4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2020-N-1602]

Revocation of Authorization of Emergency Use of an In Vitro Diagnostic Device for Detection of Antibodies Against SARS-CoV-2, the Virus that Causes Coronavirus Disease 2019 (COVID-19)

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the revocation of the Emergency Use Authorization (EUA) (the Authorization) issued to Chembio Diagnostic Systems, Inc. ("Chembio") for the DPP COVID-19 IgM/IgG System. FDA revoked this Authorization on June 16, 2020, under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), in consideration of new information from three evaluations performed since the Authorization of the device that demonstrate its performance may be both inconsistent and lower than that described in the request for Authorization. The revocation, which includes an explanation of the reasons for revocation, is reprinted in this document.

DATES: Chembio's Authorization is revoked as of June 16, 2020.

ADDRESSES: Submit written requests for single copies of the revocation to the Office of Counterterrorism and Emerging Threats, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, Rm. 4338, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your request or include a fax number to which the

revocation may be sent. See the SUPPLEMENTARY INFORMATION section for electronic access to the revocation.

FOR FURTHER INFORMATION CONTACT: Jennifer J. Ross, Office of Counterterrorism and Emerging Threats, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, Rm. 4332, Silver Spring, MD 20993-0002, 240-402-8155 (this is not a toll-free number).

SUPPLEMENTARY INFORMATION:

I. Background

Section 564 of the FD&C Act (21 U.S.C. 360bbb-3) allows FDA to strengthen the public health protections against biological, chemical, radiological, or nuclear agent or agents. Among other things, section 564 of the FD&C Act allows FDA to authorize the use of an unapproved medical product or an unapproved use of an approved medical product in certain situations. On April 14, 2020, FDA issued an EUA to Chembio, for the DPP COVID-19 IgM/IgG System, subject to the terms of the Authorization. Notice of the issuance of the Authorization is publishing elsewhere in the *Federal Register* with this revocation, as required by section 564(h)(1) of the FD&C Act. Subsequent to the Authorization, FDA considered new information from three additional evaluations, including two conducted by independent entities, demonstrating performance below the performance information submitted in the original EUA request and reflected in the authorized labeling for the device.

II. EUA Criteria for Issuance No Longer Met and Other Circumstances Make Revocation Appropriate to Protect the Public Health or Safety

Under section 564(g)(2)(B) and (C) of the FD&C Act, the Secretary of HHS may revoke an EUA if, among other things, the criteria for issuance are no longer met or other circumstances make such revocation appropriate to protect the public health or safety. On June 16, 2020, FDA

revoked the EUA for Chembio's DPP COVID-19 IgM/IgG System because the criteria for issuance were no longer met and other circumstances make such revocation appropriate to protect the public health or safety. Under section 564(c)(2) of the FD&C Act an EUA may be issued only if FDA concludes that, based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing such disease or condition and the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product. Given the poor device performance observed in multiple evaluations since the Authorization, FDA has concluded it is not reasonable to believe the product may be effective in detecting antibodies against SARS-CoV-2 or that the known and potential benefits of the device outweigh its known and potential risks. In addition, based on the same information and the risks to public health from false test results, FDA has concluded under section 564(g)(2)(C) of the FD&C Act that other circumstances make revocation appropriate to protect the public health or safety. Accordingly, FDA has revoked EUA200179 for the DPP COVID-19 IgM/IgG System, pursuant to section 564(g)(2)(B) and (C) of the FD&C Act.

III. Electronic Access

An electronic version of this document and the full text of the revocation are available on the internet at https://www.regulations.gov/ and https://www.fda.gov/media/139109/download.

IV. The Revocation

Having concluded that the criteria for revocation of the Authorization under section 564(g) of the FD&C Act are met, FDA has revoked the EUA for Chembio's DPP COVID-19

IgM/IgG System. The revocation in its entirety follows and provides an explanation of the reasons for revocation, as required by section 564(h)(1) of the FD&C Act.

