SUMMARY OF SAFETY AND PROBABLE BENEFIT (SSPB)

I. GENERAL INFORMATION

Device Generic Name: Anterior Vertebral Body Tethering System

Device Trade Name: REFLECT™ Scoliosis Correction System

Product Code: QHP

Applicant's Name and Address: Globus Medical, Inc.
Valley Forge Business Center
2560 General Armistead Avenue
Audubon, Pennsylvania 19403

Date(s) of Panel Recommendation: None

Humanitarian Device Exemption (HDE): H210002

Humanitarian Use Device (HUD) Designation Number: DEV-2019-0433

Date of HUD Designation: February 6, 2020

Date of Notice of Approval to Applicant: May 15, 2023

II. INDICATIONS FOR USE

The REFLECT™ Scoliosis Correction System is indicated for skeletally immature patients who require surgical treatment to obtain and maintain correction of progressive idiopathic scoliosis, who have a major Cobb angle of 30 to 65 degrees whose osseous structure is dimensionally adequate to accommodate screw fixation, as determined by radiographic imaging. Patients should have failed bracing and/or be intolerant to brace wear.

Modifications from the HUD Designation

The indication for use statement has been modified from that granted for the HUD designation. The HUD designation was, "for treatment of skeletally immature patients (Risser <5) with a major Cobb angle ≥30°, who require surgical treatment to obtain and maintain correction of progressive idiopathic scoliosis, and who have failed bracing and/or are intolerant to bracing." It was modified for the HDE approval as follows: removed Risser sign as a Risser score less than 5 is synonymous with skeletally immature patients; and, identified Cobb angle range to better reflect the study population. The resulting Indications for Use statement falls within the HUD designation.

III. CONTRAINDICATIONS

The REFLECT™ Scoliosis Correction System should not be implanted in patients with the following conditions:

1. Presence of any systemic infection, local infection, or skin compromise at the surgical site;
2. Prior spinal surgery at the level(s) to be treated;
3. Known poor bone quality defined as a T-score -1.5 or less;
4. Skeletal maturity;
5. Any other medical or surgical condition which would preclude the potential benefit of spinal surgery, such as coagulation disorders, allergies to the implant materials, and patient unwillingness or inability to cooperate with post-operative care instructions.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the REFLECT™ Scoliosis Correction System labeling.

V. DEVICE DESCRIPTION

The REFLECT™ Scoliosis Correction System is a non-fusion spinal device intended for treatment of idiopathic scoliosis. It is designed for continued growth and mobility and deformity correction, and accomplishes this by holding spinal segments in a natural, anatomic position using non-rigid materials (**Figure 1**). The system consists of a polymeric cord used in conjunction with monoaxial screws, locking caps, and staples.

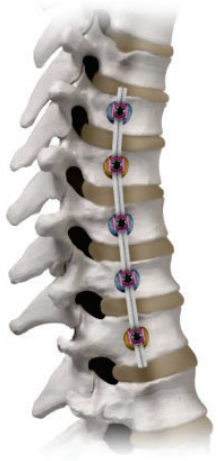


Figure 1. REFLECT™ construct.

The size and number of screws are dependent on the desired correction as well as the length and position of the cord. The cord is placed into the screw head and secured with a locking cap. Single or dual staples may be used for additional fixation of screws to the vertebral bodies and are intended for anterior use only. Manual surgical instruments are used to tension the implant assembly to provide corrective forces.

The REFLECT™ Scoliosis Correction System consist of polyethylene terephthalate (PET) cords, monoaxial screws, locking caps, and staples (**Figure 2**). The PET cord has an attached collet made from titanium alloy, which is removed following tensioning. REFLECT™ screws are composed of titanium alloy, and are available with or without hydroxyapatite (HA) coating. Locking caps and staples are made from titanium alloy.

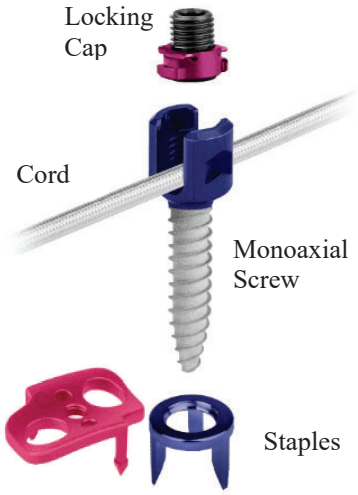


Figure 2. REFLECT™ implants.

The REFLECT™ Scoliosis Correction System is similar to a traditional anterior screw and rod construct except that a REFLECT™ cord is used instead of a rod. Surgery is performed using an anterior thoracoscopic or mini-open technique.

The screws are implanted on the convex side of the curve, with staples for additional fixation, and the cord is inserted into each screw head. After the cord is tensioned, locking caps secure the entire construct.

The REFLECT™ Scoliosis Correction System employs a growth modulation technique in which the growth of the patient is used to achieve scoliosis correction**.** Compression is applied to the convex side of the spine by tensioning the cord. Single or dual cords may be used for each curve per the preference of the surgeon to meet the surgical goals of each patient.

Compression is achieved by securing the most cephalad screw and tensioning the intervening cord segment at another screw using a tensioner instrument until the desired initial correction is achieved. Tensioning can be performed at each level or for the overall construct. Once the desired initial correction is achieved, the set screw on the locking cap is final tightened. Tensioning allows for some intraoperative deformity correction.

The patient's subsequent growth is modulated by the cord, allowing for additional curve correction as growth occurs over time. If over-correction is observed or the deformity continues to progress, cord tension may be removed by severing the cord, or by replacing and re-tensioning the cord. If cord breakage is observed, the need for cord replacement may depend on the patient's anticipated remaining growth and other patient factors.

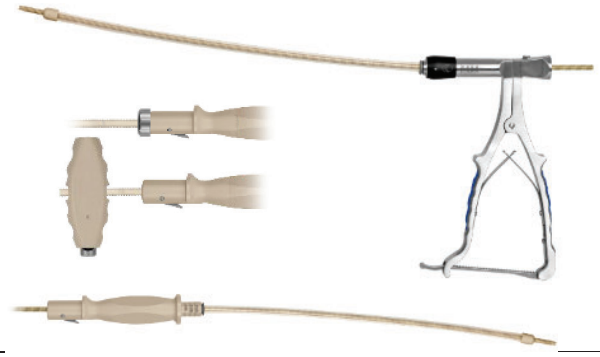
The REFLECT™ Scoliosis Correction System components are summarized in **Table 1**.

Table 1. REFLECT™ Scoliosis Correction System Components, Sizes and Materials

Implant	Image	Sizes	Materials
Cord		Diameters: 4.0, 5.0mm Lengths: 125, 250, 350mm	Cord: PET Collet: Titanium Alloy TAV (ASTM F136)
Monoaxial Screw		Lengths: 20-100mm (2.5mm increments) 100-120mm (10mm increments) Diameters: 4.0-6.5mm (0.5mm increments) 6.5-10.5mm (1mm increments)	Titanium Alloy TAV (ASTM F136) HA Coating – optional (ASTM F1185)
Locking Cap		One Size	Titanium Alloy TAV (ASTM F136)
Staples		Single: 4.0-7.5mm Dual: Small, Medium, Large, Extra Large	Titanium Alloy TAV (ASTM F136)

The surgical technique for the REFLECT™ Scoliosis Correction System involves standard instruments for access, preparation, and screw insertion, including ports, rib shears, probes, taps, drivers, counter-torques. The MIS Compressor Assembly is used to tension the cord and apply compression across the vertebrae, and the Staple Inserter and Dual Staple Holder are used to insert single and dual staples, respectively, into the vertebrae, and are shown in **Table 2**.

Table 2. MIS Compressor, Staple Inserter, and Dual Staple Holder

Instrument	Image	Use	Materials
MIS Compressor Assembly		Tensions cord along implant construct and allows for fine adjustment; Inline or T-handle	Stainless steel, aluminum, tantalum, silicone, Radel R5500, PEEK, fluorinated ethylene propylene (FEP)
Staple Inserter		Attaches to single staple for insertion into vertebral body	Stainless steel, titanium alloy, silicone
Dual Staple Holder		Attaches to double staple for insertion into vertebral body	Stainless steel

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Idiopathic scoliosis is characterized by a lateral spinal curvature in excess of 10 degrees with vertebral rotation due to an unknown cause. Treatment options for idiopathic scoliosis depend on the severity, progression and skeletal maturity of the patient and include observation, physical therapy, bracing and/or surgical intervention. Surgical treatment options include growing rods and posterior stabilization with fusion.

VII. MARKETING HISTORY

The REFLECT™ Scoliosis Correction System has not been marketed in the United States. However, the REFLECT™ system was CE-marked on March 8, 2017 and is available in a number of countries outside of the United States.

VIII. PROBABLE ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (i.e., complications) associated with the use of the device.

Potential Device- or Procedure-Related Adverse Events (AEs)

- Overcorrection of the coronal deformity, potentially requiring revision or removal of implants
- Inadequate curve correction
- Loss of curve correction
- Development of new curves above and/or below the instrumented levels
- Trunk imbalance
- Worsening of existing deformities in non-tethered spine segments
- Unintended spontaneous fusion at the instrumented levels
- Pulmonary complications including atelactasis, pneumonia or adverse events related to temporary single lung ventilation
- Anesthesia complications
- Wound infection, superficial or deep
- Wound dehiscence
- Damage to surrounding organs and structures including blood vessels, spinal cord, nerves, lungs, or vertebral bodies
- Vascular complications including bleeding, hemorrhage, or vascular damage leading to anemia or requiring blood transfusion
- Neurologic complications including damage to neurological structures, cerebrospinal fluid leakage, or meningocele
- Problems during device placement including anatomic/technical difficulty and device-sizing issues
- Loosening or migration of the implants
- Bending, fracturing, fraying, kinking, loosening, or breaking of any or all implant components
- Fretting and crevice corrosion at interfaces between components
- Pain, discomfort, or abnormal sensations due to device presence
- Material sensitivity reactions and/or particulate wear debris

Systemic AEs

- Deep vein thrombosis
- Pulmonary embolism
- Atelectasis, pneumonia
- Cardiovascular
- Dysphagia
- Dysphonia
- Gastrointestinal (ileus, ulceration, bleeding, malnutrition)
- Foreign body reaction
- Pressure sores
- Genitourinary (infection, urinary retention)
- Infection (systemic)
- Hematologic
- Endocrine/metabolic
- Hepatobiliary
- Immunologic
- Gynecologic
- Ophthalmologic
- Psychological

- Surgical procedure (non-spinal)
- Wound infection (non-spinal)
- Death

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NON-CLINICAL STUDIES

Mechanical and Biomechanical Testing

The following mechanical and biomechanical tests were conducted on the REFLECT™ Scoliosis Correction System as described in **Table 3**. The objectives of these studies were to characterize and evaluate the performance of the REFLECT™ Scoliosis Correction System in a worst-case construct. All angled tension bending testing was conducted on a worst-case test block angle of 20 degrees.

Table 3. Summary of REFLECT™ Scoliosis Correction System Laboratory Tests

Test Name	Purpose	Method	Acceptance Criteria	Results
Static Tension	To characterize performance of the REFLECT™ Scoliosis Correction System under static axial tension	Six (6) device constructs were tested under static tension in a 37°C 0.9% phosphate buffered saline (PBS) bath at a rate of 25 mm/min until failure	Demonstrate that the device can withstand loads of a safety factor of ≥ 2 compared to expected physiological loads (900N)	Pass – Acceptance criterion met
Dynamic Cord Tension	To characterize performance of the REFLECT™ Scoliosis Correction System under dynamic axial tension	Six (6) device constructs were tested under dynamic tension in a 37°C 0.9% PBS bath to 10 million cycles	Demonstrate that the device can withstand loads of a safety factor of ≥ 2 compared to expected physiological loads (900N)	Pass – Acceptance criterion met
Creep Testing	To characterize the creep behavior of the REFLECT™ cord	Increasing static and dynamic load cycles were applied to five (5) cords over a 35-hour period and resulting deformation was measured	No acceptance criteria – for characterization only	n/a
Stress Relaxation	To characterize the stress relaxation behavior of the REFLECT™ cord	Six (6) cords were tensioned to 450N and held for 168 hours (7 days). The resulting change in displacement was measured	No acceptance criteria – for characterization only	n/a
Static Angled Tension Bending	To characterize performance of the REFLECT™ Scoliosis Correction System under static tension in a	Six (6) device constructs were tested under static tension in a 37°C 0.9% PBS bath at a rate of 25 mm/min until failure	Demonstrate that the device can withstand loads of a safety factor of ≥ 2 compared to expected	Pass – Acceptance criterion met

