



June 21, 2024

Tempus Labs, Inc.
Alain Silk
Senior Director, Regulatory Affairs
600 W Chicago Ave.
Chicago, Illinois 60654

Re: K233549

Trade/Device Name: Tempus ECG-AF
Regulation Number: 21 CFR 870.2380
Regulation Name: Cardiovascular machine learning-based notification software
Regulatory Class: Class II
Product Code: SBQ
Dated: May 24, 2024
Received: May 24, 2024

Dear Alain Silk:

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
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

Indications for Use

510(k) Number (if known)

K233549

Device Name

Tempus ECG-AF

Indications for Use (Describe)

Tempus ECG-AF is intended for use to analyze recordings of 12-lead ECG devices and detect signs associated with a patient experiencing atrial fibrillation and/or atrial flutter (collectively referred to as AF) within the next 12 months. It is for use on resting 12-lead ECG recordings collected at a healthcare facility from patients:

- 65 years of age or older,
- without pre-existing or concurrent documentation of atrial fibrillation and/or atrial flutter,
- who do not have a pacemaker or implantable cardioverter defibrillator, and
- who did not have cardiac surgery within the preceding 30 days.

Performance of repeated testing of the same patient over time has not been evaluated and results SHOULD NOT be used for patient monitoring.

Tempus ECG-AF only analyzes ECG data. Results should be interpreted in conjunction with other diagnostic information, including the patient's original ECG recordings and other tests, as well as the patient's symptoms and clinical history.

Tempus ECG-AF is not for use in patients with a history of AF, unless the AF occurred after a cardiac surgery procedure and resolved within 30 days of the procedure. It is not for use to assess risk of occurrence of AF related to cardiac surgery.

Results do not describe a person's overall risk of experiencing AF or serve as the sole basis for diagnosis of AF, and should not be used as the basis for treatment of AF.

Results are not intended to rule out AF follow-up.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

Tempus ECG-AF

K233549

Sponsor Name:	Tempus AI, Inc. 600 W Chicago Ave Ste #510, Chicago, IL 60654 Phone: (833) 514-4187
Contact Person:	Alain Silk, Ph.D Senior Directory, Regulatory Affairs Tempus AI, Inc Phone: (240) 547-9430 alain.silk@tempus.com
Device Trade Name:	Tempus ECG-AF
Common Name:	AI-based ECG analysis software
Classification Name:	Atrial Fibrillation Risk Prediction machine learning-based notification software
Regulation Number:	21 CFR § 870.2380
Product Code:	SBQ
Predicate Device:	Viz HCM
Submission Number:	DEN230003
Product Code:	QXO

Indications For Use

Tempus ECG-AF is intended for use to analyze recordings of 12-lead ECG devices and detect signs associated with a patient experiencing atrial fibrillation and/or atrial flutter (collectively referred to as AF) within the next 12 months. It is for use on resting 12-lead ECG recordings collected at a healthcare facility from patients:

- 65 years of age or older,
- without pre-existing or concurrent documentation of atrial fibrillation and/or atrial flutter,
- who do not have a pacemaker or implantable cardioverter defibrillator, and
- who did not have cardiac surgery within the preceding 30 days.

Performance of repeated testing of the same patient over time has not been evaluated and results SHOULD NOT be used for patient monitoring.

Tempus ECG-AF only analyzes ECG data. Results should be interpreted in conjunction with other diagnostic information, including the patient's original ECG recordings and other tests, as well as the patient's symptoms and clinical history. Tempus ECG-AF is not for use in patients with a history of AF, unless the AF occurred after a cardiac surgery procedure and resolved within 30 days of the procedure. It is not for use to assess risk of occurrence of AF related to cardiac surgery.

Results do not describe a person's overall risk of experiencing AF or serve as the sole basis for diagnosis of AF, and should not be used as the basis for treatment of AF.

Results are not intended to rule out AF follow-up.

Device Description

Tempus ECG-AF is a cardiovascular machine learning-based notification software intended to analyze recordings of 12-lead ECG devices from patients 65 years of age and older. The software employs machine learning techniques to analyze ECG recordings and detect signs associated with a patient experiencing atrial fibrillation and/or atrial flutter (collectively referred to as AF) within the next 12 months. The device is designed to extract otherwise unavailable information from ECGs conducted under the standard of care, to help health care providers better identify patients who may be at risk for undiagnosed AF in order to evaluate them for referral of further diagnostic follow up and address the unmet need of reducing the number of undiagnosed AF patients.

As input, the software takes data from a patient's 12-lead resting ECG (including age and sex). It is only compatible with ECG recordings collected using 'wet' Ag/AgCl electrodes with conductive gel/paste, and using FDA authorized 12-lead resting ECG machines manufactured by GE Medical Systems and Philips Medical Systems with a 500 Hz sampling rate. It checks the format and quality of the input data, analyzes the data via a trained and 'locked' machine-learning model to generate an uncalibrated risk score, converts the model results to a binary output (or reports that the input data are unclassifiable), and evaluates the uncalibrated risk score against pre-set operating points (thresholds) to produce a final result. Uncalibrated risk scores at or above the threshold are returned as 'increased risk' information; uncalibrated risk scores below the threshold are returned as 'no increased risk' information. This information is used to support clinical decision making regarding the need for further referral or diagnostic follow-up. Typical diagnostic follow-up could include ambulatory ECG monitoring to detect previously undiagnosed AF, as described in device labeling. Results should not be used to direct any therapy against AF itself, including anticoagulation therapy.

Tempus ECG-AF does not have a dedicated user interface (UI). Input data comprising ECG tracings, tracing metadata (sample count, sample rate, etc.), patient age and patient sex, will be provided to Tempus ECG-AF through standard communication protocols (e.g. API, file exchange) with other medical systems (e.g., electronic health record systems, hospital information systems, or other medical device data display, transfer, storage, or format-conversion software). Results from Tempus ECG-AF will be returned to users in an equivalent manner.

Intended Use and Technological Characteristics Comparison

The intended use of the candidate and predicate devices is the same. Both are intended for the analysis of 12-lead resting ECG recordings, using machine-learning techniques to detect signs of cardiovascular conditions for further referral or diagnostic follow-up. The indications for use of the candidate and predicate devices are similar. The candidate device is indicated to analyze ECG tracings in patients aged 65 and older, to detect signs associated with likelihood of a patient experiencing AF in the next 12 months. The predicate device is indicated to analyze ECG tracings in patients aged 18 and older to detect signs associated with current hypertrophic cardiomyopathy (HCM).

The candidate device has the same technological characteristics as the predicate device. Both are machine-learning based software used to analyze recordings of resting 12-lead ECGs.

Summary of Non-Clinical Studies

The performance of Tempus ECG-AF was evaluated based on the non-clinical testing as follows: software verification and validation; and cybersecurity and human factors testing.

Summary of Clinical Studies

Clinical performance of Tempus ECG-AF for analysis of ECG tracings to identify signs associated with a clinical diagnosis of AF in the next 12 months was validated in a retrospective observational cohort study, when the device was used as intended in a representative intended use population. The Tempus ECG-AF model was trained on data from > 1,500,000 ECGs and > 450,000 patients, with 80% of data used for training and 20% of the data used for model tuning. The average age of patients in the training dataset was 59.6 years. 52% of subjects were female and 48% were male. The racial distribution of the patients in the training dataset was 96% White, and 3% Black, and 3% Asian/Other/Unknown. The model was locked prior to clinical performance validation in an independent real-world dataset derived from 3 geographically distinct clinical sites.

Patients were included in the clinical performance validation study based on receiving an ECG as part of the standard of care, and sufficient pre- and post-ECG data available to determine that the patient was part of the intended use patient population and to enable at least 1 year of follow-up to determine the presence or absence of a clinical diagnosis of AF. Each clinical site contributed >1000 patient records, from which the AF status of each patient was determined based on duplicate manual chart review. The total study size was 4017 patients, with one ECG analyzed per patient. The average age of study participants was 75.3 years. 56% of subjects were female and 44% were male. The racial distribution of the study population was 82% White, 11% Black, 3% Asian, and 5% Other/Unknown. Clinical characteristics of heart failure, hypertension, diabetes, stroke and vascular disease were broadly represented in the study. Seven models of 12-lead ECG machines were represented in the study as providing ECG inputs to the Tempus ECG-AF software. These were: CSYS, MAC2K, MAC35, MAC55 and MAC5K (GE Medical Systems) and PageWriter TC and PageWriter Touch (Philips Medical Systems).

