DOCUMENT VERIFICATION

Prior to using this document, the user is responsible for verifying that the revision and effective date are current.

REVISION HISTORY

Rev.	Effective Date	Changes Made to Document
1	06-Jan-2022	First Issue

1. Content

1. Content
2. Introduction
3. Reference documents
4. Standards and guidelines
5. Methodology
6. Findings /Results
   - 6.1 In-House manufacturing inspection at Biotime
   - 6.2 Receiving inspection - Intertek Testing in the UK
   - 6.3 Product complaints & Qualtrics Survey
   - 6.4 Combined Complaints Data (Yellow Card, Control Tower and Qualtrics Complaints) – Trending
   - 6.5 Real World Performance Monitoring
   - 6.6 CAPA
   - 6.7 SCAR – Supplier Corrective Action Report
   - 6.8 Risk Management
   - 6.9 Literature Review & State of the Art (SOTA)
7. Conclusion & Risk-Benefit Determination
8. Recommended Actions
9. Attachments
10. Author

2. Introduction

The LFD kit is an IVD medical device intended by DHSC to be used *in vitro* for the examination of combined throat and nasal specimens derived from the human body solely for the purpose of providing information concerning Covid-19 infection. The device is classified as a **general IVD for self-testing.**

The PMS report outlines, analyses and reports on the activities that were undertaken by DHSC to ensure the performance and safety of the DHSC LFD during its life cycle in line with the PMS Procedure and PMS Plan.

This was performed thorough the continuous data generation and assessment of the DHSC LFD performance post market and aims to address the questions below:

a) Were there any new hazard or hazardous situation(s) identified for the DHSC LFD's or has the risk acceptability changed?
b) Has any misuse of the DHSC LFDs occurred?
c) Do the DHSC LFD's still meet the user's needs after medium/long term clinical use?
d) Do users experience any usability issues?
e) Are there any recurring quality issues DHSC LFD's and can significant increasing/decreasing trends be identified for DHSC LFD' inadequate performance?

3. Reference documents

Doc ID	Doc name	Revision
QM-01	Quality manual	1
QOP-25	Post- Market Surveillance (PMS) Procedure	3
PMS-0001	PMS Plan for the DHSC COVID-19 LFD device (3 and 7 kit)	2
RMF-001	Risk Management File	5
QP08-F02	LFD Hazard Traceability Matrix	1

Table 1: Reference to internal documentation

4. Standards and guidelines

- ISO 9001:2000 Quality management systems – Requirements.
- ISO 13485:2016 Medical devices - Quality management systems - Requirements for regulatory purposes.
- ISO 14971:2019 Medical devices -- Application of risk management to medical devices.

5. Methodology

- Data is gathered as per the PMS Plan referenced in Table 1.
- All inputs are stored in a centralised LFD PSR location on SharePoint
- All inputs are submitted via the relevant departments as per the PMS plan.
- Inputs are divided into Reactive Methods and Pro-active Methods

6. Findings /Results

6.1 In-House manufacturing inspection at Biotime

There were no inspections carried out for the reporting period of 20th November to 17th December 2021. This is following the conclusion of QC contract on the 30th August 2021. No further DHSC COVID-19 self-test Kit product has been procured during this reporting window.

6.2 Receiving inspection - Intertek Testing in the UK

No product has been procured from Innova in the specified reporting window of this report, meaning no QC activities have taken place during this time. We have placed a large emergency order with Innova and there will be future batch-release QC actions.

6.3 Product complaints & Qualtrics Survey

The number of kits distributed in this reporting period is ~12.3 Million which is an increase of ~2.3 Million kits from the previous reporting period.

A total of 176 user reports were received from the Qualtrics survey in this reporting window. Thirty-nine of which were non product related classified as “Reporting Issues”. Thirty-seven of these user reports were relating to “QR/Barcode Issues” and were predominantly attributed to the issues with scanning the QR code on the website and were subsequently sent to the relevant department for triage.

