COVID-19 NATIONAL TESTING PROGRAMME SERVICE EVALUATION EVIDENCE REPORT

This report documents that a service evaluation was conducted on behalf of the Department of Health and Social Care, England (DHSC), intending to either support or refute the hypothesis detailed below in relation to the COVID-19 national testing programme. Details of the nature of the experiment, the hypothesis, conducting labs, results and policy recommendation from the result are included below.

Experiment ID	SE-SWTC1
Date Experiment Requested	16/04/20
Control used for experiment	Throat and nose swabs collected by trained[1] operator qRT-PCR controls at [redacted]
Protocol version	1
Type of validation	Service Evaluation
Hypothesis	MWE951S swab is suitable for use in self-swabbing collection of samples for COVID-19 antigen test-based diagnosis.
What product being tested	MW951S Sigma Virocult kit
What time incubation	• Up to 24 hours post swab collection
Objectives	<u>Primary objective</u> • To determine whether self-swabbing is as effective as swabs taking by trained operators[2] for diagnosing SARS-CoV-2 positive patients. <u>Secondary Objective</u> • To determine whether Medical Wire swabs are suitable for binding and elution of SARS CoV-2 without RNA degradation for up to 24 hours at room temperature.

Details of the experiment including the conducting lab, time frames, results and additional observations of the experiment are detailed below.

Date Experiment Started	19/04/20
Experiment Conducting Lab	[redacted] and [redacted]
Date Experiment Completed	21/04/20
Inclusion criteria	• Subjects have agreed to take part in the self-swabbing exercise and are ≥18 years old • Subjects have read and understood the self-swabbing instructions. • Minimum of 50% of cohort to be composed of individuals who do not have experience of performing medical procedures
Summary of methods	1. Subject will swab their throat and nose according to the self-swabbing instructions. Swabbing will be monitored by a trained testing operator and technique will be noted in the case report form. The swab will be placed in the viral transport medium. 2. 4 identical barcodes will be produced and these should be:

	a. One attached to the tube with the self-swab b. One attached to the bag holding the self-swab tube c. One attached to the case report form d. One given to the subject 3. A trained testing operator will swab the patient's throat and nose according to standard diagnostic requirements and placed into the viral transport medium. 4. 4 identical barcodes will be produced and these should be: a. One attached to the tube with the assisted-swab b. One attached to the bag holding the assisted-swab tube c. One attached to the case report form d. One given to the subject 5. The samples will be collated and sent to [redacted] with the case report forms at the end of the day for processing using the standard diagnostic workflow. Samples will be stored and transported together, and run together on the same qRT-PCR plate. UK Biocentre workers will be blinded to: a. Which samples belong to which subject b. The collection mode of the sample 6. qRT-PCR Ct value data for the samples will be sent to Workstream 2 for unblinding, matching to electronic case report forms and analysis.
Results (high level summary report)	• A total of 97 subjects were successfully recruited into the Service Evaluation, and 97 pairs of swabs were taken. o 1 complete pair did not arrive at the [redacted] for qRT-PCR analysis (SE062). 96 pairs of samples were then subjected to qRT-PCR analysis. • 6/192 (3%) of swabs were reported as 'invalid' following qRT-PCR analysis (i.e. a non-concordant positive or negative result was obtained across the 3 SARS-CoV-19 genes assayed). All 4 of these were from self-swab samples. The matched assisted swab results for these 6 individuals were 2 positive and 4 negative diagnoses. • The remaining 90 pairs of samples were complete and were analysed. • Overall 82 of 90 (91%; 95% confidence interval: 83%-96%) subjects were concordant for positive or negative diagnosis. o 63 of these were diagnosed as COVID-19 negative o 19 of these were diagnosed as COVID-19 positive o 8 of 90 subjects had discordant results across both samples, of whom: § 2 would be diagnosed as COVID-19 positive according to the self-collected sample, and

	as COVID-19 negative according to the assisted-test sample § 6 would be diagnosed as COVID-19 negative according to the self-collected sample, and as COVID-19 positive according to the assisted-test sample (1 was a subject with clinical experience) o For these subjects, there was no significant difference between the swabbing method, according to the confidence interval of proportion of assisted swabs being negative in discordant pairs (0.03-0.65; P=0.29). • In order to obtain more information on possible differences between self-swabbing and assisted swabbing, the quantitative Ct results were analysed. The results are shown in Appendix 1. o Results were divided (arbitrarily) into high viral load (Ct<25); low viral load (Ct>=25 & Ct<35) and undetectable o Quantitative Ct concordance was 76 of 90 (84% 95% confidence interval; 75%-91%) o There were 14 pairs of samples that were discordant for quantitative Ct result. Of these, 8 had a higher viral load in the self-swab sample and 6 had a higher viral load in the assisted swab sample. • Of note, when the quantitative viral load was compared between samples in for the 19 subjects diagnosed as COVID-19 positive across both samples, the self-swabbing results were significantly higher than the assisted swabs. The mean Ct difference between a subject's samples (assisted swab minus self-swab) was 3.24; 95% confidence interval: 5.30-1.18, P<0.004). A Ct difference of 3.24 corresponds to about a 9.4 fold higher viral load. A scatter plot of these Ct values is given in Appendix 2
Additional Observations	• Observational data comparing aggregate rates of positive, negative and void diagnoses across self-testing, assisted testing and 'hybrid' (i.e. mixed) channels for 44.6k individuals tested to date at Regional Testing Centres demonstrates a low level of variability between channels (see Appendix 2)
Summary of conclusions	• There is no convincing evidence of any overall difference between self-swabbing and assisted swabbing. It is unclear why the 4 'invalid' results were all in the self-swabbing group and the imbalance between self-swabbing and assisted swabbing could well have happened by chance. • However, self-swabbing produced about a 10-fold higher viral load compared to assisted swabbing. It is possible that some participants (about 25% (6/25)) failed to swab correctly thereby obtaining a negative result. In contrast, those who did swab correctly obtained substantially higher viral loads. This may have been the cause of 10%

