DE NOVO CLASSIFICATION REQUEST FOR
INFRASCAN, INC.'S INFRASCANNER MODEL 1000

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Near Infrared Brain Hematoma Detector. A Near Infrared (NIR) Brain Hematoma Detector is a noninvasive device that employs near-infrared spectroscopy that is intended to be used to evaluate suspected brain hematomas.

NEW REGULATION NUMBER: 882.1935

CLASSIFICATION: II

PRODUCT CODE: OPT

BACKGROUND

DEVICE NAME: INFRASCANNER MODEL 1000

SUBMISSION NUMBER: K080377

DATE OF DE NOVO: APRIL 10, 2010

CONTACT: BARUCH BEN DOR, PH.D.
INFRASCAN, INC.
3508 MARKET STREET, SUITE 215
PHILADELPHIA, PA 19104

REQUESTER'S RECOMMENDED CLASSIFICATION: CLASS II

INDICATIONS FOR USE

The Infrascanner Model 1000 is indicated for the detection of traumatic supratentorial hematomas of greater than 3.5 mL in volume that are less than 2.5 cm from the brain surface, as an adjunctive device to the clinical evaluation in the acute hospital setting of patients 18 years old or greater with suspected traumatic supratentorial intracranial hematoma. The device is indicated to assess patients for CT scans but should not serve as a substitute for these scans. The Infrascanner Model 1000 is indicated for use by physicians, or under the direction of a physician, who has been trained in the use of the device.

LIMITATIONS

In the clinical study of the device, patients were scanned with the Infrascanner Model 1000 within 30 minutes of receiving CT scan. The Infrascanner Model 1000 is intended for use as a device that

detects hematomas by detecting differences in the absorption of near infrared light at corresponding locations on the left and right sides of the skull. It is not indicated for detection of symmetrical conditions such as may occur with bilateral hematomas, or when there is massive scalp edema or bleeding (open or subgaleal). It is not indicated to detect hematomas deeper than 2.5 cm below the cortical surface. The performance of the Infrascanner Model 1000 in detecting subarachnoid hemorrhage has not been established.

The safety and effectiveness of this device in subjects less than 18 years of age have not been adequately evaluated.