Test Name	Purpose	Method	Acceptance Criteria	Results
	worst case 20° angled configuration		physiological loads (900N)	
Dynamic Angled Tension Bending with Wear Analysis	To characterize performance of the REFLECT™ Scoliosis Correction System under dynamic axial tension bending in a worst case 20° angled configuration, and evaluate wear in runout specimens	Six (6) device constructs were tested under dynamic tension in a 37°C 0.9% PBS bath. Constructs were tested at 5 Hz to 10 million cycles; wear particulate analyzed in two (2) runout specimens	Demonstrate that the device can withstand loads of a safety factor of ≥ 2 compared to expected physiological loads (900N) Wear rate < 4 mg per 4.2 kg patient weight[3]	Pass – Acceptance criterion met
Dynamic Angled Tension Bending at Lower Frequency	To characterize the performance of the REFLECT™ Scoliosis Correction System under dynamic axial tension bending at 2 Hz to confirm original run-out loads and identify any frequency-related differences	Two (2) device constructs were tested under dynamic tension in a 37°C 0.9% PBS bath at 2 Hz to 5 million cycles to confirm runout loads and identify any frequency-related differences	Demonstrate that the device was able to meet an equal run-out load compared to the standard Dynamic Tension Bending testing	Pass – Acceptance criterion met
Dynamic Angled Tension Bending with Repositioned Locking Cap	To characterize the performance of the REFLECT™ Scoliosis Correction System under dynamic tension bending in a worst case 20° angled configuration, where the cord is tightened and then repositioned intraoperatively	Three (3) device constructs were tested under dynamic tension in a 37°C 0.9% PBS bath to 10 million cycles to confirm runout loads following intraoperative repositioning of cord	Demonstrate that the device was able to meet an equal run-out load compared to the standard Dynamic Tension Bending testing	Pass – Acceptance criterion met

Biocompatibility Testing

The REFLECT™ Scoliosis Correction System is designed for permanent (>30 days) contact with bone/tissue. REFLECT™ Scoliosis Correction System materials (**Table 4**) have a well-established history of clinical use for human implant applications, and are identical to those of FDA-cleared and legally marketed devices for pediatric populations. A biocompatibility risk assessment was conducted on the REFLECT™ construct. Per ISO 10993-1:2018, *Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process* and the FDA guidance, *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process*," issued on September 4, 2020, the following endpoints were considered: cytotoxicity, sensitization, irritation or intracutaneous reactivity, acute systemic toxicity, subchronic/subacute toxicity, genotoxicity, implantation, chronic toxicity, and carcinogenicity. The results of this assessment support the conclusion that the REFLECT™ system is biocompatible for its intended use. A similar analysis was conducted for instruments used with the REFLECT™ system, and results support the conclusion that these instruments are biocompatible for their intended use.

Table 4. Summary of REFLECT™ Scoliosis Correction System Materials and Patient Contact Type

Component	Materials	Patient Contact
Cord	Polyethylene terephthalate (PET)	Direct, permanent implant – bone/tissue contacting
Screw, Locking Caps, Staples	Titanium Alloy (Ti6Al4V, Ti6Al7N)	
Screw Coating	Hydroxyapatite	

Sterilization, Reprocessing, Packaging, and Shelf-Life Testing

The REFLECT™ cord and HA coated screws are only supplied sterile, using gamma radiation with a standard medical device sterilization dose of 25-40kGy. A sterilization validation per ISO 11137-2:2013 was performed to ensure a Sterility Assurance Level (SAL) of 10^{-6}. All other implants of the REFLECT™ Scoliosis Correction System are offered in non-sterile and sterile variants (using the same method described above). All REFLECT™ Scoliosis Correction System instruments are provided non-sterile, with the exception of the MIS Compressor Threaded Shaft and End Cap which may be provided sterile (using the same method described above) or non-sterile, and the MIS Compressor Tube which is offered sterile only (using the same method described above). End users must sterilize the non-sterile implants and instruments prior to use. A steam sterilization validation rationale was created for non-sterile implants and instruments. Sterile implants are packaged in a double Tyvek pouch (cord only), or an inner plastic tube and outer Tyvek pouch (all other implants). Sterile instruments are packaged in a double Tyvek pouch (MIS Compressor Tube), an inner plastic tube and outer Tyvek pouch (MIS Compressor End Cap), or an inner Tyvek Pouch and outer container (MIS Threaded Shaft). For all packaging, shelf life was validated to 7 years. Sterilization, packaging, shipping, and shelf life validations for sterile parts were either conducted or adopted; the latter included comparison to previously validated families of device components.

Magnetic Resonance Imaging (MRI) Safety Information

The REFLECT™ Scoliosis Correction System has not been evaluated for safety and compatibility in the MR environment. It has not been tested for heating, migration, or image artifact in the MR environment. The safety of the REFLECT™ Scoliosis Correction System in the MR environment is unknown. Scanning a patient who has this device may result in patient injury.

X. SUMMARY OF CLINICAL INFORMATION

Clinical Data Overview

Globus Medical collected the clinical data used to support this HDE submission per an institutional agreement, as part of prospectively enrolling FDA-Approved Investigator-initiated Investigational Device Exemption (IDE) clinical study (G170023) for all subjects (N=20), who were enrolled and treated with Globus Medical implants for scoliosis correction. The study was approved by the site's Institutional Review Board (IRB). All study subjects were previously surgically treated using components of CREO® and TRANSITION® implants that are FDA-cleared for spinal fusion (K124058, K073439, respectively), and are nearly identical to components of the REFLECT™ Scoliosis Correction System; the REFLECT™ screws have a more rounded edge at the screw head

opening compared to the CREO® screws and the REFLECT™ locking caps were modified to accommodate this change.

