FDA Executive Summary

Prepared for the **Spring 2021,** Meeting of the FDA's Pediatric Advisory Committee

H190005

The Tether™ – Vertebral Body Tethering System

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I. INTRODUCTION

In accordance with the Pediatric Medical Device Safety and Improvement Act, this review provides a safety update based on the post-market experience with the use of The Tether™ – Vertebral Body Tethering System ("The Tether™") in pediatric patients since approval in 2019. The purpose of this review is to provide the Pediatric Advisory Committee (PAC) with post-market safety data so the committee can advise the Food and Drug Administration (FDA) on whether they have any new safety concerns and whether they believe that the HDE remains appropriate for pediatric use. This document summarizes the safety data the FDA reviewed since HDE approval in August 2019. It includes data from the sponsor's Annual Report, post-market medical device reporting (MDR) of adverse events, and peer-reviewed literature.

II. INDICATIONS FOR USE

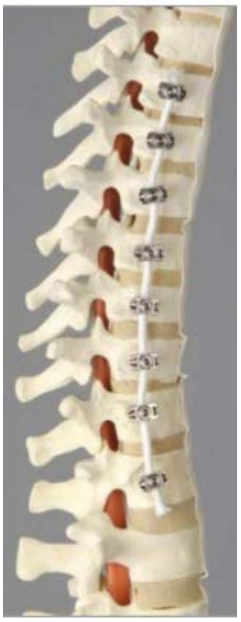
The Tether™ – Vertebral Body Tethering System is indicated for skeletally immature patients that require surgical treatment to obtain and maintain correction of progressive idiopathic scoliosis, with a major Cobb angle of 30 to 65 degrees whose osseous structure is dimensionally adequate to accommodate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

Modifications from the Humanitarian Use Designation (HUD) Designation:
The Indication for Use statement was modified from that granted for the HUD designation. The HUD designation was for "use in the treatment of juvenile and adolescent idiopathic scoliosis in patients, age 5 to 19 years, who are skeletally immature and have a Risser Score of less than 5, that require surgical treatment or have failed non-surgical treatments to obtain and maintain correction of severe, progressive spinal deformities with a Cobb angle of $\geq 30°$." It was modified for the HDE approval as follows: removed age ranges, as well as "juvenile and adolescent," as chronologic age and skeletal maturity vary among populations; added language to specify the patient should have dimensionally adequate osseous structures representative of the age range and diagnosis; removed reference to a specific skeletal maturity scoring system as there are different existing methods, and the HUD analysis was not closely linked to a specific method; and, identified a Cobb angle range to better reflect the study population. The resulting Indications for Use statement above falls within the HUD designation.

III. BRIEF DEVICE DESCRIPTION

The Tether™ – Vertebral Body Tethering System is a non-fusion spinal device intended for treatment of idiopathic scoliosis. Anchors and vertebral body screws are placed laterally from a thoracoscopic or thoracotomy approach into the vertebral body on the convex side of a spinal deformity. A SULENE® polyethylene terephthalate (PET) tensioning cord is secured to the vertebral body screws with set screws to connect the levels of the construct. The device provides a lateral tension band across the convex side of the spine that, on insertion and tensioning, partially corrects the curvature, and subsequently can arrest or correct the deformity through modulation of remaining spinal growth. In addition, the subject system includes instrumentation for insertion, manipulation, and removal of the implants.

Device Type	Image	Sizes	Material
Vertebral Body Screw		Lengths: 20-50 mm (2.5 mm increments) Diameters: 5.5-7.0 mm (0.5 mm increments)	Ti-6Al-7NV (ISO 5832-11) Hydroxyapatite (ISO 13779-2)
Set Screw		Diameter: 7 mm Height: 5.7 mm	Ti-6Al-4V ELI (ASTM F136)
Anchor		Diameter: 12 mm	Ti-6Al-4V ELI (ASTM F136)
Tensioning Cord		Diameter: 4.1 mm Implantable length: 300 mm	Polyethylene terephthalate (PET)



IV. REGULATORY HISTORY AND CURRENT STATUS

The Tether™ – Vertebral Body Tethering System received Humanitarian Use Device designation (HUD DEV-2018-0410) on March 28, 2019. The HDE was approved on August 16, 2019 by the Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (H190005). A summary of the HDE and PAS annual reports submitted for The Tether™ are presented in Table 1.

