August 6, 2020

Autobio Diagnostics Co. Ltd.
c/o Andre Hsiung
Hardy Diagnostics
1430 West McCoy Lane
Santa Maria, CA 93455

Re: Revocation of EUA200349

Dear Mr. Hsiung:

This letter is to notify you of the revocation of EUA200349, the Emergency Use Authorization (EUA) for Autobio Diagnostics Co. Ltd.'s (you, your, or Autobio's) Anti-SARS-CoV-2 Rapid Test, issued on April 24, 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 24, 2020, FDA authorized the emergency use of Autobio's Anti-SARS-CoV-2 Rapid Test for the qualitative detection and differentiation of IgM and IgG antibodies to SARS-CoV-2 in human plasma from anticoagulated blood (Heparin/ EDTA/ sodium citrate) or serum as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. The authorized labeling for your test included clinical performance estimates, for all samples collected regardless of time since symptom onset, of 85.43% (346/405) positive percent agreement (PPA) for IgM, 86.17% (349/405) PPA for IgG, 88.15% (357/405) PPA for combined IgM/IgG, and 99.04% (309/312) negative percent agreement (NPA) for combined IgM/IgG. For samples collected 15 or more days after onset of symptoms, the performance estimates were 95.7% (289/302) PPA for IgM, 99.0% (299/302) PPA for IgG, and 99.0% (299/302) PPA for combined IgM/IgG.

FDA determined that the Anti-SARS-CoV-2 Rapid Test may be effective for the qualitative detection and differentiation of IgM and IgG antibodies to SARS-CoV-2 in human plasma from anticoagulated blood (Heparin/ EDTA/ sodium citrate) or serum, and that the known and potential benefits of the test outweigh the known and potential risks for its use, based on the information available to the Agency at the time of that determination, including clinical performance data submitted by Autobio. Based on the results of new testing, FDA has determined that the Anti-SARS-CoV-2 Rapid Test does not meet current clinical performance estimates for serology tests that are generally necessary to satisfy the effectiveness and risk/benefit standards for issuance of an EUA. Specifically, the Agency has concluded that it is unlikely that this test is effective in detecting SARS-COV-2 IgM antibodies and that the known and potential benefits of its use do not outweigh the known and potential risks.

Therefore, the Agency believes that the criteria for issuance of an authorization are no longer met and is revoking the EUA.

As you know, after authorization of EUA for your device, its performance was evaluated at the National Institutes of Health's (NIH) Frederick National Laboratory for Cancer Research (FNLCR), part of the National Cancer Institute (NCI), using a well-characterized sample panel of 30 positive and 80 negative human plasma and serum specimens (referred to herein as the NCI evaluation). The evaluation was performed on June 24, 2020. As we first explained to you on July 6, 2020, the IgM sensitivity reported In the NCI study was 50% (15/30), while the IgM sensitivity in your device's labeling is 85.43% (346/405) for all samples collected regardless of time since symptom onset, and 95.7% (289/302) for samples collected 15 or more days after symptom onset. FDA requested that you reply with information adequate to demonstrate that the health risks posed by the device performing differently than the labeled performance can be adequately mitigated/addressed in a timely manner.

On July 8, 2020, you provided a written response that summarized your investigations into the poor observed IgM performance in the NCI evaluation and proposed different potential mitigations. You proposed that a combination of factors could have contributed to the low IgM PPA/sensitivity observed in the NCI evaluation, as follows:

1. You proposed that the device's (b) (4) such that it is possible that (b) (4) In this scenario, you proposed that (b) (4) You proposed that (b) (4)

2. You indicated that the SARS-CoV-2 (b) (4) domain was selected as a capture antigen for the device to focus on an IgM detection window in an early and acute infection period defined as two-to-three weeks after symptom onset. Other antigens such as the (b) (4) were rejected during test design based on indications that these antigens would likely extend IgM detection beyond the three-week period that you considered desirable for the test.

3. You noted that the average number of days post symptom onset for the 15 false negative samples was 29.9 days, and that the NCI samples contained low IgM titers (100 and 400). (b) (4) (b) (4)

You also cited other independent investigations in support of your test's performance. This included tables and figures taken from the following publications:

- The Lassaunière, et al pre-print (medRxiv 2020.04.09.20056325) included data from your test on a panel of 30 positive serum samples from PCR positive patients and 32 negative serum samples. Your test's performance was only summarized for IgM/IgG combined, and so the article does not directly address IgM detection concerns.

- The Demey B, et al. article (J Infect. 2020;81(2):e6-e10.) described a study serially testing 22 PCR positive patients with your test up to 24 days after symptom onset. Table 1 reported Autobio test IgM sensitivity up to 86.36% (19/22 subjects) on day 14 through day 24 after symptom onset.
- The Candel FJ, et al. article (Rev Esp Quimioter. 2020;33(4):258-266.) described a study in samples tested from 35 PCR positive patients between days 16 – 48 after symptom onset. In this study, your test's IgM detection > 15 days after symptom onset was 74% (26/35).

You also cited data from other sources:
(b) (4)

The additional information you provided represents an assortment of data from studies with varying levels of documentation and rigor. Based on the limited information available, we were unable to fully assess these studies. Some data were derived from serially sampling the same PCR positive individuals over time to assess IgM detection, and some appears to be from testing single samples collected from unique individuals, similar to the studies described in the authorized labelling. In the additional studies, IgM detection for samples collected more than 14 days after symptom onset ranged from 74% - 86%. This is higher than the performance observed with the NCI sample set; however, this is significantly lower than IgM performance reported in the authorized labeling when considering the similar subset of samples collected 15 or more days after symptom onset (i.e., IgM PPA 95.7%, 289/302, 95% CI: 92.8 - 97.5%).

In your July 8 email, you proposed the following mitigations:

1. You proposed to modify (b) (4) the instructions for use to reduce the likelihood of (b) (4) You proposed to re-test the NCI panel with the same device lot (b) (4)
2. You proposed to re-design the plastic cassette housing to (b) (4) (b) (4)
3. You indicated that you could re-design (b) (4) .

On July 16, 2020, you also proposed the following possible revisions to the instructions for use (b) (4)

1. Revising the (b) (4)
2. Revising the intended use to indicate that the IgM portion of the device is specifically designed "for

the detection of IgM in the early stages of the disease process and not during the rehabilitation stages."

Your proposed actions do not adequately address FDA concerns regarding the authorized device, as discussed below.

Your proposal to modify (b) (4) the package insert (b) (4) would not ensure that the high IgM false negative rate would not continue to occur during clinical use (b) (4) (b) (4) Even assuming your theory were correct, this would indicate a design flaw that makes the test prone to error and that would require consistent attention and action by the end user to avoid false negatives with low titer positive samples that are close to the test cutoff. You have not provided adequate evidence to demonstrate that the proposed labeling changes would mitigate the risks to individuals and the public health as a result of false negative IgM results. (b) (4) (b) (4)

Further, your proposal to modify the intended use language is not consistent with the intended use of the currently authorized device, and so is not appropriate. You proposed to indicate that the IgM portion of the device is specifically designed for the detection of IgM in the early stages of disease. This intended use language could be misinterpreted as a claim to aid in the diagnosis of early disease. In contrast, the intended use language of SARS-CoV-2 antibody tests includes the following statements that contraindicate the use of these tests to diagnose early disease:

- [The test] should not be used to diagnose acute SARS-CoV-2 infection.
- The sensitivity of [the test] after early infection is unknown.

The other actions you proposed (b) (4) would be considered a re-design of the device. These changes are significant design modifications that can affect both the sensitivity and specificity, particularly the change to the capture antigen, which alters the operating principle of the device. Modifications such as these would need to be validated. As such, these proposed mitigations would not address, in a timely manner, the concerns with the device as currently authorized, and it is unclear whether these changes would successfully improve the performance of the device if you were to proceed with attempts to implement and validate these changes.

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 Anti-SARS-CoV-2 Rapid Test. 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 regarding IgM sensitivity observed in the NCI evaluation after authorization of your device, FDA has concluded it is not reasonable to believe the product may be effective in detecting IgM antibodies to 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 EUA200349 for the Anti-SARS-CoV-2 Rapid Test, pursuant to section 564(g)(2)(B) and (C) of the Act. As of the date of this letter, the Anti-SARS-CoV-2 Rapid Test that was authorized by FDA for emergency use under EUA200349 is no longer authorized by FDA. As such, you are no longer authorized to distribute the Anti-SARS-CoV-2 Rapid Test. If you would like to work with FDA to resolve these issues, you may address the issues identified above and continue to work with us through a new pre-EUA or EUA request. In the event you submit a new notification to FDA for this test, or a notification for a re-designed and/or new test, note that FDA does not intend to place that test on the Section IV.D notification list, unless and until an EUA has been issued for such test.

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,

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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration