DE NOVO CLASSIFICATION REQUEST FOR BRAINTEMP NEONATE SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Brain temperature measurement system. A brain temperature measurement system is an externally placed, prescription device intended to measure brain temperature.

NEW REGULATION NUMBER: 21 CFR 882.1565

CLASSIFICATION: Class II

PRODUCT CODE: QSL

BACKGROUND

DEVICE NAME: BrainTemp Neonate (BTNeo) System

SUBMISSION NUMBER: DEN200042

DATE DE NOVO RECEIVED: June 26, 2020

SPONSOR INFORMATION:

BrainTemp Inc.
P.O. Box 823
Bryn Mawr, PA 19010

INDICATIONS FOR USE

The BTNeo System is indicated for measurement of a neonate's brain temperature. The brain temperature may be displayed with a compatible vital sign monitor system and is intended to be displayed along with core temperature.

The BTNeo System is indicated for use by qualified healthcare professionals that care for neonates (from birth through the first 28 days of life) in intensive care units, operating rooms, and recovery rooms.

LIMITATIONS

The sale, distribution, and use of the device are restricted to prescription use in accordance with 21 CFR 801.109.

The safety and effectiveness of the BTNeo System to inform diagnosis or therapy has not been evaluated.

The device is not intended for use in neonates less than 35 weeks gestational age.

The device is not intended for use in neonates that do not have intact skin for sensor placement.

The device is not intended to measure core body temperature.

Sensor accuracy may be reduced if the sensor or radiometer are placed in direct contact with an active temperature management device.

Sensor accuracy may be reduced if there is anything (e.g., hair, tape) between the sensor and the skin.

The device has been validated in a laboratory study to measure the brain temperature at a depth of approximately 2 cm below the external forehead sensor. The safety and effectiveness of the device measurement at other depths of the brain has not been evaluated or demonstrated.

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

DEVICE DESCRIPTION

The BrainTemp Neonate (BTNeo) System is an external brain temperature measurement system that measures temperature at a depth of approximately 2.0 cm below the forehead sensor. The device system consists of the following components:

- **Sensor**: Used to measure temperature of the brain beneath the sensor. Single-use and affixed to the patient's forehead via medical grade adhesive.
- **Sensor Connector**: Connects the system to the disposable sensor.
- **Cable with In-line Radiometer with Switch Module**: Converts sensor readings to brain temperature measurements via a proprietary algorithm.
- **Display Interface**: Connected to the Radiometer and displays brain temperature data and warning lights. There is an optional connection to a compatible vital sign monitor for display of brain temperature data in comparison to core body temperature.

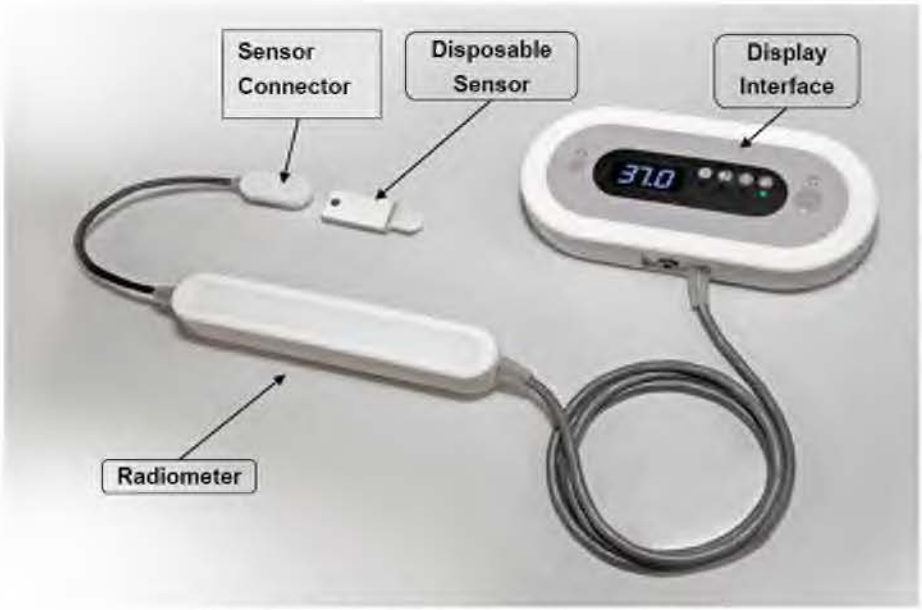

Figure 1: BTNeo System Components

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY

The sensor component of the BTNeo System is a surface device contacting intact skin for a prolonged duration (> 24 hours to 30 days) based on cumulative use. The following testing was conducted to assess the biocompatibility of the tissue-contacting components of the device:

- Cytotoxicity testing in accordance with ISO 10993-5, "Biological evaluation of medical devices — Part 5: Tests for *in vitro* cytotoxicity."
- Sensitization and irritation testing in accordance with ISO 10993-10, "Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization."