The remaining 80 user reports were analysed, and no lot specific trends were identified. There was an increase of 13 user reports over the last reporting period which can be attributed to the additional volume of kits distributed. In contrary, the “Damaged Item” category saw a reduction from 25 in the last reporting period to 4 in this reporting period. Similarly, the “Missing Item” category saw a reduction from 27 in the last reporting period to 19 in this reporting period. In the interest of continuous product improvement, it is recommended that a Quality Alert is instigated and routed to the relevant department for investigation of all QC related issues reported, see Section 8.

One product complaint was received via Control Tower relating to missing buffer sachets and recorded as complaint LFD-21-12-0024. Analysis was performed and no lot trend was identified but investigation is still on-going and further information has been requested.

No MHRA Yellow Cards were received during this reporting window. The last Yellow card response was received from the MHRA on the 15th November 2021. This sudden reduction in yellow card responses was queried with the MHRA via email communications, the DHSC was advised that due to staffing issues (relating to illness) there has been a reduction in the ability to send over Yellow Cards to the DHSC. We can therefore expect an increased volume of Yellow Cards in the next reporting window.

6.4 Combined Complaints Data (Yellow Card, Control Tower and Qualtrics Complaints) – Trending

Figure 1 shows the trending data for the combined LFD complaints received (Yellow Card, Through Control Tower and Qualtrics Complaints) vs distributed LFD test kits for the last reporting periods.

Alert and Action thresholds were established using an average derived from the last reporting periods. These thresholds remained consistent to provide an ongoing benchmark for identifying trends through continual monitoring.

As per the discussion in the PSR-011, CAPA-21-06-0039 has now been instigated to review this current trending methodology previously used. For continuity, the combined complaints data graph is presented below however DHSC is currently working on a Risk-Based trending approach which will provide a more representative continual monitoring trending process.