Table 1. H190005 Regulatory History

File	Content
H190005/R001	HDE annual report
H190005/R002	PAS 6-month annual report

V. SUMMARY OF CLINICAL DATA USED TO SUPPORT HDE APPROVAL

A clinical study (conducted under Investigational Device Exemption) was performed to support the safety and probable benefit of Tether™ – Vertebral Body Tethering System for subjects with idiopathic scoliosis and documented in the Summary of Safety and Probable Benefit (SSPB). Zimmer Biomet Spine conducted a single-center, non-randomized, clinical study in 57 subjects. The majority of the subjects were female (49/57, 86.0%), and the mean age at time of surgery was 12.4 years. Spinal tethering subjects were retrospectively evaluated for clinical and radiographic outcomes and were then prospectively followed until 30 out of 57 (47.4%) reached skeletal maturity by the time of database lock. All subjects were surgically treated utilizing components of the Dynesys® Top-Loading Spinal System which is cleared for spinal fusion (K133164). The Tether™ - Vertebral Body Tethering System includes similar components (including the identical tensioning cord) but differs from the Dynesys® System in that screws have a lower profile head. A common primary assessment collected for all subjects was curve

magnitude as determined by Cobb angle. Radiographic images were analyzed using a single core laboratory for assessment of coronal Cobb angle, device loosening, and device breakage. AEs were also reported and assessed by each investigator.

The primary probable benefit endpoint of the study evaluated the Cobb angle at 24 months post-implantation, with success defined as a major Cobb angle of less than 40 degrees following treatment with The Tether™ - Vertebral Body Tethering System. This probable benefit endpoint was chosen as 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.

Individual subject success was defined as achievement of a Cobb angle less than or equal to 40 degrees at 24 months post-surgery. Forty-three (43) out of 44 subjects with 24-month data (97.7%) met the success criteria in this study. At the last follow-up visit greater than 24 months, 52 out of 56 subjects (92.8%) had a coronal Cobb angle of less than 40 degrees. The mean major Cobb angle improved 65% from 40.4 degrees to 14.3 degrees at 24 months. At the last available follow-up visit after surgery (at or beyond 24 months), the mean major Cobb angle correction was maintained or improved compared to pre-operative baseline curve magnitude with correction from 40.4 degrees to 17.6 degrees (56.4% curve improvement).

The risks of this device are based on data collected in a clinical study conducted to support HDE approval. In this clinical study there were 132 adverse events (AEs) reported in 49 out of 57 subjects (86%). Twenty-six (26) AEs were classified as either serious or device-related, with the most common event types reported as overcorrection of the instrumented curve (N=13 in 12 subjects), tensioning cord breakage (N=8), and bone screw migration (N=3). Six (6) subjects with overcorrection events required subsequent surgical procedures and six (6) subjects were diagnosed with radiographic overcorrections which did not require surgical treatment and were not considered at risk for clinically important future curve progression which would require future additional surgical treatment.

Serious adverse events (SAEs), 6.8% of total events, occurred in 8 out of 57 subjects (14.0%) who were treated with The Tether™ – Vertebral Body Tethering System, with overcorrection also reported as the most common event type for SAEs, accounting for 6 of the 9 total SAEs due to the necessity for secondary surgery. There was one (definitive) cord breakage which resulted in a reoperation SAE. None of the screw migrations required reoperation.
The revision rate reported for subjects in the study was 12.3% (7 events in 57 subjects), and the reoperation rate was 3.5% (2 events in 57 subjects), resulting in an overall 14.0% rate of subsequent surgery. One subject underwent both a revision and reoperation procedure. There were no deaths or neurologic AEs, and only one subject so far has required conversion to fusion.