ELECTROMAGNETIC COMPATIBILITY (EMC) AND ELECTRICAL SAFETY

The BTNeo System was tested in accordance with the following consensus standards and passed the following EMC, immunity, electrical, mechanical, and thermal safety tests.

Table 1. EMC and Electrical Safety Testing Completed for the BTNeo System

Standard	Name
ANSI/AAMI ES 60601-1-1:2005/(R)2012	Medical Electrical Equipment - Part 1: General Requirements for Safety
IEC 60601-1-2:2014	Medical Electrical Equipment - Part 1-2: General Requirements for Safety - Section 2: Collateral Standard: Electromagnetic

Standard	Name
	Compatibility - Requirements and Tests
IEC 61000-4-39:2017	Medical Electrical Equipment - Part 4-39: Testing and Measurement Techniques – Radiated Fields in Close Proximity, Magnetic Field, 10-150 kHz
IEC 60601-1-8/AMD1:2012	Medical Electrical Equipment - Part 1-8: General Requirements for Safety - Section 8: Collateral Standard: General Requirements, Tests, and Guidance for Alarm Systems in Medical Electrical Equipment and Medical Electrical Systems

SOFTWARE/CYBERSECURITY

Software verification and validation testing and documentation was provided according to the FDA guidance, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." Per this guidance, the BTNeo System was determined to have a moderate level of concern. Documentation describing the firmware, software specifications, architecture design, software development environment, traceability, revision level history, and unresolved anomalies conclude that the software will operate in the manner described in the specifications. The hazard analysis characterized software and cybersecurity risks, including device malfunction, measurement-related errors, sensor, cable and other hardware failures, and unauthorized access by malicious end users during manufacturing. The submission describes verification and validation testing to address the potential hazards with satisfactory results.

The cybersecurity documentation included all the recommended information from the FDA guidance, "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices." This includes a cybersecurity hazard analysis and mitigation information, an upgrade and maintenance plan, other information for safeguarding the device during manufacturing and upon commercial distribution, and warning and precaution information in the product labeling.

HUMAN FACTORS-USABILITY

Testing and evaluation was conducted in conformance with the IEC 60601-1-6: 2010+A1:2013 standard for "Medical Electrical Equipment - Part 1-6: General Requirements for Safety - Section 6: Collateral Standard: Usability," which included establishing procedures for identifying potential hazards, evaluating key use characteristics such as sensor placement, sensor re-application, basic cleaning instructions, and optional connection to a compatible vital signs monitor, and evaluating labeling instructions and use by anticipated users. The testing passed all defined success criteria in support of the basic safety and essential performance of the device given risks associated with use. Additionally, peer-reviewed literature evaluating the placement, application, and adhesion of other commercially available devices with similar physical designs was provided to support use of silicone adhesive to attach the sensor component

of the device to the neonatal population for the intended duration. This testing and associated evaluation of similar devices informed corresponding warning and precaution statements and other use instructions in the product labeling regarding application and positioning of the sensor component to prevent thermal, pressure or other injuries that may cause trauma to the patient's skin.

PERFORMANCE TESTING – BENCH

Testing to demonstrate the accuracy of the BTNeo System was conducted in accordance with Clause 201.101.2 of the IEC 80601-2-56: 2017 standard for "Medical Electrical Equipment - Part 2-56: Particular Requirements for Basic Safety and Essential Performance of Clinical Thermometers for Body Temperature Measurement." This involved evaluation of the device performance across the operating temperature range, using a phantom model consisting of adult human scapula covered with synthetic pediatric skin, intended to simulate neonatal use, and an antenna simulator intended to simulate the BTNeo System and calibrate the skin temperature function. Separate testing sessions were performed at constant temperatures at different parts of the operating temperature range (low, middle, and high) and over the 24-hour use period (middle of operating range). To evaluate at a constant temperature, the device was placed on top of the phantom apparatus, which was then placed inside a (b)(4) and (b)(4) (b)(4) to allow for representation of the dielectric and flow properties of cerebrospinal fluid. For evaluation over the 24-hour period, the sensor was placed in a (b)(4) to ensure that any water loss of the phantom due to evaporation over the test period did not impact the accuracy of the device performance. The running average was evaluated for accuracy within ± 0.3 °C. Results indicated that the running average met the criteria per Clause 201.101.2 of the IEC 80601-2-56 standard for each test run across the operating temperature range and over a 24-hour period.

