March 15, 2024

Endostart s.r.l.
% Fabio Pasquale
Sr. Director, QA/RA
QA & RA Medical Device Consulting, Ltd.
842 Clarke Road
Brentwood Bay, BC V8M 2G1
Canada

Re: K232327
Trade/Device Name: Endorail
Regulation Number: 21 CFR 876.1500
Regulation Name: Endoscope And Accessories
Regulatory Class: Class II
Product Code: ODC
Dated: February 16, 2024
Received: February 16, 2024

Dear Fabio Pasquale:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Shanil P. Haugen -S

Shanil P. Haugen, Ph.D.
Assistant Director
DHT3A: Division of Renal, Gastrointestinal, Obesity and Transplant Devices
OHT3: Office of GastroRenal, ObGyn, General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K232327

Device Name
ENDORAIL

Indications for Use *(Describe)*
ENDORAIL is an accessory to an endoscope and is intended to ensure positioning of a standard endoscope (i.e., an endoscope with an instrument channel that is at least 3.7mm diameter and is used for standard endoscopic visualization) during endoscopy of the large intestine.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Section 8 – 510(k) Summary

(in accordance with 21 CFR 807.92)

510(k) Number:

I. Applicant Information

Applicant:

Endostart s.r.l.
Via delle Regioni 265
50052 Certaldo (FI)
ITALY

Contact Person:

Alessandro Tozzi
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Endostart s.r.l.
Tel: +39-0571-843-033
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Application Correspondent:

Fabio De Pasquale
Sr. Director QA/RA
QA & RA Medical Device Consulting, Ltd.
Tel: 1-250-920-6501
e-mail: qa.ra.meddev@outlook.com

Date Prepared: July 28, 2023

II. Subject Device Identification

Proprietary Name:	**ENDORAIL**
Classification Name:	Endoscope Channel Accessory
Regulation Name:	Endoscope and Accessories
Regulation Number:	21 CFR 876.1500
Product Code:	ODC
Regulatory Class:	Class II
Classification Panel:	Gastroenterology/Urology

III. Predicate Devices

The subject device, the **ENDORAIL**, is substantially equivalent to the following two cleared predicate devices. The subject and predicate device have the same fundamental scientific technology and intended use.

Primary Predicate Device (#1):

510(k) Number:	**K111760**
Proprietary Name:	**NaviAid BGC** (later renamed "NaviAid ABC")
Manufacturer Name:	Smart Medical Systems, Ltd.
Common/Usual Name:	NaviAid Balloon Guided Colonoscopy
Classification Name:	Endoscope Channel Accessory
Regulation Name:	Endoscope and Accessories
Regulation Number:	21 CFR 876.1500
Product Code:	ODC
Regulatory Class:	Class II
Classification Panel:	Gastroenterology/Urology

Predicate Device (#2):

510(k) Number:	**K183057**
Proprietary Name:	**PUMA-G System**
Manufacturer Name:	CoapTech LLC
Common/Usual Name:	Gastrointestinal Tube Accessory
Classification Name:	Tube, Gastro-Enterostomy
Regulation Name:	Gastrointestinal Tube and Accessories
Regulation Number:	21 CFR 876.5980
Product Code:	KGC
Regulatory Class:	Class II
Classification Panel:	Gastroenterology/Urology

IV. Subject Device Description

ENDORAIL is a colonoscopy add-on device developed to be used without any modification to colonoscopes and peripheral devices currently utilized. It is an accessory for colonoscopy aimed at facilitating progression of the endoscope in the large intestine. The device works as a magnetic anchor that allows the operator to guide the colonoscope and to straighten colon curves and loops.

ENDORAIL includes a Balloon Guide that can be introduced, when needed, through the endoscope instrument channel during the colonoscopy, if this procedure becomes challenging. The system does not require to be pre-mounted and does not interfere with the normal colon examination process. The Balloon Guide is advanced beyond the colonoscope tip where the balloon is filled with a ferromagnetic fluid and magnetically anchored to a magnetic Handpiece placed on the patient's abdomen. Once anchored, the colonoscope can be easily straightened and guided along the device, allowing a fast and safe inspection of the entire colon. Once the challenging segment of the colon is resolved, or the colonoscopy procedure is completed, the Balloon Guide can be retrieved.

As discussed in the following sections, the intended use, technological characteristics, principles of operation and materials of the subject device are substantially equivalent to the respective ones of the predicate devices.

V. Indications for Use

ENDORAIL is an accessory to an endoscope and is intended to ensure positioning of a standard endoscope (i.e., an endoscope with an instrument channel that is at least 3.7mm diameter and is used for standard endoscopic visualization) during endoscopy of the large intestine.