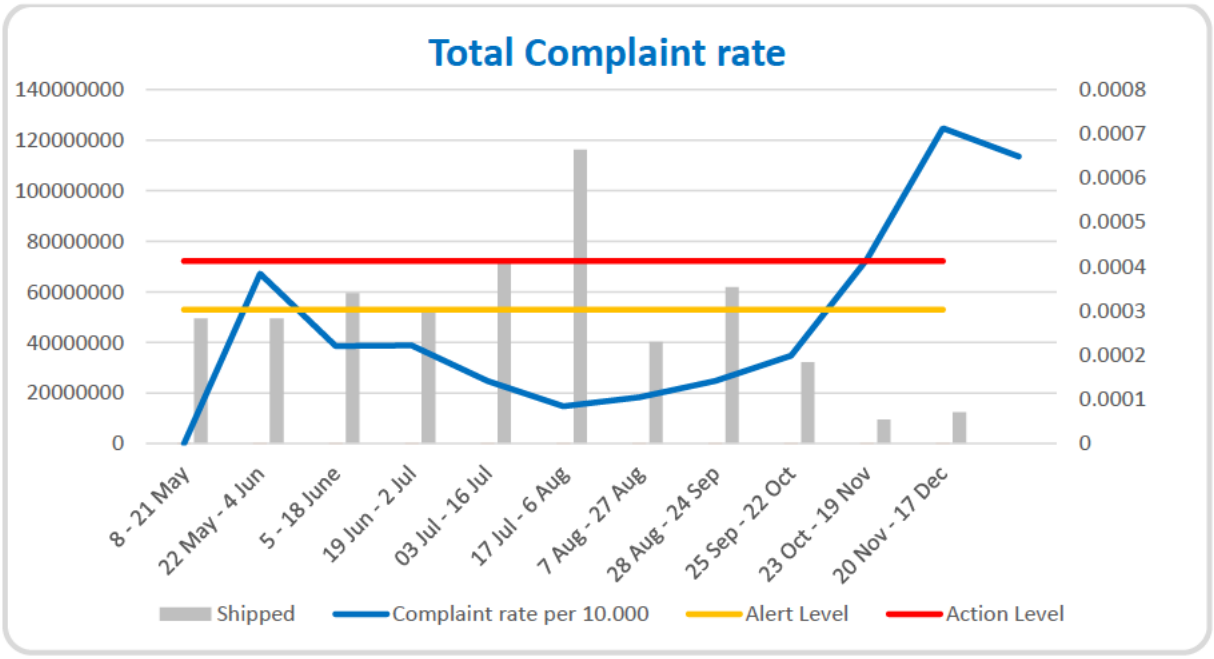
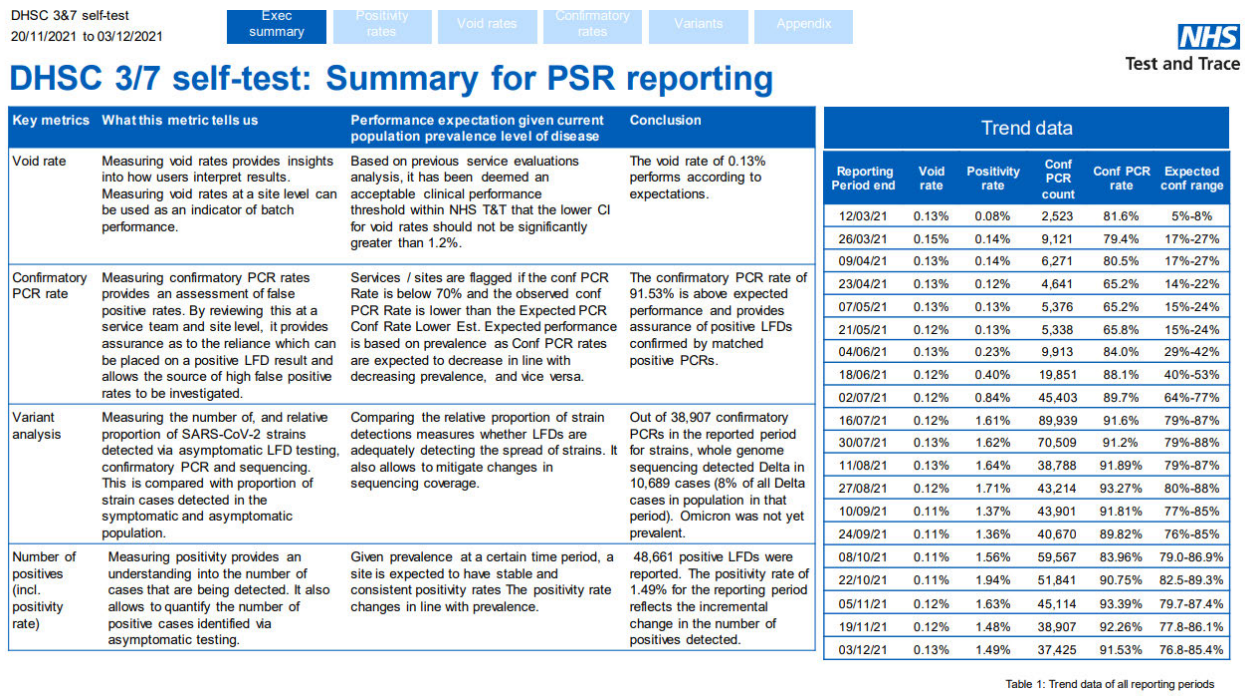


Figure 1: Graph showing total complaints vs distribution with action & alert levels set

6.5 Real World Performance Monitoring

The Real-World Performance Monitoring Team carry out routine performance of device and service performance using real-world data generated within NHS Test & Trace covering all services and devices.

Figure 2 and Figure 3 are summaries for the Void rates, confirmatory PCR rates, variant analysis, and the number of positives (i.e., positivity rates), for the reporting period 20th November – 17th December 2021.



