FDA Executive Summary

Prepared for the
Fall 2025 Review by the
FDA's Pediatric Advisory Committee

Enterra® Therapy System
(H990014)

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I. INTRODUCTION

In accordance with the Pediatric Medical Device Safety and Improvement Act, this document provides the Pediatric Advisory Committee (PAC) with post-marketing safety information to support its annual review of the Enterra® Therapy System ("Enterra"). The purpose of this annual review is to: (1) ensure that the Humanitarian Device Exemption (HDE) for this device remains appropriate for the pediatric population for which it was granted, and (2) provide the PAC an opportunity to advise FDA about any new safety concerns it has about the use of this device in pediatric patients.

This document summarizes the safety data FDA reviewed in the year following our 2024 report to the PAC. It includes data from the manufacturer's annual report, post-market medical device reports (MDR) of adverse events and peer-reviewed literature.

II. INDICATIONS FOR USE

The Enterra Therapy System for Gastric Electrical Stimulation (GES) is indicated for the treatment of patients with chronic intractable (drug-refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology in patients aged 18 to 70 years.

III. BRIEF DEVICE DESCRIPTION

Enterra is a surgically implanted gastric electrical stimulator (GES). The mechanism(s) by which Enterra works is not well understood but may involve indirect neuromodulation of parasympathetic nerves and/or ganglia, which regulate gastric function.

Enterra consists of the following:

1. A neurostimulator placed in a subcutaneous pocket in the abdomen, which functions like a pacemaker in delivering electrical pulses to the stimulation leads. The neurostimulator contains a sealed battery and electronic circuitry.
2. Two intramuscular leads that connect to the neurostimulator, implanted into the muscularis propria on the greater curvature at the limit of the corpus-antrum. The leads deliver electrical pulses to the stomach muscle.
3. An external clinician programmer.

Schematic diagrams of the implantable components and device placement are provided in Figure 1 and Figure 2, respectively.

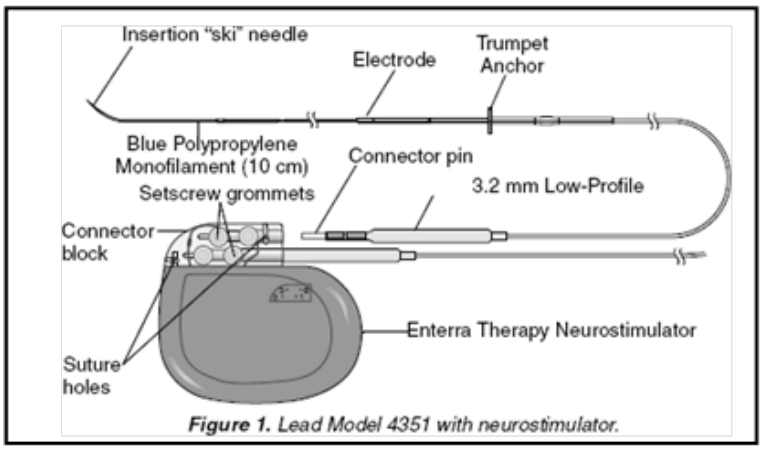

FIGURE 1: Implantable components

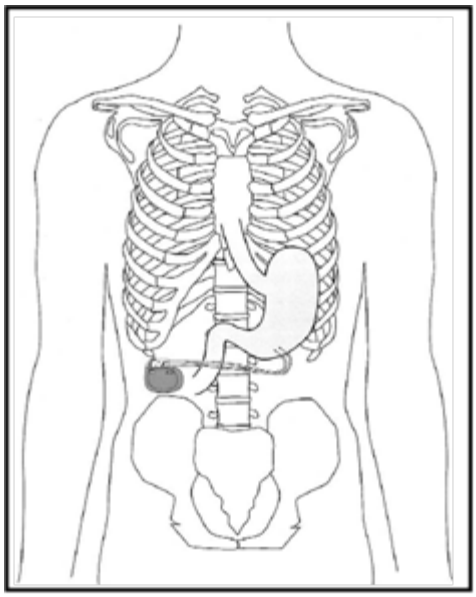

FIGURE 2: Device placement

IV. REGULATORY HISTORY

September 23, 1999: Granting of Humanitarian Use Device (HUD) designation for Enterra (HUD#990014)

March 30, 2000: Approval of Enterra HDE (H990014)

March 25, 2013: Approval to profit on the sale of Enterra

V. DEVICE DISTRIBUTION DATA

Section 520(m)(6)(A)(ii) of the Food, Drug, and Cosmetic Act (FD&C Act) 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. The approved ADN for Enterra is 8,000 total per year.

The total number of Enterra devices sold/distributed in the U.S. for the current and previous reporting periods is detailed in Table 1; the estimated number of devices implanted in pediatrics is detailed in Table 2

TABLE 1: Distribution Numbers

Model Number & Component Name	Devices Sold From 02/01/24 – 01/31/25	Devices Sold From 02/01/22 – 01/31/23	Devices Sold From 02/01/22 – 01/31/23	Devices Sold From 02/01/21 – 01/31/22	Devices Sold From 02/01/20 – 01/31/21	Devices Sold From 02/01/19 – 01/31/20	Devices Sold From 02/01/18 – 01 /31/19	Devices Sold From 02/01/17 – 01/31/18	Devices Sold from 02/01/16 – 01/31/17
37800 Implantable Neurostimulator	3099	2923	2410	2127	1895	2053	1951	2017	1865
*3116 Implantable Neurostimulator	0	0	0	0	0	0	0	0	0
4351 Intramuscular Lead	3269	3027	2345	2131	1874	1988	2106	2535	2462

**3116 Implantable Neurostimulator was discontinued by Medtronic prior to transfer to Enterra Medical*

TABLE 2: Estimated Number of Devices Implanted in Pediatric Patients*

Reporting Period: 02/01/24 –01/31/25	Total N (newly implanted this period)	Female by age in years			Male by age in years			Gender Unknown by age in years		
		<2	2<18	≥18<22	<2	2<18	≥18<22	<2	2<18	≥18<22
Newly implanted pediatric patients during this reporting period*	Unknown									
Total pediatric patients with active implants this reporting period*	423									

** Annual Report was finally submitted by sponsor on July 25, 2025, after multiple attempts to reach out, however the information provided is currently incomplete. Table cannot be filled out at this time.*

VI. ANNUAL REPORT REVIEW

This year's annual report included annual distribution information; a summary changes including design, manufacturing**,** and labeling; reports of scientific investigations and literature; clinical experience including medical device reports; and a pediatric safety report. The annual report did not include any information that affects the safety of the Enterra System. FDA conducted the independent MDR and literature reviews that follow.

VII. MEDICAL DEVICE REPORT REVIEW

Overview of MDR database

The MDR database is one of several important post-market surveillance data sources used by the FDA. Each year, the FDA receives several hundred thousand medical device reports 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 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
  - 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 important post-market surveillance data sources. Other limitations of MDRs include, but are not necessarily limited to:

- MDR data alone cannot be used to establish rates of events, evaluate a change in event rate 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 actually caused a specific event can be difficult based solely on information provided in a given 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 subject 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 Enterra Therapy System
The Enterra System labeling includes a summary of known adverse events. The Enterra labeling summary includes the following adverse events that were reported as MDRs in the current reporting year: impedance out of range, change in stimulation (described as a shocking, jolting, or tingling sensation), loss of therapeutic effect, neurostimulator system ceases to function due to battery depletion or telemetry issues, lead or neurostimulator erosion or migration, infections, stomach wall perforation, upper gastro-intestinal (GI) symptoms including nausea, vomiting, abdominal pain, discomfort, persistent pain at the neurostimulator site.

MDR Search Methodology
The MDR database was searched using the following search criteria:

- Product Code: LNQ
- Manufacturer name: Enterra, Enterra Medtronic Inc, Medtronic, Puerto Rico Operations CO
- Report Entered: between May 1, 2024, and April 30, 2025

The MDR search yielded 157 reports received between May 1, 2024, and April 30, 2025. The MDRs included 8 deaths, 113 injuries, and 36 malfunction events. Of the 157 reports there were seven (7) pediatric patient MDRs. It should be noted that three (3) pediatric MDRs may be from the same patient due to all sharing the same birth date.

The following are reported issues that occur in both adult and pediatric patients.

- Pain and inappropriate simulation/shocking secondary to positioning of the device or battery and lead issues
- Symptoms of nausea and vomiting and/or loss of therapeutic effect secondary to impedance issues or battery issues
- Component failures such as lead, battery, and erosion issues that could lead to infection

Event Type by Patient Age

Table 3 provides the distribution of the MDRs by reported event type and age grouping. In this year's reporting period, there were seven (7) patients in the pediatric age category of <22 years old with five (5) MDRs from patients <18 years old and two (2) MDRs from patients 18-21 years old. Four (4) events were related to injury, with two (2) reports each from patients <18 years old and 18-21 years old. Three (3) events were related to malfunctions for patients <18 years old. The age range for all pediatric MDRs was 9-21 years old. There were no reports of deaths among the pediatric MDRs. However, it should be noted that four (4) MDRs were listed with an

indeterminate age, and at this time there is no additional information on the demographics of these patients.

TABLE 3: Overall event type distribution by patient age

Event Type	Total MDR Count 5/1/2024 – 4/30/2025	MDR Count by Patient Age (years)			
		Pediatric (< 18)	Pediatric (18-21.9)	Adult (≥ 22)	Indeterminate (Age blank)
Death	8	0	0	4	4
Injury	113	2	2	72	37
Malfunction	36	3	0	27	6
Total MDR Count	157	5*	2	103	47

** Three (3) reports may be from same patient due to matching birth dates and year*

Comparison of Current Patient Event Type Information with Previous Years

Table 4 compares the event type distribution of current reporting period to previous years. This data is for both adult and pediatric patients.

TABLE 4: Overall event type distribution by reporting year

	Total MDR Count							
Event Type	2018 PAC Meeting 5/2017 - 4/2018	2019 PAC Meeting 5/2018 - 4/2019	2020 PAC Meeting 5/2019 - 4/2020	2021 PAC Meeting 5/2020 - 4/2021	2022 PAC Meeting 5/2021 - 4/2022	2023 PAC Meeting 5/2022 - 4/2023	2024 PAC Meeting 5/2023 - 4/2024	2025 PAC Meeting 5/2024 – 4/2025
Death*	0	1	0	0	0	0	1	9**
Injury	285	184	117	127	116	170	37	113
Malfunction	150	120	61	57	57	56	69	36
Total MDR Count	435	305	178	184	173	226	107*	157

** No deaths have been reported for pediatric patients or patients with an indeterminate age.*

*** Six (6) deaths occurred outside of the current reporting period but were not included in prior annual reports. It's unclear to the FDA why these reports were never previously documented and the company was*

requested to include in their current annual report for review.

Patient Gender and Age Information

In the 157 MDRs received from May 2024 to April 2025, only 110 reports contained information on patient age. 103 patients were identified as adult (≥22 years old) and 47 MDRs did not provide a patient age (indeterminate age reports). Seven (7) MDRs contained pediatric patients between the ages of 9-21. Three (3) reports were from a patient with the same birth date and year.

There were 95 MDRs that noted the gender of the patient: 77 MDRs were identified as female with three (3) associated with pediatric patient events; and 18 MDRs were identified as male with two (2) associated with pediatric patient events. The remaining 62 MDRs did not include the patient gender.

Review of the 62 unknown gender report narrative sections to determine gender identifiers (male or female, she or her, he or him, etc.) did not result in identifying additional female or male noted events. These MDRs identified the individual involved in the event only as "the patient".

Time to Event Occurrence

An analysis of the Time to Event Occurrence (TTEO) was performed. The TTEO is based on the implant duration and was calculated as the time between the date of implant and the date of event. For those MDRs without a date of event, the TTEO was calculated using the reported date of implant removal. A total of 33 MDRs (out of 157) provided a valid event date and date of implant. Four (4) MDRs documented events which occurred intraoperatively or on the same day as implantation (TTEO=0).

The remaining 124 reports did not include a valid event or explant date (i.e., one or both of Date Implanted and Event Date fields were missing or incorrectly entered). A TTEO could not be determined for these reports.

Table 5 provides the MDR count for the TTEO for the pediatric, adult, and indeterminate age patient populations.

TABLE 5: MDR count for the TTEO by patient age

Time to Event Occurrence (TTEO)	MDR Count by Patient Age (years)			
	Pediatric (<18)	Pediatric (18-21)	Adult (≥22)	Indeterminate (Age blank)
≤ 30 days	0	0	5	1
31 days - ≤ 1 year	0	0	6	0

> 1 year – ≤ 5 years	2	0	7	5
> 5 years	0	0	1	0
Totals (N=27)	2	0	19	6

Characterization of the MDR Narratives of the Pediatric Events per TTEO

> 1 year – ≤ 5 years

- MDR: 3027386225-2025-00015- "On March 4th 2024, a report of a 20-year-old female patient possibly needing surgery to replace neurostimulator. Neurostimulator EOS (End of Service) after ~1.5 years since replacement. Patient provided update that device was removed on 1/15/25 so that she could proceed with MRI testing. Provider plans to place a temporary stimulator while they complete testing needs. Patient reports return of symptoms since stimulator removal. Patient had device removed in order to proceed with MRI; battery was EOS. No further action to be take."

- MDR: 3027386225-2024-00101- "On September 3rd 2024, a 15-year-old male patients surgery nurse called to say that patient has an infection in the pocket area. Pocket infection post 6/27/24 gen change. Patient had his generator explanted on 8/6/24 according to surgery Nurse A. Model 37800 SN NHX722600h. Infection is being treated. Patient will have a debridement possibly 8/9 and then has a follow up appointment on 8/13. Implant date will depend on how the patient is healing."

Characterization of the Time to Event Occurrences in the Adult, Pediatric, and Indeterminate Age Populations

For the adult and indeterminate age population with TTEO data, issues with the use of the device occur most frequently in the "1 year – ≤ 5 years" from the date of implant category, followed by issues occurring between "≤ 30 days" and "31 days - ≤ 1 year" categories. Last year's analysis, issues with the use of the device occurred most often between 31 days - ≤ 1 year. Two (2) of the seven (7) reported pediatric use of device issues occurred > 1 year – ≤ 5 years from the date of implant this reporting period.

The following issues continue for both adult and pediatric patients.

- Pain and inappropriate simulation/shocking secondary to positioning of the device or battery and lead issues

- Symptoms of nausea and vomiting and/or loss of therapeutic effect secondary to impedance issues or battery issues

- Infection, lead, battery, and erosion issues

In the current analysis, 93 MDRs noted failure of implant. This was the most common complaint. 74 of these 93 MDRs noted failure of implant as the primary issue. The second most common complaint was electric shock/implant pain/discomfort noted. This was included in 40 MDRs with 31 MDRs noting electric shock as the primary issue. These MDR narratives often note pain due to inappropriate stimulation/shocking as well as positioning/migration of the device or its components. Patients experiencing pain complained of it most often around the implant site. Patient device interaction problems were reported in some patients due to losing weight after implant; device battery/lead position; or setting of the device. Device repositioning, battery or leads revision/replacement or turning down the voltage setting relieved the problems in most cases.

Failure of implant continued to occur this reporting period. Examples include:

- (Pediatric) 3027386225-2025-00015- " On 03-04-2025 possible surgery needed to replace neurostimulator. Neurostimulator EOS after ~1.5 years since replacement. Patient provided update that device was removed on 1/15/25 so that she could proceed with MRI testing. Provider plans to place a temporary stimulator while they complete testing needs. Patient reports return of symptoms since stimulator removal. Patient had device removed to proceed with MRI; battery was EOS. No further action to be taken."

- (Pediatric) 3027386225-2024-00088- "On 07-23-2024, Dead battery. Date of implant 5/2/2023. Gen change 6/27/2024. Physician A knows the settings are extremely high causing the battery to drain quickly. Mom knows they are high and wants them left high. Consulted Physician A that we could get longer battery life if we lowered the rate and pulse width as both are high. The motility GI raised the setting when he was at UF and because it works so well, everyone wants to keep the setting as is even though the battery life will be short. Generator was collected to be sent back.

Electric shock, pain and discomfort reports continued to occur this reporting period with 40 MDRs, examples include:

- (Pediatric) 3027386225-2024-00134: "A Nurse Practitioner from Facility A called me to report an adverse event. Patient reported a shocking sensation shortly after leads were changed. Patient had her leads changed on July 9th by General Surgeon A at Facility B in State A. Patient arrived at Facility A for an appointment on Tuesday September 17th. NP lowered patient's voltage from 8.5v to 7v to see if the shocking sensation resolves. The impedance between 2 & 3 is 503 ohms, c & 2 345 ohms. Patient was feeling shocking sensations."

- 3027386225-2024-00058- "A patient was implanted on 3/15/24. Two weeks after implant, she developed shocking and an impedance greater than 20,000. Pt was sent

back to OR for a revision. While in the OR for a revision, it was discovered that one of the screws was loose and would not properly seat. It is believed that the screw had backed out at some point after the device was implanted. The explanted device serial number is NHX721886h. This device is being sent to Medtronic for testing. Only effect was patient shocking while implanted with initial battery. "Patient stated on the call that they are experiencing shocking problems (did not specify more), they cannot lay on their left side."

- 3027386225-2024-00078: "A patient stated 'She is having constant discomfort around her pocket site since receiving her Enterra implant in the fall of 2023 by her doctor. Says she can feel her stimulator 'flipping' around in the pocket. Is consulting her surgeon to see if she is in need of a revision.' She also listed several other health issues that could be contributing to her abdominal discomfort, and upcoming procedures to address those issues. She and her doctor are planning to discuss waiting on a revision until those other procedures are done, to see if they have an impact on the discomfort."

Infection/Unspecified Bacteremia was reported in 23 MDRs this reporting period. In report 3027386225-2025-00024:

- Initial report: "A patient complained of a potential pocket infection and the IPG was removed. Patient was scheduled 2/6/25 for a system replacement. Upon arrival to the case, [reporter] was informed the patient showed up to the ER with a potential pocket infection 1/2/25. Her most recent system replacement was 9/12/24.The IPG was explanted by the ER physician approximately 1/2/25 and the leads were cut but left implanted."

- Follow-up: "The case today, 2/6/25 was to remove the leads left behind and replace the entire system. Patient was explanted due to infection. Explanted product was disposed of; no further actions to be taken."

Nausea/vomiting continued to occur this reporting period. There were 15 MDRs of nausea/vomiting which often led to weight loss. In one report (3027386225-2024-00057), On 06-12-2024:

- Initial Report: "Patient reports a return of nausea and vomiting symptoms about 2 months ago. Patient called and states about 2 months ago her nausea and vomiting symptoms came back. She states she went to see her managing physician and she states he increased the device to the highest settings, and she did not notice a change in symptoms. She states she has the device checked every couple of months and she had replacement surgery in February 2023. Referred the patient back to her provider for device management. She states she has an appointment with Enterra therapy provider next week."