VI. Substantial Equivalence

Intended Use/Indications for Use

ENDORAIL and its Primary Predicate device have substantially equivalent Intended Use/Indications for Use, with the minor difference being that the primary predicate device is meant to facilitate positioning of standard endoscopes in both the small and large intestine, whereas **ENDORAIL** is meant to ensure positioning of standard endoscopes exclusively in the large intestine.

Technological Characteristics

The *Substantial Equivalence Comparison Table* provided in the following pages includes a comparison of each of the technological features of the **ENDORAIL** device with those of the primary predicate and the reference devices.

The following two main differences in technological characteristics between the subject and the predicate devices are summarized in the following sections.

The Primary Predicate device (**NaviAid BGC**) achieves its balloon anchoring function by inflating the balloon with air and stretching it beyond the diameter of the colon, whereas the subject **ENDORAIL** achieves its balloon anchoring function by filling the balloon with a ferromagnetic fluid in combination with the placement of a permanent magnet externally over the patient abdomen.

The magnetic anchoring of the **ENDORAIL** balloon functions in a similar fashion to the magnetic anchoring system utilized by the Reference device, the **PUMA-G System**, which is an accessory to enteral feeding tubes that enables ultrasound-based placement of percutaneous gastrostomy feeding tubes.

The following table summarizes the substantial equivalence comparison between the subject and the predicate devices.

Substantial Equivalence Comparison Table

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed "NaviAid ABC")	Reference Device (#2): (K183057) PUMA-G System
Product Code	ODC	ODC	KGC **(N/A)**
Regulation #	876.1500	876.1500	876.5980 **(N/A)**
Class	II	II	II
Intended Use	ENDORAIL is an accessory to an endoscope and is intended to ensure positioning of a standard endoscope (i.e., an endoscope that has an instrument channel that is at least 3.7mm diameter and is used for standard endoscopic visualization) during endoscopy of the large intestine.	The NaviAid BGC is an accessory to an endoscope and is intended to ensure positioning of a standard endoscope (i.e., an endoscope that has an instrument channel that is at least 3.7mm diameter and is used for standard endoscopic visualization) during endoscopy of the small and large intestine.	The new PUMA-G system is an accessory to enteral feeding tubes that enables ultrasound-based placement of percutaneous gastrostomy feeding tubes. **(N/A)**
Indications for Use	ENDORAIL is an accessory indicated for a fast and easy colonoscopy	The NaviAid BGC is an accessory indicated for fast and easy colonoscopy, ileoscopy and upper	The new PUMA-G system is an accessory to enteral feeding tubes that enables ultrasound-based

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed "NaviAid ABC")	Reference Device (#2): (K183057) PUMA-G System
	procedure with a standard endoscope. The device allows keeping all the advantages of an endoscopic procedure, such as back-and-forth navigation, real-time operation, video imaging, or the capability to stop propagation if needed, and to use an instrument channel for patient treatment as necessary.	enteroscopy procedures with a standard endoscope. The device allows keeping all the advantages of an endoscopic procedure, such as back-and-forth navigation, real-time operation, video imaging, or the capability to stop propagation if needed, and to use an instrument channel for patient treatment as necessary.	placement of percutaneous gastrostomy feeding tubes. **(N/A)**
Sterility and Reusability	The Balloon Catheter component of ENDORAIL is supplied as "non-sterile" and for "single-use".	The NaviAid BGC system is supplied as "non-Sterile" and for "single use".	The procedural kit (guidewire, balloon catheter and other accessories) is supplied as "sterile" and for "single-use".

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed "NaviAid ABC")	Reference Device (#2): (K183057) PUMA-G System
	The ENDORAIL Handpiece (external magnet) is supplied as "non-sterile" and "re-usable".		The External Magnet component is supplied as "non-sterile" and "re-usable".
Environment of Use	ENDORAIL is intended for use in hospitals or clinics by specialized medical staff.	The NaviAid BGC is for use in hospitals or clinics by specialized medical staff.	The PUMA-G system is for use in hospitals or clinics by specialized medical staff.
Limitations of Use	To be used during endoscopy of the large intestine only.	To be used during endoscopy of the small and large intestine.	None known.
Principles of Operation	ENDORAIL facilitates the advancement and placement of an intestinal endoscope. The system utilizes a specialized balloon, inserted in the endoscope using an inflation tube catheter, which is alternately inflated and deflated in order to	The NaviAid BGC facilitates the advancement and placement of an intestinal endoscope. The system utilizes a specialized balloon, inserted in the endoscope using an inflation tube catheter, which is alternately inflated and	The PUMA-G System facilitates feeding tube insertion that can be performed at a patient's bedside. The system relies on a balloon catheter containing a small magnetic needle that is fed through a patient's mouth and guided into the