	(2/19) assisted swabs, giving false results. Although the data is not sufficient, it is possible that self-swabbing will do substantially better than assisted swabbing in individuals with low viral loads. Larger studies are required to confirm or refute this possibility.
Supporting graphs / data (to attach in the appendix)	Appendix 1 (Quantitative Ct data analysis) Appendix 2 (Ct scatter plot for concordant positive subjects) Appendix 3 ('Real World' observational data on positive, negative and void rates by channel from currently operating Regional Test Centres)

Policy recommendation from this data (to be completed by DHSC)	The current approach of self and assisted swabbing should continue. A larger service evaluation should be undertaken. Where appropriate this should be coordinated to additionally meet data requirements for the MHRA approval of different kit types to be used for both self and assisted swabbing

The signatures below confirm that requesting authority is satisfied that the experiment was conducted was conducted successfully (regardless of outcome) and that the above details are complete and correct.

[redacted]

Requesting Authority (16/04/20202)

Dr Tom Fowler

Workstream 2 Public Health Lead

[redacted]

Conducting Group (25/04/2020)

[redacted]

University of Oxford

(1) Corrected from "medically trained" in previous version; (2) Corrected from "Health Care Worker"

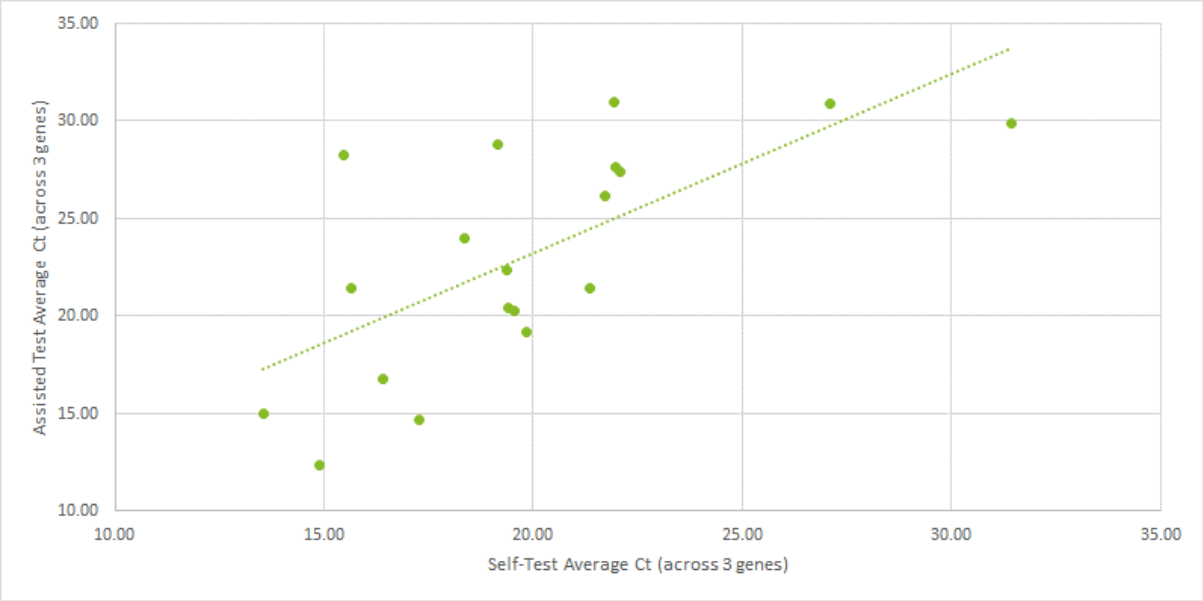
SE-SWTC1 - Appendix 1

Quantitative Ct data analysis

	Assisted CT groups			
Self-swabs CT groups	**<25 (High viral load**	**>=25 - <35 (Low viral load)**	**Undetectable viral load**	**Total**
<25 (high viral load)	11	6	0	17
>=25 – 35 (low viral load)	0	2	2	4
Undetectable	1	5	63	69
Total	**12**	**13**	**65**	**90**

SE-SWTC1 - Appendix 2

Scatter Plot of quantitative Ct results from concordant positive subjects



SE-SWTC1 - Appendix 3

Aggregate observational data from Regional Testing Centre tests conducted to 24/04/2020

RTC	Total	Positive	Negative	Void	Positive	Negative	Void	Total
Assisted	32252	9425	21845	982	29%	68%	3%	100%
Hybrid	6894	1990	4666	238	29%	68%	3%	100%
Self-administered	3197	886	2196	115	28%	69%	4%	100%
Not classified	2302	669	1554	79	29%	68%	3%	100%
Total	**44645**	**12970**	**30261**	**1414**	29%	68%	3%	100%