DHSC 3&7 self-test
20/11/2021 to 03/12/2021

Exec summary | Positivity rates | Void rates | Confirmatory rates | Variants | Appendix

NHS Test and Trace

DHSC 3/7 self-test: Summary for PSR reporting

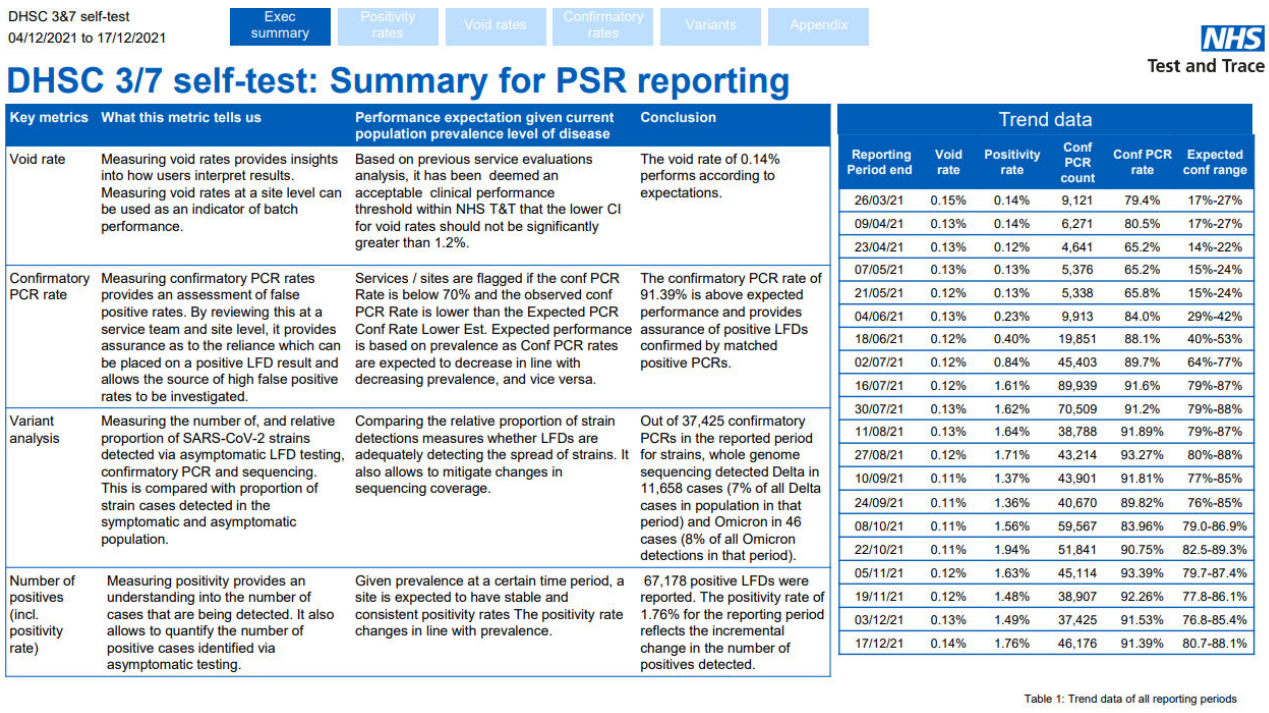
Key metrics	What this metric tells us	Performance expectation given current population prevalence level of disease	Conclusion
Void rate	Measuring void rates provides insights into how users interpret results. Measuring void rates at a site level can be used as an indicator of batch performance.	Based on previous service evaluations analysis, it has been deemed an acceptable clinical performance threshold within NHS T&T that the lower CI for void rates should not be significantly greater than 1.2%.	The void rate of 0.13% performs according to expectations.
Confirmatory PCR rate	Measuring confirmatory PCR rates provides an assessment of false positive rates. By reviewing this at a service team and site level, it provides assurance as to the reliance which can be placed on a positive LFD result and allows the source of high false positive rates to be investigated.	Services / sites are flagged if the conf PCR Rate is below 70% and the observed conf PCR Rate is lower than the Expected PCR Conf Rate Lower Est. Expected performance is based on prevalence as Conf PCR rates are expected to decrease in line with decreasing prevalence, and vice versa.	The confirmatory PCR rate of 91.53% is above expected performance and provides assurance of positive LFDs confirmed by matched positive PCRs.
Variant analysis	Measuring the number of, and relative proportion of SARS-CoV-2 strains detected via asymptomatic LFD testing, confirmatory PCR and sequencing. This is compared with proportion of strain cases detected in the symptomatic and asymptomatic population.	Comparing the relative proportion of strain detections measures whether LFDs are adequately detecting the spread of strains. It also allows to mitigate changes in sequencing coverage.	Out of 38,907 confirmatory PCRs in the reported period for strains, whole genome sequencing detected Delta in 10,689 cases (8% of all Delta cases in population in that period). Omicron was not yet prevalent.
Number of positives (incl. positivity rate)	Measuring positivity provides an understanding into the number of cases that are being detected. It also allows to quantify the number of positive cases identified via asymptomatic testing.	Given prevalence at a certain time period, a site is expected to have stable and consistent positivity rates The positivity rate changes in line with prevalence.	48,661 positive LFDs were reported. The positivity rate of 1.49% for the reporting period reflects the incremental change in the number of positives detected.