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed "NaviAid ABC")	Reference Device (#2): (K183057) PUMA-G System
	allow the proper progression and to ensure a suitable positioning of the endoscope in the intestine. ENDORAIL uses a single disposable balloon. The balloon traverses ahead of the endoscope through the endoscope's instrument channel and thus it can be applied on demand without the need for a pre-procedure preparation of the device. The balloon is connected to a dedicated inflation tube that runs inside the instrument channel of the endoscope and is connected at its proximal (user) end to	deflated in order to allow the proper progression and to ensure a suitable positioning of the endoscope in the intestine. The NaviAid BGC uses a single disposable balloon. The balloon traverses ahead of the endoscope through the endoscope's instrument channel and thus it can be applied on demand without the need for a pre-procedure preparation of the device. The balloon is connected to a dedicated inflation tube that runs inside the instrument channel of the endoscope and is connected at its proximal	stomach using an external magnet. The balloon is made to be "grabbed" by an external magnet placed over the patient stomach. The balloon is inflated with saline and ultrasound guides the treating physician as they insert a needle through the stomach and into the balloon. The balloon catches a wire that is then pulled back up and out the mouth as the balloon is removed. A feeding tube can then be pushed back down over the wire and safely out the stomach.

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed "NaviAid ABC")	Reference Device (#2): (K183057) PUMA-G System
	an inflation/deflation system. The user manually operates and controls the inflation and deflation of the balloon through the inflation/deflation system. The balloon can be advanced ahead of the endoscope tip or pulled back through a pushing/pulling action on the inflation tube at its proximal end, outside the patient's body. The balloon and inflation tube do not compromise in a significant way the endoscope's flexibility, its field of view or the	(user) end to an inflation/deflation system. The user manually operates and controls the inflation and deflation of the balloon through the inflation/deflation system. The balloon can be advanced ahead of the endoscope tip or pulled back through a pushing/pulling action on the inflation tube at its proximal end, outside the patient's body. The balloon and inflation tube do not compromise in a significant way the endoscope's flexibility, its field of view or the	

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed "NaviAid ABC")	Reference Device (#2): (K183057) PUMA-G System
	manoeuvrability of its tip, and do not limit the usage of any standard endoscopy tools such as biopsy forceps, snare, needle etc. The balloon catheter system can be pulled back at any time during the procedure in order to allow use of therapy tools. When the balloon is advanced beyond the endoscope distal end, inflated and anchored, it behaves as a distal "anchor" towards which the endoscope tip is advanced. Endoscope advancement is thus performed using the inflation tube as a guide wire, allowing the endoscope to be more	manoeuvrability of its tip, and do not limit the usage of any standard endoscopy tools such as biopsy forceps, snare, needle etc. The balloon catheter system can be pulled back at any time during the procedure in order to allow use of therapy tools. When the balloon is advanced beyond the endoscope distal end, inflated and anchored, it behaves as a distal "anchor" towards which the endoscope tip is advanced. Endoscope advancement is thus performed using the inflation tube as a guide wire, allowing the	

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed "NaviAid ABC")	Reference Device (#2): (K183057) PUMA-G System
	easily guided through the straightened curves and loops of the colon. The ENDORAIL balloon is filled with a magnetorheological ferromagnetic fluid composed of solid micrometric carbonyl iron powder dispersed in a water solution of Sodium Chloride and Sodium Citrate, by means of a syringe. The balloon is inflated with a ferromagnetic fluid and "anchored" to the colon wall.	endoscope to be more easily guided through the straightened curves and loops of the colon. The NaviAid BGC balloon is filled with ambient air using an air supply unit and control pump. The balloon is inflated with air increasing the balloon volume until its diameter is enough large to fill the entire intestine lumen.	The PUMA-G balloon is filled with saline solution using a syringe. The balloon is inflated with saline solution and "anchored" to the stomach wall.