To compare secondary surgery rates for The Tether™ – Vertebral Body Tethering System with spinal fusion, a literature review was conducted to identify the subsequent surgery rates at 24 months for patients undergoing spinal instrumentation and fusion for treatment of idiopathic scoliosis in the US. For US patients who undergo treatment with spinal instrumentation and

fusion for idiopathic scoliosis, the rates of subsequent surgery have been reported as 4.1% at 24 months[1] and 9.9% at 60 months[2]. Compared to spinal fusion treatment, the subsequent surgery rate of 14% associated with treatment with The Tether™ – Vertebral Body Tethering System in this IDE study at 24 months is numerically higher. In assessing the AEs reported for The Tether™ – Vertebral Body Tethering System in this IDE study, the categories of AEs such as implant loosening, implant failure and nausea/vomiting are similar to those AEs reported for spinal fusion. Based on the available data, The Tether™ – Vertebral Body Tethering System was considered safe for its indication for use, based upon the similar types of AEs observed, types of revisions and reoperations reported in this IDE study, and the fact that only one subject required a subsequent surgical procedure which resulted in spinal fusion.

The Indications for Use of The Tether™ - Vertebral Body Tethering System is to correct and stabilize a spinal deformity without fusion by harnessing the patient's remaining growth. This device offers the patient 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 or breakage, and the need for subsequent surgical intervention.

Additional factors were considered in determining probable benefits and risks for the device, including patient and surgeon perspectives.

1. Patient Perspectives

    - Adolescent Pediatric Pain Tool (APPT): The APPT results include a word graphic rating scale (WGRS), which is a 10-point graphic to measure pain intensity from 'no hurt' to 'hurts worst' and a list of pain quality descriptors. The APPT results for the study subjects reported low pain levels (mean score 20% of the maximum pain level) at the last visit greater than or equal to 24 months.

    - Pediatric Quality of Life Inventory (PedsQL): The PedsQL is a brief, standardized, generic assessment instrument that assesses patients' and parents' perceptions of health-related quality of life in pediatric and adolescent patients with chronic health conditions. The highest possible total PedsQL score is 2300; the mean score reported for study subjects was 2117 (90.8%), indicating a positive quality of life.

    - The Scoliosis Research Society outcomes questionnaire (SRS-22): The SRS-22, designed to evaluate domains of physical and mental function in patients with adolescent idiopathic scoliosis, is a self-administered instrument that contains 22 questions organized in five (5) domains covering the following aspects of patients' quality of life: function/activity, pain, self-image, mental health (5 items each), and satisfaction with treatment (2 items). The mean total SRS-22 score reported for study subjects was 4.5/5 (89.9%), indicating overall good patient satisfaction and function.

2. Surgeon Perspectives

   Leading scoliosis surgeons wrote letters of support that were included in the HDE application expressing the preference of patients and surgeons for a non-fusion option for progressive scoliosis.

In conclusion, given the available information above, the data on The Tether™ – Vertebral Body Tethering System collected under the study support that the probable benefits outweigh the probable risks for use of this device for treatment of select skeletally immature patients with progressive pediatric idiopathic scoliosis.

VI. POSTMARKET DATA: ANNUAL DISTRIBUTION NUMBER

Section 520(m)(6)(A)(ii) of The Food, Drug, and Cosmetic Act (FD&C) allows HDEs indicated for pediatric use to be sold for profit as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). On December 13, 2016, the 21st Century Cures Act (Pub. L. No. 114-255) updated the definition of ADN to be the number of devices "reasonably needed to treat, diagnose, or cure a population of 8,000 individuals in the United States." Based on this definition, FDA calculates the ADN to be 8,000 multiplied by the number of devices reasonably necessary to treat an individual. Since The Tether™ system includes one tensioning cord and an average of 6.79 instrumented vertebral levels, the total ADN for the tensioning cords is 8,000 and the total ADN for the vertebral body assemblies (one vertebral body screw and one set screw) and the anchors is 54,320.

The first HDE Annual Report (H190005/R001) was submitted on August 31, 2020 which included the Reporting Period from August 16, 2019 through August 15, 2020. Table 2 provides the number of device components distributed in the first year (August 2019-August 2020) in the United States. To date, there have been 405 cases of HDE approved The Tether™ on the U.S. market, with the first case performed on September 11, 2019.

Table 2. Annual Distribution Number - Reporting Period: August 2019-August 2020

Device Type	Annual Distribution Limit	2019 Total (as of 9/11/19)	2020 Total (as of 8/15/20)	Reporting Period Total
Vertebral Body Assemblies	54,320	375	2,330	2,705
Anchors	54,320	361	1,404	1,765
Tensioning Cords	8,000	54	351	405

VII. POSTMARKET DATA: POST-APPROVAL STUDY (PAS)

PAS Conditions of Approval:

The Tether™ HDE (H190005) was approved on August 16, 2019.

The objective of the PAS study is to assess the ongoing safety and probable benefit of The Tether™ – Vertebral Body Tethering System in a registry population.

The PAS is a prospective, multi-center, single-arm, prospective post-approval US registry study to provide ongoing safety and probable benefit assessment of The Tether™ – Vertebral Body Tethering System in treatment of skeletally immature patients with idiopathic scoliosis. Skeletal maturity will be assessed using both the Risser grade and Sanders score. It is planned that all patients treated in the first 18-months (up to a maximum of 200 patients) should be enrolled and followed through 60-months from the time of each patient's index surgery, with interim visits at immediate post-operative time point up to 6-weeks, 6-months, 12- months, 24-months and 60-months post-procedure. Two-hundred (200) patients will be enrolled in this study, with at least 50 patients enrolled by 24-months, 100 patients enrolled by 36-months (should enrollment still be ongoing), and 200 patients enrolled by 48-months (should enrollment still be ongoing). This study will include a minimum of 10 US centers 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 probable benefit endpoint is maintenance of major Cobb angle less than or equal to 40 degrees at 60-months post-surgery.

Secondary probable benefit 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 Tether™– Vertebral Body Tethering 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 degrees at defined follow-up visit OR any progression of the major curve at defined follow-up compared to baseline OR death OR permanent disability.

All 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-operative time points. This study is estimated to last a total of 84-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 study population is comprised of skeletally immature patients (children ages 2-12, adolescents ages 13-18) that require surgical treatment to obtain and maintain correction of progressive idiopathic scoliosis who receive the device in the post market environment. There is no comparator group.

PAS Study Status:

Subject enrollment and data collection will be managed by the Harms Study Group (HSG) and Setting Scoliosis Straight Foundation (SSSF) Registry. Institutions that are HSG members or affiliates, with Investigators/surgeons that are trained and approved to perform surgeries with The Tether, will participate in the registry. Ten sites from this group will be identified as study sites specific to this Tether post-approval study (PAS).

The PAS was approved on January 13, 2020. The six-month report was received on August 31, 2020. As of this date, six (6) clinical sites have been selected for patient enrollment and have initiated the Institutional Review Board (IRB) submission process, but no formal site-specific IRBs have been approved and no patients have been enrolled in the PAS. Therefore, the results from the PAS are still pending. Per the HDE Approval Letter, this PAS study is estimated to be completed by January 2027, 84-months from the date of PAS approval.

VIII. ADVERSE EVENTS

Known Adverse Events

Adverse events (AEs) collected during the clinical study that were used to support the safety and probable benefit of The Tether™ in subjects with pediatric idiopathic scoliosis were presented in the SSPB at the time of HDE approval. One hundred and thirty-two (132) AEs were identified in 49 of the 57 subjects in the study population. Table 3 lists all AE types reported in the clinical study that were classified as related to the device or procedure. Twenty-four (24) device-related AEs were identified in 23 out of 57 subjects (40.4%). The most common device or procedure-related AEs by subject occurrence include overcorrection of the instrumented curve (12/57, 21.1%), nausea/vomiting (12/57, 21.1%), and definite/suspected cord breakage (8/57, 14.0%).

