March 15, 2023

Anumana, Inc.
Alana O'Brien Del Campo, MD
Head of Clinical Innovation
1 Main Street, Suite 400 East Arcade
Cambridge, MA 02142

Dear Dr. O'Brien Del Campo:

On May 11, 2020, based on a request from Eko Devices, Inc., the Food and Drug Administration (FDA) issued a letter determining that the electrocardiogram (ECG) Low Ejection Fraction Tool ("ELEFT") [1] (hereinafter the ELEFT or your product) met the criteria for issuance under section 564(c) of the Act to be eligible for authorization under the March 31, 2020, Emergency Use Authorization (EUA) to be used by healthcare professionals (HCP) to provide an assessment of Left Ventricular Ejection Fraction (LVEF) [2] for use as a diagnostic aid to screen[3] for potential cardiac complications associated with Coronavirus Disease 2019 (COVID-19) or underlying cardiac conditions that may affect clinical management of COVID-19, in adult patients having or suspected of having COVID-19.

On June 17, 2022, you requested to revise this EUA. Based on that request, and having concluded that revising the May 11, 2020 EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), FDA is reissuing the May 11, 2020, letter in its entirety with the revisions incorporated.[4] Accordingly, your

[1] This EUA includes the emergency use of the ELEFT. In general, ELEFT is a machine learning algorithm that is used as an aid to screen for an LVEF less than or equal to 40% based on the input of one or more ECG vectors at the point-of-care. LVEF is a standard measure of cardiac efficiency and is used in the evaluation of patients such as those suspected of having heart failure with reduced ejection fraction. LVEF is typically, and most accurately, calculated through analysis of imaging, but acquisition of imaging at the point of care can be challenging in the current emergency, and often a cause of delay in evaluation or assessment. Additionally, recognizing that imaging resources may be limited, there may be patients who are not indicated for imaging who may benefit from an assessment of whether they are presenting with a reduced LVEF such that further evaluation can be performed. The ELEFT analysis software is available via application program interface (API) or distributed via electronic media for implementation in a healthcare facility's own server. The ELEFT is not FDA-cleared or approved for marketing in the United States. In addition, the ELEFT does not have a marketing authorization in another country.

[2] The ELEFT algorithm defines low LVEF as less than or equal to 40%, in accordance with clinical practice guidelines.

[3] The ELEFT algorithm is not intended as a sole means of diagnosis and is intended to be used when echocardiography is not available or is not indicated.

[4] On June 17, 2022, FDA received a joint request from Anumana, Inc. and Eko Devices, Inc. to amend the EUA for ELEFT to transfer ownership, title, rights and all interests from Eko Devices Inc. to Anumana, Inc. The Health Care Provider Fact Sheet, the Patient Fact Sheet, and the Instructions for Use were revised to replace references to Eko Devices, Inc. with Anumana, Inc. Additionally, minor edits to the labeling were included to provide additional clarity of the device function.

product is hereby authorized pursuant to section 564 of the Act when used pursuant to the Scope of Authorization (Section II) and Conditions of Authorization (Section IV) of this reissued letter.

On February 4, 2020, pursuant to section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.[5] Pursuant to section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared on March 24, 2020, that circumstances exist justifying the authorization of emergency use of medical devices, including alternative products used as medical devices, pursuant to section 564 of the FD&C Act, subject to the terms of any authorization issued under that section.[6]

There are no FDA approved or cleared devices to screen for cardiac dysfunction in patients with confirmed or suspected COVID-19 during the public health emergency. There is published evidence that patients with cardiac comorbidities are at substantially increased risk for complications from COVID-19, and COVID-19 may exacerbate or introduce cardiac comorbidities which is associated with higher risk of in-hospital mortality.

Based on published evidence, there has been a recognition that screening for cardiac conditions is an important part of managing patients with confirmed or suspected COVID-19. While the current recommendation[7] is that patients with confirmed or suspected COVID-19 demonstrating heart failure, arrhythmia, ECG changes or cardiomegaly should undergo echocardiography, this is not indicated for all patients. Additionally, echocardiography may not be an immediately available option. Thus, having additional tools to quickly screen for cardiac dysfunction may provide benefit to patients for whom an echocardiogram would otherwise not be indicated or is not available. The ELEFT algorithm was trained on and evaluated with datasets containing linked ECG and echocardiogram records from electronic health records. The validation was performed using retrospective and prospective methods to define the performance of the algorithm. Based on this validation data and published studies describing the performance of the algorithm, FDA has concluded that the ELEFT may be effective as a diagnostic aid to screen patients diagnosed with or suspected of having COVID-19 for LVEF less than or equal to 40%.