PERFORMANCE TESTING - ANIMAL

Objective

A Good Laboratory Practices (GLP) animal study was conducted to evaluate the performance of the final, finished version of the device in comparison to a brain temperature probe inserted approximately 2 cm below the skin surface in a weanling porcine model. This evaluation served as the primary basis for the device performance validation.

Study Design

Three (n=3), 4-week-old piglets were assessed under general anesthesia. The following temperature signals were measured: rectal, esophageal, and brain via thermocouple; the device when placed on the forehead; skin temperature (obtained from the device); and air temperature delivered into the nasal cavity. The brain temperature was measured by placing a thermocouple approximately 2 cm below the skin surface into a cerebral hemisphere. Animals then underwent several warming and cooling procedures, with the objective of demonstrating that the device accurately measured changes in brain temperature in comparison to measurements made using the invasive thermocouple.

Table 2. Piglet Physical Characteristics

Piglet	Weight	Skin Thickness	Skull Thickness	Probe Placement depth into Brain Tissue
#1	7.6kg	.37cm	.42cm	1.73cm
#2	8.0kg	.37cm	.34cm	1.73cm
#3	7.8kg	.36cm	.35cm	1.74cm

Methods

Each animal underwent the following procedures:

1. Recording started when both the brain and device temperature (the 2 key temperatures) were stable between 38 and 39 °C (± 0.2 °C) for at least two minutes. A heating blanket was set to 42 °C and animals were warmed, with whole-body heating being maintained until either the two key temperatures stabilized (± 0.2 °C) for at least two minutes, rectal temperature reached 42 °C, or 30 minutes had elapsed.
2. When the first procedure concluded, the second procedure started immediately. Some heat sources were removed, and 15 mL/min air flow was introduced to the nasal passages to induce selective brain/head cooling. Dry air was supplemented with saline pumped into the nasal cavity. Selective cooling was maintained until either the two key temperatures stabilized (± 0.2 °C) for at least two minutes, or when 45 minutes had elapsed. At this point, nasal air flow was turned off and heating blankets set at 42 °C were used to return the animal to its pre-experimental brain temperature of 38 °C (± 1 °C).
3. Once the piglet's brain temperature returned to approximately 38 °C or 45 minutes had passed, the blanket settings were changed to 10 °C to cool the piglet to induce whole-body hypothermia until the two key temperatures stabilized (± 2 °C) for at least two minutes, the rectal temperature fell to 34 °C, or 45 minutes had elapsed. Once the procedures were concluded, the animals were euthanized.