Trend data

Reporting Period end	Void rate	Positivity rate	Conf PCR count	Conf PCR rate	Expected conf range
12/03/21	0.13%	0.08%	2,523	81.6%	5%-8%
26/03/21	0.15%	0.14%	9,121	79.4%	17%-27%
09/04/21	0.13%	0.14%	6,271	80.5%	17%-27%
23/04/21	0.13%	0.12%	4,641	65.2%	14%-22%
07/05/21	0.13%	0.13%	5,376	65.2%	15%-24%
21/05/21	0.12%	0.13%	5,338	65.8%	15%-24%
04/06/21	0.13%	0.23%	9,913	84.0%	29%-42%
18/06/21	0.12%	0.40%	19,851	88.1%	40%-53%
02/07/21	0.12%	0.84%	45,403	89.7%	64%-77%
16/07/21	0.12%	1.61%	89,939	91.6%	79%-87%
30/07/21	0.13%	1.62%	70,509	91.2%	79%-88%
11/08/21	0.13%	1.64%	38,788	91.89%	79%-87%
27/08/21	0.12%	1.71%	43,214	93.27%	80%-88%
10/09/21	0.11%	1.37%	43,901	91.81%	77%-85%
24/09/21	0.11%	1.36%	40,670	89.82%	76%-85%
08/10/21	0.11%	1.56%	59,567	83.96%	79.0-86.9%
22/10/21	0.11%	1.94%	51,841	90.75%	82.5-89.3%
05/11/21	0.12%	1.63%	45,114	93.39%	79.7-87.4%
19/11/21	0.12%	1.48%	38,907	92.26%	77.8-86.1%
03/12/21	0.13%	1.49%	37,425	91.53%	76.8-85.4%

Table 1: Trend data of all reporting periods

Figure 2: DHSC 3/7 self-test summary Period 20-Nov-2021 to 03-Dec-2021



DHSC 3&7 self-test
04/12/2021 to 17/12/2021

Exec summary | Positivity rates | Void rates | Confirmatory rates | Variants | Appendix

NHS Test and Trace

DHSC 3/7 self-test: Summary for PSR reporting

Key metrics	What this metric tells us	Performance expectation given current population prevalence level of disease	Conclusion
Void rate	Measuring void rates provides insights into how users interpret results. Measuring void rates at a site level can be used as an indicator of batch performance.	Based on previous service evaluations analysis, it has been deemed an acceptable clinical performance threshold within NHS T&T that the lower CI for void rates should not be significantly greater than 1.2%.	The void rate of 0.14% performs according to expectations.
Confirmatory PCR rate	Measuring confirmatory PCR rates provides an assessment of false positive rates. By reviewing this at a service team and site level, it provides assurance as to the reliance which can be placed on a positive LFD result and allows the source of high false positive rates to be investigated.	Services / sites are flagged if the conf PCR Rate is below 70% and the observed conf PCR Rate is lower than the Expected PCR Conf Rate Lower Est. Expected performance is based on prevalence as Conf PCR rates are expected to decrease in line with decreasing prevalence, and vice versa.	The confirmatory PCR rate of 91.39% is above expected performance and provides assurance of positive LFDs confirmed by matched positive PCRs.
Variant analysis	Measuring the number of, and relative proportion of SARS-CoV-2 strains detected via asymptomatic LFD testing, confirmatory PCR and sequencing. This is compared with proportion of strain cases detected in the symptomatic and asymptomatic population.	Comparing the relative proportion of strain detections measures whether LFDs are adequately detecting the spread of strains. It also allows to mitigate changes in sequencing coverage.	Out of 37,425 confirmatory PCRs in the reported period for strains, whole genome sequencing detected Delta in 11,658 cases (7% of all Delta cases in population in that period) and Omicron in 46 cases (8% of all Omicron detections in that period).
Number of positives (incl. positivity rate)	Measuring positivity provides an understanding into the number of cases that are being detected. It also allows to quantify the number of positive cases identified via asymptomatic testing.	Given prevalence at a certain time period, a site is expected to have stable and consistent positivity rates The positivity rate changes in line with prevalence.	67,178 positive LFDs were reported. The positivity rate of 1.76% for the reporting period reflects the incremental change in the number of positives detected.

