

**DE NOVO CLASSIFICATION REQUEST FOR
ECHO TIP® INSIGHT™ PORTOSYSTEMIC PRESSURE GRADIENT MEASUREMENT SYSTEM**

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Endoscopic transhepatic venous access needle. An endoscopic transhepatic venous access needle is inserted through the liver into the patient's portal/hepatic venous system under endoscopic ultrasound guidance. It is connected to a separate device intended to measure a physiological parameter.

NEW REGULATION NUMBER: 21 CFR 876.1050

CLASSIFICATION: Class II

PRODUCT CODE: QIJ

BACKGROUND

DEVICE NAME: EchoTip® Insight™ Portosystemic Pressure Gradient Measurement System

SUBMISSION NUMBER: DEN180062

DATE DE NOVO RECEIVED: November 19, 2018

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INDICATIONS FOR USE

The EchoTip® Insight™ Portosystemic Pressure Gradient Measurement System is indicated to directly measure pressures in the hepatic and portal venous vasculatures and is used in conjunction with an ultrasound endoscope.

LIMITATIONS

The sale, distribution, and use of the EchoTip® Insight™ Portosystemic Pressure Gradient Measurement System are restricted to prescription use in accordance with 21 CFR 801.109.

The device is not intended for uses other than that described in the labeling.

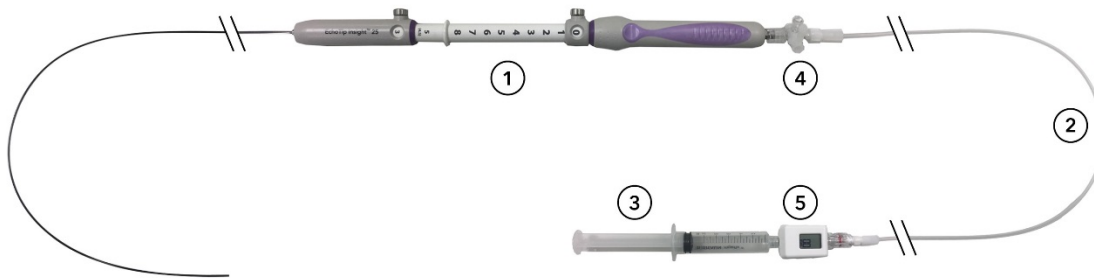
PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The EchoTip® Insight™ Portosystemic Pressure Gradient Measurement System is a system used to provide endoscopic access to the portal and hepatic veins to measure local blood pressure.

As shown in Figure 1, the system is composed of:

1. EchoTip Insight Endoscopic Ultrasound Needle
2. Connecting Tube
3. 10 mL syringe
4. Stopcock
5. Compass CT Pressure Transducer (K133624).



| | | |
|-----------------------------|------------------------------------|------------|
| 1. EchoTip® Insight™ Needle | 2. Connecting Tube | 3. Syringe |
| 4. Stopcock | 5. Compass® CT Pressure Transducer | |

Figure 1. EchoTip Insight needle, with Connecting Tube and Compass CT transducer

The EchoTip® Insight™ Needle functions to provide access to the venous vasculature related to the portal circulation and hepatic outflow to facilitate the measurement of physiological pressure by the Compass® CT pressure transducer, a disposable manometer (cleared under K133624).

The needle is enclosed within a 5.2 Fr. outer sheath for protection. The sheath has an adjustable length (0-5 cm) to allow the user to adjust for the working length of the endoscope. The sheath length extension lock ring allows the sheath to be secured in place by tightening the thumbscrew.

The needle extension is also adjustable and ranges from 0-8 cm. The “zero” reference ensures complete needle retraction within the sheath. The handle has a safety ring that slides and locks using the thumbscrew at the desired needle extension.

The Connecting Tube is used for the transfer of liquids (heparinized saline) between the

EchoTip® Insight™ Needle and the Compass® CT pressure transducer. The Connecting Tube uses a female Luer lock to connect to the Compass CT pressure transducer, and a male Luer lock to connect to the stopcock. The Compass CT is a disposable, point-of-use blood pressure measurement and monitoring device that incorporates an embedded pressure sensor and an integrated, pre-programmed diagnostic computer chip with a liquid crystal display.

Once the system is connected and primed with heparinized saline, the EchoTip® Insight™ Needle is passed through the accessory channel of an ultrasound endoscope and the needle is advanced to the desired vasculature (portal or hepatic vein) through the liver parenchyma. Using ultrasound guidance, the needle is placed at the desired location, allowed to stabilize, and a measurement reading is taken.