Table 3. Known Adverse Event (AE) Types Related to The Tether™ Device or Procedure

AEs Related to Device or Procedure
1. Acidosis 2. Anemia 3. Bone screw migration 4. Bradycardia 5. Tensioning cord break, definite 6. Tensioning cord break, suspected 7. Development of new curve 8. Hyperchloremia & hypocalcemia 9. Intraoperative hemorrhage 10. Nausea/vomiting 11. Overcorrection of instrumented curve, requiring revision

12. Overcorrection, no revision required
13. Perioperative peripheral nerve injury
14. Pleural effusion
15. Pneumothorax
16. Sympathetic dysfunction
17. Transfusion requirement
18. Worsening of pre-existing secondary curve

From the AEs reported in Table 3, Table 4 summarizes the five (5) AE types were classified as device- or procedure-related Serious Adverse Events (SAEs). Nine (9) total SAEs were reported for this study. Overcorrection of the major curve following AVBT which required additional spinal surgery was the most common SAE type, and accounted for 6 of the 9 total SAEs. Overcorrection was defined as any major curve that corrected to any degree in the opposite direction of the original curve convexity. Seven (7) overcorrection AEs did not require secondary surgery based on curve magnitude (<10 degrees, N=3; 11-20 degrees, N=3; 24 degrees, N=1), and the subject's skeletal maturity status. Overcorrection less than 10 degrees may be referred to as spinal asymmetry given that scoliosis is defined as curvature of the spine greater than 10 degrees and represents a radiographic finding which is not associated with any known adverse clinical effect. These subjects have been monitored with radiographs at subsequent follow-up visits. Only one (definite) cord breakage resulted in a reoperation SAE and none of the screw migration events required reoperation.

Table 4. Known Serious Adverse Event (SAE) Types Related to The Tether™ Device or Procedure

SAEs Related to Device or Procedure
1. Overcorrection of instrumented curve
2. Tensioning cord break, definite
3. Tensioning cord break, suspected
4. Development of new curve
5. Bone screw migration

Literature Review

The sponsor performed a clinical literature search in their Annual Report (H190005/R001) of articles published from February 2019 through August 2020. Scoliosis, tether, spine, anterior vertebral body tethering, and investigators' last names who previously published on AVBT including Samdani, Larson, Miyanji, Diab, Hoernschemeyer, Betz, Cuddihy, and Antonacci, were used as search terms and the following inclusion/exclusion criteria were used to further refine the articles to criteria relevant for this HDE.

Inclusion Criteria:

- It provides relevant information regarding technical and clinical features of the device subject of
- the search, or
- It provides relevant information regarding performance and/or safety of the device subject of the

- Search, or
- It provides information relevant to determining the probable benefit of the subject device, and
- It contains sufficient information for a rational and objective assessment, and
- It is based on an appropriate study design

Exclusion Criteria:

- Those involving implants other than those of interest
- Isolated case reports
- Random experience
- Reports lacking sufficient detail to permit scientific evaluation
- Unsubstantiated opinions
- Non-clinical study
- Foreign language (non-English) literature

After removing duplicates, and reading the titles, abstracts, and full-texts, six (6) articles were determined to be relevant based on the inclusion and exclusion criteria.[3-8]

An additional clinical literature search in PubMed was performed by FDA for articles published from January 2019 to November 2020. The following search terms were used: scoliosis, tether. After reading the titles, abstracts, and full-texts, and excluding non-clinical studies, review papers, tethered spinal cord studies, and non-AVBT (anterior vertebral body tethering) studies, four (4) additional articles were found.[9-12]

Out of the ten (10) total articles, five (5) were from US sites and five (5) were from outside the United States sites. It is important to note that the literature articles do not indicate the specific device type used. However, all literature articles did study AVBT devices and therefore were included in this analysis. A total of 334 patients were reported on across these 10 articles with 132 adverse events:

- Spinal curvature overcorrection (progression of Cobb angle beyond correction provided by intraoperative tethering)
    - 3.6% (n = 12) compared to 22% from clinical data results in the SSPB
- Loss of spinal curvature correction
    - 0.3% (n = 1) compared to 0 from clinical data results in the SSPB
- Broken tethers
    - 12.6% (n = 42) compared to 14.0% from clinical data results in the SSPB
- Broken tethers that required revision
    - 2.4% (n = 8) compared to 1.8% from clinical data results in the SSPB
- Other mechanical complications (screw loosening/pullout/migration/misplacement, tether loosening)
    - 1.8% (n = 6) compared to 5.3% from clinical data results in the SSPB
- Pulmonary/thoracic complications (pneumothorax, pleural effusion, chylothorax, pulmonary edema, pneumonia, pulmonary embolism)
    - 8.4% (n = 28) compared to 14.0% from clinical data results in the SSPB

- Radiculopathy
    - 0.3% (n = 1) compared to 1.8% from clinical data results in the SSPB
- Horner's syndrome
    - 0.3% (n = 1) compared to 0 from clinical data results in the SSPB

Summary of Literature

The studies found in this literature review suggest probable benefits of AVBT systems such as The Tether™ with respect to the treatment of skeletally immature patients with idiopathic scoliosis. From the clinical data documented in the SSPB used to support safety and probable benefit for The Tether™, a total of 91 adverse events were observed for 49 of the 57 total subjects. All event types from the literature search were identified at time of HDE approval as potential adverse effects (e.g., adverse events) as documented in the SSPB except for Horner's syndrome. Horner's syndrome has been documented following high chest tube insertion and therefore is unlikely to be related to the tether device components or intraoperative spinal curvature correction.[13] While the list of adverse events is much more comprehensive in the SSBP as compared to the literature, this search demonstrates that the types of adverse events documented in the literature are expected given the clinical data published in the SSPB for The Tether™ – Vertebral Body Tethering System. It does not appear that any additional safety signals nor concerns have arisen since HDE approval.

Overview of MDR Database

Strengths and Limitations of MDR Data

Each year, the FDA receives several hundred thousand MDRs of suspected device-associated deaths, serious injuries and malfunctions. The MDR database houses MDRs submitted to the FDA by mandatory reporters (manufacturers, importers and device user facilities) and voluntary reporters such as health care professionals, patients and consumers. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products. MDR reports can be used effectively to:

- Establish a qualitative snapshot of adverse events for a specific device or device type
- Detect actual or potential device problems used in a "real world" setting/environment, including:
    - Rare, serious or unexpected adverse events;
    - Adverse events that occur during long-term device use;
    - Adverse events associated with vulnerable populations;
    - Off-label use; and
    - Use error

Although MDRs are 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. Because of this, MDRs comprise only one of the FDA's several

important post-market surveillance data sources. Other limitations of MDRs and FDA's internal MDR database include:

- 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.
- Confirming whether a device caused a specific event can be difficult based solely on information provided in each report. Establishing a cause-and-effect relationship is especially difficult if circumstances surrounding the event have not been verified or if the device in question has not been directly evaluated.
- MDR data is subjected to reporting bias, attributable to potential causes such as reporting practice, increased media attention, and/or other agency regulatory actions.
- MDR data does not represent all known safety information for a reported medical device and should be interpreted in the context of other available information when making device-related or treatment decisions.

MDRs Associated with The Tether™

FDA's internal MDR Database was searched on December 1, 2020 utilizing the following search criteria:

1. Product code QHP (Vertebral Body Tethering System)
    - 38 MDRs found
2. Brand name, generic name, or concomitant product "Tether"
    - 54 MDRs found; 16 reports found to be not relevant, 38 relevant MDRs identical to results from search criterion 1
3. Catalog numbers beginning with "203H", "204H", or "211H"
    - 38 MDRs found; identical results to search criterion 1
4. Voluntary reports with narrative text containing "Tether" or "Tethering"
    - 0 MDRs found

The search resulted in thirty-eight (38) MDRs. In two cases, an MDR was submitted for every component that was implanted into the patient accounting for 21 and 15 MDRs, respectively. Therefore, a total of four (4) unique patient events were reported. All four events occurred within the U.S., involved pediatric patients, and were received in 2020.