U.S. FOOD & DRUG ADMINISTRATION

June 16, 2020

Chembio Diagnostic Systems, Inc.
c/o Louise M. Sigismondi, Ph.D.
3661 Horseblock Road
Medford, NY 11763

Re: Revocation of EUA200179

Dear Dr. Sigismondi:

This letter is to notify you of the revocation of the Emergency Use Authorization (EUA200179) for Chembio Diagnostic Systems, Inc.'s (you, your, or Chembio) DPP COVID-19 IgM/IgG System, issued on April 14, 2020. The authorization of a device for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3) may, pursuant to section 564(g)(2)(B) and (C) of the Act, be revoked when the criteria in section 564(c) for issuance of such authorization are no longer met, or other circumstances make such revocation appropriate to protect the public health or safety. FDA has decided to revoke your EUA based on both of these grounds.

On April 14, 2020, based on information available to the Agency at that time, FDA determined that the DDP COVID IgM/IgG System may be effective for the detection of IgM and IgG antibodies against SARS-CoV-2 in serum and plasma (EDTA or lithium heparin), venous whole blood, or fingerstick whole blood specimens collected from individuals suspected of COVID-19 by their healthcare provider and that the known and potential benefits of the test outweigh the known and potential risks for its use. The DPP COVID-19 IgM/IgG System was authorized for use with the DPP Micro Reader (MRI) and the DPP Micro Reader II (MRII). Authorization of your test was based on data demonstrating clinical performance estimates of 77.4% positive percent agreement (PPA)/sensitivity for IgM, 87.1% PPA for IgG, 93.5% PPA for combined IgM/IgG, and 94.4% negative percent agreement (NPA)/specificity for combined IgM/IgG.

New information from three evaluations performed since authorization of the device demonstrates its performance may be both inconsistent and lower than that described in your original submission. As we first explained to you on April 29, 2020, data generated from an independent evaluation of your device by the Department of Health and Human Services (HHS) National Institutes of Health (NIH) National Cancer Institute (NCI) (NCI evaluation) demonstrate an observed PPA of 57.1% for IgM, 78.6% for IgG, and 82.1% for combined IgM/IgG, which indicates a high false negative rate. The overall NPA was 81.2%, which indicates a high false positive rate. On April 29, 2020, you provided additional data demonstrating poor performance. Specifically, the combined data for (b) (4) (b) (4) hospital patients and employees with positive PCR results showed PPAs of (b) (4) for IgG, (b) (4) for IgM, and (b) (4) for combined IgM/IgG. On May 15, 2020, you provided the draft manuscript for a study of health care workers at (b) (4) that showed an overall sensitivity for your test of (b) (4) and an overall specificity of (b) (4) A

separate analysis in the study of results from (b) (4) healthcare workers showed that the sensitivity of the test in a cohort of (b) (4) patients with positive PCR results was (b) (4) All three of these additional evaluations, including two conducted by independent entities, demonstrate performance below the performance information submitted in your original EUA request and reflected in your authorized labeling.

The performance observed in these additional evaluations is also below the clinical performance we generally expect for serology tests to meet the effectiveness and risk/benefit standards for issuance of an EUA, as set forth in section 564(c). Under our current thinking, based on the totality of scientific evidence currently available to the Agency regarding the clinical performance estimates for serology tests, and under the current circumstances of this public health emergency, clinical agreement data for SARS-CoV-2 antibody tests with 30 positive samples and 75 negative samples generally should demonstrate a minimum combined PPA/sensitivity, of 90%; a minimum NPA/specificity, of 95%; and for tests that report specifically IgM and IgG, a minimum PPA/sensitivity for IgG of 90% and a minimum PPA/sensitivity for IgM of 70%. Moreover, clinical agreement data for SARS-CoV-2 antibody tests with greater than 30 positives and 75 negative samples generally should demonstrate a minimum overall (i.e., IgM/IgG combined) and IgG PPA of 87% with a lower bound of the 95% confidence interval greater than 74.4%, a minimum IgM PPA of 67% with a lower bound of the 95% confidence interval greater than 52.1%, and a minimum NPA of 93% with a lower bound of the 95% confidence interval greater than 87.8%.