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act are met, I am authorizing the emergency use of the ELEFT, as described in the Scope of

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[5] U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. 85 FR 7316 (February 4, 2020) (accessible at https://www.fda.gov/media/135010/download).

[6] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 17335 (March 27, 2020).

[7] American College of Cardiology. "ACC President Message: ACC Issues COVID-19 Clinical Guidance For the CV Care Team." March 6, 2020, https://www.acc.org/latest-in-cardiology/articles/2020/03/06/15/01/acc-issues-covid-19-clinical-guidance-for-the-cv-care-team.

Authorization section of this letter (Section **Error! Reference source not found.**) and pursuant to the Conditions of Authorization (Section III) of this letter.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the ELEFT, as described in the Scope of Authorization (Section **Error! Reference source not found.**) of this letter, for use by HCP to provide an assessment of low Left Ventricular Ejection Fraction (LVEF), for use as diagnostic information to screen for potential cardiac complications associated with COVID-19 in patients 18 years of age or older with suspected or confirmed COVID-19 meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. SARS-CoV-2, the virus that causes COVID-19, can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the ELEFT may be effective for use by HCP to provide an assessment of LVEF for use as a diagnostic aid to screen for potential cardiac complications associated with COVID-19 or underlying cardiac conditions that may affect clinical management of COVID-19, in adult patients with suspected or confirmed COVID-19 and that the known and potential benefits of ELEFT, for such use, outweigh the known and potential risks; and

3. There is no adequate, approved, and available alternative to the emergency use of the ELEFT for use by HCP to provide an assessment of low LVEF for use as a diagnostic aid to screen for potential cardiac complication associated with COVID-19, or underlying cardiac conditions that may affect clinical management of COVID-19, in adult patients having or suspected of having COVID-19.[8]

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the ELEFT by HCP to provide an assessment of LVEF for use as a diagnostic aid to screen for potential cardiac complications associated with COVID-19 or underlying cardiac conditions that may affect clinical management of COVID-19, in adult patients having or suspected of having COVID-19. The software should not replace an echocardiogram in cases where an echocardiogram is indicated. The software does not detect any possible cardiac abnormality besides low LVEF. It is not intended for monitoring of patients diagnosed with heart failure. The software is not intended as a sole means of diagnosis and is intended to be used when echocardiography is not yet available or is not indicated.

[8] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

The Authorized ELEFT

ELEFT is software as a medical device that detects whether a patient has a LVEF less than or equal to 40% based upon the input of one or more ECG vectors at the point-of-care. The tool analyzes a collected ECG, and within seconds displays a binary prediction of likelihood of LVEF less than or equal to 40% on a smartphone, tablet, or PC device.

The ELEFT contains the following components:

- A cloud-based software application program interface (API) that allows a user to upload 12 lead ECG data for analysis. The API can be electronically interfaced and perform analysis with data transferred from 12 lead ECG devices.

The above described ELEFT is authorized to be accompanied with labeling entitled "Instructions for use, ELEFT" (available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations) together with the following product-specific information pertaining to emergency use, which is required to be made available to HCP and patients, respectively:

- Fact Sheet for Healthcare Providers: Emergency Use of the ELEFT During the COVID-19 Pandemic
- Fact Sheet for Patients: Emergency Use of the ELEFT During the COVID-19 Pandemic

The above described product, when accompanied with the sponsor's developed Instructions for use (identified above) and the two Fact Sheets (referred to as "authorized labeling") is authorized to be distributed under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of ELEFT, when used as described in the Scope of Authorization of this letter (Section **Error! Reference source not found.**), outweigh the known and potential risks of this product.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized ELEFT may be effective use by HCP to provide an assessment of LVEF for use as a diagnostic aid to screen for potential cardiac complications associated with COVID-19 or underlying cardiac conditions that may affect clinical management of COVID-19, in adult patients having or suspected of having COVID-19 when used consistently with the Scope of Authorization of this letter (Section **Error! Reference source not found.**), pursuant to section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that the authorized

ELEFT, as described in the Scope of Authorization of this letter (Section **Error! Reference source not found.**), meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.
The emergency use of the authorized ELEFT must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section **Error! Reference source not found.**) and the Conditions of Authorization (Section III). Subject to the terms and conditions of this EUA and under the circumstances set forth in the Secretary of HHS's determination under section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the ELEFT described above is authorized for use by HCP to provide an assessment of LVEF for use as a diagnostic aid to screen for potential cardiac complications associated with COVID-19 or underlying cardiac conditions that may affect clinical management of COVID-19, in adult patients having or suspected of having COVID-19.

