December 3, 2021

Fifth Eye Inc.
% Donna-Bea Tillman
Senior Consultant
Biologics Consulting Group
1555 King Street, Suite 300
Alexandria, Virginia 22314

Re: K212219
Trade/Device Name: AHI System
Regulation Number: 21 CFR 870.2220
Regulation Name: Adjunctive hemodynamic indicator with decision point
Regulatory Class: Class II
Product Code: QNV, QNL
Dated: November 3, 2021
Received: November 4, 2021

Dear Donna-Bea Tillman:

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 (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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 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 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 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,

for

LCDR Stephen Browning
Assistant Director
Division of Cardiac Electrophysiology,
Diagnostics, and Monitoring Devices
Office of Cardiovascular 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)*
K212219

Device Name
AHI System

Indications for Use *(Describe)*

The AHI System is intended for use by healthcare professionals managing patients 18 years or older who are receiving continuous physiological monitoring with electrocardiography (ECG) in hospitals.

AHI provides a frequently updated binary output over time based on pattern analysis of a lead-II ECG waveform intended to describe a patient's hemodynamic status and indicate if a patient is showing signs of hemodynamic stability or instability. Signs of hemodynamic instability (HI) are defined as hypotension (systolic blood pressure <90 mmHg or mean arterial pressure (MAP) <70 mmHg) combined with tachycardia (heart rate ≥ 100 bpm).

AHI-PI provides the clinician with physiological insight into a patient's likelihood of a future episode of HI. An episode of HI is defined as 10 continuous minutes or more where HI is present.

The goal of this adjunctive monitoring method is to enable identification of patients who are showing HI or are likely to experience a future episode of HI, and to allow clinicians an opportunity to increase vigilance. This device is intended for adjunctive use with other physical vital sign parameters and patient information and is not intended to independently direct therapy.

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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In accordance with 21 CFR 807.87(h) and 21 CFR 807.92 the 510(k) Summary for the AHI System is provided below.

1. SUBMITTER

Applicant:	Fifth Eye Inc. 110 Miller Avenue, Suite 300 Ann Arbor, MI 48104
Contact:	Jen Baird Chief Executive Officer Fifth Eye Inc. 734.260.4800 jbaird@fiftheye.com
Submission Correspondent:	Donna-Bea Tillman, Ph.D. Senior Consultant Biologics Consulting 1555 King St, Suite 300 Alexandria, VA 22314 410.531.6542 dtillman@biologicsconsulting.com
Date Prepared:	November 2, 2021

2. DEVICE

Device Trade Name:	AHI System
Device Common Name:	Hemodynamic Indicator
Classification Name	21 CFR 870.2220 Adjunctive Hemodynamic Indicator with Decision Point
Regulatory Class:	II
Primary Product Code:	QNV
Subsequent Product Code:	QNL

3. PREDICATE DEVICE

Predicate Device:	Analytic for Hemodynamic Instability (AHI) - DEN200022
Secondary Predicate Device:	CLEWICU System (ClewICUServer And ClewICUnitor) – K200717

4. DEVICE DESCRIPTION

The AHI System is a multiparameter system designed to meet clinicians' need to identify patient hemodynamic status and predict patient hemodynamic instability episodes using two analytics:

1. Analytic for Hemodynamic Instability (AHI) (as granted in DEN200022): Utilizing data from a single existing lead of a non-invasive electrocardiograph (ECG), AHI analyzes heart rate variability (HRV) and ECG morphology features to rapidly detect signs of hemodynamic stability or instability and categorize each window of data as either "AHI Stable" or "AHI Unstable." Time trending of AHI outputs is also provided.

2. Analytic for Hemodynamic Instability Predictive Indicator (AHI-PI): Utilizing AHI outputs from up to the most recent 30 minutes of ECG data, AHI-PI indicates the likelihood of a future episode of hemodynamic instability, defined as ten continuous minutes or more where signs of hemodynamic instability are present.

5. INTENDED USE/INDICATIONS FOR USE

The AHI System is intended for use by healthcare professionals managing patients 18 years or older who are receiving continuous physiological monitoring with electrocardiography (ECG) in hospitals.

AHI provides a frequently updated binary output over time based on pattern analysis of a lead-II ECG waveform intended to describe a patient's hemodynamic status and indicate if a patient is showing signs of hemodynamic stability or instability. Signs of hemodynamic instability (HI) are defined as hypotension (systolic blood pressure <90 mmHg or mean arterial pressure (MAP) <70 mmHg) combined with tachycardia (heart rate ≥ 100 bpm).

AHI-PI provides the clinician with physiological insight into a patient's likelihood of a future episode of HI. An episode of HI is defined as 10 continuous minutes or more where HI is present.