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

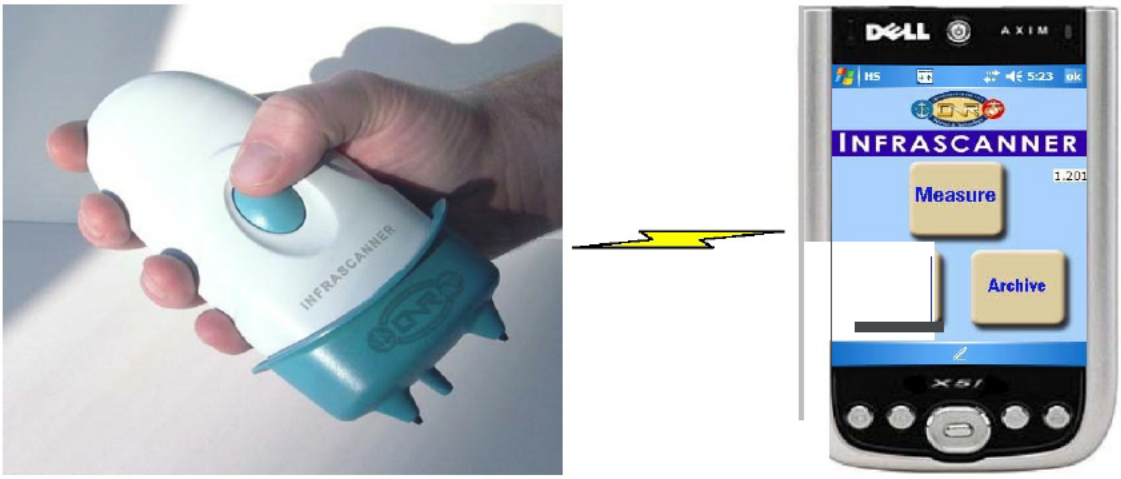
DEVICE DESCRIPTION

The Infrascanner System

The system includes two components: the Sensor and a Personal Digital Assistant (PDA). The Sensor includes an 21 CFR 1040 Class I NIR 808nm diode laser and a silicon detector. The light to and from the laser and detector are optically coupled to the patient's head through two 19mm long disposable light guides. The light guides are long enough to reach through hair and contact the scalp. The light guides are placed 4 cm apart allowing detection of hematomas. The detector light passes through an optical bandpass filter centered at 808nm to minimize background light interference. Electronic circuitry is included to control laser power and the detector signal amplifier gain. The detector signal is digitized and transmitted via a Bluetooth wireless link to the PDA. The wireless link is also used to receive and set the hardware parameters of the Sensor. The PDA receives the data from the Sensor and automatically adjusts the settings of the Sensor to ensure good data quality. The data is further processed by the PDA and the results are displayed on the PDA screen.

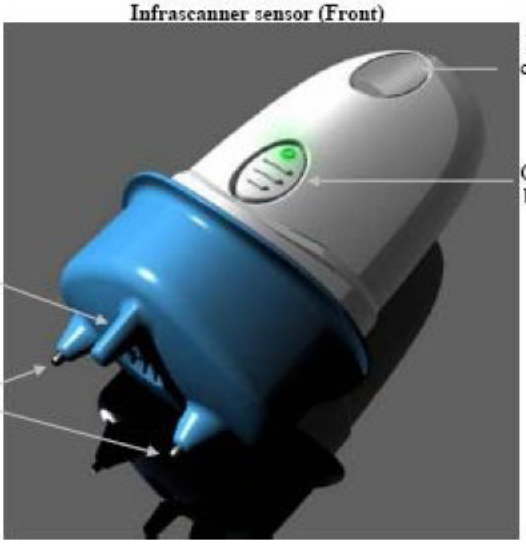
The Sensor has a power On/Off switch and a Measure Button. When the Sensor is turned on, pressing and releasing the Measure Button activates a measurement sequence at a given head location. The measurement includes an initial adjustment phase and then the data collection. The adjustment of laser power and detector signal gains is only done at the first head location of a pair. The contra-lateral location uses the same Sensor hardware parameters as the ipsi-lateral location. After a measurement, the PDA will display the optical density for that location. The absolute value of optical density is not relevant, just the relative difference between left and right sides of the head.

Audible signals indicate whether the data is acceptable or unacceptable. If the data is unacceptable, the measurement is to be repeated before proceeding to the next head location.



Photographs of the Infrascanner Model 1000

Infrascanner sensor (Front)



Infrascanner Sensor (Back)

Principles of Operation

Basic Near Infrared Theory

All biological tissue is, to a varying extent, permeable to electromagnetic (EM) radiation of different frequencies and intensities. This can also be considered permeability to photons of different energy levels. This permeability to EM energy is the basis of all imaging based on transmission/scattering characteristics such as x-ray, Computed Tomography (CT), and Near Infrared (NIR) imaging. From the principles of spectroscopy, it is also known that different molecules absorb different wavelengths of EM radiation (which is synonymously referred to as light at smaller wavelengths). Similarly, tissue scatters EM radiation to different degrees. The Infrascanner Model 1000 operates using NIR imaging of the hemoglobin molecule.

From any light source, photons follow a characteristic path through the target tissue back to a detector on the same approximate plane as the source. While the light is severely attenuated due to the scattering and absorption process, it is nonetheless encoded with the spectroscopic signatures of the molecules encountered en route to the detector. By carefully choosing the wavelengths that are produced by the source, it is possible to detect the relative concentration of hemoglobin in the target tissue. By comparing these levels to tissue in a "baseline" state, and using some basic knowledge about clinically relevant conditions for the tissue, it is possible to draw conclusions from these levels.

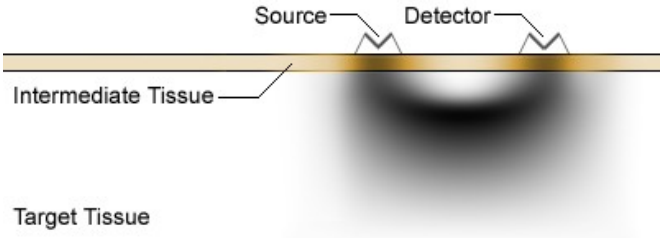


Figure 1: Simulated photon diffusion path through target tissue from source to detector. This simulation shows the photon path density, not the overall transmission level.

