DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
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Silver Spring, MD 20993-0002

December 21, 2016

Flashback Technologies, Inc.
c/o Paul Dryden
ProMedic, LLC
1215 Spruce Street, Suite #101
Boulder, Colorado 80302

Re: DEN160020
CipherOx CRI™ Tablet
Evaluation of Automatic Class III Designation – *De Novo* Request
Regulation Number: 21 CFR 870.2200
Regulation Name: Adjunctive cardiovascular status indicator
Regulatory Classification: Class II
Product Code: PPW
Dated: May 22, 2016
Received: May 24, 2016

Dear Mr. Dryden:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your *de novo* request for classification of the CipherOx CRI™ Tablet, a prescription device under 21 CFR Part 801.109 that is indicated for the following:

> *The CipherOx CRI Tablet is indicated for continuous noninvasive monitoring of functional oxygen saturation of arterial hemoglobin (SpO2), pulse rate (measured by an SpO2 sensor), and the Compensatory Reserve Index (CRI), which trends changes in intravascular volume relative to the individual patient's response to hypovolemia.*
>
> *For patients with a finger thickness of 0.3" to 1" in hospital and pre-hospital settings.*
>
> *CRI trends with changes in intravascular volume relative to the individual patient's response to hypovolemia, and should only be used by qualified medical providers as an adjunct to rather than as a replacement for traditional hemodynamic measures. CRI is indicated for adults (19-36 years old) in the supine position under non-motion conditions and without cardiovascular disease. CRI has not been studied in trauma patients.*

FDA concludes that this device should be classified into class II. This order, therefore, classifies the CipherOx CRI™ Tablet, and substantially equivalent devices of this generic type, into class II under the generic name adjunctive cardiovascular status indicator.

FDA identifies this generic type of device as:

> **Adjunctive cardiovascular status indicator.** The adjunctive cardiovascular status indicator is a prescription device based on sensor technology for the measurement of a physical parameter(s). This device is intended for adjunctive use with other physical vital sign parameters and patient information and is not intended to independently direct therapy.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This new law provides two options for *de novo* classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may, within 30 days of receiving notice of the NSE determination, request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device type.

On May 24, 2016, FDA received your *de novo* requesting classification of CipherOx CRI™ Tablet into class II. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the CipherOx CRI™ Tablet into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

After review of the information submitted in the *de novo* request, FDA has determined that the CipherOx CRI™ Tablet indicated for the following:

> *The CipherOx CRI Tablet is indicated for continuous noninvasive monitoring of functional oxygen saturation of arterial hemoglobin (SpO2), pulse rate (measured by an SpO2 sensor), and the Compensatory Reserve Index (CRI), which trends changes in intravascular volume relative to the individual patient's response to hypovolemia.*
>
> *For patients with a finger thickness of 0.3" to 1" in hospital and pre-hospital settings.*
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> *CRI trends with changes in intravascular volume relative to the individual patient's response to hypovolemia, and should only be used by qualified medical providers as an adjunct to rather than as a replacement for traditional hemodynamic measures. CRI is indicated for adults (19-36 years old) in the supine position under non-motion conditions and without cardiovascular disease. CRI has not been studied in trauma patients.*

can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in Table 1.

Table 1 – Identified Risks to Health and Mitigation Measures

Identified Risk	**Mitigation Measures**
Delayed or incorrect treatment due to erroneous output as a result of software malfunction or algorithm error	Software verification, validation, and hazard analysis Non-clinical performance testing Clinical performance testing Labeling
Delayed or incorrect treatment due to user misinterpretation	Usability assessment Labeling

In combination with the general controls of the FD&C Act, the adjunctive cardiovascular status indicator is subject to the following special controls:

1. Software description, verification and validation based on comprehensive hazard analysis must be provided including:
    a. Full characterization of technical parameters of the software, including any proprietary algorithm(s);
    b. Description of the expected impact of all applicable sensor acquisition hardware characteristics on performance and any associated hardware specifications;
    c. Specification of acceptable incoming sensor data quality control measures;
    d. Mitigation of impact of user error or failure of any subsystem components (signal detection and analysis, data display, and storage) on accuracy of patient reports;

2. Scientific justification for the validity of the status indicator algorithm(s) must be provided. Verification of algorithm calculations and validation testing of the algorithm using a data set separate from the training data must demonstrate the validity of modeling;

3. Usability assessment must be provided to demonstrate that risk of misinterpretation of the status indicator is appropriately mitigated;

4. Clinical data must be provided in support of the intended use and include the following:
    a. Output measure(s) must be compared to an acceptable reference method to demonstrate that the output measure(s) represent(s) the predictive measure(s) that the device provides in an accurate and reproducible manner;
    b. The data set must be representative of the intended use population for the device. Any selection criteria or limitations of the samples must be fully described and justified;
    c. Agreement of the measure(s) with the reference measure(s) must be assessed across the full measurement range;
    d. Data must be provided within the clinical validation study or using equivalent datasets to demonstrate the consistency of the output and be representative of the range of data sources and data quality likely to be encountered in the intended use population and relevant use conditions in the intended use environment;

5. Device labeling must include the following:
    a. The type of sensor data used, including specification of compatible sensors for data acquisition;
    b. A description of what the device measures and outputs to the user;
    c. Warnings identifying sensor reading acquisition factors that may impact measurement results;
    d. Guidance for interpretation of the measurements, including warning(s) specifying adjunctive use of the measurements;
    e. Key assumptions made in the calculation and determination of measurements;
    f. The measurement performance of the device for all presented parameters, with appropriate confidence intervals, and the supporting evidence for this performance; and
    g. A detailed description of the patients studied in the clinical validation (e.g., age, gender, race/ethnicity, clinical stability) as well as procedural details of the clinical study.

In addition, this is a prescription device and must comply with 21 CFR 801.109. Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the adjunctive cardiovascular status indicator they intend to market prior to marketing the device and receive clearance to market from FDA.

Please be advised that FDA's decision to grant this *de novo* request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD & C 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD & C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the **Federal Register**. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the *de novo* request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Nathalie Yarkony at 301-796-1235.

Sincerely,

Jonette R. Foy -S

Jonette Foy, Ph.D.
Deputy Director
for Engineering and Science Review
Office of Device Evaluation
Center for Devices and
Radiological Health