The purpose of collecting this clinical data was to assess the safety and probable benefit of the subject device in the idiopathic scoliosis target population. Study subjects were prospectively evaluated for clinical and radiographic outcomes. A primary probable benefit assessment collected for all subjects was curve magnitude as determined by Cobb angle. Radiographic images were qualitatively analyzed using independent radiologists for assessment of device loosening, device migration, and device breakage; and, using an independent radiologist for quantitative assessment of scoliosis measures including Cobb angles. Adverse Events (AEs) were reported and assessed by the investigator and an independent Clinical Events Committee (CEC).

Enrollment Criteria

The following enrollment criteria were utilized to select subjects for the aforementioned IDE study.

Inclusion Criteria

- Males or females 8 to 16 years old at time of enrollment (inclusive)
- Diagnosis of idiopathic scoliosis
- Sanders stage of less than or equal to 4
- Thoracic curve of greater than or equal to 35° and less than or equal to 60°
- Lumbar curve less than 35°
- Subject has already been identified for and recommended to have surgical intervention
- Spina bifida occulta is permitted

Exclusion Criteria

- Pregnancy (current)
- Prior spinal or chest surgery
- MRI abnormalities (including syrinx greater than 4mm, Chiari malformation, or tethered cord)
- Neuromuscular, thoracogenic, cardiogenic scoliosis, or any other non-idiopathic scoliosis
- Associated syndrome, including Marfan Disease or Neurofibromatosis
- Sanders stage greater than 4
- Thoracic curve less than 35° or greater than 60°
- Lumbar curve greater than or equal to 35°
- Unable or unwilling to firmly commit to returning for required follow-up visits
- Investigator judgement that the subject/family may not be a candidate for the intervention

Safety and Probable Benefit Assessments

Safety was evaluated through analysis of all AEs reported and assessed by each investigator. All AEs were also assessed and adjudicated by an independent CEC. The primary probable risk was assessed by evaluating all reported safety data. The study did not include hypothesis-driven safety endpoints. The investigator ranked each AE by type, severity (e.g., Serious Adverse Event (SAE)), and relationship to the device- and/or

procedure. AEs were collected based on a complete review of each subject's medical record at the study site.

Probable benefit was assessed by measurement of coronal curve correction (Cobb angle) on post-operative radiographs. A subject was considered a success if the Cobb angle of their major curve was less than 40 degrees at 24 months following treatment (Month 24) with the study devices. Success rates at 12 months following treatment (Month 12) were also assessed.

All treated subjects (N=20) were included in the safety and probable benefit analysis population. All subjects (20/20) have reached 12-month follow-up, with 85% 17/20) having completed their Month 24 follow-up visit.

Study Population Demographics and Baseline Parameters

A total of 20 subjects were enrolled in this study and had evaluable data. Study population demographics and baseline characteristics are shown in **Table 5**. The majority of subjects were female (16/20, 80% , and the mean age was 12.3 years. All subjects were skeletally immature at the time of surgery, as assessed by Sanders Stage[1] or Risser Score[2]. More than half of the subjects (13/20, 65%) had baseline major curves with a measured Cobb angle between 45 and 65 degrees.

Table 5. Demographics and Baseline Parameters for Study Subjects

Demographic Measure		Value/N (%)
Subjects		20
Gender	Female	16 (80%
	Male	4 (20%
Age at time of surgery	Mean (SD)	12.3 (1.9)
	Min, Max	9.0, 16.4
Height (cm)	Mean (SD)	155.6 (12.4)
Weight (kg)	Mean (SD)	46.4 (13.8)
BMI	Mean (SD)	18.9 (4.2)
FEV1 (L)	Mean (SD)	2.2 (0.5)
FVC (L)	Mean (SD)	2.6 (0.6)
Risser Score	0	15 (75%
	1	1 (5%
	2	2 (10%
	3	0
	4	0
	5	0
	NR	2 (10%
Sanders Stage	0	0
	1	0
	2	2 (10%
	3	10 (50%
	4	8 (40%
	5	0
	6	0
	7	0
	NR	0

Demographic Measure		Value/N (%)
Cobb Angle	30°-44°	7 (35.0%
	45°-65°	13 (65.0%

NR=Not reported

Safety Results

Total AEs

A total of 148 AEs were reported in the 20 subjects. These AEs are summarized in **Table 6**, and the majority of AEs were non-SAEs; 6 subjects (6/20, 30%) experienced an AE classified as an SAE following treatment with the study devices.

Table 6. AE Summary (N=20 subjects)

Adverse Events	All AEs	Non-SAEs	SAEs
Number of Events, N % of events)	148	142/148 (95.9%)	6/148 (4.1%)
Number of Subjects with AE, N % of subjects)	20	14/20 (70%)	6/20 (30%)

AEs Categorized by Relationship

A listing of AEs by relationship/category is presented in **Table 7**. The most common AEs include Respiratory - Diminished Bases/Sounds/Capacity (15/20, 75%), Gastrointestinal (13/20, 65%), Pain - Thorax (12/20, 60%), Pain - Upper Extremities (7/20, 35%), and Respiratory - Pneumothorax (7/20, 35%).

Table 7. All IDE Study AEs by Relationship

Adverse Event Category	Number of AEs (N)	Number of Subjects with AE [N (%)]	Days to AE [Mean (range)]
Cardiovascular	1	1 (5%	1 (1, 1)
Dysesthesia - Thorax	1	1 (5%	21 (21, 21)
Gastrointestinal	17	13 (65%)	3 (0, 20)
Infection - Other	3	3 (15%	48 (6, 94)
Muscle Spasms	2	2 (10%	22 (5, 38)
Musculoskeletal	4	4 (20%	249 (1, 699)
Neurological Focal - Other	1	1 (5%	23 (23, 23)
Other	4	2 (10%	24 (1, 86)
Pain - Back	8	6 (30%	179 (1, 807)
Pain - Hip	2	2 (10%	219 (66, 372)
Pain - Lower Extremities	3	2 (10%	59 (36, 85)
Pain - Other	2	1 (5%	26 (4, 48)
Pain - Thorax	15	12 (60%	10 (0, 85)
Pain - Upper Extremities	8	7 (35%	79 (0, 372)
Paresthesia - Lower Extremities	1	1 (5%	21 (21, 21)
Paresthesia - Other	4	4 (20%	22 (1, 43)
Paresthesia - Upper Extremities	1	1 (5%	5 (5, 5)
Psychological	1	1 (5%	12 (12, 12)
Radiographic - Suspected Screw/Staple Issue	1	1 (5%	386 (386, 386)
Radiographic - Suspected Cord Finding	4	4 (20%	650 (363, 765)

Adverse Event Category	Number of AEs (N)	Number of Subjects with AE [N (%)]	Days to AE [Mean (range)]
Respiratory - Atelectasis	4	4 (20%	2 (1, 3)
Respiratory - Congestion/Cough	6	5 (25%	10 (0, 51)
Respiratory - Diminished Bases/Sounds/Capacity	24	15 (75%	6 (0, 49)
Respiratory - Pleural Effusion/Edema	6	6 (30%	2 (1, 6)
Respiratory - Pneumothorax	7	7 (35%	1 (0, 3)
Respiratory - Other	4	4 (20%	1 (0, 1)
Surgery - Index Levels	6	6 (30%	499 (253, 755)
Trauma	2	2 (10%	80 (44, 115)
Wound Issue	6	5 (25%	401 (9, 807)

AEs Categorized by Relatedness

All AEs in the clinical study that were categorized as related to the device or are listed in **Table 8**. A total of 106 device- or procedure-related AEs were identified. The most common device- or procedure-related AE was Respiratory – Diminished Bases/Sounds/Capacity observed in 75% (15/20) of subjects.

Table 8. Adverse Events Related to Device or Procedure

Adverse Event Category	Number of AEs (N)	Number of Subjects with AE [N (%)]	Days to AE [Mean (range)]
Cardiovascular	1	1 (5%	1
Dysesthesia – Thorax	1	1 (5%	21
Gastrointestinal	14	12 (60%	2 (0, 8)
Muscle spasms	2	2 (10%	22 (5, 38)
Musculoskeletal	1	1 (5%	1
Other	3	2 (10%	3 (1, 7)
Pain – Back	2	2 (10%	1 (1, 1)
Pain – Other	1	1 (5%	4
Pain – Thorax	13	11 (55%	4 (0, 43)
Pain – Upper extremities	1	1 (5%	0
Paresthesia – Other	2	2 (10%	11 (1, 21)
Radiographic – Suspected Screw/Staple Finding	1	1 (5%	386
Radiographic – Suspected Cord Finding	4	4 (20%	650 (363, 765)
Respiratory – Atelectasis	4	4 (20%	2 (1, 3)
Respiratory – Congestion/Cough	5	5 (25%	2 (0, 6)
Respiratory – Diminished Bases/Sounds/Capacity	22	15 (75%	2 (0, 23)
Respiratory – Pleural Effusion/Edema	6	6 (30%	2 (1, 6)
Respiratory – Pneumothorax	7	7 (35%	1 (0, 3)
Respiratory – Other	4	4 (20%	1 (0, 1)
Surgery – Index Levels	6	6 (30%	499 (253, 755)
Wound Issue	6	5 (25%	401 (9, 807)

AEs Categorized by Seriousness

There were 6 SAEs reported during the clinical study and all resulted in secondary surgery, as shown in **Table 9**. Four subjects had a suspected cord breakage (4/20, 20%), one subject's curve progressed (1/20, 5%), and one subject had overcorrection (1/20, 5%).

Table 9. Adverse Events Classified as Serious Adverse Events (SAEs)

Adverse Event	Total Events (N)	SAEs (N)	SAEs Requiring Secondary Surgery	Subjects with SAE [N (% of 20)]	Days to SAE [Mean (range)]
Progression of Instrumented Curve	1	1	1	1 (5%	755
Overcorrection of Instrumented Curve	1	1	1	1 (5%	519
Suspected Cord Break	4	4	4	4 (20%	429 (253, 720)
Total	**6**	**6**	**6**	**6 (30%)**	**499 (253, 755)**

Secondary Surgeries

All secondary surgeries are listed in **Table 10**. Secondary surgeries were classified as Revision, Reoperation, or Removal. Revision surgery (e.g., cord adjustment) is a procedure in which the cord is removed, replaced and re-tensioned. Reoperation (e.g., posterior spinal fusion) involves conversion to a fusion construct using pedicle screws and rods, and may or may not involve removal of all implants. Removal is defined as removal of some or all of the original implants. Cord adjustment surgery provides the potential benefit of arresting curve progression and avoiding fusion surgery.

Overall, a total of 6 subjects (6/20, 30%) underwent secondary surgery involving the originally treated levels. One subject (1/20, 5%) with curve progression and four subjects (4/20, 20%) with suspected cord breakages had a reoperation to convert to posterior spinal fusion, and one subject (1/20, 5%) with overcorrection of their curve underwent partial implant removal/revision without posterior fusion.

Table 10. Secondary Surgeries Listing*

Revision Subject	Secondary Surgery Type	Levels Treated	Months to Secondary Surgery	AE Term and Description
1	Reoperation (Fusion)	T7-L1	37	Tether breakage between T11-T12. Breakage assumed based on increased screw angulation and increased Cobb angle. Underwent posterior spinal fusion from T4-L2 with pedicle screws, hooks, and cobalt chrome rods.
2	Reoperation (Fusion)	T6-T12	18	Tether failure at T10-T11. Underwent posterior spinal fusion.
3	Reoperation (Fusion)	T5-T11	30	Implant reoperation. Progression of curve without evidence of cord breakage. Underwent posterior spinal fusion from T5-L3 with pedicle screws, hooks, and cobalt chrome rods.

Revision Subject	Secondary Surgery Type	Levels Treated	Months to Secondary Surgery	AE Term and Description
4	Reoperation (Fusion)	T6-T11	22	Tether breakage at T7-T8 and at T8-T9. Underwent posterior spinal fusion from T2-T12 with pedicle screws, hooks and rods.
5	Removal/ Revision (Removed some implants)	T6-L1	18	Overcorrection of curve. Underwent removal of the cord and screws at T10, T11, T12 and L1; staples remained in place. REFLECT™ devices remain implanted at T6, T7, T8 and T9.
6	Reoperation (Fusion)	T5-T12	21	Tether breakage at T10-T11. Breakage assumed based on increased screw angulation and increased Cobb angle. Underwent posterior spinal fusion from T4-L2 with pedicle screws, hooks, and cobalt chrome rods.

*T=Thoracic spine; L=Lumbar spine

Probable Benefit Results

The primary probable benefit endpoint of this single-arm study was based on Cobb angle measurement of the subject's major coronal curve at Month 24. Individual subject success was defined as a major curve less than or equal to 40 degrees at Month 24. For Cobb angle measurements, the superior and inferior end vertebrae of the curve were determined pre-operatively and held constant across all timepoints for direct comparison.

Mean Cobb Angle Correction

The change in Cobb angle from baseline, Month 12 and Month 24 is described in **Table 11**. At Month 12, the mean major Cobb angle improved 21.9% from 48.0 degrees to 26.1 degrees. At Month 24, the mean major Cobb angle improved 21.2% from 48.0 degrees to 26.8 degrees.

Table 11. Change in Cobb Angle from Baseline at Month 12 and Month 24

		Cobb Angle				
		Pre-Op (N=20)	Month 12 (N=20)		Month 24 (N=17)	
Cohort	N	Mean (SD) [min, max]	Mean (SD) [min, max]	Δ %Δ)	Mean (SD) [min, max]	Δ %Δ)
All subjects	20	48.0 (8.1) [34.1, 62.4]	26.1 (8.6) [6.1, 47.7]	21.9 45.2%	26.8 (11.3) [3.5, 47.3]	21.2 44.7%

Individual Subject Probable Benefit Success

Individual subject success was defined as achievement of a Cobb angle less than or equal to 40 degrees at Month 24. Fifteen 15) out of 17 subjects with Month 24 data 88.2%) met the success criteria in this study. Success rates at Month 12 and Month 24 stratified by pre-operative Cobb angle are provided in **Table 12**.

Table 12. Overall Study Success (Cobb Angle Less Than or Equal to 40 degrees) at Month 12 and Month 24 by Pre-operative Cobb Angle

Cohort	N	Success % (n/N)		Month 24 Cobb Angle (n, %)
		Month 12	Month 24	
All subjects	20	95% (19/20)	88.2% (15/17)	< 30° (12, 70.6%) < 35° (14, 82.4%) < 40° (15, 88.2%)
Pre-Op Cobb < 45°	7	85.7% (6/7)	100% (6/6)	< 30° (5, 83.3% < 35° (6, 100%) < 40° (6, 100%)
Pre-Op Cobb ≥ 45°	13	100% (13/13)	81.8% (9/11)	< 30° (7, 63.6% < 35° (8, 72.7% < 40° (9, 81.8%)

Sensitivity analyses were also performed to determine how the results were affected by changing the Cobb angle reduction threshold for the probable benefit success endpoint, as shown in **Table 12**. For all treated subjects, the probable benefit success rates were 82.4% (14/20) and 70.6% 12/20) when the probable benefit success is defined as a major Cobb angle of less than 35 degrees and 30 degrees, respectively.

Results were further stratified for subjects with pre-op Cobb angles less than 45 degrees (N=7) and greater than or equal to 45 degrees (N=13), respectively. For subjects with pre-op Cobb angles less than 45 degrees, probable benefit success rates were 100%, 100%, and 83.3% based on a major Cobb angle of less than 40 degrees, 35 degrees, and 30 degrees, respectively, at Month 24. For subjects with pre-op Cobb angles greater than or equal to 45 degrees, probable benefit success rates were 81.8%, 72.7%, and 63.6% based on a major Cobb angle of less than 40 degrees, 35 degrees, and 30 degrees, respectively, at Month 24.

Improvement in Patient Reported Outcomes

Patient-reported outcomes included the Scoliosis Research Society (SRS) outcomes questionnaire (SRS-30). Overall outcomes are positive and show improvement in self-image and patient satisfaction with treatment.

Spinal Alignment

Spinal alignment was measured on radiographs at each timepoint, in terms of thoracic kyphosis, lumbar lordosis, sagittal balance, coronal balance, and total vertical thoracic spine length. On standing images, sagittal balance was measured by the distance between the C7 plumb line and the posterior S1 vertebral body; anterior displacement of the plumb line corresponds to positive sagittal balance, and posterior displacement corresponds to negative sagittal balance. Coronal balance was measured by the distance between a C7 plumb line and the central sacral vertical line (CSVL); plumb line right of the CSVL corresponds to positive coronal balance and left corresponds to negative coronal balance. Radiographic parameters at each time point are summarized for all subjects in **Table 13**.

Table 13. Radiographic Data by Timepoint [mean (SD)]

Timepoint	N	Thoracic Kyphosis (°)	Lumbar Lordosis (°)	Sagittal Balance (mm)*	Coronal Balance (mm)**	Total Vertical Thoracic Spine Length (mm)
Pre-Op	20	15.6 (10.4)	50.7 (7.1)	-5.7 (26.0)	8.1 (17.0)	204.8 (16.9)
Month 12	20	18.4 (8.1)	48.9 (7.6)	-2.4 (31.1)	-0.1 (14.7)	220.4 (16.0)
Month 24	17	19.6 (9.2)	48.5 (8.5)	7.0 (24.2)	-3.6 (14.9)	223.8 (11.4)

**Sagittal balance: positive value indicates anterior shift; negative indicates posterior shift.*
***Coronal balance: positive value indicates right coronal shift; negative value indicates left coronal shift.*

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The clinical study included one investigator who had no financial interests/arrangements, as defined in 21 CFR 54.2(a), (b), (c) and (f). The applicant has adequately disclosed the financial interest/arrangements with its clinical investigator. Furthermore, the applicant collected all data from one site under an IDE, and adjudicated AEs as well as radiographic data using independent third parties. The information provided does not raise any questions about the reliability of the data.

XII. SAFETY AND PROBABLE BENEFIT ANALYSIS

Devices representative of the REFLECT™ Scoliosis Correction System were implanted in 20 subjects with idiopathic scoliosis in a single site prospective non-randomized study under G170023. Safety was evaluated based on reported AEs as assessed by the study investigators and adjudicated through an independent CEC. Secondary surgeries, classified as either Revisions, Reoperations, or Removals, were also assessed. AEs and secondary surgery data were also compared to literature describing posterior instrumented spinal fusion for treatment of idiopathic scoliosis.

Probable benefit was evaluated based on correction of the Cobb angle of the major curve provided by the REFLECT™ Scoliosis Correction System at Month 24. The data provide a sufficient basis upon which to draw conclusions regarding the safety and probable benefit of the REFLECT™ Scoliosis Correction System.

A. Probable Benefit Conclusions

The primary probable benefit endpoint of the study evaluated the scoliotic curve at Month 24, with success defined as a major Cobb angle of less than 40 degrees following treatment with study devices. This probable benefit endpoint was selected because curves of this magnitude at skeletal maturity are not expected to progress to the point where surgical intervention with spinal fusion would be required later in life. Spinal curves in skeletally immature subjects with progressive idiopathic scoliosis who have failed bracing and/or are intolerant to brace wear are

likely to increase in magnitude and approach or exceed the threshold where spinal fusion is considered.

REFLECT™ is intended to use the patient's inherent remaining growth to correct and stabilize the spinal deformity without fusion. The device provides a non-fusion treatment with the potential to avoid the adverse consequences associated with fusion which include decreased spinal motion, pseudarthrosis, adjacent spinal segment degeneration, neurological complications, pain, implant failure/breakage, and subsequent or repeated surgical intervention.

At Month 12, 19 out of 20 subjects (95%) with evaluable data were considered a success due to having a Cobb angle of less than 40 degrees. At Month 24, 15 out of 17 subjects (88.2%) with evaluable data were determined to be a probable benefit success. Sensitivity analyses were performed to determine how probable benefit success was affected by changing the endpoint threshold for Cobb angle reduction. For all treated subjects, success rates at Month 24 were 82.4% 14/20) and 70.6% (12/20) when the probable benefit success is defined as a major Cobb angle of less than 35 degrees and 30 degrees, respectively. The probable benefit results were further stratified by subjects with pre-op Cobb angles of less than 45 degrees (N=7) and greater than or equal to 45 degrees (N=13). For subjects with pre-op Cobb angles less than 45 degrees, probable benefit success rates were 100%, 100%, and 83.3% based on probable benefit success defined as a major Cobb angle of less than 40 degrees, 35 degrees, and 30 degrees, respectively, at Month 24. For subjects with pre-op Cobb angles greater than or equal to 45 degrees, probable benefit success rates were 81.8%, 72.7%, and 63.6% based on probable benefit success as defined as a major Cobb angle of less than 40 degrees, 35 degrees, and 30 degrees, respectively, at Month 24.

The mean major Cobb angle correction was 45.2% 21.9°) at Month 12, and 44.7% (21.2°) at Month 24. The amount of correction achieved in the current study is lower than the approximately 63% correction reported for posterior pedicle screw and rod stabilization systems intended for spinal fusion.[3] However, the mean Cobb angle improvements of between 21.2 degrees and 21.9 degrees observed in these study subjects are highly similar to the 21.9 degrees of improvement reported for posterior pedicle-screw-based stabilization in a meta-analysis.[5]

Analyses of the probable benefit endpoint suggest that patients are likely to experience the benefit of improved Cobb angle and avoidance of spinal fusion during the study time period. Based upon the improvements in Cobb angle observed in the study, the REFLECT™ Scoliosis Correction System achieves a level of correction in a comparable range to posterior spinal stabilization and fusion.

B. Safety Conclusions

The risks of the REFLECT™ Scoliosis Correction System are based on data collected in a clinical study that was used to support HDE approval as described above. The REFLECT™ Scoliosis Correction System is an implantable device requiring anterior exposure of the spine and general anesthesia, which have inherent

risks. This study involved subjects treated through a surgeon-initiated IDE to use existing marketed devices for growth modulation. The site initially performed more reoperations and treated fewer levels of the curve, and over time has had fewer reoperations, possibly due to adjusting surgical plans for correction and anticipated growth.

In the clinical study, there were 148 AEs reported in all 20 subjects. Six (6) AEs were classified as an SAE and/or device-related AE (6/20, 30%), and included 4 suspected cord breakages, 1 curve progression, and 1 overcorrection. All 6 subjects required subsequent surgery. The subjects with suspected cord breakage (4) and curve progression (1) underwent reoperation to posterior spinal fusion, and the subject with overcorrection had some implants removed without spinal fusion. Two (2) of the reoperations occurred after 30 months. The revision rate was 5%, and the reoperation rate was 25%, for an overall 30% rate of subsequent surgery. Fusion was avoided in 17 of the 20 subjects (85%) through Month 24, and in 15 of the 20 subjects (75%) by 37 months post-operatively following treatment (Month 37). There were no deaths or serious neurological AEs.

Based on the available data, the REFLECT™ Scoliosis Correction System can be considered safe for its indication for use, based upon the similar types of AEs observed, and the types of revisions and reoperations reported in this IDE study.

C. Probable Benefit-Risk Conclusions

The probable benefits of the REFLECT™ Scoliosis Correction System are based on data collected in a clinical study conducted to support HDE approval as described above.

The primary probable benefit of the REFLECT™ Scoliosis Correction System is correction and maintenance of the magnitude of the patient's major spinal curve below the threshold where spinal fusion is indicated, thereby potentially avoiding associated adverse consequences of spinal fusion. Based on the data provided, the probable benefit success rate of curve correction and maintenance below 40 degrees, is 88.2% at Month 24. Additionally, the rate of fusion avoidance was 75% of subjects through Month 37, which suggests a likely probability of a patient experiencing the benefit of avoiding spinal fusion.

The probable risks of the device are also based on data collected in a clinical study conducted to support HDE approval as described above. Device risks reported as SAEs include (from most frequent to least frequent): cord breakage, curve progression, and overcorrection.

Additional factors considered in determining probable risks and benefits for the device included patient perspectives.

1. Patient Perspectives

Patient-perspectives considered for the REFLECT™ Scoliosis Correction System included results from the SRS-30 outcome questionnaire as described above. These

patient-reported outcomes were considered as part of the benefit-risk assessment for the subject device, and as noted above, were generally positive in terms of patient self-image and patient satisfaction with treatment.

In conclusion, given the available information above, the data on the REFLECT™ Scoliosis Correction System collected under the study support treatment of progressive idiopathic scoliosis, and the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data collected in this HDE application support the reasonable assurance of safety and probable benefit of the REFLECT™ Scoliosis Correction System when used in accordance with the indications for use. This device can be considered safe for its intended use, based upon consideration of the types of SAEs, device- and procedure- related AEs, and subsequent surgical procedures reported. The probable benefit success rate, defined as maintenance of a Cobb angle of less than 40 degrees, is 88.2% at Month 24. This probable benefit endpoint is considered representative of the likelihood of avoidance of the need for spinal fusion during this time period. The benefit of a device which avoids spinal fusion during the study time period but does not preclude treatment with spinal fusion if needed, is considered to outweigh those of posterior stabilization and fusion in which the spine is immobilized during growth.

Therefore, it is reasonable to conclude that the probable benefit to health from using the device for the target population outweighs the risk of illness or injury, taking into account the probable benefits and risks of currently available devices or alternative forms of treatment when used as indicated in accordance with the directions for use.

XIII. PANEL RECOMMENDATION

This HDE was not taken to a meeting of the Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee because the information in this HDE did not raise any unanticipated safety concerns.

XIV. CDRH DECISION

CDRH has determined that, based on the data submitted in the HDE, REFLECT™ Scoliosis Correction System will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from using the device outweighs the risks of illness or injury. CDRH issued an approval order on May 15, 2023. The final conditions of approval cited in the approval order are described below.

Based on the protocol summary received on April 20, 2023, the REFLECT™ Scoliosis Correction System Registry PAS is a multi-center, single-arm, prospective post-approval US registry to provide ongoing safety and probable benefit assessment of the REFLECT™ Scoliosis Correction System in treatment of skeletally immature patients with idiopathic

scoliosis. Skeletal maturity will be assessed using both the Risser grade and Sanders score. Once enrolled, the patients will be followed through 60-months from the time of each patient's index surgery, with interim visits at immediate post-operative up to 6-weeks, 6-months, 12-months, 24-months, and 60-months post-procedure. One hundred (100) patients will be enrolled in this study. This study will include a minimum of 5 US centers, with a maximum of 20 patients at any one site, with sequential enrollment from each site that agrees to participate.

The primary safety endpoints are serious adverse events (SAEs), and device- or procedure-related AEs. Additional safety analyses will include the rate of AEs, including by relatedness to device or procedure and severity, time-to-event, including means and ranges if applicable, and rate of reoperation, including by type of reoperation.

The primary probable benefit endpoint is maintenance of major Cobb angle less than or equal to 40 degrees at 60-months post-surgery. Secondary endpoints will be analyzed up to 60-months post-surgery, and will include the following:

1. Curve progression no greater than 10 degrees of any secondary curve above or below the implant, or development of a new curve equal to or greater than 40 degrees.

2. Device integrity failures including cord breakage and screw migration

3. Composite endpoint analysis (maintenance of major Cobb angle less than or equal to 40 degrees AND freedom from SAEs during the REFLECT™ Scoliosis Correction System procedure and procedure/device-related SAEs following surgery).

4. Analysis of the failure attributable to conversion to another spinal implant OR major Cobb angle that exceeded 40° at defined follow-up visit OR any progression of the major curve at defined follow-up compared to baseline OR death OR permanent disability.

5. Mean score of Scoliosis Research Society 22r (SRS-22) patient questionnaire.

These safety and probable benefit data will be collected from each patient at pre-operative, immediate post-operative up to 6-weeks, 6 months, 12-months, 24-months, and 60-months post-operatively.

From the date of study protocol approval, the applicant must meet the following timelines for the REFLECT™ Scoliosis Correction System Registry PAS as follows:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 24 months
- 100% of subjects enrolled within 36 months

Descriptive statistics and 95% confidence intervals will be presented for all analyses. For continuous variables, means and standard deviations will be shown. For categorical variables, frequencies and percentages will be presented.

The applicant's manufacturing facilities have been found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), via the supporting documentation provided in H210002, and through a risk-based assessment.

XV. APPROVAL SPECIFICATIONS

Directions for use: See the device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Potential Complications in the labeling.

Post-Approval Requirements and Restrictions: See Approval Order.

XVI. REFERENCES

1. Sanders JO, Khoury JG, Kishan S, Browne RH, Mooney JF 3rd, Arnold KD, McConnell SJ, Bauman JA, Finegold DN. Predicting scoliosis progression from skeletal maturity: a simplified classification during adolescence. JBJS 2008, 90(3):540-553.
2. Risser JC. The iliac apophysis: an invaluable sign in the management of scoliosis. Clinical Orthopedics 1958, 11:111-119.
3. Cunningham BW, Hallab, NJ, Hu N, McAfee PC. Epidural application of spinal instrumentation particulate wear debris: a comprehensive evaluation of neurotoxicity using an in vivo animal model. J Neurosurg Spine 2013, 19(3):336-350.
4. Min K, Sdzuy C, Farshad M. Posterior correction of thoracic adolescent idiopathic scoliosis with pedicle screw instrumentation: results of 48 patients with minimal 10-year follow-up. Eur Spine J. 2012, 22(2):345-354.
5. Lykissas MG, Jain VV, Nathan ST, Pawar V, Eismann EA, Sturm PF, Crawford AH. Mid- to long-term outcomes in adolescent idiopathic scoliosis after instrumented posterior spinal fusion: A meta-analysis. Spine 2013, 38(2):E113-E119.