Public Health England

Protecting and improving the nation's health

Public Accountability Unit
Wellington House
133-155 Waterloo Road
London SE1 8UG

www.gov.uk/phe

By email
request-774968-216e6db7@whatdotheyknow.com

Our ref: 14/08/21/cf/1047

13 September 2021

Dear P Newton,

Re: 1047 - Internal review of Case ref: 790

I refer to your email 14 August 2021 requesting an internal review of the handling of case reference 790, in relation to your request for information under the Freedom of Information Act 2000 (FOI) "the Act".

Your Request case ref: 790

Public Health England (PHE) received your information request on 18 July 2021.

Under the Act a public body, such as PHE is required to 'respond to requests promptly' and no later than '20 working days after the request is received within the organisation'.

Under the Act PHE, had until the 13 August 2021 to respond to your request.

Response Case ref: 790

PHE sent you its response on the 13 August and correctly confirmed it partially holds the information you requested and provided you with advice and assistance under Section 16 of the Act.

Internal review decision

PHE has now conducted the internal review and concludes that PHE sent you its response to your request for information the statutory deadline.

PHE could have been clearer in setting out its response and would like to apologise for any inconvenience caused as a result of its omission. As requested, please see our response to your request below, set out point by point.

Response to request 1047 [Linked to case ref: 790]

In accordance with Section 1(1)(a) of the Act, PHE can confirm that it partially holds the information requested.

1. The validation study for each of the RT-PCR and Rapid Lateral Flow tests currently in use on or in England.

RT-PCR test:
There are over 85 different SARS-CoV-2 RT-PCR assays/platforms in use across the UK. Most tests used in England are commercial. Each test/platform comes with its own standardised interpretation and have a slightly different limit of detection (LoD) – the lowest concentration of virus that can be reliably and consistently detected by the assay and will be configured according to local arrangements.

Each testing kit manufacturer includes the criteria for interpretation in the Information for Use (IFU) leaflets provided with their kits. All testing centres are required to follow the manufacturer's interpretation. Validation is performed by the manufacturer; all labs are expected to test the kits in house to determine limit of detection and use this for interpretation. PHE has performed some assessments of PCR – see https://www.gov.uk/government/publications/covid-19-phe-laboratory-assessments-of-molecular-tests

Lateral Flow Devices:
This paper shows the evaluation of LFD kits:
https://www.gov.uk/government/publications/assessment-and-procurement-of-coronavirus-covid-19-tests/protocol-for-evaluation-of-rapid-diagnostic-assays-for-specific-sars-cov-2-antigens-lateral-flow-devices

Also see publication of report:
https://www.ox.ac.uk/sites/files/oxford/media_wysiwyg/UK%20evaluation_PHE%20Porton%20Down%20%20University%20of%20Oxford_final.pdf

2. The known error/accuracy rate.

RT-PCR test:
The RT-PCR assays used for the UK's COVID-19 testing programme have been verified by PHE. RT-PCR tests are highly sensitive and highly specific, but can show, as every diagnostic test, low rates of false negative and false positive results. These false negative and false positive results cannot be entirely eliminated. A test result is called 'false positive' when it gives a positive result for a person who is not infected with the infectious agent the test is designed for.

RT-PCR test show over 95% sensitivity and specificity. This means that under laboratory conditions, these RT-PCR tests should never show more than 5% false positives or 5% false negatives.

The proportion of false positives will increase as prevalence decreases and (for the same reason) the proportion of positive results that are false positive will be higher among vaccinated individuals: https://www.bmj.com/content/369/bmj.m1808/rr-22"

Lateral Flow Devices:
For known error/accuracy rate of LFDs please see:
https://www.gov.uk/government/publications/assessment-and-procurement-of-coronavirus-covid-19-tests/protocol-for-evaluation-of-rapid-diagnostic-assays-for-specific-sars-cov-2-antigens-lateral-flow-devices.

Lateral flow tests show high specificity and are effective at identifying most individuals who are infectious, Oxford University and a PHE evaluation confirmed. The specificity of the test was recorded as 99.68% - the overall false positive rate was 0.32%, although this was lowered to 0.06% in a lab setting. It has an overall sensitivity of 76.8% for all PCR positive individuals but detects over 95% of individuals with high viral loads, and minimal difference between the ability of the test to pick up viral antigens in symptomatic and asymptomatic individuals.