Trend data

Reporting Period end	Void rate	Positivity rate	Conf PCR count	Conf PCR rate	Expected conf range
26/03/21	0.15%	0.14%	9,121	79.4%	17%-27%
09/04/21	0.13%	0.14%	6,271	80.5%	17%-27%
23/04/21	0.13%	0.12%	4,641	65.2%	14%-22%
07/05/21	0.13%	0.13%	5,376	65.2%	15%-24%
21/05/21	0.12%	0.13%	5,338	65.8%	15%-24%
04/06/21	0.13%	0.23%	9,913	84.0%	29%-42%
18/06/21	0.12%	0.40%	19,851	88.1%	40%-53%
02/07/21	0.12%	0.84%	45,403	89.7%	64%-77%
16/07/21	0.12%	1.61%	89,939	91.6%	79%-87%
30/07/21	0.13%	1.62%	70,509	91.2%	79%-88%
11/08/21	0.13%	1.64%	38,788	91.89%	79%-87%
27/08/21	0.12%	1.71%	43,214	93.27%	80%-88%
10/09/21	0.11%	1.37%	43,901	91.81%	77%-85%
24/09/21	0.11%	1.36%	40,670	89.82%	76%-85%
08/10/21	0.11%	1.56%	59,567	83.96%	79.0-86.9%
22/10/21	0.11%	1.94%	51,841	90.75%	82.5-89.3%
05/11/21	0.12%	1.63%	45,114	93.39%	79.7-87.4%
19/11/21	0.12%	1.48%	38,907	92.26%	77.8-86.1%
03/12/21	0.13%	1.49%	37,425	91.53%	76.8-85.4%
17/12/21	0.14%	1.76%	46,176	91.39%	80.7-88.1%

Table 1: Trend data of all reporting periods

Figure 3: DHSC 3/7 self-test summary Period 04-Dec-2021 to 17-Dec-2021

6.6 CAPA

- Since the last reporting period the DHSC Quality team have closed 2 CAPA's.
- Refer to Table 2 for a CAPA Status Overview
- Refer to Table 3 for List of open CAPA's and current progress and due dates.

CAPA Status	No
Completed	02
Implementation	01
Investigation	00
VOE	04
Open	02
Total	**09**