III. Conditions of Authorization

Pursuant to section 564(e) of the Act, I am establishing the following conditions on this authorization:

Anumana, Inc., as Sponsor of Authorized Product

A. Anumana, Inc. must comply with the labeling requirements under 21 CFR 801 Subpart A (general labeling provisions) and 21 CFR 801.109 (labeling for prescription devices), as well as those described in Section **Error! Reference source not found.** of this letter, Scope of Authorization. As such, compliance with unique device identification regulations (see Subpart B of 21 CFR Part 801) is not required under this EUA.

B. Anumana, Inc. will make the ELEFT available with authorized labeling. Anumana, Inc. may request changes to the authorized labeling. Such changes require review and concurrence from Office of Health Technology 2 (OHT2)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH).

C. Anumana, Inc. may request changes to the Scope of Authorization (Section **Error! Reference source not found.** in this letter) of the authorized ELEFT. Such requests will be made by Anumana, Inc. in consultation with OHT2/OPEQ/CDRH and require concurrence of the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and OHT2/OPEQ/CDRH.

D. Anumana, Inc. may request changes to the device. Such requests will be made in consultation with and require concurrence of OHT2/OPEQ/CDRH.

E. Anumana, Inc. will have process in place for reporting, and will report to FDA, adverse events of which they become aware to FDA under 21 CFR Part 803. Anumana, Inc. will establish a process to collect adverse event information from healthcare facility customers.

F. Anumana, Inc. will notify FDA of any authorized distributor(s)[9] of the ELEFT, including the name, address, and phone number of any authorized distributor(s), and provide authorized distributor(s) with a copy of this EUA and any updates.

Anumana, Inc., and any Authorized Distributor(s)

G. Anumana, Inc. and authorized distributors will distribute the authorized ELEFT with the authorized labeling only to healthcare facilities with HCP who are adequately equipped, trained, and capable of using the ELEFT according to the criteria set forth by Anumana, Inc.

H. Anumana, Inc., and authorized distributors will make authorized labeling available on their websites.

I. Authorized distributors will make Anumana, Inc., aware of any adverse events of which they become aware.

J. Through a process of inventory control, Anumana, Inc. and authorized distributors will maintain records of the healthcare facilities to which they distribute the ELEFT and the number of each product they distribute.

K. Anumana, Inc., and authorized distributor(s) are authorized to make available additional information relating to the emergency use of the product that is consistent with, and does not exceed, the terms of this letter of authorization.

L. Anumana, Inc., and authorized distributor(s) will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

Healthcare Facilities

M. Healthcare facilities using the authorized ELEFT must make available to patients the accompanying Patient Fact Sheet and make available to HCP the accompanying Healthcare Provider Fact Sheet. Healthcare facilities using the authorized ELEFT must also make available the Instructions for use for the ELEFT to patients and HCP.

N. Healthcare facilities using the ELEFT must make Anumana, Inc. and FDA aware of any adverse events under 21 CFR Part 803.

O. Healthcare facilities will ensure HCPs using the ELEFT are adequately equipped, trained,

[9] "Authorized Distributor(s)" are identified by Anumana, Inc. in an EUA submission as an entity allowed to distribute the device.

capable, and will maintain records of device usage.

Conditions Related to Advertising and Promotion

P. All descriptive printed matter, including advertising and promotional materials, relating to the use of the authorized ELEFT shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

Q. No descriptive printed matter, including advertising or promotional materials, relating to the use of the authorized ELEFT may represent or suggest that this product is safe or effective for screening of patients diagnosed with or suspected of having COVID-19 for low LVEF

R. All descriptive printed matter, including advertising and promotional materials, relating to the use of the authorized ELEFT shall clearly and conspicuously state that:

- The ELEFT has neither been cleared or approved for use by HCP to provide an assessment of low LVEF, for use as a diagnostic aid to screen for potential cardiac complications associated with COVID-19 or underlying cardiac conditions that may affect clinical management of COVID-19, in adult patients having or suspected of having COVID-19;

- The ELEFT has been authorized for the above emergency use by FDA under an EUA;

- The ELEFT has been authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of medical devices under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures