October 25, 2023

Implicity Inc.
Caroline Florequin – Head of Quality and Reguatory Affairs
185 Alewife Brook Parkway; Suite 210
Cambridge, Massachusetts 02138

Re: K230842
Trade/Device Name: SignalHF
Regulation Number: 21 CFR 870.2210
Regulation Name: Adjunctive Predictive Cardiovascular Indicator
Regulatory Class: Class II
Product Code: QNL
Dated: September 25, 2023
Received: September 25, 2023

Dear Caroline Florequin:

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,

Stephen C. Browning -S

LCDR Stephen Browning
Assistant Director
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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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K230842

Device Name
SignalHF

Indications for Use *(Describe)*
The SignalHF System is intended for use by qualified healthcare professionals (HCP) managing patients over 18 years old who are receiving physiological monitoring for Heart Failure surveillance and implanted with a compatible Cardiac Implantable Electronic Devices (CIED) (i.e., compatible pacemakers, ICDs, and CRTs).
The SignalHF System provides additive information to use in conjunction with standard clinical evaluation.
The SignalHF HF Score is intended to calculate the risk of HF for a patient in the next 30 days.
This System is intended for adjunctive use with other physiological vital signs and patient symptoms and 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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510(k) Summary

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of 21 CFR 807.92

1 Submitter

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Date prepared: October, 25th 2023
510(k) number: K230842

2 Device Information

Trade Name	SignalHF
Common Name	IM008
Classification	21CFR- 870.2210 - Adjunctive predictive cardiovascular indicator, Class II – Medium

Product Code QNL

3 Predicate Device

The predicate and reference device for SignalHF are:

Predicate Device Acumen™ Hypotension Prediction Index (HPI), Edwards Lifesciences, LLC K203224

	Subject Device	Predicate Device	Comparison to Predicate Device
Device Name	SignalHF	Acumen™ Hypotension Prediction Index (HPI)	
Manufacturer	IMPLICITY INC	Edwards Lifesciences, LLC	
510(k) #		K203224	
Regulation Number	21 CFR 870.2210	21 CFR 870.2210	Same
Class	II	II	Same
Device Class / Name	Medium term adjunctive predictive cardiovascular indicator.	Adjunctive predictive cardiovascular indicator.	Same
Product Code	QNL	QAQ	Similar, Product codes are not the same, but similar. Both devices are SaMD. Incoming data is similar but not the same. Product Code QAQ specifically identifies hypotension as the target area.
Product Code Device Definition	Medium-Term Adjunctive Predictive Cardiovascular Indicator The adjunctive predictive cardiovascular indicator is a prescription device that uses software algorithms to analyze cardiovascular vital	Adjunctive Predictive Cardiovascular Indicator The adjunctive predictive cardiovascular indicator is a prescription device that uses software algorithms to analyze cardiovascular vital signs and predict	Same

	signs and predict future cardiovascular status or events within a defined medium-term period. This device is intended for adjunctive use with other physical vital sign parameters and patient information and is not intended to independently direct therapy.	future cardiovascular status or events. This device is intended for adjunctive use with other physical vital sign parameters and patient information and is not intended to independently direct therapy.	
Software Level of Concern	Moderate	Moderate	Same

4 Device Description

SignalHF is a software as medical device (SaMD) that uses a proprietary and validated algorithm, the SignalHF HF Score, to calculate the risk of a future worsening condition related to Heart Failure (HF). The algorithm computes this HF score using data obtained from (i) a diverse set of physiologic measures generated in the patient's remotely accessible pre-existing cardiac implant (activity, atrial burden, heart rate variability, heart rate, heart rate at rest, thoracic impedance (for fluid retention), and premature ventricular contractions per hour), and (ii) his/her available Personal Health Records (demographics). SignalHF provides information regarding the patient's health status (like a patient's stable HF condition) and also provides alerts based on the SignalHF HF evaluation. Based on an alert and a recovery threshold on the SignalHF score established during the learning phase of the algorithm and fixed for all patients, our monitoring system is expected to raise an alert 30 days (on median) before a predicted HF hospitalization event (see Figure 1).