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed "NaviAid ABC")	Reference Device (#2): (K183057) PUMA-G System
	The "anchoring" of the balloon is ensured by magnetic force using an external magnet over the patient abdomen in correspondence of the balloon. The anchoring of the balloon allows the straightening of the colon curves and loops, facilitating the endoscope progression.	The "anchoring" of the balloon is ensured by the friction force exerted by the filled balloon against the intestine wall. The anchoring of the balloon allows the straightening of the colon curves and loops, facilitating the endoscope progression.	The "anchoring" of the balloon is ensured by magnetic force using an external magnet over the patient abdomen in correspondence of the balloon.
Orifice of Use	The ENDORAIL catheter is passed via the colonoscope through anus into the colon.	The NaviAid BGC catheter is passed via the colonoscope through anus into the colon.	The PUMA-G catheter is passed through the mouth into the stomach of the patient. **(N/A)**
Balloon Inflation/Deflation Mechanism	The user may manually operate and control the inflation and deflation of	The user may manually operate and control the inflation and deflation of	The user may manually operate and control the inflation and deflation of

Comparison Elements	Subject Device: ENDORAIL	Primary Predicate Device (#1): (K111760) NaviAid BGC (renamed “NaviAid ABC”)	Reference Device (#2): (K183057) PUMA-G System
	the balloon through the syringe.	the balloon through the power air supply/foot pedal control system. **(N/A)**	the balloon through the syringe.

VII. Non-Clinical Performance Data

Endostart s.r.l. has conducted extensive verification and validation testing of **ENDORAIL**, as an accessory for colonoscopy capable of facilitating progression of the endoscope in the large intestine. The subject device was tested to ensure that it can provide all the capabilities necessary to operate safely and effectively.

Acceptance criteria have been established to ensure that the subject device performs in a manner that is substantially equivalent to the cited predicate devices. Testing was conducted to verify the safety and performance requirements of the subject device and the test results support substantial equivalence to the predicate devices. The following table lists the nonclinical tests performed on the subject **ENDORAIL** for a determination of substantial equivalence.

ENDORAIL – Non-Clinical Tests Performed
Biocompatibility Testing
Electrical Safety Testing
Electromagnetic Compatibility Testing
Software Verification and Validation Testing
Mechanical Testing
Components Testing
Human Factors Validation Testing
Microbiological Bioburden Testing
Shelf Life and Stability Testing
Packaging Testing
Environmental Conditioning and Shipping Testing
Characterization and Functional Testing

ENDORAIL complies with all the applicable voluntary recognized standards related to its regulations and product code and successfully passed all respective testing.

The following guidance documents and standards were followed to determine appropriate methods for evaluating the performance of the subject device.

Guidance Documents and Recognized Standards Applicable to ENDORAIL	
Standard/Guidance	**Title**
FDA Guidance	Design Control Guidance for Medical Device Manufacturers
FDA Guidance	Format for Traditional and Abbreviated 510(k)s
FDA Guidance	The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]
FDA Guidance	Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions

Guidance Documents and Recognized Standards Applicable to ENDORAIL	
Standard/Guidance	**Title**
FDA Guidance	Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"
FDA Guidance	General Principles of Software Validation
FDA Guidance	Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices
FDA Guidance	Content of Premarket Submissions for Device Software Functions
FDA Guidance	Applying Human Factors and Usability Engineering to Medical Devices
FDA Guidance	Content of Human Factors Information in Medical Device Marketing Submissions [Draft]
FDA Guidance	Acceptance of Clinical Data to Support Medical Device Applications and Submissions: Frequently Asked Questions
FDA Guidance	Shelf-life of Medical Devices
FDA Guidance	Device Labeling Guidance #G91-1 (Blue Book Memo)
FDA Guidance	Testing and Labeling Medical Devices for Safety in the Magnetic Resonance (MR) Environment
FDA Guidance	Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex
FDA Guidance	Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices
FDA Guidance	Refuse to Accept Policy for 510(k)s
FDA Guidance	Financial Disclosure by Clinical Investigators
FDA Guidance	eCopy Program for Medical Device Submissions
ANSI AAMI ES60601-1:2005/(R)2012 & A1:2012, C1:2009/(R)2012 & A2:2010/(R)2012	Medical Electrical Equipment - Medical Electrical Equipment - Part 1: General Requirements for Basic Safety and Essential Performance
ANSI AAMI IEC 60601-1-2:2014	Medical Electrical Equipment – Part 1-2: General Requirements for Basic Safety and Essential Performance – Collateral Standard: Electromagnetic Disturbances – Requirements and Tests
IEC/TR 60601-4-2 Edition 1.0 2016-05	Medical electrical equipment - Part 4-2: Guidance and interpretation - Electromagnetic immunity: performance of medical electrical equipment and medical electrical systems
IEC 60601-1-6 Edition 3.2 2020-07	Medical Electrical Equipment-Part 1-6: General Requirements for Basic Safety and Essential Performance – Collateral Standard: Usability
ANSI AAMI IEC 62304:2006/A1:2016	Medical device software – Software Life Cycle Processes
ANSI AAMI IEC 62366-1:2015+AMD1:2020 (Consolidated Text)	Medical Devices – Part 1: Application of Usability Engineering to Medical Devices
ISO 10993-1 Fifth edition 2018-08	Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing within a Risk Management Process