Table 1 provides a technological description of the device.

Table 1. Description of Technology for the EchoTip Insight Portosystemic Pressure Gradient Measurement System.

| Device Component | Attribute |
|--------------------------------|--|
| Needle | 25 gauge 0-8 cm length Beveled tip Stainless steel Echogenic texturing |
| Sheath | 5 Fr. 142 cm 0-5 cm adjustable length Polyetheretherketone (PEEK) Material |
| Handle | Proximal female luer Sheath and needle adjustment controls |
| Connectors | Luer connection |
| Access/visualization technique | Manually advanced through the working channel (2.8 mm) of an ultrasound endoscope under ultrasound visualization |

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Connecting Tube, stopcock, and syringe are externally communicating devices with indirect contact with blood for a limited (≤ 24 hrs) duration. As such, the following tests are expected: Cytotoxicity, Sensitization, Irritation, Acute systemic toxicity, material mediated pyrogenicity, hemocompatibility. The EchoTip Insight needle is categorized as an externally communicating device in direct contact with circulating blood for a limited (≤ 24 hrs) duration. As such, the same tests were expected, with the addition of genotoxicity. The device system therefore, has components that have direct and indirect

patient contact. All device components were evaluated according to the [FDA guidance](#) (2016), “Use of International Standard ISO 10993-1, Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process,” and the ISO 10993-4:2017, “Biological evaluation of medical devices – Part 4: Selection of tests for interactions with blood.” From the evaluations and supporting information, the components of the device were found to be biocompatible for its use.

SHELF LIFE/STERILITY

The EchoTip® Insight™ Portosystemic Pressure Gradient Measurement System is a sterile, single use system. All device components are single use devices provided sterile to the end user. Device components in contact with blood were also tested for pyrogenicity using the LAL (*Limulus Amebocyte* Lysate test).

Sterilization methods for the EchoTip Insight needle and Connecting Tube have been validated in accordance with ISO 11135-1:2007 “Sterilization of Health Care Products- Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices,” to ensure a sterility assurance level of 10^{-6} before the device is marketed.

Accelerated aging to support a 3-year shelf life was performed for the EO sterilized EchoTip Insight needle and Connecting Tube per ASTM F1980-07, Standard Guidance for Accelerated Aging of Sterile Medical Device Packages. The expiration date of 3 years was verified by demonstrating package integrity through dye penetration and burst testing on the stored products.

PERFORMANCE TESTING - BENCH

Non-clinical performance data was generated to mitigate the risk associated with the failure of the device components and/or materials. The following tests were conducted and passed: needle crumple testing, tensile strength testing, product integrity testing for Connecting Tube, dimensional verification for needle and Connecting Tube, package integrity testing on all device components post distribution, and design verification/validation testing.

A simulated use test was performed to measure pressures of known values. The simulated use testing consisted of design verification and validation of the EchoTip Insight Portosystemic Pressure Gradient Measuring System. After passing the device through an echoendoscope, the device was tested for its ability to measure three known pressures, which were created by filling a column of liquid at three different points. A statistically significant number of distinct needle devices, connecting tubes, and Compass CT transducers were tested, and the ability of an end user to accomplish each of the tasks conducted to obtain a pressure measurement under simulated use conditions was verified.

PERFORMANCE TESTING – ANIMAL TESTING

The EchoTip® Insight™ Portosystemic Pressure Gradient Measurement System was compared versus the standard trans-jugular approach, in which an indirect portal/hepatic pressure is obtained with the use of a balloon catheter¹. In this study, 17 pressure measurements were carried out in three swine at baseline, and then following induction of portal hypertension (PH) by rapid peripheral infusion of Dextran-40. Manometric data were obtained using an interventional radiologic (IR) trans-jugular balloon catheter tip from the right hepatic vein (both free and wedged pressures) and then using the subject device to obtain pressure gradients of the portal and hepatic veins. The correlation between the 2 methods of measurement was charted in scatter plots, and the Pearson's correlation coefficient (R) was calculated. Among other measurements, the authors calculated the correlation of 17 paired manometric data points from Wedge Hepatic Venous Pressure (WHVP) using the transjugular method, and Portal Venous Pressure (PV) using the subject device. There was excellent correlation between the subject device and transjugular approach at all pressure ranges. The authors calculated a Pearson's correlation coefficient of 0.999 for all vessels, 0.985 for all veins, 0.988 for PV and WHVP, and 0.986 for free HV pressure.