Results

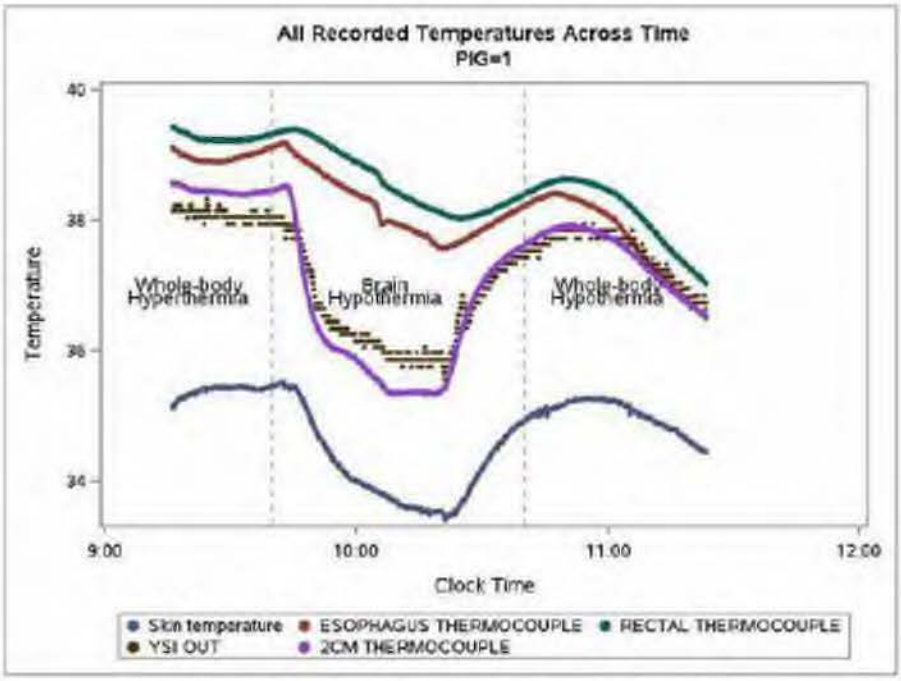

Figure 2: Experimental Temperature Data of Pig 1

Figure 2 shows the temperature data for Pig 1 comparing the invasive brain probe (2 cm Thermocouple), the test device (YSI Out), core temperatures (rectal and esophagus thermocouple), and skin temperature, with the vertical dotted lines dividing the different experimental procedures. For whole body hyperthermia, all temperatures trended downward, then upward. For brain hypothermia, the brain, skin and device temperatures decreased rapidly while the core body temperatures (rectal and esophageal) decreased more gradually. All probes trended upward when nasal cooling stopped and warming was initiated. For whole body hypothermia, temperatures trended downward for all probes, with skin temperature consistently being less than the brain or core body temperatures.

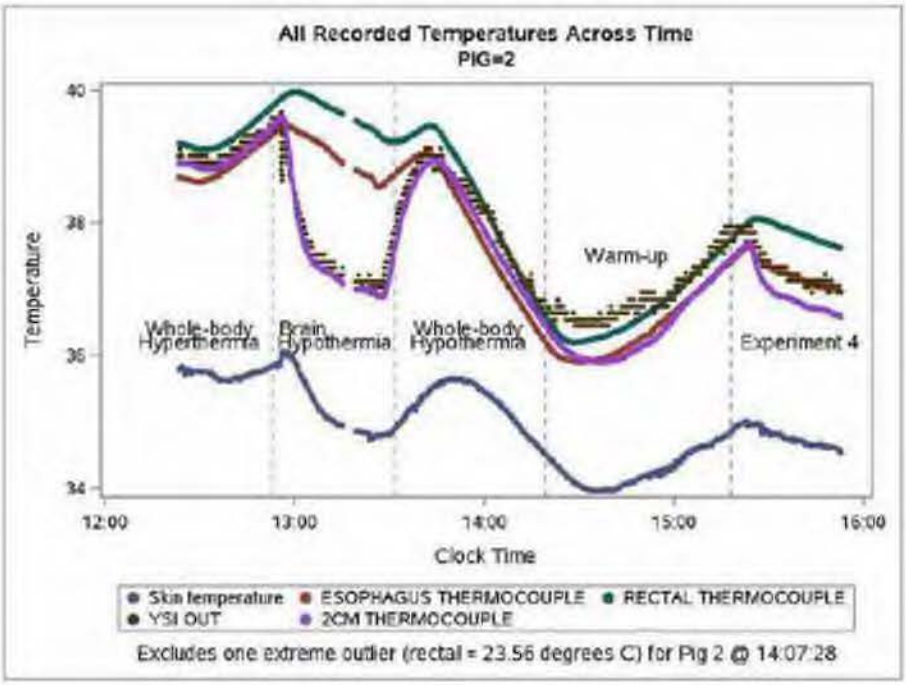

Figure 3: Experimental Temperature Data of Pig 2

Figure 3 shows the temperature data for Pig 2. As with Pig 1, core (esophageal and rectal) thermocouples, brain and the device temperatures trended in the same direction. When selective head/brain cooling was applied (brain hypothermia), the brain and device probes decreased more rapidly in comparison to the core (esophageal and rectal) probes. Additionally, skin temperature was consistently less than brain or core temperatures.