- Follow-up: “the patient called and said she found out that battery died, and she had replacement surgery on 1/22/24. She said she went in for adjustments and said they weren't helping and states she has been so miserable for almost a month with vomiting, nausea, and pain. She stated today she saw dr. And he told her one of the leads is not in the stomach and she will have to go back in for surgery again. She requested to be transferred to the tech services line. Patient had a revision and battery replacement 4/29/24.”

There were 29 reports of “No Clinical Signs or Symptoms or similar Conditions”. This type of report can mean there were no health consequences or impact to the patient. These MDRs can also vary and include reports of patients needing a physician to replace a lead(s), reports of patients with batteries depleted and replaced and patients with devices out of range and requiring the voltage adjustment. This reporting year also included reports with insufficient information, reports not device related and reports with no lasting health impact to patients. In report 3027386225-2024-00068 a patient reported:

- Initial report: “That her simulator is currently turned off and is awaiting removal because a piece of it allegedly corroded (couldn't specify what piece, but sounded as if it was internally). Says symptoms have progressed.”
- Follow-up: “patient was explanted due to ineffective treatment of symptoms. No corrosion was found in explanted device.”

Most Commonly Reported Patient Problem Codes (PPC)[1]

Table 6. provides the most prevalent patient problem codes found in the MDRs reviewed during this reporting period classified by patient age. The top reported patient problems this reporting period are “Failure of Implant” (n=93), which increased from the previous year (n=9). The second highest category is Electric Shock/Implant Pain/Discomfort (n=40), which is characterized by inappropriate stimulation/shocking/burning as well as cramping/discomfort and migration of the device or its component, which decreased from last year (n=42). The third most prevalent code “No Clinical Signs, Symptoms or Conditions, Symptoms, Conditions Term / Code Not Available/Insufficient Information” (n=29), is characterized by no findings and/or problem being detected after an investigation, decreasing from first placed compared to last year (n=37). The fourth patient problem code is Unspecified Infection/Bacteremia (n=23). The Fifth most reported patient problem code is Infection(n=13) is predominately characterized by infection of the pocket site. This year’s patient problem codes do not present significantly new or increased safety concerns when compared to last year.

[1] The total patient problem code (PPC) does not equal the total MDR count since one MDR might have multiple patient problems. Patient problem codes indicate the effects that an event may have had on the patient, including signs, symptoms, syndromes, or diagnosis.

TABLE 6: Most commonly reported patient problem codes in MDRs received by patient age

Patient Problem	Total Patient Problem Code	Total Patient Problem Code by Patient Age (years)			
		Pediatric (< 18)	Pediatric (18 to 21)	Adults (≥ 22)	Indeterminate (Age blank)
Failure of Implant	93	2	1	71	19
Electric Shock/Implant Pain/Discomfort	40	0	1	29	10
No Clinical Signs, Symptoms or Conditions/ Insufficient Information	29	1*	0	19	9
Unspecified Infection/Bacteremia	23	2*	0	18	3
Obstruction/Occlusion	3	0	0	2	2
Internal Organ Perforation	1	0	0	1	0
Total Count	189	5	2	139	43

** Might be from the same patient due to patient having the same birth date (< 18).*

Most Commonly Reported Device Problem Codes (DPC)[2]

Table 7. provides the most prevalent reported device problems for all MDRs classified by patient age. The top three reported device problem codes this year are "Adverse event without identified device or use problem" (n=30) ranking first, "Unintended Electrical Shock, Intermittent Shock/Stimulation" (n=24) ranking second, and "Patient Device Interaction Problem, Patient-

[2] The total Device Problem Codes (DPC) does not equal the total MDR count since one MDR might have multiple patient problems. Device problem codes describe device failures or issues related to the device that are encountered during the event.

Device Incompatibility" (n=19) ranking third. The reports with "adverse event without identified device or use problem" are related to patient issues in which the device was functioning or had no identified device problems. The other reports most often included reports of pain with device intolerance issues. Most of the corresponding patient problem codes were nausea/vomiting, shocking sensation, and infection. Adjustments to the device voltage, device placement and replacement of the leads or battery were reported interventions in these patients. The reports of "Inappropriate Shock" typically involved the position of device, or electromagnetic compatibility/interference. "Energy output problem" and "Failure to deliver energy are related to nausea, vomiting, shocking and decreased therapeutic effect issues. Recognized Device or Procedural Complication are Hospitalizations or Prolonged Hospitalizations are common health impact codes associated interventions as well as Device Revision or Replacement in many of the reports.

TABLE 7: Most commonly reported device problem codes in MDRs received by patient age

Device Problem	Total Device Problem Code	Total Device Problem Code by Patient Age (years)			
		Pediatric (< 18)	Pediatric (18 to 21)	Adults (≥ 22)	Indeterminate (Age blank)
Insufficient Information Adverse Event Without Identified D Appropriate Term/Code Not Available device or Use Problem/	171	2*	2	122	45
Migration, Malposition of Device, Unintended Movement	10	0	0	10	0
Battery Problem, Premature Discharge of Battery, Battery Problem: High Impedance	3	1	0	2	0
Break, Material Erosion,	2	0	0	1	1
Premature Discharge of Battery, Failure to Deliver Shock/Stimulation	2	1	0	0	1
Patient-Device Incompatibility, Biocompatibility, Loose or Intermittent Connection/ Misconnection	4	0	0	4	0

Total Device Problem Code Count	192	4	2	139	47

Discussion of Pediatric Patient Problem as it relates to Device Problem Information

Table 8 identifies the MDR occurrences of the top patient problems and issues in pediatric patients only in comparison to the prior reporting periods. There were seven (7) pediatric MDRs this reporting period. Previous pediatric MDRs have involved complaints of nausea, vomiting, pain, shock, and infection, corresponding to device issue related to "Therapeutic Response, unexpected/decreased", and "inappropriate shock." These complaints and device problems were most often due to device setting, battery, and lead issues. Adjustments of the device settings, follow up with the treating physician, hospitalization, and request to explant the device were noted interventions.

TABLE 8: Clinical events identified with pediatric patients - year-to-year comparison*

Clinical Events	Occurrences in MDRs** 5/1/2024-4/30/2025	Occurrences in MDRs** 5/1/2023-4/30/2024	Occurrences in MDRs** 5/1/2022-4/30/2023	Occurrences in MDRs** 5/1/2021-4/30/2022	Occurrences in MDRs** 5/1/2020-4/30/2021	Occurrences in MDRs** 5/1/2019–4/30/2000
Nausea/Vomiting	0	0	1	1	1	1
Unintended Revision Surgery	4	0	0	0	1	3
Pain/Discomfort/Abdominal pain/ Burning sensation	0	0	0	0	2	2
Electric Shock/Nerve Stimulation, Undesired/ Inappropriate	1	3	1	0	0	1
Infection	2	1	0	0	0	1
Therapeutic Effects, Unexpected	0	0	0	0	1	0
Insufficient Information/Complaint Ill-Defined	0	0	0	1	1	0

**Only the most observed patient problems and issues in pediatric MDR narratives are included.*
***The total MDR Occurrences may not equal the total pediatric MDR count since one MDR might have multiple clinical events.*

Re-Interventions in Pediatric Patients this reporting period

Re-interventions addressing clinical events are listed in Table 9. This table summarizes the re-interventions identified in the narratives and the causal events leading to these re-interventions. Re-interventions are events that required an additional procedure after the initial placement of the device. There were four pediatric MDRs this reporting period.

TABLE 9: Re-interventions in pediatric patients*

Re-Interventions	# of Re-Interventions	Causal Event	Outcome of Intervention
Device Revision or Replacement	4	• Needed MRI • Battery was EOS	• Provider plans to place a temporary stimulator while they complete testing needs. • Return of symptoms • Replaced the IPG at a later date
Infection	1	• Against physician orders the patient went swimming in a lake post generator charge	• Move the device site to the other side of the body • and reimplant the device
Shock	1	• Patient reported a shocking sensation shortly after leads were changed.	• Patient's shocking sensations have ceased since adjustment. No further action to be taken.
Under stimulation- Non-surgical	1	• Reduced efficacy post physical assault at school	• Patients experienced some relief after Enterra INS settings re-adjustment

**Note that the total counts may not equal the number of MDRs since one MDR might have multiple noted re-interventions.*

MDR Review Conclusions

- There were seven (7) pediatric MDR reports submitted for the Enterra Therapy System between May 1, 2024 and April 30, 2025, none involving a death. Three (3) patient reports might be from the same patient due to patient having the same birth date.

- The number and type of pediatric MDRs this year are similar to previous reporting periods.

- The age range for all confirmed pediatric MDRs reported in this current reporting period ranged from 9 to 21 years old. All seven (7) pediatric

MDRs were malfunction reports.

- The valid event date and date of implant were provided correctly for 33 event(s). There were 4 event(s) which occurred intraoperatively or on the same day as implantation (TTEO=0). Time to Event could not be calculated for 124 event(s).

- Patient problems observed this reporting period were similar to patient problem codes observed in the last reporting period. Complaints of pain and incidences of shock appear to be related to the position of device and/or connection/malfunction issues involving the leads or batteries.

- Device problems observed this reporting period were similar to device problem codes observed in the last reporting period. Reports continue to identify device functionality issues including migration, reduced efficacy and battery depletion issues.

- The device continues to be sold as an effective way for patient's regulate their gastric function. The device continues to be used for the pediatric population and the FDA has no new safety concerns about the use of this device in pediatric patients.

Purpose

A systematic literature review was conducted to evaluate the safety and probable benefit of Enterra gastric electrical stimulator (GES) in the pediatric population (<22 years old). This review is an update to the literature reviews presented at the Pediatric Advisory Committee (PAC) meetings from 2014 through 2024. Specifically, the literature review was conducted to address the following questions:

1. What is the probable benefit of Enterra for the following clinical endpoints: improvement in upper GI symptoms; reduction in need for nutritional support; and improved gastric emptying time (GET)?
2. What adverse events are reported in the literature after treatment with Enterra?