Guidance Documents and Recognized Standards Applicable to ENDORAIL	
Standard/Guidance	**Title**
ISO 10993-2 Second edition 2006-07-15	Biological evaluation of Medical devices Part 2: Animal welfare requirements
ISO 10993-5 Third edition 2009-06-01	Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity
ISO 10993-10 Fourth edition 2021-11	Biological evaluation of medical devices - Part 10: Tests for skin sensitization
ISO 10993-11 Third edition 2017-09	Biological evaluation of medical devices - Part 11: Tests for systemic toxicity
ISO 10993-12 Fifth edition 2021-01	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials
ISO 10993-23 First edition 2021-01	Biological evaluation of medical devices - Part 23: Tests for irritation
ISO 20695 First edition 2020-03	Enteral feeding systems - Design and testing
ASTM F2528-06 (Reapproved 2014)	Standard Test Methods for Enteral Feeding Devices with a Retention Balloon
ISO 80369-7 Second edition 2021-05	Small-bore connectors for liquids and gases in healthcare applications - Part 7: Connectors for intravascular or hypodermic applications
ISO 11737-1 Third edition 2018-01	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on product
ISO 7886-1 Second edition 2017-05	Sterile hypodermic syringes for single use - Part 1: Syringes for manual use
ISO 20696 First edition 2018-06; Corrected 2019-12	Sterile urethral catheters for single use
ASTM F1886/F1886M-16	Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection
ASTM F1929-15	Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration – Method B
ASTM F88/F88M-21	Standard Test Method for Seal Strength of Flexible Barrier Materials
ASTM D4332-14	Standard Practice for Conditioning Containers, Packages, Or Packaging Components For Testing
ASTM F1980-21	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
ASTM D4169-22	Standard Practice for Performance Testing of Shipping Containers and Systems
The United States Pharmacopeia (USP) and National Formulary (NF) USP 42–NF 37; M98900_01_01	<151> Pyrogen Test (USP Rabbit Test)
ISO 14155 Third edition 2020-07	Clinical investigation of medical devices for human subjects - Good clinical practice

Guidance Documents and Recognized Standards Applicable to ENDORAIL	
Standard/Guidance	**Title**
ISO 15223-1 Fourth edition 2021-07	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements
ISO 20417 First edition 2021-04 Corrected version 2021-12	Medical devices - Information to be supplied by the manufacturer
ISO 14971 Third Edition 2019-12	Medical Devices – Application of Risk Management To Medical Devices

VIII. Clinical Performance Data

Clinical validation testing was conducted with **ENDORAIL** to confirm the safety and effectiveness of the device. A summary of the design of the Multicenter Post-Market Single Arm Open Label Interventional Study performed, together with a summary of the key results, are provided below. The following table summarizes the main elements of the study.

Title	Multicentre Clinical Trial for the evaluation of the safety and effectiveness of ENDORAIL in patients with long-lasting colonoscopy
Short Title	ENDORAIL Clinical Study
Study Type	Multicentre post-market single arm open label interventional study
Trial centres	1. **IRCCS Humanitas Research Hospital** Via Manzoni 56, I-20089 Rozzano (Milan, Italy) (Principal Investigator: Prof. Alessandro Repici) 2. **GastroZentrum Lippe** Lange Str 55 32105 Bad Salzuflen (Germany) affiliated with **Universität Mainz** Langenbeck Street 1, D-55131 Mainz (Germany) (Principal Investigator: Prof. Helmut Neumann) 3. **University Hospitals Leuwen** Herestraat 49, B-3000 Leuwen (Belgium) (Principal Investigator: Prof. Raf Bisschops)
Sponsor / Manufacturer	Endostart s.r.l., Via delle Regioni 265, 50052 Certaldo (FI), ITALY
Trial period **(first subject in-last subject out)**	First Patient In: 24 January 2023; Last Patient In: 17 May 2023; Last Patient Last Visit: 24 May 2023.

Background

This Multicenter Post-Market Single Arm Open Label Interventional Study was intended to expand the clinical knowledge in support of the safety and efficacy of the ENDORAIL device.

Reported incomplete colonoscopy rates range from 4% to 25% of all screened patients. However, while international guidelines recommend a rate of less than 10% for diagnostic colonoscopies, the risk is at least 20% in the more challenging subset of patients characterized by long-lasting procedures.

A colonoscopy can be defined as “long-lasting” when caecal intubation time is longer than 10 minutes. As data from literature shows that about 80% of all diagnostic colonoscopies are typically completed in less than 10 minutes, the long-lasting colonoscopy subset represents approx. 20% of the total procedures. Indeed, since virtually all incomplete colonoscopies are also long-lasting, the risk of incompleteness in this subset of patients increases nearly five-fold (i.e., for a 5X increase, the lower bound of the rate increases from 4% to 20%).

ENDORAIL is intended to facilitate the positioning of a standard colonoscope. One of the main advantages of this system is that it can be used “as needed” during the procedure to prevent incomplete procedures without requiring any “preloading” ahead of time. This makes ENDORAIL particularly indicated for patients in which caecal intubation time gets longer and the risk of incompletion increases.

The aim of this study is to test the efficacy of ENDORAIL in ensuring low incompletion rate in long-lasting colonoscopies.

Primary Objectives

Efficacy (Timeframe: day 1)

To validate the efficacy of ENDORAIL in long-lasting colonoscopies by reaching a colonoscopy incompletion rate ≤ 10%.

Safety (Timeframe: day 1 to day 7)

To validate the safety of ENDORAIL in long-lasting colonoscopies, by demonstrating that colonoscopy serious adverse events (SAEs) are not increased using the device (i.e., absence of any device-related SAEs).

Methodology

Multicentre, post-marketing, single-arm, open-label, interventional study: Outpatients of either sex aged between 22-75 years (inclusive), undergoing elective colonoscopy for diagnostic or surveillance procedure, who signed a written ICF and presenting caecal intubation time greater than 10 minutes, took part in the study.

The study plan included: a Screening/Baseline/Treatment visit (Visit 1/Day 1), during which colonoscopy with ENDORAIL was performed; and a phone follow-up visit (Visit 2), scheduled at 7 (± 1) days post-treatment with ENDORAIL.

Sample Size Determination

Efficacy (first primary objective) is assessed by measuring the colonoscopy completion rate in long-lasting procedures, which is a measurable parameter of clinical value recognized by international medical societies. Safety (second primary objective) is assessed by measuring the rate of adverse events. Adverse events are classified into four groups: serious gastrointestinal events; myocardial infarction; stroke; and pneumonia. Based on the data from the literature; the adverse events occurrence rates for those 4 groups, for screening or surveillance colonoscopy, are 47, 4, 7 and 10 patients per 100,000, respectively.

These two objectives are merged in one indicator for each subject, which is either equal to 1 if the procedure is incomplete or an adverse event occurs, or equal to 0 otherwise.

The non-completion rate of long-lasting colonoscopies conducted with ENDORAIL is expected to be around 10%. This will be compared to the above-mentioned threshold of 20% for incomplete procedures. It should be noted that this threshold is conservative and represents the most critical setting for comparison with respect to the state of the art, as it is derived from the lower bound of the range from the literature.

When including the safety to provide the expected value of the indicator for ENDORAIL and the corresponding threshold, the above values of 10% minimally change, as the adverse event occurrence rate is 0.068% (given by the sum of the occurrence of the 4 events reported above per 100,000 persons, expressed in percentage).

With a significance level α of 5%, assuming a proportion of outcome of 10.1%, 85 patients allow to test with a power of 80% the H0: $p \geq 20\%$ vs H1: $p < 20\%$, where 20% is the estimated percentage of incomplete procedure from literature.

The chosen number is then increased by the 10% to account for possible drop-out (e.g., cases to be discarded, losses to follow-up, etc.), resulting in 85/0.90 = 95 patients to be actually enrolled.

Inclusion and Exclusion Criteria

Inclusion Criteria

1. Patients of both sexes aged between 22 – 75 years (inclusive).
2. Outpatients undergoing long-lasting diagnostic or surveillance colonoscopy. A long-lasting colonoscopy is defined as follows: colonoscopy completion (caecal intubation) not achieved after 10 minutes from endoscope insertion through the anal canal.
3. Patients have signed a written informed consent form (ICF) for participation in the study at the time of enrolment or before.
4. Patients able to understand the full nature and the purpose of the investigation, including possible risks and side effects, able to cooperate with the Investigator and to

comply with the requirements of the entire investigation based on Investigator's judgement.

