse Insert as the Insert may obscure images.
- The Eclipse Insert and the Pump are for single-patient use only.

Precautions

- This device should only be prescribed by physicians with expertise in the evaluation of pelvic floor anatomy.
- Prior to each use, inspect the Eclipse Insert and Pump for possible damage. If damaged, do not use.
- Patients should continue the use of any treatment they are using for vaginal atrophy (e.g., topical estrogen cream).
- Care should be taken to avoid use in patients with severe vaginal atrophy that would prevent safe, effective, or comfortable use of the Insert.
- The safety and effectiveness of the Eclipse System have not been evaluated in patients with pelvic organ prolapse beyond the plane of the hymen or who are pregnant.
- The safety and effectiveness of the Eclipse System have not been evaluated in women who use an IUD.
- Use of the Eclipse System after a recent hysterectomy may compromise the integrity of the vaginal cuff repair.
- The safety and effectiveness of the Eclipse System for use in women with less than 4 episodes of fecal incontinence over a 2-week period have not been demonstrated.

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

DEVICE DESCRIPTION

Device Description

The Eclipse System is a device intended to treat women with fecal incontinence (FI), also referred to as "accidental bowel leakage", or "bowel control disorder". The Eclipse System contains the Eclipse Insert and the Pump, including Regulator. The Eclipse Insert

is used intra-vaginally, is insertable/removable by the patient, and includes a balloon that when inflated, exerts a force posteriorly (trans-vaginally) against the wall in the rectum resulting in a decrease in the lumen of the rectum (Figure 1). The compression of the rectal space results in decreased frequency of fecal incontinence events. The Eclipse Insert consists primarily of a silicone and stainless steel base with an inflatable silicone balloon. The pump is used by the patient for inflating and deflating the balloon with a goal of improving control over bowel movements.

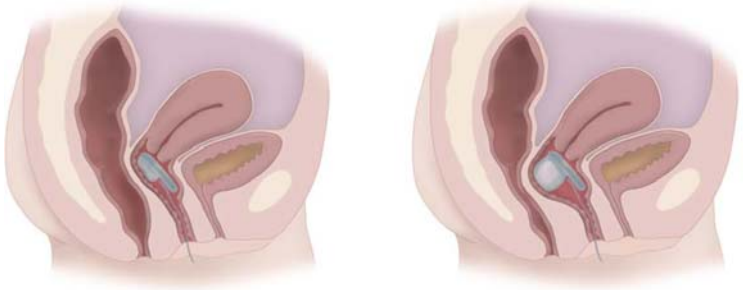


Figure 1. Eclipse Insert; balloon deflated (left) and inflated (right)

The Eclipse System is composed of: The Eclipse Insert and a Patient Pump (or simply called "the pump").

Eclipse Insert (Figure 2): The insert is composed of a base portion, an inflatable balloon portion, and inflation tube (also called a tube), and a valve (also referred to as inflation valve or self-closing Luer valve). The base portion positions the balloon and helps maintain the placement of the Insert in the vagina; its exterior (patient contact) is silicone with internal stainless steel and silicone components. The base is flexible to allow for ease of insertion and removal. The balloon is made of thin walled silicone, with an enclosed, non-body contacting polyurethane liner to enhance its impermeability to air, minimizing air loss. The silicone inflation tube connects the balloon on one end, and on the other end, terminates in a self-closing Luer valve. A silicone cap is included to keep contaminate out of the valve. An optional extension tube is also provided that can be added to the existing tube to increase its length.