Methods

The search was limited to studies published since the last PAC meeting update (May 1, 2024 to April 30, 2025). The results were filtered for studies in human subjects, studies published in English, and excludes articles indexed to animals when not also indexed to humans. This search yielded a total of 548 citations (197 in PubMed, 150 in Embase and 201 in Google Scholar). After a review of titles, abstracts, and selected full texts, 26 articles were selected for full review and assessment. On June 7, 2025, searches in PubMed, Embase, and from MDRs were performed using the following search terms:

- PubMed
    - ("Enterra" OR "gastric electric stimulation" OR "gastric electrical stimulation" OR "gastric electrostimulation" OR "gastric pacemaker" OR "gastric pacing" OR (stimulation AND (gastroparesis OR "stomach paresis")) OR (gastrointestinal

neuromodulat*)) AND English [la] AND ("infant, newborn" [mh] OR "infant" [mh] OR "child, preschool" [mh] OR "Child"[Mesh] OR "adolescent" [mh] OR "young adult" [mh] OR newborn* OR infant* OR child* OR preschool* OR adolescent* OR "young adult" OR pediatric* OR boy OR girl OR toddler*) AND ("2024/05/01"[Date - Create] : "2025/04/30"[Date - Create] OR "2024/05/01"[Date - Publication] : "2025/04/30"[Date - Publication]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])
= 10 references after date limits applied

- Embase
  - (('enterra'/exp OR enterra OR 'gastric pacemaker'/exp OR 'gastric pacemaker' OR 'gastric electrical stimulation'/exp OR 'gastric electrical stimulation' OR 'gastric electric stimulation'/exp OR 'gastric electric stimulation' OR 'gastric electrostimulation' OR 'gastric pacing'/exp OR 'gastric pacing' OR (stimulation AND ('gastroparesis'/exp OR gastroparesis OR 'stomach paresis')) OR 'gastrointestinal neuromodulation') AND [english]/lim AND ([newborn]/lim OR [infant]/lim OR [child]/lim OR [preschool]/lim OR [adolescent]/lim OR [young adult]/lim OR newborn* OR neonat* OR infant* OR child* OR preschool* OR adolescen* OR 'young adult' OR pediatric* OR boy OR girl OR toddler*) AND [01-05-2024]/sd NOT [30-04-2025]/sd) NOT ([animals]/lim NOT [humans]/lim)
  = 5 references after date limits applied

- Google Scholar
  "Enterra" AND ("gastric electrical stimulation" OR "gastric electrostimulation" OR "gastric pacemaker" OR "gastric pacing" OR gastroparesis OR "gastric neuromodulation") AND (infant OR child OR adolescent OR pediatric OR "young adult")
  Limited to 2024-2025
  = 11 references after date limits applied)

Literature Review Summary

Similar to literature reviews presented at the Pediatric Advisory Committee (PAC) meetings from 2014 through 2024 our identification of relevant articles was determined on finding articles that were:

- Relevant to the safety and probable benefit of Enterra/Gastric Electric Stimulators; and
- Analysis of the pediatric population

Within the period of this search limited to studies published since the last PAC meeting update (May 1, 2024 to April 30, 2025) there was one article that fit these above criteria.

Summary of Relevant Article

Hawa K, Sanchez RE, Usman AP, Diefenbach KA, et al. 999 GASTRIC ELECTRICAL STIMULATION IS EFFECTIVE FOR CHILDREN WITH REFRACTORY NAUSEA AND

VOMITING: RESULTS OF A CONTROLLED, BLINDED TRIAL. Gastroenterology. Volume 166, Issue 5, Supplement,2024, Pages S-244-S-245, ISSN 0016-5085, https://doi.org/10.1016/S0016-5085(24)01047-3.

Background: Gastric electrical stimulation (GES) has been shown in controlled trials to be effective for adults with refractory nausea and vomiting, but evidence of its benefit in children has thus far been limited to retrospective and prospective cohort studies. Our objective was to perform the first controlled trial of GES in children with refractory nausea and vomiting.

Methods: We performed a controlled, single-blinded trial of GES for children with refractory nausea and vomiting. Participants were recruited prior to starting a two-week trial of temporary GES delivered by a nasogastric pacing lead. Patient characteristics, medical history, diagnostic testing, clinical symptoms, route of nutrition, Symptom Monitor Worksheet (SMW), and nutrient drink test were collected at baseline. Participants and families were blinded to the status of the stimulator during the trial. After starting temporary GES, stimulators were turned off for the initial 3-4 days of the trial. Symptoms, SMW, and drink test were collected with the stimulator off (OFF). Stimulators were then turned on (10.0 volts for adolescents and 7.0 volts for children, pulse width 330 μs, frequency 28 Hz, 1 second on, 4 seconds off). Participants returned 3-4 days later and symptoms, SMW, and drink test were collected with the stimulator on (ON). Outcomes were compared between baseline and follow-up as well as with the stimulator OFF and ON.

Results: From October 2019-November 2023, 34 children with refractory nausea and vomiting were treated with temporary GES at our institution and 28 children (79% F, median age 16 years, IQR 14- 17, range 4-19) participated in the trial. Prior diagnoses included gastroparesis (89%), functional dyspepsia (32%), cyclic vomiting syndrome (7%), and rumination syndrome (7%). Comorbid conditions included postural orthostatic tachycardia syndrome (43%), anxiety (25%), Ehlers-Danlos syndrome (18%), and depression (11%). Most children (75%) required supplemental nutrition, with 68% on tube feeding and 11% on parenteral nutrition. Symptom severity based on SMW total score improved from baseline both while OFF (35.5 vs. 25.5, $p=0.001$) and ON (35.5 vs. 21, $p<0.001$), but SMW was improved when ON compared to OFF ($p=0.02$). The maximum volume that participants were able to drink as measured by nutrient drink test was also improved from baseline both while OFF (90 ml vs. 105 ml, $p=0.02$) and ON (90 ml vs. 120 ml, $p=0.002$), but again the volume was greater when ON compared to OFF ($p=0.02$). 23/28 (82%) experienced significant clinical improvement during the trial and underwent implantation of the stimulator.

Conclusion: In this controlled trial of GES for children with refractory nausea and vomiting, children experienced greater improvement in symptoms and oral intake with GES compared to sham stimulation.

Probable Benefit from Literature

The single article found in this search is an American Gastroenterological Association (AGA) abstract describing a controlled, single-blinded trial of GES where 34 children with refractory nausea and vomiting were treated with temporary GES, of which 28 had participated in the study.

These pediatric subjects had prior diagnoses which included gastroparesis, functional dyspepsia, cyclic vomiting syndrome, and rumination syndrome. Most subjects required supplemental nutrition through tube feeding and parenteral nutrition.

The study reported subjects responding favorably GES upon initiation of therapy through reduction in associated symptoms and improved oral intake during GES stimulation compared to baseline and sham therapies.

Probable Benefit from Literature

Most children (75%) required supplemental nutrition, with 68% on tube feeding and 11% on parenteral nutrition. No other safety data was reported in the study and none of the information included in the abstract indicates the presence of safety signal.

Critical Assessment of the Literature

The current systematic literature review found one relevant citation (meeting abstract), out of 548 publications.

The study included a total of 28 pediatric patients. The AGA abstract provides some evidence that GES can improve associated symptoms and oral intake for a small sample size of pediatric patients with refractory vomiting and nausea.

The results of this systematic literature review should be interpreted with consideration of the key limitations. First, the literature review only evaluates the use of GES being used in a sample of pediatric patients but makes no mention of the Enterra Therapy System. The sample size of subjects in this prospective study was on a limited sample size of non-randomized patients from a single institution which makes it difficult to determine the generalizability of the results to the total patient population. There was no true control arm, instead the therapy was toggled on and off with single blinding. The use of self-reporting for symptom monitoring introduces bias of the treatment signals selected along with lack of any information on adjudication of the endpoints selected. The meeting abstract is missing key details regarding safety findings. FDA was not able to obtain additional information on this study or abstract.

None of the considered articles raised any additional safety concerns. However, several articles do note that greater efforts are needed to ameliorate the negative impact of gastroparesis on pediatric health which references therapies such as GES.

Literature Review Conclusion
The current findings were based on the same approach as last year's literature review. No pertinent literature was located during this literature review that would suggest a need to revise prior conclusions about the safety of using the Enterra Medical INS System in the pediatric population or any general safety concerns when utilizing the Enterra Medical INS system.

VIII. OVERALL SUMMARY

FDA did not identify any new safety signals during this year's review of the Enterra annual report, MDRs or the peer-reviewed literature published since the last report to the PAC. FDA concludes the HDE for this device remains appropriate for the pediatric population for which it was granted.

However, we will be requesting Enterra Medical capture more specific data regarding their pediatric safety reports as part of their future annual reports.

FDA will continue routine surveillance including MDR and literature reviews.

FDA will report the following to the PAC in 2025:

- Annual distribution number,
- Literature review,
- MDR review

IX. REFERENCES

1. Hawa K, Sanchez RE, Usman AP, et al. 999 GASTRIC ELECTRICAL STIMULATION IS EFFECTIVE FOR CHILDREN WITH REFRACTORY NAUSEA AND VOMITING: RESULTS OF A CONTROLLED, BLINDED TRIAL. Gastroenterology. 2024;166(5):S-244-S-245. doi:https://doi.org/10.1016/S0016-5085(24)01047-3