The principle used in identifying intracranial hematomas with the Infrascanner Model 1000 is that extravascular blood absorbs NIR light more than intravascular blood. This is because there is a greater (usually 10-fold) concentration of hemoglobin in an acute hematoma than in normal brain tissue where blood is contained within vessels. The Infrascanner Model 1000 compares the left and right side of the brain in four different areas. The absorbance of NIR light is greater (and therefore the reflected light less) on the side of the brain containing a hematoma, than on the uninjured side.

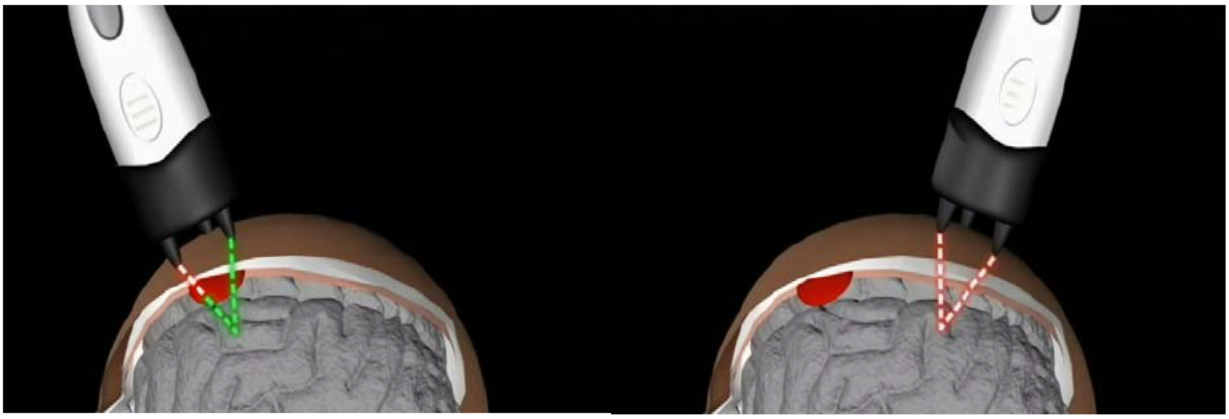


Figure 2: NIR method of detecting intracranial hematomas

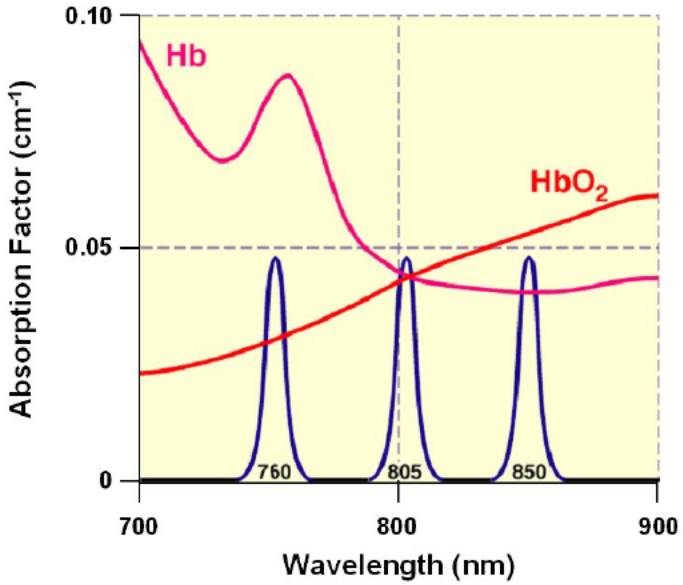


Figure 3: Absorption of light by hemoglobin

The wavelength of 805nm is sensitive only to blood volume, not to oxygen saturation in the blood. The Infrascanner Model 1000 is placed successively in the left and right frontal, temporal, parietal, and occipital areas of the head and the absorbance of light at 805 nm is recorded and compared.

Frontal Left/Right forehead, above the frontal sinus
Temporal In the Left/Right temporal fossa in front of the top of the Left/Right ear
Parietal Above the Left/Right ear, midway between the ear and the midline of the skull
Occipital Behind the top of the Left/Right ear, midway between the ear and the occipital protuberance

The difference in optical density (ΔOD) in the different areas is calculated from the following formula:

$$\Delta OD = \log_{10}\left(\frac{I_N}{I_H}\right)$$

Where I_N = the intensity of reflected light on the normal side, I_H = the intensity of reflected light on the hematoma side.