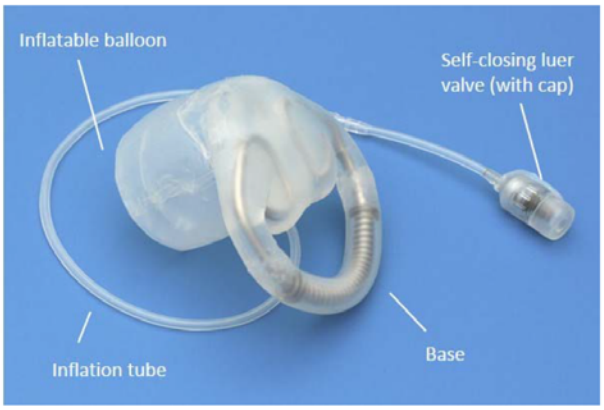


Figure 2. Eclipse Insert (inflated)

The following is recommended regarding the Insert:

- The initial fitting and placement of the Eclipse should be done by a physician, to estimate the size of the vagina, and to match the appropriate Eclipse size with the patient's anatomy
- It can remain in the vagina continuously up to a week, but can be removed by the patient at any time
- It should be removed during sexual intercourse
- Air should be added to the balloon at least three times daily (minimally including morning, night and after bowel movements), as some air will leak out over time
- It should be removed and cleaned on a weekly basis
- It should be removed and cleaned daily during menstruation
- It should be disinfected if it becomes soiled
- For bowel movements, air is removed from the balloon and then when the patient has defecated, the device is re-inflated
- The device should be replaced yearly
- Special instructions are provided for women with a prior hysterectomy

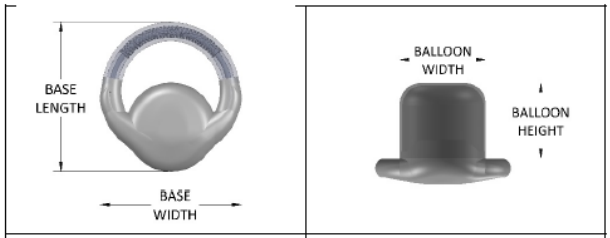
Table 1 shows the different sizes that are available to clinicians for ensuring the best fit for the patients.

Table 1. Balloon Measurements

Product Code	Base Measurement Length x Width (mm)	Balloon Measurement Height x Width (mm)
48ES	48x48	37x36
48EL	48x48	47x42
51US	51x48	37x36
51UL	51x48	47x42
51ES	51x51	37x36
51EL	51x51	47x42
54ES	54x54	37x36
54EL	54x54	47x42
55US	55.5x51	37x36
55UL	55.5x51	47x42
57US	57x54	37x36
57UL	57x54	47x42
57ES	57x57	37x36
57EL	57x57	47x42
62US	62x57	37x36

Table 1. Balloon Measurements, continued

Product Code	Base Measurement Length x Width (mm)	Balloon Measurement Height x Width (mm)
62UL	62x57	47x42
64ES	64x64	37x36
64EL	64x64	47x42
70US	70x64	37x36
70UL	70x64	47x42
70ES	70x70	37x36
70EL	70x70	47x42
76US	76x70	37x36
76UL	76x70	47x42
76ES	76x76	37x36
76UL	76x76	47x42
83US	83x76	37x36
83UL	83x76	47x42



Patient Pump (Figure 3): As shown in Figure 3a, the patient pump (external to the patient) has two ends that connect to the valve: one end for adding air, and the other end for removing air (labeled with a "+" and "-", respectively). The patient pump interfaces with the Eclipse insert via the self- closing Luer valve (Figure 3b). The pump is fitted with a regulating valve (also called a Regulator), also external to the patient, which regulates the amount of air introduced to the inflatable balloon portion of the Eclipse insert. Air is moved through the pump by squeezing the pump body. During inflation, the Pump is squeezed seven to ten times. Typically, fewer than seven pumping motions are necessary to adequately fill the balloon and any excess air is vented out by the regulator. Regulators are removable so that different balloon pressures can be achieved. Regulators are provided as single –patient use only. The patient pump is:

- Supplied non-sterile
- For single-patient use

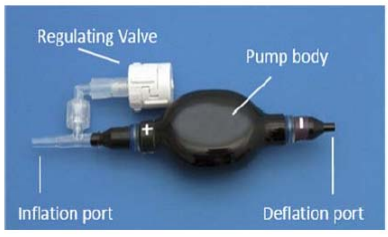


Figure 3a. Patient Pump.