The goal of this adjunctive monitoring method is to enable identification of patients who are showing HI or are likely to experience a future episode of HI, and to allow clinicians an opportunity to increase vigilance. This device is intended for adjunctive use with other physical vital sign parameters and patient information and is not intended to independently direct therapy.

6. SUBSTANTIAL EQUIVALENCE

Comparison of Indications

The subject device and both of the predicate devices are all software decision support systems that receive patient data, process it, and display calculated insights into patient hemodynamic and cardiovascular status to support meaningful clinical decisions.

The subject and both predicate devices are all prescription devices intended for use by healthcare professionals. They are intended for use in adult patients 18 years and older and are intended for adjunctive use with other monitoring and patient information and are not intended to

independently direct therapy. The subject device and primary predicate device are both intended for use on patients in hospitalized settings who are receiving continuous physiological monitoring with electrocardiography (ECG). The subject device and secondary predicate device both are intended to provide physiological insight into a patient's likelihood of future hemodynamic instability.

Technological Comparisons

The table below compares the key technological feature of the subject devices to the predicate devices.

Table 1: Technological Comparison

	AHI System	**Primary Predicate**	**Secondary Predicate**
510(k) Number		DEN200022	K200717
Applicant	Fifth Eye Inc.	Fifth Eye Inc.	CLEW Medical Ltd.
Device Name	AHI System	Analytic for Hemodynamic Instability (AHI)	CLEWICU System (ClewICUServer And ClewICUnitor)
Classification Regulation	860.2220. Adjunctive Hemodynamic Indicator With Decision Point 870.2210. Medium-Term Adjunctive Predictive Cardiovascular Indicator	860.2220. Adjunctive Hemodynamic Indicator With Decision Point	870.2210. Medium-Term Adjunctive Predictive Cardiovascular Indicator
Product Code	QNV, QNL	QNV	QNL
Type of Device	Software-as-a-medical-device	Software-as-a-medical-device	Software-as-a-medical-device
Timing of Analytic Inputs	Near-real-time patient health data	Near-real-time patient health data	Near-real-time patient health data
Analytic Inputs	Inputs are based on signals received from FDA-cleared patient monitoring systems, specifically: For AHI: ECG-II For AHI-PI: AHI Outputs	Inputs are based on signals received from FDA-cleared patient monitoring systems, specifically: ECG-II	Inputs are based on signals received from FDA-cleared patient monitoring systems and other values stored in the electronic health record (EHR) system, specifically: Up to 80 EHR inputs including vital signs, nursing assessments,

	AHI System	Primary Predicate	Secondary Predicate
			flowsheet data, medications, and lab data
Technical Method	Uses analysis of patient data (ECG-II) to detect current signs of a hemodynamic condition (AHI) and combines patient data from patient monitors to produce a single value (AHI-PI) that estimates the likelihood of a future adverse cardiovascular event or condition from a single model mathematically derived from AHI inputs.	Uses pattern analysis of patient data (ECG-II) to detect current signs of a hemodynamic condition	Combines patient data collected from patient monitors and/or electronic health records to produce a single value that estimates the likelihood of a future adverse cardiovascular event or condition using two models, a high risk model and a low risk model.
Analytic Outputs	AHI: A frequently updated binary output over time AHI-PI: A single indicator that estimates the likelihood of a future adverse cardiovascular event (hemodynamic instability episode)	AHI: A frequently updated binary output over time	Single CLEWICU indicator that estimates the likelihood of a future adverse cardiovascular event (hemodynamic instability)
Visual Alerts	AHI: Signs of hemodynamic status provided by red and green color-coded indicators AHI-PI: Risk of future hemodynamic episode provided by red, yellow, and green color-coded indicators	AHI: Signs of hemodynamic status provided by red and green color-coded indicators	CLEWICU: Risk of hemodynamic instability provided by red, yellow, and green color-coded indicators

In conclusion, the differences in the intended use and technological characteristics do not raise new questions of safety and effectiveness. Based on the detailed comparison between the predicate devices and the subject device, the performance testing, and conformance with applicable standards, the AHI System can be found substantially equivalent to the predicate devices.

7. PERFORMANCE DATA

Biocompatibility Testing

The AHI System is a software only device. There are no direct or indirect patient-contacting components of the subject device; therefore, patient contact information is not needed for this device.

Electrical safety and electromagnetic compatibility (EMC)

Not applicable. The AHI System is a software-only device. It contains no electric components, generates no electrical emissions, and uses no electrical energy of any type.

Software Verification and Validation Testing

Software verification and validation testing were conducted and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device was considered as a moderate level of concern. Testing was conducted to ensure the AHI System works as designed.

Bench Testing

Fifth Eye conducted a summative usability study according to the FDA's guidance on Applying Human Factors and Usability Engineering to Medical Devices. Fifth Eye recruited 30 users to participate in the study. The results of the human factors validation study were positive and demonstrated that mitigations addressing use-related risk made during device development were effective.

Animal Testing

Not applicable. Animal studies are not necessary to establish the substantial equivalence of this device.

Clinical Data

The clinical data to support AHI was provided in DEN200022. There have been no changes to AHI since that submission.

To validate that AHI-PI predicts a patient's likelihood of a future hemodynamic instability episode, defined as 10 continuous minutes or more where signs of hemodynamic instability are present, we compared AHI-PI outputs to episodes of hemodynamic instability as observed using a hemodynamic vital signs reference standard – Hypotension (systolic blood pressure <90mmHg or mean arterial pressure (MAP) <70 mmHg) combined with tachycardia (heart rate ≥100 bpm).

The targeted patient population for the AHI System is hospitalized patients 18 years or older who are receiving continuous physiological monitoring with electrocardiography (ECG) and are not contraindicated. While ideally the clinical study would reflect the full spectrum of levels of care for ECG-monitored patients, study design considerations required limiting the primary study population to only patients who were invasively monitored with an arterial line. Therefore,

beginning at the study start date, data were prospectively collected from consecutive patients in equipped beds (those that could store continuous measures of ECG, arterial line numeric data, and other vital signs) at Michigan Medicine.

As requested by FDA, and using bootstrapping to account for multiple measurements per subject, Fifth Eye has demonstrated that AHI-PI can distinguish the risk of developing hemodynamic instability for patients in different risk groups, i.e., those that are at low risk (green), moderate risk (yellow), and high risk (red).

Table 2: Probability estimates of the occurrence of an episode of hemodynamic instability in the prediction window for each of the AHI-PI indicators (Study Population).

AHI-PI Indicator	**Windows in Primary Analysis Set** (total 65,969 windows) n (%) [2]	**Probability of an Episode of Hemodynamic Instability in the next 1 hour measured using continuous vital signs** [1] (Observed [95% confidence interval])	**Likelihood Ratio**
AHI-PI Low Risk Indicator (Green)	43,443 (65.8%)	**0.7%** [0.4%, 1.3%]	N/A
AHI-PI Moderate Risk Indicator (Yellow)	4,999 (7.6%)	**6.5%** [3.7%, 10.3%]	An AHI-PI Moderate Risk indication is **9x** more likely to have an episode of hemodynamic instability in the next 1 hour than an AHI-PI Low Risk Indicator.
AHI-PI High Risk Indicator (Red)	17,527 (26.6%)	**35.9%** [28.1%, 44.0%]	An AHI-PI High Risk indication is **51x** more likely to have an episode of hemodynamic instability in the next 1 hour than an AHI-PI Low Risk Indicator.

[1] The unit of analysis here is at the windows level and not the patient level.

[2] Windows included in the analysis total 65,969 to ensure that a full one hour is available for each AHI-PI in order to determine whether an episode of hemodynamic instability is present or not.

As seen in Table 2, with the prevalence of 10.5% seen in the Primary Analysis Set population using the continuous vital signs reference standard, the probability of an episode of hemodynamic instability in the next 1 hour measured using continuous vital signs was 0.7%, 6.5%, and 35.9% for green, yellow, and red AHI-PI indicators respectively. An AHI-PI High Risk (red) indication is **51** times more likely and an AHI-PI Moderate Risk (yellow) indication is **9** times more likely to have an episode of hemodynamic instability in the next hour as compared to an AHI-PI Low Risk (green) indication. Thus, the risk predication and likelihood performance data show significant discrimination between the risk of future hemodynamic instability events between the different AHI-PI indications, demonstrating a clinical benefit by providing

adjunctive information to the clinician to facilitate fewer missed diagnoses of emerging hemodynamic instability/patient deterioration.

The other relevant metric is lead time. Of those patients who had an episode of hemodynamic instability, AHI-PI High Risk predicted patient deterioration in 89% of cases. The median lead time was calculated as 48 minutes. Although this lead time is less that the 3 hours reported for CLEWICU, it still provides an advance warning to clinicians that the patient is at risk of future hemodynamic instability. The differences in the performance do not impact the safety or effectiveness, as neither device is intended to be the sole factor upon which a patient's clinical care is based.

8. CONCLUSION

The subject AHI System and the predicate devices have equivalent intended uses. The differences in technological characteristics do not raise different questions of safety and effectiveness, and the results of software verification, human factors and clinical validation demonstrate that the subject device performs in accordance with specifications and meets user needs and intended uses. Therefore, the AHI System has been demonstrated to be substantially equivalent to the predicate devices.