Table 2: CAPA Status Overview

No	CAPA No	Start Date	Problem statement	Status/ progress	Due date	Reason for extension if overdue
04	CAPA-21-06-0011	08-Jun-21	CAPA raised to address the lack of unified complaints system for receiving direct complaints under the design and responsibility of DHSC	Complete Pending VOE	VOE due: 31-Dec-21	N/A
06	CAPA-21-06-0013	08-Jun-21	CAPA raised to strengthen the PMS plan and appropriate PMS activities	Complete pending VOE	Voe Due: Mid Feb 2022	N/A
10	CAPA-21-06-0017	08-Jun-21	CAPA raised to address the lack of evidence identified in LFD technical file to demonstrate whether the tests continue to be fit for purpose and that they meet the intended performance stated by DHSC.	Complete pending VOE	VOE Due: 15-Feb-22	N/A
23	CAPA-21-06-0032	11-Jun-21	CAPA raised to demonstrate DHSC's compliance towards nonconformity identified in Innova USA voluntary recall notice with regards to QMS requirements	Complete pending VOE	VOE due 31-Dec-21	N/A
24	CAPA-21-06-0037	26-Nov-21	CAPA raised due to Barcode labels being procured from two different manufacturers (although through a single supplier) that have the same TC number.	Action Implementation Stage. Meeting to be had in the new year.	31-Jan-21	N/A
25	CAPA-21-06-0038	26-Nov-21	CAPA raised as a preventative measure to monitor and react to cases of Positive LFD tests being followed by Negative PCR tests	Open	Mid Feb 2022	N/A
26	CAPA-21-06-0039	26-Nov-21	CAPA raised due to a spike in LFD complaints taking them over the acceptable threshold	Open	31-Mar-21	N/A

Table 3: List of open CAPA's, Status & Due date

6.7 SCAR – Supplier Corrective Action Report

No SCARs raised for DHSC LFD's in this reporting period of 20th November to 17th December 2021.

6.8 Risk Management

LFD Risk management File (RMF) has been updated to RMF-0001 Revision 5 and HTM Hazard traceability Matrix Rev5. The RMF updated to new template for compliance with ISO 14971:2019.

All identified known or reasonably foreseeable risks associated with the design, use and manufacture of the LFD device are considered to have been identified and addressed through implementation of the Risk Management Plan as documented in the risk management report (QOP08-F03). Appropriate control measures have been identified and implemented, which resulted in all the risks being reduced as low as possible (with no new hazards introduced). The results of both individual and overall risk-benefit analysis demonstrated that the intended medical benefits of the LFD device outweigh the residual risks.

6.9 Literature Review & State of the Art (SOTA)

In collaboration with an external consultancy, DHSC has developed a Literature Search Protocol. The intention of the literature search is to review the continued clinical safety and effectiveness of the Lateral Flow Device kit when used for the intended purpose.

The literature search is carried out monthly in line with the PSR reporting schedule and utilizes multiple electronic search databases (e.g., PubMed, Embase & Medboard) as highlighted in the protocol. It is worth highlighting that due to the frequency and timing of the LFD PSR reports, it is not practical nor feasible to provide a detailed analysis and conclusions of findings. However, the literature searches will be continuously reviewed with the support of PHCO for on-going performance evaluation and separately, a high-level summary is provided in the monthly PSR report.

In a study by *Cubas-Atienzar A.I., et al (Attachment 7, Ref: 202111.1, Appendix D,Pg 29),* the author is analyzing the Limit Of Detection (LOD) in different matrices of 19 commercially available rapid antigen tests for the detection of SARS-COV-2 using live SARS-COV-2 spiked in different matrices. The author found that fourteen of 19 Ag-RDT's exceeded the LOD performance criteria defined by the WHO, of these fourteen Ag-RDT's Innova LFD is named.

Similarly a publication by *Lamb G.,et al* discusses the real-world evaluation of COVID-19 lateral flow devices in mass-testing in healthcare workers at London Hospital *(Attachment 7, Ref: 202111.2, Appendix D, Pg 29).* The authors conclude that the PPV of Innova LFD is high when used amongst hospital staff during periods of high prevalence of Covid-19 and goes on to discuss how LFD testing allows earlier isolation of infected workers and facilitates detection of individuals whose symptoms do not qualify for PCR testing.

Another publication by Peto T.,et al *(Attachment 7,Ref: 202111.5, Appendix D, Pg 32)* where the author is performing a national systematic evaluation of sensitivity & specificity of Rapid Antigen mass-testing, suggests that LFD's have promising performance characteristics for mass population testing. The author goes on to discuss how LFD's can be used to identify infectious positive individuals and how the Innova LFD shows good viral antigen detection/sensitivity with excellent specificity. In contrast, the author does discuss how kit failure rates and the impact of training are potential issues. However, the results supported the expanded evaluation of LFD's and assessment of greater access to testing on Covid-19 transmission.

