Department of Health & Social Care

Summary of Incident and corrective and preventative action report. MHRA incident reference: 2021/006/011/601/004

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Background

On Thursday, June 10, the FDA released a notice warning US citizens against using the Innova SARS-CoV-2 Antigen Rapid Qualitative Test for diagnostic testing. This was due to “significant concerns” and findings from an FDA inspection of an Innova facility in Pasadena, California. DHSC only became aware after the FDA safety recall notice. These concerns detailed in a warning letter to Innova included:

- Innova distributing the product in the US without prior FDA approval
- Innova including clinical performance information with Innova 25s which did not match performance evidence observed by the FDA at the time of their inspection
- Failures in the quality management system in the US company

Innova did not provide an adequate response to the audit which resulted in the FDA issuing a safety notice. DHSC became aware of the audit, findings, and letter after the issue of the safety notice which covered the following products in the US:

- Innova COVID-19 Self-Test kit (3T Configuration)
- Innova SARS-CoV-2-Antigen Rapid Qualitative test (7T Configuration)
- Innova SARS-CoV-2-Antigen Rapid Qualitative Test (25T Configuration)

DHSC is the legal manufacturer of DHSC Covid-19 Self-Test Kits, provided under a supply contract by Innova and manufactured by Xiamen Biotime. DHSC is also a distributor of Innova branded tests, that are manufactured by Xiamen Biotime used for assisted testing. DHSC in its role as the legal manufacturer has always had additional measures in place to meet regulatory requirements and ensure quality of supply.

Upon becoming aware of the FDA concerns, DHSC commissioned a formal review of its role as a legal manufacturer of self-test kits and a distributor of Innova assisted test products to determine if the FDA's claims represented any risk to public health in the UK. DHSC notified the MHRA of a potential safety incident.

DHSC Investigations

DHSC has investigated each claim made by the FDA to determine the impact on UK public health.

Claim 1: Not authorised to be made available in the US

Innova was lawfully introduced into the UK market as a CE marked test for use by professionals. Following this, DHSC applied for Exceptional Use Authorisation from the Medicines and Healthcare Products Regulatory Agency (MHRA) in December 2020, as part of the national testing strategy, which allowed DHSC specified tests to be used for self-test, without the need of a professional to assist. These tests were supplied directly from Xiamen Biotime and followed the correct regulatory procedures including usability and performance testing.

Upon review, DHSC has concluded that it followed the correct regulatory approvals to ensure Innova's product was permitted for use in the UK.

Claim 2: Unsupported performance claims

The performance of packs of 25 Innova antigen tests stated in the instructions could not be confirmed by the FDA. While the FDA has noted they have not received any reports of injuries or deaths related to the use of Innova tests, they were concerned by:

- False-negatives results (whereby the test would produce a negative result in an infected person)

- False – positive results (whereby the test would produce a positive result for a person who was not infected)

False positive Results

DHSC has analysed the positivity rates of Innova antigen tests and has found that they provide a specificity of greater than 99.97%. This indicates a very low chance of the test producing a positive result in a person who was not infected.

False Negative Results

For those doing one-off or regular asymptomatic testing, false negative results could result in individuals believing they are not infectious which may lead to risky actions such as not adhering to social distancing guidelines or good hygiene standards. This increases the chance of a potentially infectious individual infecting other people. For those doing outbreak, high risk, or daily contact testing, the potential risks are the same. However, the impact of these risks is higher in these settings as they will usually involve more vulnerable people. It is important to note that LFD use in vulnerable settings usually form part of a testing regime which involves other testing methods, for example PCR tests.

The latest evidence from the use of Innova antigen tests shows that 95% of true positive results are detected for those with a high viral load. This indicates that there is a low chance of the test producing a negative result in someone who is infectious. There is also additional information in the Innova test instructions for users which advises those who receive a negative result to continue to follow national and local guidelines on COVID-19, further preventing the chances of the virus spreading. Furthemore, in many vulnerable settings LFDs form an adjunct too, rather than the sole approach, to a regular testing programme, usually alongside PCR tests

Interruption or cessation of LFD testing

For the purposes of the NHS Test and Trace programme, LFD antigen tests are used on asymptomatic individuals. In order to identify asymptomatic infectious people in the general population so they can self-isolate, testing had to be delivered on a large scale

while providing rapid results and, at present, only LFD antigen tests are capable of doing this.

If the supply of LFD tests stopped, asymptomatic mass testing would need to be reduced or stopped entirely. The public health impact would be an increase in infection rates and a likely increase in deaths. In this event, other public health services would need to be considered as a replacement.

Published data on the performance of LFDs, including Innova based tests, can be found here:

Asymptomatic testing for SARS-CoV-2 using antigen-detecting lateral flow devices

Lateral flow device specificity in phase 4 (post marketing) surveillance.

Conclusion

Substantial work has been undertaken to understand the performance of Innova LFDs and ensure they are safe and effective at detecting COVID-19.

Claim 3: Significant deficiencies in the Quality Management System

The FDA warning letter highlighted failures in the quality management system of Innova in the US. These included:

- Failure to establish procedures for control and distribution of finished devices.
- Failure to establish procedures to control product that does not conform to specified requirements.
- Failure to establish procedures for corrective and preventative action.
- Failure to establish procedures for receiving, reviewing, and evaluating complaints
- Failure to establish procedures to ensure that all purchased or otherwise received products and services conform to specified requirements.
- Failure to develop, maintain, and implement written Medical Device Reporting (MDR) procedures.

DHSC is the legal manufacturer of DHSC Covid-19 Self-Test Kits which are obtained directly from Xiamen Biotime. Because of this, we have in place a quality management system and quality assurance processes that apply to all DHSC Covid-19 Self-Test Kits

purchased. We have reviewed each of the above issues raised by the FDA warning letter to determine whether we have any of these issues in our own quality management system. After reviewing our own systems and processes, DHSC is satisfied that we do have quality processes in place for each of the issues raised by the FDA, and each of these processes are in use and working.

Failure of Innova to notify DHSC of the FDA audit and findings in the USA

Innova's current contract requires them to share concerns and information related to quality, performance, and safety. DHSC has consistently maintained contact with Innova, yet the voluntary recall and FDA investigation had not been brought to DHSC's attention.

In response to this, DHSC have decided to:

- Strengthen contracts with LFD suppliers and remind them of the need to provide such information to DHSC without delay.

- Arrange a process to request this information on a monthly basis from suppliers who will need to confirm that they have not had any concerns or regulatory contact and to inform us of these discussions if they have

- Request an update on the US regulatory position and Innova's strategy for that market.

Conclusion

DHSC immediately reviewed each of the concerns raised by the FDA regarding the US operations of Innova group and the use of their lateral flow devices to determine whether these issues applied to the UK. A response was provided to the MHRA within 4 days of notification.

DHSC has complied with UK requirements and obtained an Exceptional Use Authorisation from the MHRA for the DHSC Covid-19 Self-Test Kits and we are satisfied that tests used by DHSC in the UK are on the market legally. DHSC also conducted a full review of our quality processes and management system and are satisfied these are operating effectively.

We are also satisfied that the DHSC Covid-19 Self-Test Kits used as part of the NHS Test and Trace programme perform at the required level and are safe to use, and that our

ongoing monitoring of their performance has not raised any concerns that indicate they are not performing as expected.

In summary, our review of the issues raised by the FDA and our subsequent investigation into our own processes has confirmed that the legal challenges raised in the US have not impacted public health in the UK. DHSC Covid-19 Self-Test Kits perform as expected and continue to play a key role in national testing. As a result, we will continue to use DHSC Covid-19 Self-Test Kits as part of our approach to test and identify infectious individuals and prevent the virus from spreading.

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