



April 5, 2024

The Surgeon General, Department of the Army (TSG-DA)  
% Chandar Thakur  
Acting Branch Chief, Medical Devices & Diagnostics, Office of Regulatory Activities  
U.S. Army Medical Materiel Research & Development Command; Attn: Fcmr-ora,  
1430 Veterans Drive  
Fort Detrick, Maryland 21702

Re: K233249

Trade/Device Name: APPRAISE-HRI  
Regulation Number: 21 CFR 870.2220  
Regulation Name: Adjunctive Hemodynamic Indicator With Decision Point  
Regulatory Class: Class II  
Product Code: SAR  
Dated: February 27, 2024  
Received: February 27, 2024

Dear Chandar Thakur:

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](mailto: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,

Diagnosics 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)  
K233249

Device Name  
APPRAISE-HRI

### Indications for Use (Describe)

The APPRAISE-HRI is a mobile health app intended to provide a means for military healthcare providers to screen U.S. Service members for hemorrhage risk after a physically traumatic event and stratify casualties who need immediate attention and emergency evacuation from those who are injured but may not be at risk for hemorrhage.

The APPRAISE-HRI is not intended to diagnose or direct treatment. Rather, it is intended to provide situational awareness and inform clinical management of potentially hemorrhagic casualties by identifying those at the greatest risk of hemorrhage.

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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**ATTACHMENT 18.1 A4  
510(k) SUMMARY****Contact Details****Applicant Details:**

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Date Prepared: March 27, 2024

**Subject Device Details**

Device Trade Name: APPRAISE-HRI  
Common Name: Adjunctive Hemorrhage Risk Indicator  
Classification: Class II  
Classification Regulation: 21.CFR.870.2220: Adjunctive Hemodynamic Indicator with Decision Point  
Product Code: SAR

**Predicate Device Details**

Device Trade Name: Analytic for Hemodynamic Instability (AHI)  
De Novo number: DEN200022  
Common Name: Adjunctive Hemodynamic Indicator with Decision Point  
Classification: Class II  
Classification Regulation: 21.CFR.870.2220: Adjunctive Hemodynamic Indicator with Decision Point  
Product Code: QNV

## Device Description

The Automated Processing of the Physiological Registry for Assessment of Injury Severity (APPRAISE)-Hemorrhage Risk Index (HRI) is an Android application developed by the U.S. Army Medical Research and Development Command (USAMRDC) that uses vital-sign data collected from a trauma patient to provide a risk score that stratifies the patient's risk of hemorrhage. When the application runs, heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) vital-sign data are collected from an external monitor [currently only the ZOLL Propaq M (K202375) is supported]. The ZOLL Propaq M monitor connects via Bluetooth with the Android platform running the APPRAISE-HRI application. The APPRAISE-HRI application continuously pulls data from the ZOLL Propaq M monitor to gather the required vital signs (HR, SBP, and DBP) and then runs the hemorrhage risk stratification algorithm to generate an output every one minute.

Once the vital-sign data from the ZOLL Propaq M monitor are transferred, the APPRAISE-HRI provides a stratification of hemorrhage into three Risk Level categories: Low (I), Average (II), or High (III). The APPRAISE-HRI application continuously displays both the input vital signs (HR, SBP, and DBP) and the Risk Level score to the caregiver to provide situational awareness and to inform clinical management of potentially hemorrhagic casualties by identifying those at the greatest risk of hemorrhage.

## Indications for Use Statement

The APPRAISE-HRI is a mobile health app intended to provide a means for military healthcare providers to screen U.S. Service members for hemorrhage risk after a physically traumatic event and stratify casualties who need immediate attention and emergency evacuation from those who are injured but may not be at risk for hemorrhage.

The APPRAISE-HRI is not intended to diagnose or direct treatment. Rather, it is intended to provide situational awareness and inform clinical management of potentially hemorrhagic casualties by identifying those at the greatest risk of hemorrhage.

## Software Functionality

APPRAISE-HRI is an application designed to run on the Android platform. It targets Android 13, but it is compatible with Android versions 9 through 13, excluding Android 12L. The application is designed to be device agnostic, supporting devices with touch screens that have resolution of at least 1200x800 dp. APPRAISE-HRI does not require any other hardware features except for Bluetooth. The software of the application is divided by function into three major components: graphical user interface, services, and the APPRAISE-HRI algorithm.

The graphical user interface (GUI) consists of three pages: the MainActivity Page, the PreferenceActivity Page, and the WebViewActivity Page. They provide functionality to control the device settings and display results of the APPRAISE-HRI algorithm. The services component of APPRAISE-HRI mobile app allows the application to communicate with the ZOLL Propaq M monitor, request and receive real-time data, and feed real-time data to the APPRAISE-HRI algorithm.

The APPRAISE-HRI algorithm, which provides the core functionality to this device, consists of three modules. The first module pre-processes the raw vital-sign data and provides minute-by-minute values as valid input for the second module, an artificial intelligence (AI) linear regression model. Then, the third module stratifies the output of the AI model to yield three

hemorrhage risk indices: HRI Levels I, II, or III. An HRI Level of I indicates that the likelihood of the patient experiencing hemorrhage is highly decreased compared to the population average; an HRI Level of II indicates that the likelihood of hemorrhage is equivalent to that of a trauma population; and an HRI Level of III indicates that the likelihood of the patient experiencing hemorrhage is highly increased compared to the population average.

## **Summary of Performance Testing**

### **Software Verification Tests**

Non-clinical software tests (Unit, Integration, and System levels) were conducted for the subject device, APPRAISE-HRI, during product development. The risk analysis was completed, and risk controls were implemented to mitigate identified hazards. The test results support that all the software specifications have met the acceptance criteria. The subject device, APPRAISE-HRI, conforms to the following voluntary standards: 1) “ISO 14971:2019 – Medical devices – application of risk management to medical devices” and 2) “IEC 62304 2016 – Medical device software – software life cycle processes.”

The level of software documentation for the subject device, APPRAISE-HRI, was determined to be “Enhanced Documentation Level,” according to the risk analysis and rationale set forth in the June 14, 2023, FDA Guidance for the Content of Premarket Submissions for Device Software Functions.

### **Summative Usability Testing (Usability Study)**

USAMRDC conducted a summative study as part of the usability assessment evaluation of the subject device, APPRAISE-HRI. The summative study was conducted to ensure that the device user interface has been designed so that user error is reduced or eliminated and that it meets the intended users’ (i.e., Army medics’) needs.

The responses of the participating Army medics on the summative study based on the Likert-scale questionnaire show that the medics found it easy to determine a patient’s hemorrhage risk using APPRAISE-HRI. In addition, they agreed that using the APPRAISE-HRI app will help to identify patients with a risk of hemorrhage. The medics also responded that the instructions for use of the APPRAISE-HRI were easy to follow. Further, the study provided evidence that participants were able to correctly interpret the device output.

Intended users (i.e., Army medics) are expected to receive training on the use and interpretation of the device prior to first use.

### **Clinical Study Validation**

A clinical utility study was conducted to evaluate the performance of the APPRAISE-HRI in real-world trauma patients. This “prospectively, retrospectively” design study prospectively validated the APPRAISE-HRI device using retrospectively collected vital-sign data both during transport of trauma patients from the point of injury to the receiving hospital (eight sites) and at a hospital’s Emergency Department (one site). The targeted population for the APPRAISE-HRI is adult trauma patients (patient age range is  $\geq 18$  and  $\leq 90$  years) who were labeled as Hemorrhage patients or Control patients based on trauma registry data, including blood transfusion information and documented hemorrhagic injuries, such as clinical notes, International Classification of Disease 10th Revision (ICD-10) codes, and Abbreviated Injury Scale (AIS) codes.

The primary endpoint used to validate the APPRAISE-HRI was the Likelihood Ratios for HRI

Levels I, II, and III, for the first HRI output of each patient. The secondary endpoints included other statistical metrics, analysis of different subgroups of interest [age, mode of injury (blunt vs. penetrating), and clinical study site], and analysis through time. The success criteria for the APPRAISE-HRI device required that it effectively and consistently differentiated between HRI Levels, I, II, and III and that the ground truth for trauma patients tracked consistently with the algorithm results.

As shown in Table 1, the primary endpoint results demonstrate that the key test statistics, the Likelihood Ratios of the APPRAISE-HRI Levels, met the success criteria: APPRAISE-HRI was at least five times less likely to output an HRI Level I for Hemorrhage patients than for Control patients; APPRAISE-HRI was almost as likely to output an HRI Level II for Hemorrhage patients as for Control patients; and APPRAISE-HRI was nearly seven times more likely to output an HRI Level III for Hemorrhage patients than for Control patients. These results indicate that the APPRAISE-HRI is a useful tool to aid in discriminating hemorrhage risk in the trauma population.

**Table 1:** APPRAISE-HRI Algorithm for the Detection or Exclusion of Hemorrhage.

Test Level	# of Hemorrhage Patients	# of Control Patients	Total # of Patients	Likelihood Ratio [95% CI*]
HRI Level I	25	1,347	1,372	0.18 [0.12, 0.26]
HRI Level II	257	3,631	3,888	0.70 [0.63, 0.76]
HRI Level III	261	374	635	6.88 [6.04, 7.84]
Total	543	5,352	5,895	

\*Confidence intervals (CI) computed based on 10,000 samples with replacement from the dataset.

The APPRAISE-HRI performed consistently across subgroups (age categories, modes of injury, and study sites), with the exception of ruling in hemorrhage patients with penetrating injury (mainly due to low numbers of the patient population recorded with penetrating injury). Based on the clinical results, the APPRAISE-HRI met the Special Control (b) (4) of 21CFR870.2220.

### **Conclusion (Substantial Equivalence Discussion)**

The subject device, APPRAISE-HRI, and its predicate (DEN200022) have the same intended use and similar indication for use, similar technological characteristics, and, overall, similar principles of operation. There is a minor difference between the subject device, the APPRAISE-HRI, and the predicate's (DEN200022) indications for use (the subject device is indicated for hemorrhage condition and the predicate is indicated for hemodynamic condition). In addition, they are used both in different patient populations and use environments. However, these differences do not constitute a new indication for use, because both the subject device and the predicate device are intended to be used adjunctively to monitor blood (hemo-) related conditions along with other cardiovascular monitoring devices.

The other minor differences between the subject device and the predicate are certain technological characteristics and principles of operation (such as different algorithm inputs and outputs). However, these differences do not raise additional safety and efficacy questions because the safety and performance of the subject device, the APPRAISE-HRI, were evaluated as per the verification and validation testing.

Traditional 510(k) Notification  
18.0 Administrative Documents

APPRAISE-HRI

Therefore, the noted differences do not raise different questions of safety or effectiveness, and the results of software verification, usability testing, and clinical validation demonstrate that the subject device performs in accordance with specifications and meets user needs. The subject device, APPRAISE-HRI, has been demonstrated to be substantially equivalent to the identified predicate device (DEN200022).