November 12, 2021

Openwater
% Prabhu Raghavan
Principal
MDQR, LLC
1790 Montemar Way
San Jose, California 95125

Re: Q211873
Trade/Device Name: Openwater LVO Stroke Alert
Received: September 13, 2021

Dear Prabhu Raghavan:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has received the above submission requesting designation as a Breakthrough Device. We regret to inform you that your device and the proposed indication do not meet the criteria for designation as a Breakthrough Device and your request has been denied. Please refer to the FDA guidance document entitled "Breakthrough Devices Program", for more information regarding the program, available at https://www.fda.gov/media/108135/download.

Designation as a Breakthrough Device is not granted for the following reasons:

1. To meet Breakthrough Device designation criterion #1 as defined by section 515B(b)(1) of the Food, Drug, and Cosmetic (FD&C) Act (21 U.S.C. 360e-3(b)(1)), you need to demonstrate a reasonable expectation that the proposed device could function as intended thereby demonstrating technical success and could provide for more effective diagnosis or treatment of the target condition compared to current available methods. In response to the October 13, 2021, request for additional information (AIRQ) letter, you clarified that the Openwater LVO Stroke Alert classified 100% of large vessel occlusion (LVO) strokes accurately (N=4), 100% of the non-LVO strokes accurately (N=3, with one intracranial hemorrhage (ICH) and two non-LVO ischemia), and 100% of controls as not LVO (N=30) based on a small human feasibility study comparing the blood volume index (BVI) and blood flow index (BFI) from the Openwater Headset and the Openwater LVO Stroke Alert output to computed tomography (CT) and magnetic resonance imaging (MRI) data. However, we believe that this sample size is too small and may not be generalizable to all suspected stroke patients in the United States (US) to understand the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the subject device and how this performance compares to alternative diagnostic methods to meet Breakthrough Device criterion #1. Therefore, we request that you submit additional clinical performance data to characterize the sensitivity, specificity, PPV, and NPV of the Openwater LVO Stroke Alert that is more representative of your device performance to be used in all suspected LVO stroke patients in the US that incorporates and addresses the following items:

a. Specify the demographics of the patient population enrolled and justify how the sample size is adequate to quantify the device performance that is representative of all suspected LVO stroke patients in the US based on stroke location, infarction size, and time from last known well. As part of the demographics of the patients enrolled, there should be a sufficient number of enrolled patients with varying degrees of skin pigmentation, including darker skin pigmentation to assess whether device performance can be affected by skin pigmentation due to the technological characteristics of the Openwater Headset. Although you state in the response to the October 13, 2021, AIRQ letter that "*skin tone should have minimal effect on Openwater LVO Alert's algorithms for various reasons*," the accompanying bench test of speckle contrast changes in response to varying light filtration and discussion of device design are insufficient justification to support this statement. While it is reasonable to state that measurements between left and right hemispheres will be affected equally by patient skin pigmentation, it is not clear how changes in the magnitude of the resulting difference would affect device performance. Furthermore, while the provided bench data may provide an initial assurance of potential resilience of the BFI to changes in skin pigmentation, we lack information about how the proprietary calculation of BVI is affected.

b. Provide a risk assessment that evaluates how poor device placement and other technical issues may affect the interpretation of the data and all of the scenarios in which the device output could be misinterpreted by the end user. This assessment should include a targeted discussion of use of the Openwater LVO Stroke Alert in the intended clinical use environment, which can include the pre-hospital emergency medical services (EMS) setting. This is important because various environmental use factors can affect device performance, such as how the end user interprets the output and how the device is applied in a moving ambulance versus at a hospital.

c. The response (p.10) to deficiency #2.a. in the October 13, 2021, AIRQ letter mentioned that "*stroke scales have shown poor sensitivity in actual practice, as low as 38% in some studies (Nguyen et al., 2021) and additionally suffer from particularly poor specificity as low as 20% in some studies (English et al., 2018)*." However, the Los Angeles Motor Scale (LAMS) and other scales have good accuracy and predictive value for LVO strokes in the pre-hospital and emergency department settings (Noorian et al., 2018). Additionally, LAMS can be used for ischemic strokes in the posterior circulation as well. Provide additional information comparing the device safety and effectiveness when compared to pre-hospital stroke scales, such as LAMS using more updated performance data. Also, provide a discussion of the intended use of the device and whether it is intended to replace stroke scales or imaging modalities.

2. The proposed indications for use (IFU) related to the Openwater Headset states:

"*The non-invasive Openwater Headset is intended for monitoring of blood flow in tissue, including the brain. The Openwater headset is intended for monitoring of adults. The prospective clinical value of data from Openwater Headset has not been demonstrated in disease states. Openwater Headset should not be used as the sole basis for diagnosis or therapy.*"

The proposed IFU related to the Openwater LVO Stroke Alert states:

"*Openwater LVO Stroke Alert is indicated for use as an early notification system to identify and communicate blood flow data on patients suspected of large vessel occlusion (LVO) of the internal carotid artery or proximal middle cerebral artery. This software as a medical device (SaMD) utilizes blood flow data from Openwater Headset in adult patients*."

The proposed IFU should include information specifying use of the device in the pre-hospital setting to align with its intended use. It should also mention information related to the triage and routing of patients to stroke facilities that are equipped to manage LVO vs. non-LVO patients, if applicable. Therefore, we request that you include these modifications to the IFU statement of the Openwater LVO Stroke Alert to better identify the patient population for which the device is intended to be used for and assist with effective diagnosis of LVO strokes to support the Breakthrough Device designation.

Even though we have determined that your device does not qualify for the Breakthrough Device designation, you may use the Pre-Submission review process, as described in the Pre-Submission guidance available at https://www.fda.gov/media/114034/download, to request feedback from FDA. This new submission should be provided as an eCopy, it should include the FDA reference number for this Pre-Submission, and should be submitted to the following address:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
IDE Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you disagree with the decision identified in this letter, please note, the most effective means for resolving disputes is through discussion with the CDRH staff who reviewed your submission. If these approaches fail to resolve the disagreement, you may request supervisory review under 21 CFR 10.75. Most actions taken by CDRH can be revisited under this Section, which is a general-purpose mechanism to request supervisory review of a decision made by CDRH staff. The general expectation is that there will be an orderly progression of interaction with CDRH review staff, followed by outreach to relevant members of Management and then engagement with the CDRH Ombudsman, prior to filing an appeal under 10.75. A request for supervisory review should be directed at the next organizational level above the level at which the action was taken.

If you have any questions, please contact Saikat Bhuiyan at 301-796-2436 or Saikat.Bhuiyan@fda.hhs.gov.

Sincerely,

Xiaolin Zheng -S

Xiaolin Zheng, Ph.D.
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