Antibody Tests: Note on Misclassification, Misunderstanding, Misuse and Mitigation to Realise Benefits and Minimize Harms.

Note from SPI-B (1 April 2020)

These tests detect those recently infected by the virus who may therefore have some immunity to it. However, it is unknown how recent the infection has to have been, the duration of any detectable antibody in this test, the performance of different test techniques, and the relationship between antibodies and immunity.

The performance of an antibody test depends on:

1. The proportion of those who have antibodies who test positive - sensitivity
2. The proportion of people without antibodies who test negative - specificity
3. The proportion of people in the population who have antibodies – prevalence

Performance of a test will affect the numbers in each of the four cells below:

	Have antibodies	Do not have antibodies
Test Antibody Positive	**A** correctly classified	**B** incorrectly classified
Test Antibody Negative	**C** incorrectly classified	**D** correctly classified

Misclassification
Misclassification is inherent to varying degrees in all tests. The test currently being considered could at best result in:
- 200 (0.5%) with no antibodies (B) misclassified as having antibodies = false reassurance
- 27 in 200 (13.5%) of those with antibodies (C) classified as having no antibodies = false concern

In a population with 10% prevalence of antibodies, this would mean that in those that test positive, in fact 1 in 20 (5%) would *not* have antibodies (Appendix 1).

Misunderstanding
All those tested retain the potential to infect others (e.g. via touching contaminated surfaces), but it is far lower in those testing positive.

Those testing antibody positive need to understand:
- They are at low but not no risk of transmission
- Hand hygiene measures remain relevant
- Front line care workers need to maintain safe working practices

Those testing antibody negative need to understand:
- They remain at risk of infection and transmission
- Hand hygiene measures remain relevant
- Social distancing and safe working practices remain relevant

Misuse
Potential concerns around the misuse of the test include:
- Misunderstanding of the limitations of the test

- Inequity in test availability
- Discrimination in the workforce *eg* employment only of those testing positive
- Legitimises unsafe work practices
- Non-standardised tests become widely available
- Profiteering – in selling tests and/or fake test certificates

Mitigating misclassifications, misunderstanding and misuse
- Establish performance of any test in a target population before use (e.g. healthcare workers vs general public)
- Develop materials to effectively communicate test results
- Tests offered free at point of testing within standardised protocols
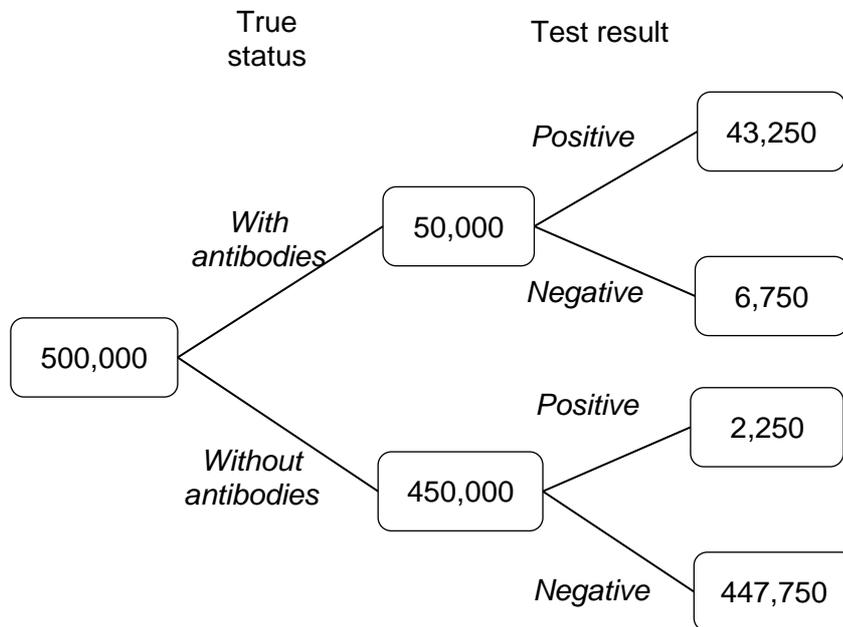- Apply existing regulations to protect workers' rights

Recommendation
PHE or DHSC, in collaboration with experts, should commence work <u>now</u> to mitigate the potential misclassifications, misunderstandings and misuse of antibody testing to ensure that its potential benefits are realised with minimal harms. This will require the collation of evidence regarding the test performance in different UK populations; the development of materials in multiple formats to explain the test and its results (e.g. pre and post-testing); guidance to employers on what the test does and does not convey and the rights of all workers within exiting HSE legislation.

Note prepared by Theresa Marteau with input from David Spiegelhalter

Appendix: Hypothetical worked example based on technical information available on website of CELLMID

https://cellmid.com.au/covid-19-rapid-test-sars-cov-2-rapid-antibody-detection-kit/#howitworks

If Sensitivity = 86.5% - of 200 people who are antibody positive, 173 will be told this correctly. 27 will be incorrectly told they do not have antibodies.

If Specificity= 99.5% - of 200 people who are antibody negative, 199 will be told this correctly. 1 will be incorrectly told they have antibodies.

If prevalence is 10%, and a hypothetical sample of 500,000 NHS workers are tested:

    o 50, 000 would truly have antibodies, of whom 86.5% (43,250) would be correctly identified, and 13.5% (6750) would be falsely told they did not.
    o 450,000 would truly not have antibodies, of whom 0.5% (2,250) would be falsely told they did have them.

Of those receiving a positive test result indicating presence of antibodies:

    5% (1 in 20 = 2250/(43250 + 2250)) do not in fact have antibodies.

Of those receiving a negative test result indicating absence of antibodies:

    1.5% (6750/(447750+6750)) so in fact have antibodies.