Also see publication of report:
https://www.ox.ac.uk/sites/files/oxford/media_wysiwyg/UK%20evaluation_PHE%20Porton%20Down%20%20University%20of%20Oxford_final.pdf

3. Information demonstrating that the RT-PCR and Rapid Lateral Flow tests are diagnostic instruments contrary to manufacturer literature.

PHE do not hold this information. Questions regarding manufacturing and production need to be directed to the commercial manufacturers. PHE does not mandate what each lab needs to do – we provide guidance – the assessment of quality is performed by UKAS (UK accreditation service). Should you wish to contact them regarding accreditation you can do so at: info@ukas.com

4. The Cycle threshold for the RT-PCR test in laboratories under the superintendence of Public Health England.

PHE have not set a specific Cycle threshold (Ct) that should be used. Ct cut offs for COVID-19 PCR tests are subjected to a standardised laboratory algorithm and this informs interpretation of positive or negative results. The algorithm is based on evaluating the limit of detection for each test using known positive control material and will differ depending on the assay used.

These data are available from the commercial manufacturer of the assay and is subject to local validation by the laboratory using the test and before using it for diagnostic purposes. The laboratories have a statutory duty to report positive cases to PHE, but they are not obliged to advise PHE which tests they are using nor submit CT values used to PHE.

Further information on understanding cycle threshold (Ct) in SARS-CoV-2 RT-PCR can be found at the following link:
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/926410/Understanding_Cycle_Threshold__Ct__in_SARS-CoV-2_RT-PCR_.pdf

Information on interpretation of Ct values during periods of low prevalence is provided at the following link: https://www.gov.uk/government/publications/sars-cov-2-rna-testing-assurance-of-positive-results-during-periods-of-low-prevalence/assurance-of-sars-cov-2-rna-positive-results-during-periods-of-low-prevalence

5. The genetic sequence UNIQUE to SARS-CoV-2 and not the sequence currently used which show up 93 times in the Human genome and 91 times in Bacteria and Fungi (microbe) genomes.

PHE does not hold the information as specified in your request. However, you may be interested in the following information on the COVID-19 variants: https://github.com/phe-genomics/variant_definitions

PHE's virology teams use the term "virus isolation" to mean culture of SARS-CoV-2 in the laboratory. This specialised technique involves adding patient samples to cell cultures and looking for virus growth. It is time consuming and highly specialised work. For this reason, the SARS-CoV-2 virus is identified most often by looking for its unique genetic material in a clinical sample and further identification is refined and confirmed by whole genome sequencing.

PHE' culture work on other SARS-CoV-2 variants is in progress and has not published in any peer-reviewed papers at present.

You may be interested in viewing:

COVID-19 variants: genomically confirmed case numbers: https://www.gov.uk/government/publications/covid-19-variants-genomically-confirmed-case-numbers

Investigation of SARS-CoV-2 variants of concern: technical briefings: https://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201

6. In isolating and purifying SARS-CoV-2 from a COVID-19 patient sample, please provide a copy of the negative control experiments to rule out other possibilities of disease causation such as toxicity, trauma and malnutrition etc.

The SARS-CoV-2 virus has been isolated in the PHE Viral Reference Lab by culturing clinical material from patients who have tested positive for the virus. The virus isolation is reported in a publication from Singanayagam et al: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.32.2001483.

PHE is not involved in further clinical investigation of individual cases of COVID-19 and so cannot comment on whether other factors are contributing to an individual patient's symptoms.

Further information can be found at the following links below regarding evidence of COVID-19, in accordance with Section 16 of the Act:

SARS-CoV-2 has been cultured and then subjected to electron microscopy. Evidence of the Electron Micrograph is available at the following link: https://publichealthmatters.blog.gov.uk/2021/02/05/what-do-we-know-about-the-new-covid-19-variants/

General information pertaining to SARS-CoV-2, which causes the disease known as COVID-19: https://www.gov.uk/government/publications/wuhan-novel-coronavirus-background-information/wuhan-novel-coronavirus-epidemiology-virology-and-clinical-features

Please note that you have the right to an independent review by the Information Commissioner's Office if a complaint cannot be resolved through the PHE complaints procedure.

The Information Commissioner's Office can be contacted by calling the ICO's helpline on 0303 123 1113, visiting the ICO's website at www.ico.org.uk or writing to the ICO at Wycliffe House, Water Lane, Wilmslow, Cheshire, SK9 5AF.

Yours sincerely,

FOI Manager