¹ Huang, J., Samarasena, J., Tsujino, T., Chang, K. EUS Guided portal pressure gradient measurement with a novel 25-gauge needle device versus standard transjugular approach: A comparison animal study. *Gastrointestinal Endoscopy*, 2016 Aug; 84(2), p. 358-362.

SUMMARY OF CLINICAL INFORMATION

A published clinical study² was provided to FDA as confirmatory evidence that the device could safely measure portal pressure gradient (PPG) (i.e the difference between hepatic and portal vein pressures). In this single center study, PPG was determined in 28 patients. Of these patients, 19 patients had clinical signs or symptoms that were highly suspicious of cirrhosis. The study excluded pregnant women, patients at risk of bleeding (International Normalized Ratio > 1.5, platelet count < 50 X 10⁹ /L), patients with active gastrointestinal bleeding, and patients with post sinusoidal portal hypertension.

No patient experienced intraprocedural or postprocedural adverse events. Specifically, no patient developed bleeding, perforation, infection, or complained of pain.

²Huang, J., Samarasena, J., Tsujino, T., Lee, J., Hu, K., McLaren, C., Chen, W., Chang, K. EUS Guided portal pressure gradient measurement with a simple novel device: a human pilot study. *Gastrointestinal Endoscopy*, 2017 May; 85(5), p. 996-1001.

Pediatric Extrapolation

In this De Novo request, existing clinical information was not leveraged to support the use of the device in a pediatric patient population.

LABELING

Labeling has been provided that includes instructions for use and an appropriate prescription statement as required by 21 CFR 801.109. The labeling includes:

- Instructions for Use Manual: The manual is the primary labeling material for the device. It provides information about the device and its components, indications, contraindications, precautions, warnings, possible adverse reactions, device functions, and guidelines for use. The manual includes instructions and diagrams that explain the steps to prepare the device for use prior to use and explains the steps to measure hepatic and portal venous pressures.
- Package Label: This provides sizing information, manufacturer information, a shelf life and product summary.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of the endoscopic transhepatic venous access needle and the measures necessary to mitigate these risks.

Table 2: Identified Risks to Health and Mitigation Measures

| Identified Risk | Mitigation Measures |
|--|---|
| Adverse tissue reaction | Biocompatibility testing Pyrogenicity testing |
| Infection | Sterilization validation Pyrogenicity testing Shelf life testing Package integrity testing |
| Use error leading to: <ul style="list-style-type: none">• Access site hemorrhage/thrombosis• Portal vein penetration leading to intrahepatic bleeding | Labeling |
| Improper patient management due to inaccurate measurement | Non-clinical performance testing Labeling |

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the endoscopic transhepatic venous access needle is subject to the following special controls:

1. The patient-contacting components of the device must be demonstrated to be biocompatible.
2. Performance data must demonstrate the sterility of the patient-contacting components of the device.

3. The patient-contacting components of the device must be demonstrated to be non-pyrogenic.
4. Performance testing must support the shelf life of device components provided sterile by demonstrating continued sterility and package integrity over the labeled shelf life.
5. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following must be tested:
 - a. Needle crumple testing;
 - b. Tensile testing;
 - c. Dimensional verification for all components; and
 - d. Simulated use testing.
6. Labeling must include the following:
 - a. Instructions for use, including specific instructions regarding device preparation;
 - b. The recommended training for safe use of the device; and
 - c. A shelf life for any sterile components.

BENEFIT-RISK DETERMINATION

The probable risks of the device include the risks associated with an endoscopic ultrasound procedure, adverse tissue reactions, infection, use error such as those leading to hemorrhage/thrombosis, portal vein penetration leading to intrahepatic bleeding and improper patient management due to inaccurate pressure measurement.

Based on the available performance data, the probability of such harmful events is low, and the incidence is reduced with the mitigation measures and special controls identified above.

The probable benefits of the device include direct measurement of both portal and hepatic venous pressures, without risks associated with trans jugular measurements, which include bleeding from the jugular puncture site, cardiac arrhythmias, and exposure to radiation and contrast agents.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

The EchoTip® Insight™ Portosystemic Pressure Gradient Measurement System is indicated to directly measure pressures in the hepatic and portal venous vasculatures and is used in conjunction with an ultrasound endoscope.

The probable benefits outweigh the probable risks for this device. The device provides benefits

and the risks can be mitigated using general controls and the identified special controls.

CONCLUSION

The De Novo request for the EchoTip® Insight™ Portosystemic Pressure Gradient Measurement System is granted and the device is classified as follows:

Product Code: QIJ

Device Type: Endoscopic transhepatic venous access needle

Regulation Number: 21 CFR 876.1050

Class: II