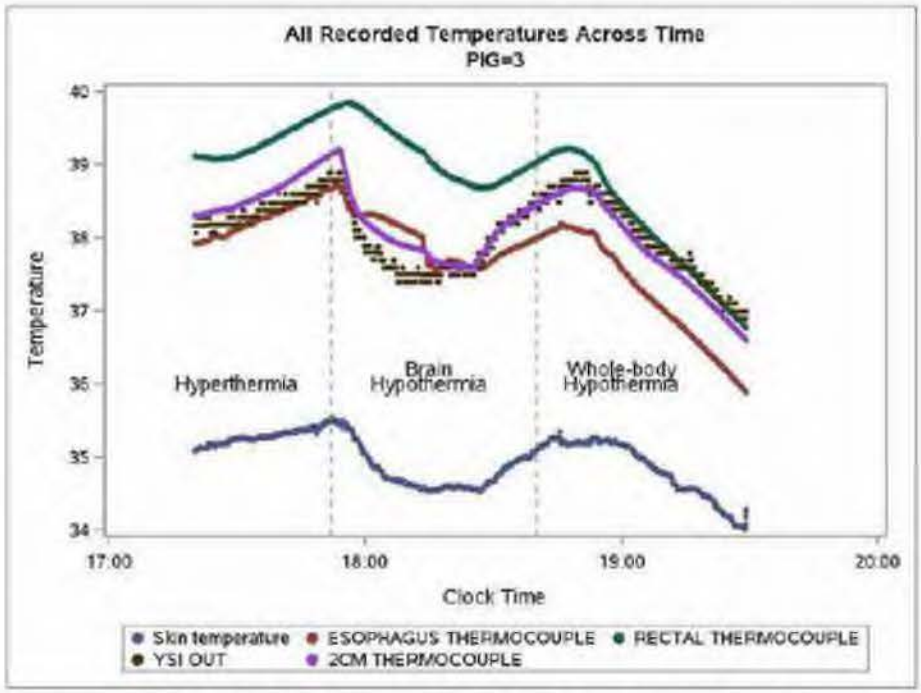

Figure 4: Experimental Temperature Data of Pig 3

Figure 4 shows temperature data for Pig 3. For this animal, the brain, device, and esophageal temperatures had similar rates of temperature change, including during selective head cooling. The rectal thermocouple shows a more gradual decrease in temperature during the brain hypothermia procedure. Skin temperature was consistently less than brain or core temperatures.

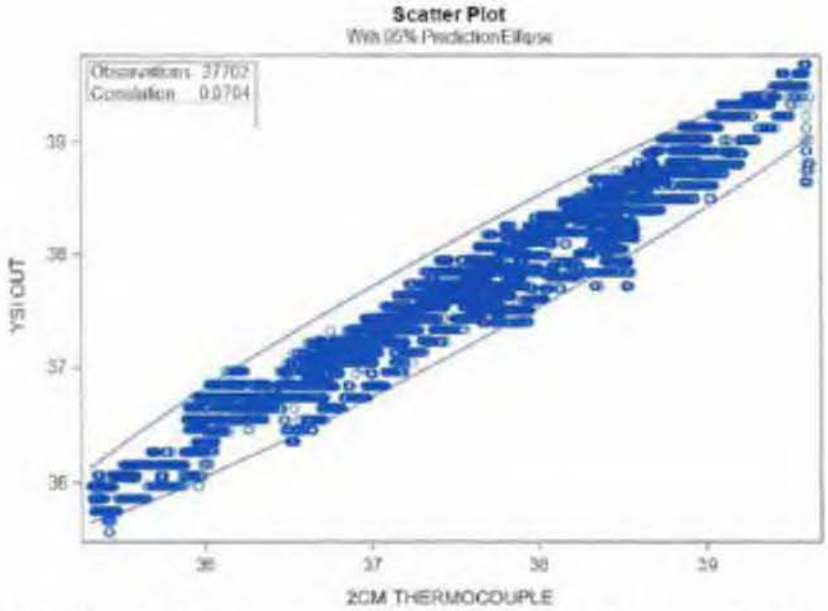

Figure 5: Point-to-point Comparison of Brain Probes for All Animals

Figure 5 shows the invasive brain probe (2 cm Thermocouple) and the test device (YSI Out) of all animals. The correlation between the temperature probes was 0.97. The dips at the top right of the graph indicate the occurrence of animal movement during recording.

LABELING

The labeling is sufficient and satisfies the requirements of 21 CFR 801.109 for prescription devices.

The labeling includes a detailed description of the device, a description of the patient population for which the device is indicated for use, contraindications, warnings, precautions, and instructions for use. The labeling also includes summary information about the animal studies performed to validate the device measures.

The labeling includes information regarding appropriate use and placement of the sensor component, reliability of the device output based on sensor application site, instructions to monitor skin integrity for duration of use, and a discussion of the limitations that the device is not intended to inform diagnosis or therapy, is not intended for use in patients less than 35 weeks gestational age, and is not intended for use in patients who do not have intact skin for sensor application.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a brain temperature measurement system and the measures necessary to mitigate these risks.