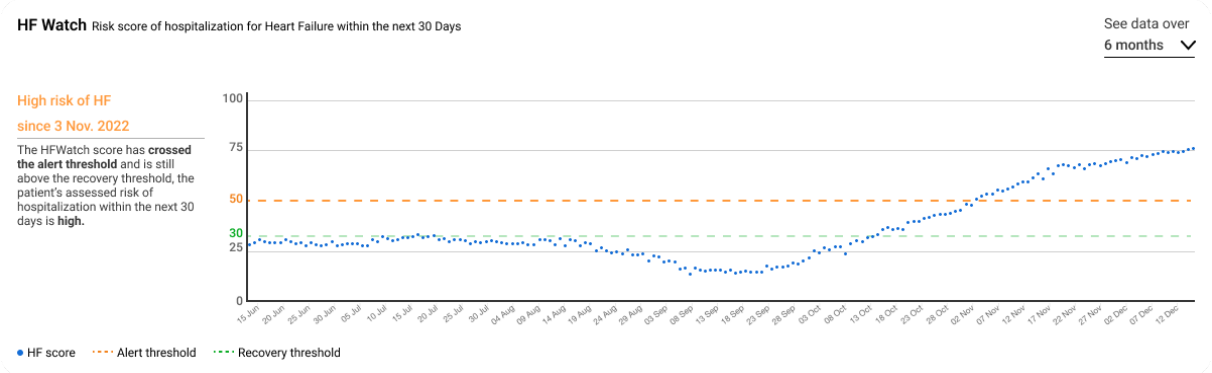

Figure 1. An example of a graph displaying the SignalHF score over time, crossing the alert threshold.

SignalHF does not provide a real-time alert. Rather, it is designed to detect chronic worsening of HF status. SignalHF is designed to provide a score linked to the probability of a future decompensated heart failure event specific to each patient. Using this adjunctive information, healthcare professionals can make adjustments for the patient based on their clinical judgement and expertise.

The score and score-based alerts provided through SignalHF can be displayed on any compatible HF monitoring platform, including the Implicity platform. The healthcare professional (HCP) can utilize the

SignalHF HF score as adjunct information when monitoring CIED patients with remote monitoring capabilities.

The HCP's decision is not based solely on the device data which serves as adjunct information, but rather on the full clinical and medical picture and record of the patient.

5 Indication for Use

Indication for use :

The SignalHF System is intended for use by qualified healthcare professionals (HCP) managing patients over 18 years old who are receiving physiological monitoring for Heart Failure surveillance and implanted with a compatible Cardiac Implantable Electronic Devices (CIED) (i.e., compatible pacemakers, ICDs, and CRTs). The SignalHF System provides additive information to use in conjunction with standard clinical evaluation. The SignalHF HF Score is intended to calculate the risk of HF for a patient in the next 30 days.
This System is intended for adjunctive use with other physiological vital signs and patient symptoms and information and is not intended to independently direct therapy.

Indication for use of predicate:

The Edwards Lifesciences Acumen Hypotension Prediction Index feature provides the clinician with physiological insight into a patient's likelihood of future hypotensive events (defined as mean arterial pressure < 65 mmHg for at least one minute in duration) and the associated hemodynamics.

The Acumen HPI feature is intended for use in surgical or non-surgical patients receiving advanced hemodynamic monitoring.
The Acumen HPI feature is considered to be additional quantitative information regarding the patient's physiological condition for reference only and no therapeutic decisions should be made based solely on the Hypotension Prediction Index (HPI) parameter.

Comparison of the two indication for use statements :

- Same target users (HCP).
- Both provided adjunctive information
- Same type of input data (physiological data)
- Both devices produce an output future risk score
- Different input data: CIEDs data for the subject device and blood pressure and associated hemodynamics for the predicate device (HPI).

6 Technological Characteristics

SignalHF (the subject device) and the Predicate Device have substantially equivalent fundamental scientific technology. Both consist of:

- physiologic data analysis performed using machine learning
- software being deployed as a cloud service`
- input data comes from cardiac vital signs monitors

Based on the assessment and comparison of the technical characteristics of the subject and predicate device, it is determined that both systems have been developed using similar methodologies, offer a future risk score as part of the intended use, and provide adjunct information to the healthcare professional in management of the patient population. The technical characteristics of both devices have been determined to be substantially equivalent.

7 Non-clinical Performance

Non-clinical testing was conducted to assess algorithm performance and to verify that SignalHF performs as intended.

Software verification and validation testing was 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 moderate level of concern. Testing was conducted to ensure that the SignalHF algorithm works as designed.

Algorithm performance testing was assessed using SNDS (the SYSTÈME NATIONAL DES DONNÉES DE SANTÉ) databases as well as Implicity proprietary databases.

The results of the testing demonstrate that SignalHF performs to its specifications and meets its intended use, which is substantially equivalent to that of the predicate device.
A traditional clinical study was not required.

FORESEE-HF Study is a non-interventional clinical retrospective study designed to evaluate a SignalHF score resulting from the combination of multiple sensor measurements collected from multi-brands CIEDs and the data stored in the French national health database "SNDS" in order to detect signs of worsening HF. The follow-up period is defined as 2017-2021.

Inclusion and exclusion criteria

All patients that meet the following criteria were included in the study:

1. Implanted with a ICD / CRT-D / PM / CRT-P, manufactured by Medtronic, Boston Scientific and Biotronik, compatible with thoracic impedance recording
2. With at least one remote monitoring data transmission during the follow-up period of 2018-2021

Patients were excluded from the trial if they presented data quality issues:

1. Patients with unspecified device type in the retrospective database
2. Patients with multiple devices between 2010 and 2021

Coprimary endpoints

The coprimary endpoints of the study for ICD/CRT-D devices are:

- Sensitivity for detecting hospitalizations with HF as primary diagnosis > 40%
- Unexplained alert rate per patient-year < 2.0
- 75% of true positive alerts are raised at least 15 days before HF hospitalization event

The coprimary endpoints of the study for pacemaker/CRT-P devices are:

- Sensitivity for detecting hospitalizations with HF as primary diagnosis > 30%
- Unexplained alert rate per patient-year < 2.0

- 75% of true positive alerts are raised at least 15 days before hospitalization event

The population size of patients who match the inclusion criteria and are not excluded is 17,974 (PM 7,360, ICD 5,642, CRT-D 4,116 and CRT-P 856; age 70.0 ± 13.3, male 70.20%).

Demographic Variable	**Train cohort**	**Validation cohort**	**Clinical cohort**
Nb of patients	***7556***	3678	6,740
Age (years)	69.2 ± 13.9	70.9 ± 12.3	70.6 ± 13.0
Sex			
Female (%)	28.43	29.50	30.03
Male (%)	71.57	70.50	69.97
Device model			
ICD (%)	33.72	28.17	30.54
CRT-D (%)	23.13	23.33	22.40
Pacemaker (%)	38.49	42.90	42.64
CRT-P (%)	4.66	5.60	4.42
Manufacturer device model			
Biotronik (%)	44.64	43.83	49.75
Boston Scientific (%)	18.99	17.64	10.01
Medtronic (%)	36.37	38.53	40.24
Comorbidities			
Renal failure(%)	10.26	10.47	11.56
Hypertension(%)	37.43	40.33	40.54
Diabetes(%)	15.62	17.84	16.25
Obesity/High BMI(%)	6.93	8.48	11.51

Coprimary Objective Results

SignalHF sensitivity, defined as sensitivity for detecting hospitalizations with HF as primary diagnosis, is above 50% for Medtronic and Boston Scientific ICD and CRT-D devices. For Biotronik ICD and CRT-D products, the

sensitivity reaches 70 %. The UAR PPY is always < 1.5 and the lower quartile on alerting time is always > 15 days for ICD and CRT-D from all the manufacturers analyzed, except for Boston Scientific ICD/CRT-D devices, where it is > 15 days on average only. Concerning IPG and CRT-P devices, the sensitivity is 50.4 % for Medtronic devices and 45.3% for Biotronik and UAR PPY is always < 1 for both manufacturers. Lower quartile on alerting time is > 15 days for Biotronik IPG/CRT-P devices, and on average due to low sample size for Medtronic IPG/CRT-Ps. Therefore, the three co-primary endpoints are reached.