<u>MDRs #1-15: 3012447612-2020-00354 through 3012447612-2020-00359</u>
A patient (age unknown) present in the emergency rooms with a pleural effusion related to a CSF leak after a tether procedure. The patient underwent a revision surgery to drain the spinal fluid. No further information was provided, and root cause could not be determined. This MDR was reported by the sponsor in the 2020 Annual Report (H190005/R001). A CSF leak would not be expected following a tether surgery given the implantation of all device components on the external surface of the anterior spinal column and do not breach the spinal canal. As a result, the sponsor is investigating this event and states that the results of the investigation and closure details will be provided within the 2021 Annual Report.

MDRs #16-36: 3012447612-2020-00544 through 3012447612-2020-00564
A 14-year old male was admitted to the hospital, two (2) weeks after undergoing a tether procedure, after presenting with increased pain on his right side. A CT was performed which revealed a hemothorax. A drain was placed with no immediate plans to return to the operating room. The patient was reported to have been discharged from the hospital. Additional information was provided stating that the patient first presented to the emergency room with shortness of breath, chest pain, and a singe syncopal episode. He was released, returned after a clinical visit, and admitted to the hospital where an x-ray showed a large pleural effusion with atelectasis and significant decrease in hemoglobin. The patient is reported to have been discharged and is in stable condition. Given the location of the implanted components within the chest cavity and the coagulation of blood vessels over the external surface of the spinal column, a hemothorax following tether surgery is not unexpected. However, the root cause of this event could not be more precisely determined.

MDR #37: 3012447612-2020-00574
A 12-year old patient was reported to need a revision surgery after their curve began to increase three (3) months postoperatively. A revision is planned to remove and retighten the cord but is not scheduled at this time. One month after this report, visual examination of the patient's x-rays confirmed that the curve had exceeded 38° postoperatively. Following the initial surgery, the patient's condition should have stabilized or improved. While there was no clear defect observed with the implants, the patient's condition did not stabilize or improve. Root cause of this curve progression could not be determined based on the limited information provided. Potential etiologies would include insufficient growth remaining to benefit from the procedure or an unrecognized tether breakage.

MDR #38: 3012447612-2020-00589
A female patient (age unknown) underwent a tether revision surgery after a thoracic tether procedure when it was discovered that their compensatory lumbar curve was increasing postoperatively. The surgeon believed that the tension in the cord needed to be released. The cord was removed and replaced. There were no additional patient impacts reported. The development of a new (compensatory) curve was observed in the clinical data for The Tether™. Given that patients are surgically treated prior to reaching skeletal maturity, it is possible for a new curve to develop (or a secondary curve to increase) in response to the correction of the primary curve.

Summary of MDRs

As of the first annual report for The Tether™ (H190005/R001), the sponsor was notified of one MDR reportable event. This event was the same event related to CSF leak found during FDA's internal MDR search (MDRs #1-15: 3012447612-2020-00354 through 3012447612-2020-00359). This MDR along with the additional three reports found during FDA's internal MDR search are all expected given the nature of tether surgery as well as immobilization and venous status while the patient is recumbent under anesthesia. Table 5 Summarizes all MDRs associated with The Tether™. Given the total of 405 tether cases, the MDRs represent a 0.99% AE incident rate.

Table 5. MDRs for The Tether™

Adverse Event Type	Number of Events	Patient Age and Sex (if known)	Relationship to Device	Source
CSF leak	1	Unknown age and gender	Unknown, investigation ongoing	H190005/R001, FDA's internal MDR search
Hemothorax	1	14, male	unknown	FDA's internal MDR search
Curve progression (primary)	1	12, unknown gender	Yes	FDA's internal MDR search
Curve progression (secondary/compensatory)	1	Unknown age, female	Yes	FDA's internal MDR search

IX. SUMMARY

Evaluation of data available to CDRH, including the first Annual Report, MDRs and published scientific literature, has identified no new safety signals compared to what was known and anticipated at the time of HDE approval in August 2019. Based on the available data, and considering the probable benefits and risks, FDA believes that the HDE remains appropriately approved for pediatric use. Therefore, FDA recommends continued surveillance and will report the following to the PAC in 2022:

- Annual distribution number
- Literature review
- MDR review

X. REFERENCES

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