Figure 3b. Eclipse insert connected to patient pump.

There are five regulators that come with the device, and they are listed in Table 2:

Table 2. Regulator Pressures.

Regulator #	Pressure at Full Inflation (mmHg)
1	45-57
2	58-69
3	70-92
4	93-113
5	114-129

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Eclipse System is comprised of an Insert and a Pump. The Insert part of the Eclipse System, when used as intended, is considered as a surface device with long term (> 30 days) contact with intact mucosal membrane. As discussed in Tables 3 and 4 below, the body-contacting materials on the portion of the Insert that typically reside inside the vagina are the *base, balloon, and tube*. The Pump part of the Eclipse System, when used as intended, is considered as a surface device with limited (< 24 hours) contact with intact skin.

Table 3. List of component materials used in the Eclipse Insert.

Part Description	Material
Parts listed below may contact vaginal mucosa:	
Base Tubing	b(4)
Adhesive	
Silicone tubing	
Straight connector	
Valve	
Parts listed below do not contact the patient:	
Spring	b(4)
Wire (for base)	
Bladder Material	

Table 4. List of component materials used in the Eclipse Pump.

Part Description	Material
Parts listed below may contact skin (hand):	
Hand Pump	b(4)
Elbow connector	
T-connector	
Primer	

Check Valve Adapter	b(4)
Check valve	
Check Valve Adapter, printed	
Relief valves (5 sizes)	
Parts listed below do not contact the patient:	
Check Valve Shim	b(4)
Filter Paper	
Polyurethane Foam	

Biocompatibility testing (Table 5) was completed based on the nature of patient contact on the test articles identified as Eclipse Insert and Eclipse Patient Pump.

Table 5. Tests Completed for the Eclipse System.

Eclipse Insert
ISO Cytotoxicity – L929 MEM Elution Test
ISO Maximization Sensitization – Guinea Pig
ISO Vaginal Irritation and Histopathology
ISO Muscle Implantation 1 week Interval
ISO Muscle Implantation 4 week Interval
Eclipse Pump
ISO Cytotoxicity – L929 MEM Elution Test
ISO Maximization Sensitization – Guinea Pig
ISO Skin Irritation

In lieu of additional recommended tests for devices of this nature of contact (Genotoxicity, Systemic Toxicity (acute), Sub Chronic Toxicity, and Chronic Toxicity), a Toxicological Risk Assessment was completed to further support the biocompatibility of the Eclipse System.

SHELF LIFE/STERILITY

The Eclipse System (Insert and Pump), is provided non-sterile with cleaning instructions and low level disinfection instructions if the device should become soiled.

The device has not been labeled with a shelf life or expiration date, although the user is instructed that the device should be replaced annually.

Please refer to the labeling for a complete list of patient cleaning and disinfecting instructions.

PERFORMANCE TESTING – BENCH

Microbiological testing on vaginal microflora and Toxic Shock Syndrome Toxin-1 (TSST-1) was performed to show that the use of the Eclipse System did not:

- Enhance the growth of *Staphylococcus aureus*
- Increase the production of TSST-1 by *S. aureus*
- Alter the growth of the normal vaginal microflora

The following bench tests were performed successfully to characterize the safety and performance of the Eclipse System:

Attribute(s)	Test Description	Acceptance Criteria
Balloon Dimensions	Measure balloon width and height at 150mmHg (Max Regulating valve pressure + 21mmHg buffer)	Balloon dimensions must be ±3mm from nominal when insert is pressurized to 150mmHg. Must also meet width and height limits.
Balloon Fatigue	Inflate balloon to 150mmHg, then cycle deflation and inflation. Repeat dimensional and leak resistance testing.	No loss of integrity or function during worst case life cycling. After cycling, balloon dimensions and leak resistance must continue to pass.
Folding Fatigue	Cycle device base between fully folded and flat configurations.	No loss of integrity or function during worst case life cycling. After cycling, base dimensions must continue to pass.
Leak Resistance	Inflate balloon to 134 mmHg under ≥ 400g load, then measure air loss over time.	Balloon must maintain fluid volume between inflations. Insert inflated to maximum clinical amount, and with a 400g applied external load must lose <0.3mL of volume per hour during a test 4-36 hours.
Inflation Tool (Pump) use	Use the Pump to inflate and deflate the	Tool must inflate Insert to its

