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Lessons learned from COVID-19 in relation to IVD regulations

CONTENTS

The Birmingham Health Partners Centre for Regulatory Science & Innovation was established in 2020 to support the development and delivery of novel therapeutics and medical devices in the UK, through advanced regulatory standards and tools. A truly multidisciplinary initiative, the CRSI aims to bring together experts in medicinal science, health policy and management, clinical trial design, medical law, and patient-reported outcomes research, from across BHP member organisations. The mission of the CRSI is to drive innovation in regulatory science to promote efficient, safe, and cost-effective implementation of new therapies, for the benefit of patients and society. **www.birminghamhealthpartners.co.uk**

The Regulatory Horizons Council (RHC) is an independent expert committee that identifies the implications of technological innovation, and provides government with impartial, expert advice on the regulatory reform required to support its rapid and safe introduction.

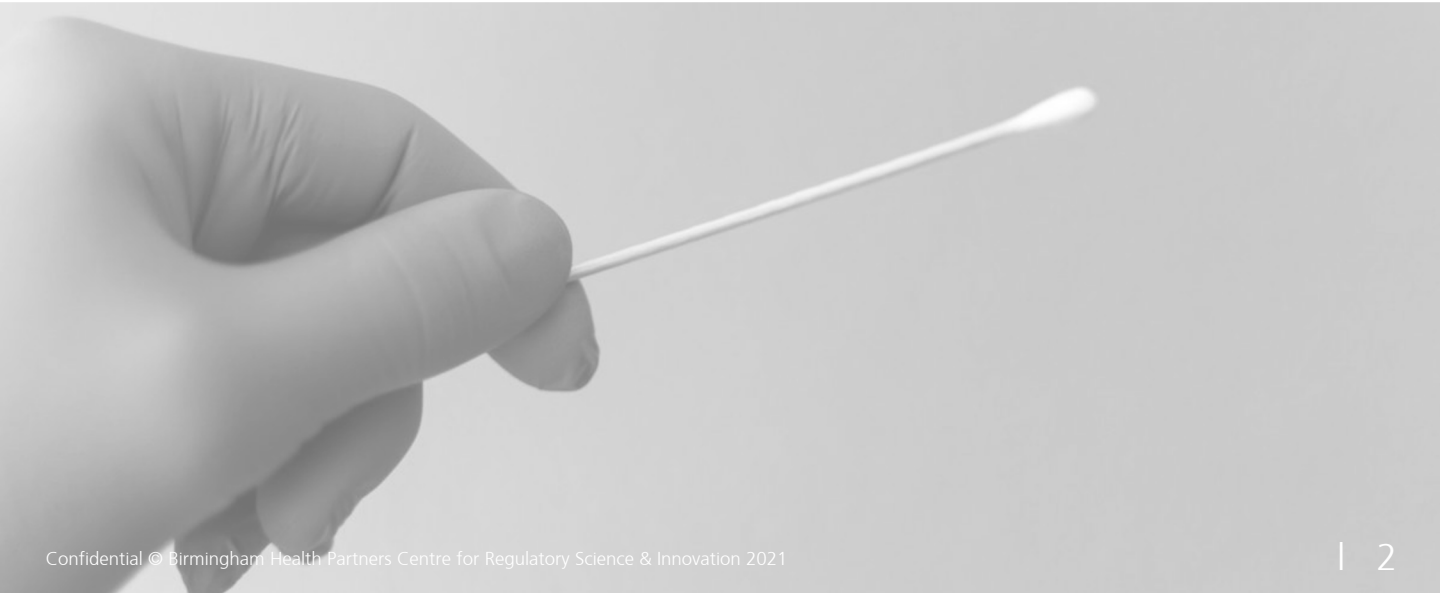
March 2021

Executive Summary

In vitro diagnostics (IVDs) are medical devices intended for use in diagnosis of disease or other conditions. The COVID-19 pandemic has clearly highlighted the importance of diagnostic tests in infectious disease outbreaks. The Regulatory Horizons Council commissioned the Birmingham Health Partners Centre for Regulatory Science and Innovation (CRSI) to collate lessons learned from COVID-19 in relation to IVD regulations by identifying the 'key challenges that have arisen around the application of IVD regulations during the COVID-19 pandemic' and the 'strategies that could be adopted to overcome the key challenges in the event of a future infectious disease outbreak'.

The CRSI team began by performing a literature review using PubMed and Google Scholar to search the published literature and Google Search Engine to search the grey literature. We then used three qualitative methods to comprehensively collate the lessons learned by stakeholders from across the medical device sector: i) one-on-one, semi-structured interviews with stakeholders were conducted; ii) a multidisciplinary stakeholder workshop was convened to review initial findings and discuss areas of agreement and disagreement; and iii) a post-workshop survey was distributed to attendees to further explore areas of contention discussed during the workshop. All data were subsequently analysed using a framework approach.