In a comprehensive comparison of antigen LFD's and virus infectivity by Pickering S, et al *(Attachment 7, Ref 202111.6, Appendix D, Pg 33),* the author found a clear relationship between Ct values, quantitative culture of infectious virus and antigen LFD positivity in clinical samples. The authors go on to conclude that the data support regular testing of target groups with LFDs to supplement PCR testing, thus helping to rapidly identify infected individuals in situations which they would otherwise go undetected.

In addition to the discussion above, a Medboard search was carried out on 02 December 2021 to obtain additional publications that are related to other manufacturers of similar LFD test kits to the DHSC LFD device. A summary of the results of the MedBoard search covering all historical reports to date is presented in Attachment 07, Appendix E.

Twenty-six publications were relevant for inclusion for **similar devices including Orient Gene, Acon, MP Biomedical and Panbio-Abott**. Recurring conclusions from these publications are favorable with regards to the rapid antigen test (LFD's) being quick, valuable, and cost-effective tools in the detection of contagious persons during the on-going pandemic.

7. Conclusion & Risk-Benefit Determination

The DHSC LFD test is intended to detect the presence of coronavirus (Covid-19) antigen in humans to enable the spread of the virus to be reduced in the community. The overall purpose of post-market surveillance activities is to ensure that the device continues to meet its intended purpose.

It is noted that performance of the device demonstrated a Void Rate (Average across 2 periods) of **0.135%** which performs according to expectations and is below the threshold of 1.2%. The confirmatory PCR rate (Average across 2 periods) of **91.46%** is above expected performance and provides assurance of positive LFDs confirmed by matched positive PCRs.

DHSC has not instigated a re-call nor issued any Field Safety Corrective Action Notices.

All identified known or reasonably foreseeable risks associated with the design, use and manufacture of the LFD device are considered to have been identified and addressed through implementation of the Risk Management Plan as documented in the risk management report (QOP08-F03). Furthermore, no new Hazards were identified during this reporting period as part of the continual monitoring through post-market surveillance activities. Benefits of use of Lateral Flow Devices continue to outweigh identified risk. These include:

a) Early indication of possible infection with Covid-19 while still asymptomatic
b) Prevention of spread of Covid-19 virus
c) Prevention of the need for unnecessary self-isolation/travel restriction therefore improving patient/user quality of life.
d) Widespread PCR testing is operationally unfeasible

Literature searches discussed in Section 6.9 provide further support that LFDs are cost quick and cost-effective means of rapid testing during the on-going pandemic and that the device continues to meet its intended purpose.

No emerging issues or safety signals identified, but opportunities for improvement were noted and actions are assigned in Section 8.

As a result of the PMS activities analysed/discussed in this report the PMS Team advice is to continue distributing the current EUA cleared product.

8. Recommended Actions

No	Added	Action	Responsible Name	Due Date	Status
1	06-Dec-2021	Raise Quality Alert for 68 reports under complaint categories "Missing", "Media Volume"," Empty Sachet", "Damaged" and "Contamination"	[redacted]	19-Jan-2022	Open
2	26-Nov-2021	CAPA instigated for complaints going above action and alert levels in PSR-010 & PSR 011.	[redacted]	05-Jan-2022	Completed
3	04-Oct-2021	Finalize review of Risk Management File after the addition of 2 new hazards identified in previous reporting periods 28th Aug to 24thSep and 25th Sept to 22nd Oct.	[redacted]	23-Nov-21	Completed

9. Attachments

Attachment 01: PMS-0001, PMS Plan for the DHSC Covit-19 LFD Devices (3 and 7 kit) Rev2, 29-July-2021
Attachment 02: DHSC PSR – Complaints & Qualtrics data
Attachment 03: RWPM Innova 3s and 7s
Attachment 04: RWPM Innova 25s
Attachment 05: RWPM Innova Assisted
Attachment 06: QP08-F02 LFD Hazard Traceability Matrix v.01 Issued 22.12.2021
Attachment 07: Literature Search Report - Lateral Flow Device rev2 20211221

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