Attribute(s)	Test Description	Acceptance Criteria
	Insert.	Regulating Valve's pressure minimum and deflate.
Inflation Tool (Pump) & Relief Valve (Regulator) Fatigue	Pump with regulating valve into device repeatedly. Repeat Pump and Regulating Valve use testing.	No loss of integrity or function during worst case life cycling. After cycling, Pump and Regulating Valve Function must continue to Pass.
Base Ring Deflection	Pull base ring mounted to a 35mm opening, with approx. 5lbs force.	No loss of integrity or function. Base dimensions must remain within tolerances and ≤3mm out of plane.
Accelerated Device Aging	Expose materials to 1 year simulated aging at accelerating temperature.	Aged materials must pass all subsequent cycling tests and functional verifications.
Simulated Cleaning and Disinfection Cycling	Expose device to simulated cycles of cleaning and disinfection.	No loss of integrity or function during worst case life cleaning and disinfection cycling.
Packaging and Effect of Distribution Stresses	Expose packaged materials to climatic conditioning and package performance testing.	Following testing, no loss of packaging or device integrity or function.

SUMMARY OF CLINICAL INFORMATION

The Eclipse System has been the subject of three clinical studies: two feasibility studies and a pivotal study. Across all studies, 219 subjects have worn the device.

Feasibility Studies

The goal of these studies was to evaluate the proof of concept of the Eclipse System by evaluating the device's stability and positioning, rectal occlusion, and patient comfort. The fitting process, comfort, and safety were evaluated, as well as usability feedback from those subjects suffering from FI.

In the 102 subjects exposed to the device, there were no serious device-related adverse events and 9 non-serious, device-related adverse events. All 9 were mild [minor

bleeding/superficial cuts due to tissue stretching upon insertion/removal (3) or minor ecchymosis (6)] and resolved quickly without medical intervention other than vaginal estrogen cream.

Pivotal Study

Study Design

The study design was a multi-center, prospective, open-label, safety and effectiveness study of the Eclipse System in women with fecal incontinence. To be eligible for treatment, patients must have met several screening criteria, including a 6-month history of FI, ≥ (greater than or equal to) 4 FI episodes (defined as major or minor soiling) during their 2-week baseline diary, and successful fitting of the Insert. The primary endpoint was reduction of FI episodes (as recorded in a patient diary) after 1 month of treatment with the Eclipse System (Treatment Period) compared to baseline without the device. A study success criterion was ≥40% of subjects reporting ≥50% reduction in FI episodes during the on-device period as compared to the baseline period. Subjects were invited to enter an Optional Treatment Period for an additional two months, for a total of 3 months of treatment.

Study Results

Two hundred (200) subjects were consented with 61 subjects (31%) entering the Treatment Period. The most common reason for screening exclusions prior to fitting was insufficient frequency of FI episodes during the baseline period (<4 FI episodes in two weeks), which accounted for 49% of exclusions prior to fitting. Of the 110 patients who continued to the fitting assessment, 49 (45%) did not achieve a successful fit or successfully complete the fitting assessment.

Safety

There were 93 AEs in 61 subjects reported as device-related/possibly device-related. There were no serious device-related adverse events reported. All device-related adverse events were rated as mild (78%) or moderate (22%) and none required medical intervention beyond a topical vaginal steroid cream for vaginal erythema and an antifungal cream/suppository for yeast infection. The most common AE was pelvic cramping or discomfort which occurred in 15% of subjects during the fitting period, 11% of subjects during the treatment period and 8% of subjects who elected to continue use during the optional treatment period. There were substantially fewer occurrences in the Treatment Period and Optional Treatment Period once subjects were successfully fit with the device and entered treatment.