Global Performance

The following presents the performance of SignalHF by device type as it relates to:

- Sensitivity for detecting hospitalizations with HF as primary diagnosis, and
- Unexplained alert rate per patient-year (PPY)
- Lower quartile on alerting time (in days)

All SignalHF performance metrics are available in the Clinical Evaluation Report (CER-IM008)

Endpoints	**ICD/CRT-D population objective**	**SignalHF performance for ICD/CRT-D devices**
Sensitivity (%)	> 40%	59.8% [54.0%; 65.4%]
Unexplained Alert Rate PPY	< 2.0	0.654 [0.614; 0.692]
Lower quartile on alerting time (in days)	> 15 days	35.0 [27.0; 52.0]

Endpoints	**Pacemaker/CRT-P population objective**	**SignalHF performance for pacemaker/CRT-P devices**
Sensitivity (%)	> 30%	45.9% [38.1%; 53.8%]
Unexplained Alert Rate PPY	< 2.0	0.470 [0.441; 0.502]
Lower quartile on alerting time (in days)	> 15 days	37 [24.5; 53.0]

Performance per manufacturer

MEDTRONIC

Endpoints	ICD/CRT-D population objective	SignalHF performance for Medtronic ICD/CRT-D
Sensitivity (%)	> 40%	52.0% [43.6%; 60.2%]
Unexplained Alert Rate PPY	< 2.0	0.30 [0.28; 0.32]
Lower quartile on alerting time (in days)	> 15 days	39.3 [21.0; 59.0]

Endpoints	Pacemaker/CRT-P population objective	SignalHF performance for Medtronic pacemaker/CRT-P
Sensitivity (%)	> 30%	50.4% [30.6%; 70.2%]
Unexplained Alert Rate PPY	< 2.0	0.71 [0.65; 0.78]
Lower quartile on alerting time (in days)	> 15 days	64.5 [8.0; 119.0]

BOSTON SCIENTIFIC

Endpoints	ICD/CRT-D population objective	SignalHF performance for Boston Scientific ICD/CRT-D
Sensitivity (%)	> 40%	62.5% [46.9%; 75.8%]
Unexplained Alert Rate PPY	< 2.0	0.89 [0.81; 0.97]
Lower quartile on alerting time (in days)	> 15 days	28.0 [13.0; 55.5]

BIOTRONIK

Endpoints	ICD/CRT-D population objective	SignalHF performance for Biotronik ICD/CRT-D
Sensitivity (%)	> 40%	70.0% [60.6%; 77.9%]
Unexplained Alert Rate PPY	< 2.0	1.09 [1.00; 1.18]
Lower quartile on alerting time (in days)	> 15 days	39.0 [25.8 ; 60.0]

Endpoints	Pacemaker/CRT-P population objective	SignalHF performance for Biotronik pacemaker/CRT-P
Sensitivity (%)	> 30%	45.3% [36.9%; 53.9%]
Unexplained Alert Rate PPY	< 2.0	0.42 [0.39; 0.46]
Lower quartile on alerting time (in days)	> 15 days	37.0 [25.5; 53.0]

SUMMARY

SignalHF performances are above target performances for all pre-defined patient groups except for Boston Scientific pacemaker/CRT-P devices, for which we did not have enough data for training and evaluation of a HF prediction algorithm.