Exclusion Criteria

1. Body mass index (BMI) > 30 kg/m².
2. Outpatients undergoing colonoscopy for colorectal cancer screening or therapeutic indication.
3. Patients in class >2 physical status of the classification system of American Society of Anaesthesiologists.
4. Any contraindication to colonoscopy.
5. Any contraindication to sedation.
6. Known allergy or hypersensitivity to any of the elements of the Endorail Set (e.g.: iron).
7. Patients with permanently or semi-permanently implanted medical devices (e.g., orthopaedic implants, trauma fixation devices, cardiac pacemakers, implantable cardioverter defibrillator, drug pumps, neurostimulators, vascular stents, cochlear implants, aneurysm clip).
8. Presence of dense diverticulosis.
9. Presence of diverticulitis.
10. Presence of ferromagnetic foreign body.
11. Presence of large abdominal hernias.
12. Urgent colonoscopy.
13. Presence of severe thrombocytopenia.
14. Presence of severe granulocytopenia.
15. Presence of severe coagulopathy.
16. Presence of peritonitis.
17. Presence of colonic wall ischemia or necrosis or injured mucosa.
18. Presence of peritoneal carcinomatosis.
19. Boston Bowel Preparation Scale <2 in at least one of the colonic segments.
20. Presence of obstructing masses and strictures of the colon.
21. History of total or subtotal colectomy.
22. Presence of angulated and fixed colon curves.
23. Pregnant or breast-feeding women.
24. Patient unable to provide the signed ICF, uncooperative patient or patient unlikely to comply with the protocol or unable to understand the nature, scope, and possible consequences of the study.
25. Presence of any other reason that, in the opinion of the Investigator, could prevent the subject from participating in the study or compromise the subject safety.
26. Concomitant participation in other clinical investigations or participation in the evaluation of any investigational product/device in the 30 days before this study or previous participation in the same investigation.

Test Device

ENDORAIL (Endostart s.r.l., Certaldo, Firenze, Italy).

Duration of Treatment

One single procedure (long-lasting diagnostic or surveillance colonoscopy).

Concomitant Treatments

Permitted Treatments:

Participants were allowed to use any concomitant medication necessary for the treatment of pre-existing concomitant pathologies or for intercurrent diseases, if they do not interfere with the parameters under investigation. Sedation was performed by an anaesthesiologist or an endoscopist according to standard of care.

Non-Permitted Treatments:

No prohibited concomitant treatments were defined.

Endpoints

Primary Efficacy Endpoint:

The primary efficacy endpoint was ≤ 10% of incomplete long-lasting colonoscopies (colonoscopy was defined as complete when caecal intubation was achieved).

Primary Safety Endpoint:

The primary safety objective was to validate the safety of ENDORAIL in long-lasting colonoscopies by demonstrating that colonoscopy SAEs are not increased using the device (i.e., the lack of any device-related SAEs). The assessed AEs were:

- general AEs and medical device incidents, and
- specific AEs: gastrointestinal (GI) bleedings, intestinal perforation, mucosal petechiae and abdominal pain.

Secondary Endpoints:

None defined.

Statistical Analysis

A total of thirty-eight (38) patients were enrolled into the study, underwent the colonoscopy procedure with ENDORAIL, and were included in the statistical analysis. As discussed in the Sample Size Determination section, a first interim analysis was planned once 40% of the total sample size (i.e., 38 patients) was reached. At this first interim analysis, the statistical significance of sample was tested and was found to be sufficient, at which, time per protocol, the trial was terminated. A total of 38 patients was therefore considered for the interim analysis.

Thirty-six (36) out of thirty-eight (38) enrolled patients (94.7%) were successfully contacted for

a phone follow-up visit, which was scheduled 7 ± 1 days after treatment. The remaining two (2) patients (i.e., 5.3%) resulted unreachable and were considered lost to follow-up. A total of 38 patients were therefore considered for the interim analysis.

The great majority of patients was enrolled in two (2) out of the three (3) study sites, as follows: 21 patients (55.3%) were enrolled at the Italian site (Milan) managed by Prof. Alessandro Repici, and 15 patients (39.5%) were enrolled at the German site (Bad Salzuflen) managed by Prof. Helmut Neumann. The remaining 2 patients (5.3%) were enrolled at the Belgian site (Leuwen) managed by Prof. Raf Bisschops.

The populations included in the analysis were the following:

Screening Set –The screening set included all patients who had signed the ICF and had been screened for inclusion in the study. Thirty-eight (38) patients were included in this population.

Intent-to-Treat (ITT) – The ITT population included all enrolled patients who underwent treatment with ENDORAIL. All 38 patients were included in this population.

Per-Protocol (PP) – The PP population included all patients of the ITT population who also met all inclusion/exclusion criteria. Again, all 38 enrolled patients were included in the PP population.

In conclusion, the three populations defined above resulted to be identical.