Effectiveness

The primary endpoint of the pivotal study was the reduction in the number of FI episodes/2 weeks during the 3rd and 4th week of study participation compared to the baseline 2 week assessment period. The study success criteria was that > 40% of the subjects would have a ≥ 50% reduction in FI episodes. FI episodes were categorized as major soiling (a large accident that required an immediate change of undergarment, pad, or clothing) or minor soiling (stool leakage that is more than just staining, but did not

require an immediate change of undergarment, pad, or clothing). Episodes of staining were not considered as FI episodes.

The primary effectiveness analysis performed on the intent to treat (ITT) Cohort demonstrated that 79% of the 61 subjects reported at least a 50% reduction in FI episodes (95% CI 66-88%), which statistically exceeded the study's predetermined 40% threshold for success ($p<0.0001$). Five (5) patients included in the ITT analysis were counted as treatment failures due to: unanalyzable diary data (2), exited due to unrelated health issues (2), and withdrew consent (1). In the Per Protocol (PP) Cohort, which included the 56 patients with fully analyzable diary data, 86% of subjects reported at least a 50% reduction in FI (95% CI 74-94%), also statistically exceeding the study's predetermined 40% threshold for success ($p<0.0001$). Twenty-three (23) subjects (41% of the PP Cohort) reported a complete elimination of FI episodes during the Treatment Period. Seventy percent (70%) of subjects reported 75% or greater reduction in FI episodes.

A secondary FI endpoint was the reduction in number of incontinent days while wearing the device during the 2 week assessment period as compared to the baseline 2 week assessment period. Patients experienced a reduction from incontinence on 49% of days to 11% of days (an average of 6.9 incontinent days in a 2-week period at baseline versus 1.6 incontinent days during the 2-week treatment diary). Additionally, patients experienced a reduction in the mean number of FI Episodes per 2-week period from 11.6±9.5 at baseline to 2.1±2.9 during the Treatment Period.

The sub-population evaluated were subjects with total hysterectomies. Of the 63 subjects with total hysterectomies in the Safety Cohort, 14 subjects reported device-related/possibly device-related adverse events (22%), which is less than the observed percentage of device-related/possibly device-related adverse events in the entire Safety Cohort (52%; 61/117). Additionally, 7/63 (11%) subjects in the Safety Cohort with total hysterectomies reported adverse events related to possible vaginal irritation or tissue damage, compared to 25/117 (21%) in the entire Safety Cohort. For the purpose of this analysis, adverse events in this category included the following: vaginal abrasion, vaginal irritation, vaginal ecchymosis or bruising, vaginal erythema/petechiae, vaginal bleeding, or vaginal spotting.

Due to the observed lower rates of device-related/possibly device-related adverse events and adverse events related to possible vaginal irrigation or tissue damage in women with a total hysterectomy, there is no increased risk of irritation, abrasion, or ulceration at the location of the vaginal cuff repair.

Quality of Life - All subscales of the Fecal Incontinence Quality of Life (FIQOL) and the Modified Manchester Health Questionnaire (MMHQ) showed significant improvements. In response to a Patient Global Impression of Improvement (PGI-I) question that asked patients to "check the item that best describes how [their] control of bowel leakage is now, compared with how it was without the [insert]", 86% of patients selected "very much better" or "much better". Patients were also asked to list their most bothersome lifestyle restriction, and rank the impact that use of the Eclipse had on it. Of the 53

respondents to this question, 89% indicated that their most bothersome restriction was "completely addressed", or had been "helped a lot" (47% and 42%, respectively). Additionally, 98% (54/55) of patients responded that they would recommend the Eclipse System to a friend with FI. Finally, after completing the Treatment Period, 54/56 subjects (96%, PP Cohort) said the Insert was comfortable or they could not feel it (48% and 48% respectively); one subject reported the Insert was slightly uncomfortable, but tolerable; one reported the Insert was uncomfortable; and 0 patients reported the Insert was painful.