The evidence gathering and stakeholder engagement process identified that, in the event of an infectious disease outbreak, high-quality diagnostic tests need to be robustly and rapidly developed, distributed, and disseminated. For that reason, we have categorised the key challenges that have arisen around the application of IVD regulations during the COVID-19 pandemic and the strategies that could be adopted to overcome them in the event of a future infectious disease outbreak into three categories: those most relevant to the quality of diagnostic tests; those most relevant to the development and distribution of diagnostic tests; and those most relevant to the dissemination of information relating to diagnostic tests.



Quality of diagnostic tests High-quality tests are crucial in containing and controlling an infectious disease outbreak. This is because the implications of inaccurate test results, in the case of false negatives, undermine containment efforts. Unfortunately, throughout the COVID-19 pandemic, many substandard tests have been made available on the market without high quality evidence as a result of inadequate IVD regulations. This is because test developers in the EU (under the In Vitro Diagnostic Directive (IVDD)) and in the US (under Emergency Use Authorization (EUA)) are able to self-certify their tests without regulatory verification. Stakeholders succinctly summarised that no test is better than a bad test; and suggested that, in the event of a future infectious disease outbreak, all claims made by test developers should be checked by regulators, and the requirements for test characteristic requirements should be reviewed with the contextual implications of inaccurate test results in mind. Stakeholders also suggested that greater emphasis should be placed on intended use and usability testing to ensure adequate test performance in the 'real world'.

Development and distribution of diagnostic tests The timely development and distribution of high-quality tests is essential in curtailing transmission. This is because, until the advent of a vaccine, testing is the most effective tool available to keep transmission under control. During the COVID-19 pandemic, the development and distribution of high-quality tests has been delayed for a number of reasons, including a lack of access to crucial SARS-CoV-2 reference materials; a lack of clear and comprehensive COVID-19 specific guidance for test developers; regulators not being able to meet the surge in demand for their IVD and non-IVD-related services; and regulators not being able to carry out important in-person physical audits due to social restrictions. Stakeholders made multiple suggestions for how to increase efficiency in test development and distribution in the event of a future infectious disease outbreak: ensure access to pathogen-specific reference materials; provide clear and comprehensive situation-specific guidance for test developers; train and retain IVD regulatory experts; plan for and permit remote auditing; establish a permanent diagnostic unit with in-house clinical and regulatory expertise; use target product profiles (TPPs); develop common specifications; make routine health data more readily available; digitise the regulatory approval process; ensure continued access to laboratory-developed tests (LDTs); and increase the emphasis placed on post-market surveillance.

Dissemination of information relating to diagnostic tests The effective dissemination of test-related information is critical in combating an infectious disease outbreak. Enormous amounts of information have been disseminated from disparate sources during the COVID-19 pandemic and the quality of the information has been hugely variable. This has created confusion amongst patients and the public and made consumers more vulnerable to scams from unscrupulous suppliers. Data sharing practice amongst scientists has also been inadequate. Strategies to improve the dissemination of information in the event of a future infectious disease outbreak include developing best practice guidance for communicating complex information to patients and the public; investing in communication campaigns; and ensuring that information is presented in standardised formats, both online and in the scientific literature.

Key Findings

Challenges that have arisen around the application of IVD regulations during the COVID-19 pandemic

Quality

Self-certification meant that many COVID-19 tests were made available on the market without regulatory verification.
The unprecedented demand for COVID-19 tests has meant that regulatory authorities have had to adapt their policies and practices to ensure that tests could be made available on the market without delay. In the EU, under IVDD, and in the US, under EUA, developers have been able to self-certify their tests without regulatory verification, which has resulted in significant numbers of substandard tests being made available on the market.

Test characteristic requirements were not reviewed with the implications of inaccurate COVID-19 test results in mind. The requirements for test characteristics such as sensitivity, specificity, positive predictive value, and negative predictive value, were not reviewed with the implications of inaccurate COVID-19 test results in mind. This meant that many poor-quality tests with high false positive rates (which increase the likelihood of an uninfected individual self-isolating and worrying unnecessarily) and false negative rates (which increase the likelihood of disease being spread unknowingly by infected individuals with undetected infection) were made available on the market.

Insufficient emphasis was placed on the intended use of different COVID-19 tests.
The implications of a test's outcomes, and, by extension, the performance requirements for that test, differ depending on the situation in which the test is used. For example, the implications of and performance requirements for a test designed to screen healthcare professionals for immunity are different to those designed to diagnose patients with active infection. During the COVID-19 pandemic, insufficient emphasis was placed on the intended use of different tests, which raised the risk of tests being used inappropriately.