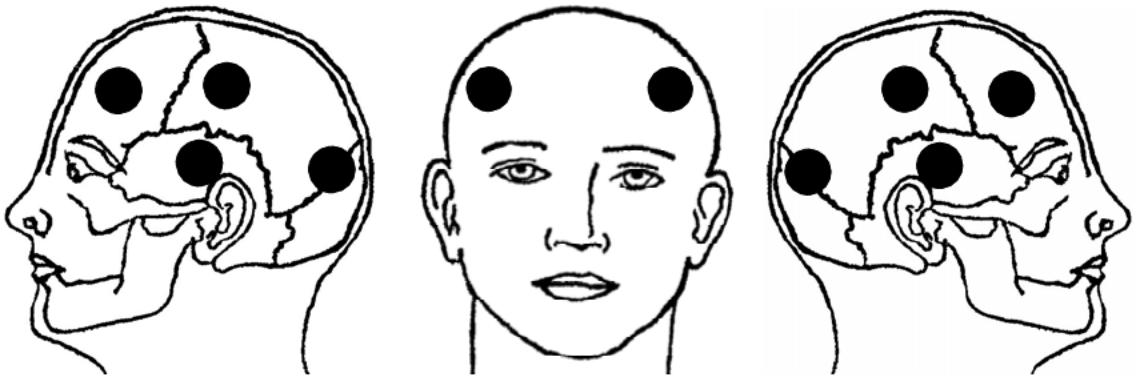


Figure 4: Head locations of NIR Measurements

SUMMARY OF NONCLINICAL/BENCH

Nonclinical performance data were provided related to the following areas: Model lab testing, Interrater Study, Biocompatibility, Electromagnetic compatibility (EMC) and Electrical Safety, and Software.

MODEL LABORATORY TESTING

InfraScan conducted three separate tests of the Infrascanner Model 1000 using a laboratory model of brain hematoma for each test. The purpose of these tests was to study the theoretical performance of NIR technology in detection of brain hematomas.

Results from this series of lab tests demonstrated that the NIR technique using the Infrascanner Model 1000 was able to detect hematomas down to about an inch (~ 2.5 cm) from the brain surface. **In addition, the results showed that the Infrascanner Model 1000 is unable to reliably detect very small hematomas (≤3.5 mL) at the detection threshold of ΔOD = 0.2.**

INTERRATER STUDY

Data collected from an interrater study was based on 7 subjects and used 20 phantoms. This study was originally designed to evaluate reproducibility results obtained from three different physicians taking Infrascan measurements on the same person. However, because of the limitations imposed by the acute hospital setting, measurements were augmented using a phantom hematoma. Because these results were simulated and not representative of actual clinical practice, the data provided limited information. Precision studies (e.g., the same operator repeating measurements on the same patient) were not conducted. However, when feasible, it is recommended that reliability studies (precision and interrater) be performed when additional clinical data is needed in support of a premarket application.

BIOCOMPATIBILITY

With respect to biocompatibility, the main material that contacts the patient is the (b)(4) used in the light guide portion of the probe. (b)(4) has a long history of safe use not only in skin-contacting applications such as this, but also for implant use in a variety of applications. The rest of the probe, which might contact the patient, is made out of a medical grade (b)(4) plastic. The following biocompatibility tests were performed in accordance with ISO 10993 on the disposable light guide portion of the Infrascanner Model 1000: cytotoxicity, sensitization, and skin irritation.

The cytotoxicity results demonstrated the device is non-cytotoxic. The sensitization results supported that the device does not elicit sensitization. Finally, the skin irritation results demonstrated the device has a negligible irritation response. In light of these results, FDA has determined that the information provided demonstrates appropriate biocompatibility of the device.

ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

InfraScan has conducted testing on the Infrascanner Model 1000 to verify compliance with the following standards:

- IEC 61000-4-2 (Edition 1.2, 2001-04) (Electrostatic Discharge);
- IEC 61000-4-3 (Edition 2.1, 2002-09) (Radiated Radiofrequency (RF) Immunity); and
- FCC Part 15, Class B, EN 55011 (Edition 3.1, 1999-08) (Radiated Emissions).
- IEC 60601-1-2 Second edition 2001-09.