Optional Treatment Period - The treatment effect was maintained at the 3-month follow-up in the Optional Treatment Period for those that elected to continue use of the Eclipse System: 38 of 44 patients achieved treatment success (86.4%, 95% CI 73-95%). Significant improvements were also shown for clinical impact, comfort, and lifestyle, as measured by the FIQOL, MMHQ, and PGI-I scales, as well as subject satisfaction, comfort, and impact on lifestyle restrictions.

LABELING

Labeling for the Eclipse System includes Physician's Instructions for Use and a Patient Instructions for Use Manual, since the device is to be used at home. A package label is also included. The labeling is sufficient and satisfies the requirements of 21 CFR 801.109. The Instructions for Use and Patient Instructions for Use Manual provide all of the elements required as part of the Special Controls. Please refer to the Instructions for Use and Patient Instructions for Use Manual for device labeling.

RISKS TO HEALTH

Table 6 identifies the risks to health that may be associated with use of the Rectal Control System and the measures necessary to mitigate these risks.

Table 6. Identified Risks to Health and Mitigation Measures.

Identified Risk	**Mitigation Method**
Vaginal Wall Trauma	• Clinical Testing • Labeling
Adverse Tissue Reaction	• Biocompatibility Testing
Infection	• Non Clinical (bench) Testing • Cleaning and Disinfection Validation • Labeling
Device Malfunction	• Non Clinical (bench) Testing • Labeling
Urinary Urgency, Incontinence or Voiding Problems	• Clinical Testing • Labeling
Fecal Urgency, or Difficulty in Evacuation	• Clinical Testing • Labeling

Identified Risk	Mitigation Method
Discomfort, Pain	• Clinical Testing • Labeling
Change in Amount, color, or consistency of vaginal discharge	• Labeling

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the rectal control system is subject to the following special controls:

1. Clinical testing must document the device acceptance data and the adverse event profile associated with clinical use, and demonstrate that the device performs as intended under anticipated conditions of use.
2. The elements of the device that contact vaginal tissue must be demonstrated to be biocompatible.
3. The cleaning and disinfection instructions for the device must be validated.
4. Non-clinical (bench) testing must demonstrate that the device performs as intended under anticipated conditions of use.
5. Non-clinical (bench) testing must demonstrate that the device does not:
    a. Enhance the growth of *Staphylococcus aureus*
    b. Increase production of Toxic Shock Syndrome Toxin -1 by *S. aureus*
    c. Alter the growth of normal vaginal flora
6. Labeling must include:
    a. Specific instructions, contraindications, warnings, cautions, limitations, and the clinical training needed for the safe use of the device.
    b. The intended patient population and the intended use environment.
    c. Information on how the device is to be fitted, how the device operates, and recommendations on device maintenance.
    d. A detailed summary of the clinical testing pertinent to the use of the device, including a summary of the device- and procedure-related complications or adverse events related to use of the device, as well as relevant safety and performance information.
7. Patient labeling must be provided and must include:
    a. Relevant contraindications, warnings, precautions, and adverse events/complications.
    b. Information on how the device operates and the recommended device maintenance (i.e., care instructions) including cleaning and disinfection.
    c. Information on the patient population for which there was a favorable benefit/risk assessment.
    d. The potential risks and benefits associated with the use of the device.

BENEFIT/RISK DETERMINATION

The data demonstrate a clinically meaningful improvement in terms of fecal incontinence episodes and fecal incontinent days along with an improvement in quality of life. This was achieved without any reported serious device-related adverse events.

The study design reflected the use of the device in clinical practice. The data demonstrated a high likelihood of success from the use of the device given the patient population as described in the indications for use, inclusion and exclusion criteria.

In conclusion, given the available information above, the data support the treatment of fecal incontinence in adult women, the probable benefits outweigh the probable risks for the Eclipse System. The device provides substantial benefits and the risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The *de novo* for the Eclipse System is granted and the device is classified under the following:

Product Code: PJH
Device Type: Rectal Control System
Class: II
Regulation: 21 CFR 876.5930