Because the data you submitted on April 29 and May 15 did not resolve our concerns regarding the poor clinical performance of your test, we emailed you on May 22, 2020, explaining our concern that the NCI evaluation data "suggest significant performance concerns with your device, which may put patients at unreasonable risk of harm due to inaccurate results." As a result, we asked you to submit, by May 25, 2020, "information adequate to demonstrate that the health risks posed by your device performing differently than the labeled performance can be adequately mitigated/addressed in a timely manner." We also notified you that if the information you provided did not adequately address the potential risk to patients, we may take steps and/or request that you take additional actions to protect the public health as appropriate.

You responded on May 24, 2020, stating that an investigation had been performed to better understand and confirm the findings of the NCI evaluation and, based on the results of your investigation, you changed the cut-off for the MRII (which was used in the NCI evaluation) from 25 to 35. You explained that your re-analysis of the NCI evaluation data using this new cut-off suggested that the specificity of your device could be improved from 81.2% to 93.5% and that the performance of the device with the MRII with the revised cut-off produces results equivalent to those of the MRI using the original cut-off that FDA authorized on April 14.

This change in the cut-off is a significant modification that affects the sensitivity and specificity of the device. The EUA Condition of Authorization IV.L for this device expressly states that changes to the Scope of Authorization (Section II) of the EUA may be made in consultation with, and require concurrence of, FDA. Chembio has not requested and FDA has not concurred on any such changes to the Scope of Authorization.[1] Therefore, you are not permitted to distribute the modified DPP COVID-

[1] The Scope of Authorization of the EUA states that IgM and IgG positive and negative results occur when those relevant

19 IgM/IgG System unless and until you receive emergency use authorization for the modified DPP COVID-19 IgM/IgG System.

More fundamentally, your proposed modification of the device has not resolved the poor clinical performance observed, as demonstrated in the re-analysis of the NCI evaluation results that you provided on May 24. In your re-analysis, although specificity improved from 81.2% to 93.5%, the sensitivity for IgG decreased from 78.6% to 75.0% and the sensitivities for IgM and combined IgM/IgG were unchanged at 57.1% and 82.1%, respectively.

In short, the information you have provided does not address our concerns about the performance issues observed with your device, and we are unaware of any other currently available information that resolves these concerns.

Conclusion

After consideration of the totality of scientific evidence available to the Agency, including all of your submissions, FDA has determined under section 564(g)(2)(B) that the criteria for issuance of emergency authorization in section 564(c) of the Act are no longer met for the DPP COVID-19 IgM/IgG System. Under section 564(c)(2) an EUA may be issued only if FDA concludes it is reasonable to believe the product may be effective and the known and potential benefits outweigh the known and potential risks. Given the poor device performance observed in multiple evaluations since authorization described above, FDA has concluded it is not reasonable to believe the product may be effective in detecting antibodies against SARS-CoV-2 or that the known and potential benefits of your device outweigh its known and potential risks. In addition, based on the same information and the risks to public health from false test results, FDA has concluded under section 564(g)(2)(C) that other circumstances make revocation appropriate to protect the public health or safety.

Accordingly, FDA revokes EUA200179 for the DPP COVID-19 IgM/IgG System, pursuant to section 564(g)(2)(B) and (C) of the Act. As of the date of this letter, the DPP COVID-19 IgM/IgG System that was authorized by FDA for emergency use under EUA200179 is no longer authorized by FDA. As such, you are no longer authorized to distribute the DPP COVID-19 IgM/IgG System.

If you have questions about this letter, please email Ellen Flannery, Deputy Center Director for Policy, Center for Devices and Radiological Health, at Ellen.Flannery@fda.hhs.gov.

Sincerely,

/s/

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

antibody results are at 25 or above or are less than 25, respectively.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903
www.fda.gov

Dated: July 8, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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