The results show that the Infrascanner Model 1000 passed the electrostatic discharge and radiated RF immunity tests. In addition, the results show that the Infrascanner Model 1000 had radiated emissions below the maximum permissible limit.

In addition, analysis of the light safety for the pulsed diode laser light source of the Infrascanner Model 1000 has been performed using the international laser safety standard, IEC 60825-1. These results demonstrate that the Infrascanner Model 1000 as a Class I laser product as per 21 CFR 1040, and does not require protective eyewear, special warnings, interlocks, or laser keys.

The company provided appropriate characterization and software validation information regarding their Blue Tooth system. The company addressed issues regarding the ability of the handheld PDA to reset use parameters and to determine whether the initial measurement was not acceptable. The process used by the PDA was clarified and the impact on subsequent measurements was adequately addressed.

SOFTWARE

The controlling software for the Infrascanner presents a "moderate" level of concern based on answers to questions listed in FDA's *Guidance for the Content of Premarket Submission for Software Contained in Medical Devices* (May 11, 2005). According to the *Guidance Document,* software for a device has a "moderate" level of concern if a failure or latent design flaw in the software could result in minor injury to the patient or operator or if a failure or latent flaw could indirectly result in minor injury to the patient or operator through incorrect or delayed information or through the action of a care provider.

Software Description

The system includes two main components: a NIR based sensor and a mobile computing platform (PDA). The system software was developed with C++ using Microsoft embedded Visual C++ 4.0 SP4, while the firmware uses Silicon Labs Integrated Development Environment, IDE Version 2.90.

The Sensor includes a (b)(4) integrated circuit micro-controller, a supervisor chip to reset the CPU on power-up and down, a crystal for the master clock oscillator, and a Bluetooth transceiver. In addition, the Sensor features an NIR diode laser and a silicon detector, both coupled optically to the patient's head through disposable plastic light guides. The Sensor's micro-controller communicates with the PDA via the Bluetooth link and adjusts the power of the laser and the gain of the detector amplifiers to ensure good data quality. The signal from the detector is digitized and transmitted via the Bluetooth link to the PDA.

The PDA is a commercial off-the-shelf system running on the Windows Mobile 5.0 operating system or higher. The CPU will be at least 100MHz and the PDA features a memory of more than 32 MB. The PDA is provided with a USB cable for data download to a computer. The system provides optical density (OD) calculations based on diffuse light measurements made by the Sensor and then displays the results to the user on the user interface template of a skull.

The system software is loaded onto the PDA and is comprised of 3 main applications:

- Parameters Program – Used to set the various software and hardware parameters of the system, which are then stored in the PDA's persistent storage. The program is managed by a dedicated parameter setting software.

- Main Infrascanner Program – The central measurement and diagnosis program. The program has the following basic modules:

    - Sensor command and parameter setting using Bluetooth communications
    - Data acquisition from Sensor via Bluetooth link
    - Data processing module
    - Storage routing for recording all raw data and the algorithm results in the persistent memory
    - Screen control, user interface, and display

- Sound control and output
- Downloading data through a USB port.

- Archive Program – Used to review previously acquired data. Data is sorted by patient name or otherwise according to user preference.

Hazard Analysis

The software portion of the Risk Analysis and Failure Mode Effect Analysis (FMEA) includes potential, undesirable effects and identifies the hardware and software features or labeling that are designed to ensure that these potentially hazardous events do not occur. The FMEA involved the consideration of all possible faults which were Single Fault in nature. After a list was compiled, the faults were analyzed using the following information:

- The Occurrence table estimates the probability of occurrence of each failure and assigns a numerical rating (1 through 10) to the fault condition.
- The Severity table considers the severity of the fault and assigns a numerical rating (1 through 10) to the fault.
- The Detection table considers the probability that the fault will be caught by the present controls and assigns a numerical value (1 through 10) to this rating.
- Finally, these ratings are multiplied to obtain the Risk Priority Number (RPN). Any faults which have an RPN rating greater than 100 are considered faults that require further attention to reduce their RPN rating.

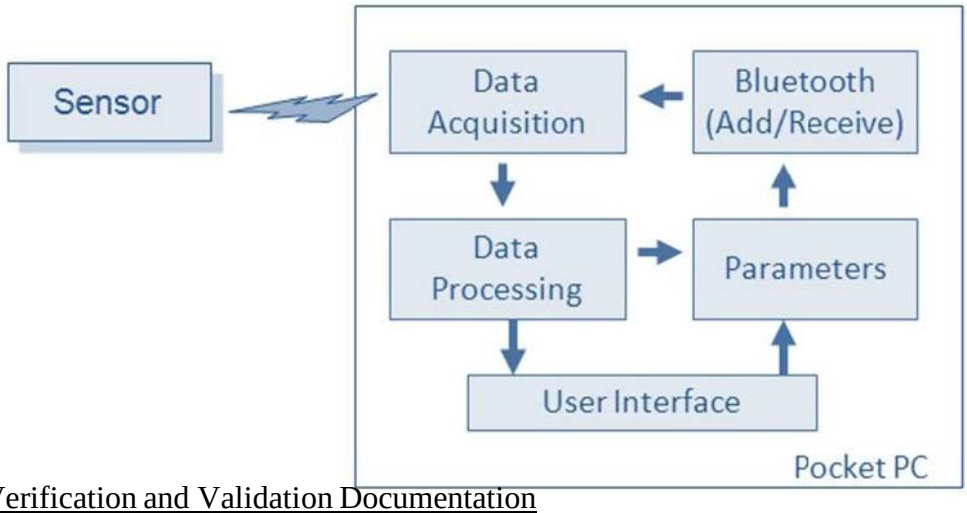
Overall, the results FMEA did not highlight any software related failure modes that carried an RPN of greater than 100.

Software Requirements Specifications (SRS)

The software requirements for the Infrascanner Model 1000 software were based on a value analysis approach, consisting of discussions with potential users, site visits, and a review of current, similar systems. The Software Requirements Specifications were developed based on these findings.

Architecture Design Chart

A basic diagram showing the Infrascanner software is provided below.



Verification and Validation Documentation

Verification and Validation Documentation

Based on the initial draft of the SRS, a baseline Software Verification and Validation Plan (SVVP) for the Infrascanner Model 1000 software was developed. The SVVP was based on the IEEE Guide for Software Verification and Validation Plans (IEEE Std 1059-1993) and FDA's *General Principles of Software Validation; Final Guidance for Industry and FDA Staff* (2002). Following completion of the Design Phase of software development, the SVVP was reviewed and revised according to the SRS and the Product Development Specifications. After that time the SVVP was again reviewed and revised, at a minimum, at the conclusion of each phase of software development. The submission indicates that all verifications and validation activities were completed and all tests were passed successfully.

Revision History Log

The submission included a software revision history log. The *de novo* is being sought for version 2.18 of the Firmware and version 2.006 of the system software, which are the most recent versions.

The software documentation has been reviewed and deemed acceptable.

Battery Testing

Canadian Standards Association (CSA) conducted testing for the scanner battery in accordance with UL1642 (passed). Hewlett-Packard (HP) provided the battery information in their detailed HP iPAQ Product Guide. The HP Product Guide lists the battery specs, battery warnings, recycling, disposal, as well as the medical electronic equipment warning. Battery usage is addressed in the Troubleshooting Section of the Infrascanner Model 1000 Operation Manual.

SUMMARY OF CLINICAL INFORMATION

A clinical study was carried out in five sites: four (4) sites US and one (1) site in India. Subjects were included in the study if they had a non-contrast CT scan for evaluation of a head

injury and signed informed consent to participate in the Infrascanner Model 1000 study. The Infrascan was to be completed within 30 minutes before or after the CT scan. Subjects were excluded if 12 hours or more had elapsed between the injury and CT scan. Subjects were also excluded if there were massive scalp lacerations or edema.

All of the CT scans were interpreted by an independent radiologist blinded to the result of the Infrascanner Model 1000 measurements. CT scans were evaluated for the location(s) and volume of hematomas. Infrascanner Model 1000 results were considered positive for hematomas if the maximum difference in optical density (ΔOD) for comparable skull regions was greater than 0.2.

Three hundred eighty-three (383) subjects age 18 years or older were enrolled in the study and are the primary analysis population.

Age	
Mean ± SD (years)	40.5±17.4
Range (years)	18-89
Sex (% male)	76%
Initial GCS*	
Mean ± SD	11.9±4.4
Range	3-15
Cause of injury	
Fall	150
Motor Vehicle Accident	172
Assault	46
Other	15
Time interval between CT scan and Infrascanner study	
Mean ± SD (minutes)	25.2±24
Range (minutes)	1-202

*: GCS = Glasgow Coma Scale (range 3 – 15, lower scores indicating greater impairment)

CT Scan Results

Infrascanner Model 1000 results	Intracranial hematoma >3.5 mL and < 2.5 cm from brain surface	No hematoma or hematoma ≤ 3.5mL or ≥2.5cm from brain surface
	(N = 63)	(N = 320)
ΔOD > 0.2 (n, %, 95% CI)	**Sensitivity** 47/63; 74.6% (62.1, 84.7%)	59/320; 18.4%
ΔOD ≤ 0.2 (n, %, 95% CI)	16/63; 25.4%	**Specificity** 261/320; 81.6% (76.9, 85.7%)

95% CI: 95% Confidence interval

The data above supports the specific technological characteristics and indicated use for the InfraScanner Model 1000 device. Clinical data may be required for future devices, or modifications to the InfraScanner Model 1000 device that may include: a. dissimilar indications, b. dissimilar designs, or c. different technology.

LABELING

The following information is included in the labeling for the Infrascanner Model 1000 device:

1. Physician Labeling

   a. Description of the technological features of the device and all steps necessary for the operation, inspection and maintenance of the device. Information regarding maintenance of the device includes: duration of use; component replacement; and quality control.

   b. Identification of all device safety features and limits of use.

   c. Applicable warnings and precautions, including patient populations where safety and effectiveness have not been established; hematoma size or bleeding location where safety and effectiveness have not been established; and specific types of hemorrhage, edema, or other conditions where safety and effectiveness have not been established.

   d. Limiting device use to physicians, or those under the direction of a physician, trained in the use of the device.

2. Operator Training

Operator training will be implemented to ensure that physicians, or those under their direction, understand appropriate device usage in the correct patient setting and patient population and understand the device limitations and patient populations where safety and effectiveness have not

been established.

3. Labeling Related to Performance Specifications

a. A summary of the clinical study.

b. Sensitivity and specificity in detecting intracranial hematomas, as well as any limitations.

In addition, the Infrascanner Model 1000 device complies with the labeling requirements under 21 CFR 807.87(e) and prescription device requirements under 21 CFR § 801.109. The device is exempt from having adequate directions for lay use. The device labeling bears the following: "Caution: Federal law restricts this device to sale by or on the order of a physician."

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of noninvasive, near- infrared spectroscopy devices to evaluate suspected intracranial hematomas and the measures recommended to mitigate these risks.

Identified Risks	**Recommended Mitigation Measures**
Excessive laser power	Electrical Safety and Electromagnetic Compatibility (EMC)
Interference with other devices	Electrical Safety and EMC Labeling
Unit (hardware) malfunction	Performance Testing (non-clinical and clinical) Software Verification, Validation and Hazard Analysis
Software Malfunction	Software Verification, Validation, and Hazard Analysis
Operator errors	Labeling Training
Incorrect result (false positive and negative)	Labeling
Adverse tissue reaction	Biocompatibility
Battery Failure (Failure of device to operate)	Labeling

SPECIAL CONTROLS:

In addition to the general controls of the Act, the Infrascanner is subject to the following special controls:

(1) The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 of this chapter;

(2) The labeling must include specific instructions and the clinical training needed for the safe use of this device;

(3) Appropriate analysis/testing should validate electromagnetic compatibility (EMC), electrical safety, and battery characteristics;

(4) Performance data should validate accuracy and precision and safety features;

(5) Any elements of the device that may contact the patient should be demonstrated to be biocompatible; and,

(6) Appropriate software verification, validation, and Hazard Analysis should be performed.

CONCLUSION

The *de novo* for the Infrascanner Model 1000 is granted and the device is classified under the following:

Product Code:	OPT
Device Type:	Near Infrared (NIR) Brain Hematoma Detector
Class:	II
Regulation:	21 CFR 882.1935