Performance analysis per manufacturer, device model type and number of leads

Medtronic ICD/CRT-D devices

Endpoints	ICD/CRT-D population objective	One lead	Two leads	Three leads
Sensitivity (%)	> 40%	43.5% [29.6%; 58.5%]	49.3% [35.8%; 63.0%]	62.7% [48.0%; 75.4%]
Unexplained alert rate PPY	< 2.0	0.24 [0.20; 0.28]	0.31 [0.27; 0.35]	0.34 [0.30; 0.38]
Lower quartile on alerting time (in days)	> 15 days	59.0 [19.0; 163.0]	31.0 [10.0; 55.0]	57.0 [16.0; 96.0]

Medtronic PM/CRT-P devices

Endpoints	Pacemaker /CRT-P population objective	One lead	Two leads	Three leads
Sensitivity (%)	> 30%	16.7% [2.3%; 63.1%]	64.6% [34.5%; 86.3%]	Not available
Unexplained alert rate PPY	< 2.0	0.61 [0.42; 0.84]	0.62 [0.56; 0.68]	0.76 [0.60; 0.93]
Lower quartile on alerting time (in days)	> 15 days	10.0 (CI not computable)	91.8 [20.0; 129.0]	106.3 [98.0; 131.0]

Boston Scientific ICD/CRT-D devices

Endpoints	ICD/CRT-D population objective	One lead	Two leads	Three leads
Sensitivity (%)	> 40%	71.2% [40.3%; 90.0%]	Not available	60.5% [39.4%; 78.4%]
Unexplained alert rate PPY	< 2.0	0.69 [0.56; 0.84]	0.49 [0.38; 0.60]	0.56 [0.49; 0.64]
Lower quartile on alerting time (in days)	> 15 days	52.5 [15.0; 140.3]	53.8 [29.0; 179.0]	43.0 [11.3; 94.0]

Biotronik ICD/CRT-D devices

Endpoints	ICD/CRT-D population objective	One lead	Two leads	Three leads
Sensitivity (%)	> 40%	73.1% [55.4%; 85.6%]	67.5% [50.3%; 81.1%]	63.1% [48.4%; 75.8%]
Unexplained alert rate PPY	< 2.0	0.88 [0.76; 1.01]	0.76 [0.64; 0.88]	0.63 [0.54; 0.71]
Lower quartile on alerting time (in days)	> 15 days	41.0 [22.0; 64.8]	62.75 [30.0; 157.0]	54.0 [18.5; 88.0]

Biotronik PM/CRT-P devices

Endpoints	Pacemaker/ CRT-P population objective	One lead	Two leads	Three leads
Sensitivity (%)	> 30%	29.4% [11.2%; 58.0%]	40.2% [30.9%; 50.2%]	48.0% [26.3%; 70.4%]
Unexplained alert rate PPY	< 2.0	0.46 [0.36; 0.58]	0.31 [0.28; 0.34]	0.45 [0.35; 0.57]
Lower quartile on alerting time (in days)	> 15 days	108.0 [3.0; 395.0]	64.0 [34.0; 105.5]	10.0 [9.0; 34.5]

SUMMARY

Defibrillators with 1, 2 or 3 leads from all manufacturers, as well as pacemakers with 2 and 3 leads from Medtronic and pacemakers with 1, 2 or 3 leads from Biotronik passed the required performances on every endpoint (sensitivity, unexplained alert rate, median alerting time). The results show in particular no specific group overperforming and causing performance overestimation.
Medtronic Pacemaker 1 lead is the only group not meeting endpoint requirements as defined in the CEP_IM008. However, this population does not have any alternative to assess a potential risk of Heart Failure based on their device data. Implicity believes bringing IM008 to this population could avoid some hospitalization in a population that is for the moment not addressed by any other solution.

Warning: In patient populations unlikely to have acute decompensation of HF, the use of the algorithm may have less and possibly poor PPV and NPV.

8 Conclusion

The results of non-clinical testing demonstrate that SignalHF meets its intended use which is equivalent to that of the predicate device. Testing also ensured that SignalHF performed as intended and does not raise different questions of safety or effectiveness to the predicate device.