Identified Risks to Health	Mitigation Measures
Inaccurate measurement made by the device, resulting in misuse or misinterpretation of device output	In vivo performance testing Non-clinical performance testing Software verification, validation, and hazard analysis Usability evaluation Labeling
Equipment malfunction leading to injury to user/patient (e.g., shock, burn, interference)	Electrical, mechanical and thermal safety testing Electromagnetic compatibility (EMC) testing Labeling
Adverse tissue reaction, including thermal or pressure injuries	Biocompatibility evaluation Usability evaluation Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the brain temperature measurement system is subject to the following special controls:

(1) In vivo performance testing must demonstrate that the device performs as intended for its anticipated conditions of use and can accurately and reliably measure brain temperature compared to a ground truth measurement.

(2) Non-clinical performance testing must demonstrate that the device can accurately measure changes in brain temperature under simulated conditions of use. Testing must assess repeatability within pre-specified, clinically relevant parameters. The technical specifications of the device's hardware and software must be fully characterized.

(3) Electrical safety, thermal safety, mechanical safety, and electromagnetic compatibility (EMC) testing must be performed.

(4) Software documentation must include a detailed technical description of the algorithm(s) used to generate the device output(s), and be accompanied by verification and validation testing to ensure device and algorithm functionality as informed by the software requirements and hazard analysis.

(5) The tissue contacting device components must be demonstrated to be biocompatible.

(6) Usability evaluation must demonstrate that the intended user(s) can safely and correctly use the device, based solely on reading the directions for use.

(7) Labeling must include:
    (i) Instructions for use, including a detailed description of the device and explanation of all device outputs.
    (ii) The following warnings:
        (A) A statement that the device is not intended to measure core body temperature, and to use an independent thermometer to measure core body temperature.
        (B) Conditions of use that may impact the accuracy and reliability of the device measurement.
        (C) Conditions of use that may affect skin integrity or cause skin injury, such as extended wear duration or placement of the device on damaged or compromised skin, skin lesions, or open wounds.
        (D) Limitations of device use to inform diagnosis or therapy.
    (iii) Summaries of in vivo testing conducted to demonstrate how the device functions as intended. The summary must include the following:
        (A) A description of each device output.
        (B) A description of the study population and the use environment.
        (C) The methods used to collect temperature data.
        (D) Any observed adverse events and complications.

BENEFIT-RISK DETERMINATION

Risks associated with use of the device are related to biocompatibility, electrical safety, electromagnetic compatibility (EMC), software verification and validation, usability, pressure on the skin, and the sensor adhesive. Risks include inaccurate measurement, inappropriate use of the device to inform diagnostic and therapeutic decisions based on its output, and injury to the skin.

The safety testing and hazard analysis performed, in conjunction with the device technical alerts regarding device malfunction and labeling contraindications, warnings, and precautions mitigate the risks presented. The product labeling also states that the safety and effectiveness of the device to inform diagnosis or therapy has not been evaluated. Use of the device is limited to patients under care in the neonatal neurocritical care environment.

The probable benefits of the device are based on bench and animal studies demonstrating the accuracy of the measurements made by the device. The BTNeo System is an externally placed device that provides an estimated measure of brain temperature below the sensor. This device allows qualified healthcare professionals to measure brain temperature, which is intended to be displayed along with core temperature.

Additional factors to be considered in determining probable risks and benefits for the BTNeo System include:

- Brain temperature is a physiological measurement that is currently not typically included in the clinical evaluation of the target population. Utility for diagnosis or making treatment decisions of this additional physiological data has not been established.

- Other methods to measure brain tissue temperature are not practical in the neonatal intensive care or are invasive.

For the reasons described above, the probable benefits of the BTNeo System outweigh the probable risks.

Patient Perspectives

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

Benefit/Risk Conclusion

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

> "The BTNeo System is indicated for measurement of a neonate's brain temperature. The brain temperature may be displayed with a compatible vital sign monitor system and is intended to be displayed along with core temperature.
>
> The BTNeo System is indicated for use by qualified healthcare professionals that care for neonates (from birth through the first 28 days of life) in intensive care units, operating rooms, and recovery rooms,"

the probable benefits outweigh the probable risks for the BTNeo System. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the BTNeo System is granted and the device is classified as follows:

> Product Code: QSL
> Device Type: Brain temperature measurement system
> Regulation Number: 21 CFR 882.1565
> Class: II