Analyses

The statistical analysis plan was finalized before the Data Base Lock and it included a more technical and detailed description of the statistical analyses summarized in this section.

All data collected in this study, and documented in the eCRFs, were listed and summarized (as appropriate):

- for quantitative variables: standard quantitative statistics (N, mean, standard deviation, median, interquartile range, minimum and maximum)
- for qualitative variables: frequency distribution [number of non-missing observations (N) and percentages (%)].

The analysis plan provided:

- Analysis of baseline characteristics for all population. Baseline characteristics included demographic data, medical history, vital signs, and physical examination.
- Analysis of endpoints for all population. This analysis included:
    - analysis of the efficacy of ENDORAIL, considering the successful completion of the colonoscopy; and
    - analysis of the safety of ENDORAIL regarding intraprocedural adverse events.
- Analysis of follow-up data for all population, regarding adverse events (AEs) and device deficiencies.

A statistical test was planned to assess the significant difference of the indicator with respect to the threshold and statistically prove efficacy of ENDORAIL in long-lasting procedures. Due to the type of variable, the exact binomial test was adopted. Additionally, considering as alternative hypothesis that the rate observed in the analysed population is less than the respective threshold, the one-tailed test was adopted.

Medical AEs and medical device AEs were collected during the study.

The number of AEs – related or not-related to the medical device – and the number and proportion of patients with at least one AE were assessed.

All AEs were tabulated by System Organ Class (SOC) and Preferred Term (PT) after medical coding using the Medical Dictionary for Regulatory Activities (MedDRA) thesaurus version 24.1. The primary SOC and the PT were used for the analysis of the frequency distribution.

The frequency of occurrence of specific AEs (gastrointestinal bleedings, intestinal perforation, mucosal petechiae, abdominal pain) were assessed by means of default descriptive statistics.

The statistical analyses were carried out using R Statistical Software (Foundation for Statistical Computing, Vienna, Austria).

Conclusions about the Study Hypothesis

This study was designed to test the null hypothesis that the proportion of “event” (intended as procedure incomplete or serious adverse event) is equal or greater than 20%. The alternative hypothesis is that the proportion of “event” is less than 20%.

The interim analysis was performed to allow the termination of the study in advance if significance was found for the first 38 enrolled patients.

The observed events were 0 out of 38 patients: the exact binomial one-tailed test shows a 95% confidence interval of 0% (95%CI: 0% - 7.6%) with a p-value <0.001. The observed percentage of events was significantly under the pre-specified threshold of 20%.

Results: The principal safety and effectiveness results from the Multicenter clinical trial for the evaluation of safety and effectiveness of **ENDORAIL** in patients with long-lasting colonoscopy are presented below.

Efficacy Results: all patients enrolled into the clinical study successfully completed the colonoscopy with **ENDORAIL** and no patient needed to interrupt the diagnostic procedure or to be withdrawn from the study for any reason. More importantly, in all the patients (100%) the endoscopist could reach and fully inspect the last segment of the colon called caecum. In conclusion, the study results have achieved the primary efficacy endpoint, which was to validate the efficacy of **ENDORAIL** in long-lasting colonoscopies by reaching a colonoscopy incompletion rate ≤ 10%. In fact, the recorded coloscopy incompletion rate over the entire **ENDORAIL** study was 0%.

Safety Results: this clinical study was also conducted to assess the safety of **ENDORAIL** in long-lasting colonoscopies. No AE/SAE, no abnormal findings,

and no overall change in the health status of any patient undergoing the colonoscopy with **ENDORAIL** were observed in the course of the clinical study. The study has therefore successfully achieved the primary safety objective, which was to validate the safety of **ENDORAIL** in long-lasting colonoscopies by demonstrating that colonoscopy SAEs are not increased by using this investigational device (i.e., absence of any device-related SAEs).

Conclusions: The **ENDORAIL** study was aimed at testing the safety and efficacy of the device in ensuring a low incompletion rate in long-lasting colonoscopies. The multicenter clinical trial for the evaluation of safety and effectiveness of **ENDORAIL** in patients with long-lasting colonoscopy confirmed that **ENDORAIL** is safe and effective for its intended use.

IX. Statement of Substantial Equivalence

Based on substantially equivalent intended use, technological characteristics and the safety and performance of non-clinical and clinical testing, the **ENDORAIL** is deemed to be substantially equivalent to its primary predicate device, the **NaviAid BGC** (subsequently renamed as “NaviAid ABC”) cleared under K111760.

The **ENDORAIL**, as designed and manufactured, does not raise new questions regarding safety and effectiveness as compared to its predicate device and is concluded to be substantially equivalent to its predicate device.