Study endpoints of sensitivity and specificity were met, with an observed sensitivity of 31% (95% CI of 25% - 37%) and specificity of 92% (95% CI of 91%-92%). The positive predictive value (PPV) observed in the study was 19% (95% CI of 15% - 23%) and the negative predictive value (NPV) was 95% (95% CI of 95% - 96%). The 1 year incidence of clinical diagnosis of AF following ECG in the study population was 6.0%. No clinically significant differences in performance were observed based on analysis of subgroups.

The observed 19% PPV can be interpreted in the context of the baseline 1-year incidence rate of AF (6%) observed in the study population as follows: if the intended use population were clinically evaluated for AF, AF would be observed in approximately 1-in-16 patients within the next 1 year. For those receiving a positive result from the test, AF would be observed in approximately 1-in-5 patients within the next 1 year.

Table 1. Clinical performance validation study and training dataset demographic characteristics

Parameter	Clinical Performance Study	Training Dataset
N (ECGs)	4107	1597424

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Parameter	Clinical Performance Study	Training Dataset
Age		
Mean (SD)	75.33 (7.16)	59.55 (16.64)
Median	74.18	60.83
Min/Max	65.00 / 89.98	18.00 / 90.00
Age groups n (%)		
< 65	0 (0)	949277 (59)
[65, 70)	1166 (29)	181254 (11)
[70, 75)	1004 (20)	160647 (10)
[75, 80)	791 (19)	131944 (8)
≥ 80	1056 (26)	174302 (11)
Sex n (%)		
Female	2254 (56)	823040 (52)
Male	1761 (44)	774144 (48)
Unknown	2 (<1)	240 (<1)
Race n (%)		
White	3281 (82)	1538164 (96)
Black	433 (11)	42294 (3)
Asian	120 (3)	10207 (1)
Other	141 (4)	2863 (<1)
Unknown	42 (1)	3896 (<1)
Ethnicity n (%)		
Hispanic	382 (10)	39213 (2)
Not Hispanic	3615 (90)	1432954 (90)
Unknown	20 (<1)	125257 (8)
CHA₂DS₂VASc* score n (%)		
< 2	128 (3)	n/a**
≥ 2	3889 (97)	
CHA₂DS₂VASc* score n (%)		
< 4	1698 (42)	n/a**
≥ 4	2319 (58)	
Clinical Characteristics n (%)***		
Heart failure	441 (11)	n/a**
Hypertension	3232 (80)	
Diabetes	1341 (33)	
Stroke/TIA/TE	622 (15)	
Vascular disease	1290 (32)	
Conduction delay on ECG****	539 (13)	
BMI:		
[0, 18.5)	83 (2)	21844 (1)
[18.5, 24.9)	899 (22)	265247 (17)
[25, 29.9)	1405 (35)	383650 (24)
≥ 30	1611 (40)	591980 (37)
Unknown	19 (<1)	334703 (21)

*The CHA₂DS₂VASc scoring system is used to estimate stroke risk in patients with AF

**not available

***Patients may have more than one clinical characteristic, therefore the percentages do not sum to 100

****Conduction delay is considered QRS > 120 msec

Substantial Equivalence Conclusion

Based on non-clinical and clinical performance testing conducted, the candidate device, Tempus ECG-AF, is substantially equivalent to the predicate device Viz HCM (DEN230003). The devices have the same intended uses, principles of operation, and technological characteristics. Differences between the candidate and predicate devices do not raise different questions of safety and effectiveness, and the results of non-clinical testing and clinical performance validation demonstrate that the candidate device is substantially equivalent to the predicate device.

Table 2. Substantial Equivalence Comparison

	Predicate (Viz HCM, DEN230003)	Candidate (Tempus ECG-AF)
Intended Use	Analysis of 12-lead resting ECG recordings using machine-learning techniques to detect signs of cardiovascular conditions for further referral or diagnostic follow-up.	Same
Rx / OTC	Rx only	Same
Cardiovascular Condition Evaluated	Hypertrophic cardiomyopathy (HCM)	Risk of atrial fibrillation/flutter (AF) in the next 12 months
Age of Intended Patient (Years)	18+	65+
For Use with Patients with Implanted Pacemakers	No	No
Locked Machine-Learning based Model	Yes	Same
Input	12-lead ECG tracing, and other physiological inputs	12-lead ECG tracing, patient age, patient sex
Output	Detection of signs associated with HCM causes ECGs to be flagged.	Detection of signs associated with AF is provided as "increased risk", "no increased risk" or "unclassifiable" to medical information systems for display to clinicians.
Prediction Window	Current disease	Future disease (12 months)
Software	Proprietary algorithm and software	Same