Development and distribution

Regulators have struggled to meet the surge in demand for their services due to the significant numbers of novel diagnostic tests that have been developed during the COVID-19 pandemic. Significant numbers of novel diagnostic tests, non-IVD devices, new drugs, and vaccines have been developed during the COVID-19 pandemic and regulators have struggled to meet the surge in demand for their services. The increased burden placed on regulators has been exacerbated by unique COVID-19 related challenges, such as the reorganisation of clinical services, which has meant that fewer clinicians are available to advise regulators, and social restrictions, which have prevented essential in-person physical audits from taking place.

Lack of clear and comprehensive COVID-19-specific guidance for IVD developers.
A lack of clear and comprehensive COVID-19 specific guidance from regulators made it difficult for IVD developers to navigate the regulatory approval process during the pandemic.

Variable access to crucial SARS-CoV-2 reference materials. Pathogen-specific reference materials are essential when developing and validating tests. During the COVID-19 pandemic, there have been issues around access to crucial SARS-CoV-2 reference materials, which have impeded test development and validation.

Dissemination of information

Lack of accessible, clear, timely, and understandable information about COVID-19 tests for patients and the public.
Enormous amounts of information about tests have been disseminated from disparate sources during the COVID-19 pandemic and the quality of this information has been hugely variable. This has made it difficult for patients and the public to compare different test types, interpret test characteristics, and, ultimately, understand what is best for them. Unscrupulous suppliers have sought to capitalise on the confusion and the increase in demand for home testing kits by selling unsafe and unlicensed tests online, sometimes seeking to scam consumers via fraudulent websites.

Insufficient emphasis was placed on the importance of using reporting guidelines for studies involving COVID-19 tests.
Reporting guidelines specify the minimum content needed when reporting a study. Their use helps to improve the design, delivery, and evaluation of studies. During the COVID-19 pandemic, insufficient emphasis was placed on the use of reporting guidelines for studies involving IVDs. This made it difficult for developers to design and deliver high-quality studies and for reviewers to effectively evaluate them.

Widespread use of preprint servers for sharing COVID-19 test-related data before peer review.
Peer review describes the process of subjecting scientific research to the scrutiny of others who are experts in the same field. It functions to ensure that unwarranted claims and interpretations are not published inappropriately. During the COVID-19 pandemic, preprint servers have been widely used to disseminate IVD-related data whilst awaiting peer review. The timely sharing of information is important during a pandemic but doing so prior to peer review increases the likelihood that poor quality, potentially misleading data are disseminated inappropriately.

Key Findings

Strategies that could be adopted to overcome the key challenges in the event of a future infectious disease outbreak

Quality

Regulatory oversight should be required for all tests. Although self-certification may be appropriate for low-risk tests most of the time, regulatory oversight should be required for all relevant diagnostic and screening tests in the event of a future infectious disease outbreak, to ensure that all claims made by IVD developers regarding test performance are reviewed.

Test characteristic requirements should be reviewed with the contextual implications of inaccurate test results in mind. In the event of a future infectious disease outbreak, the requirements for test characteristic requirements should be reviewed, with the contextual implications of inaccurate test results in mind, as these are likely to be different than they would be during normal times. Where possible, some aspects of test characteristic requirements can be prespecified based on lessons learned during the COVID-19 pandemic to increase readiness for a future infectious disease outbreak.

Greater emphasis should be placed on usability testing. The usability of a test is a key determinant of whether it will work when deployed at scale. For this reason, greater emphasis should be placed on usability testing in the event of a future infectious disease outbreak.

Development and distribution

Train and retain IVD regulatory experts. The ability for regulatory bodies to respond to surges in demand for their IVD-specific services during a future infectious disease outbreak could be improved by investing in training new, and retaining existing, IVD regulatory experts.

Plan for and permit remote auditing. It is possible that social restrictions that prevent in person physical audits from taking place will be re-instituted in the event of a future infectious disease outbreak. To prepare for such an eventuality, it is important for regulators to plan for and permit remote auditing.

Establish a national diagnostic unit with in-house clinical and regulatory expertise. Having a national diagnostic unit with in-house clinical and regulatory expertise in place that could be mobilised when needed would enable healthcare authorities to efficiently respond to a future infectious disease outbreak. In the UK, this could sit within the Department of Health and Social Care (DHSC).

Provide clear and comprehensive situation-specific guidance for IVD developers. In the event of a future infectious disease outbreak, clear and comprehensive situation-specific guidance would help IVD developers more easily overcome any challenges that they may face whilst navigating the regulatory approval process. Some guidance could potentially be prespecified.

Use target product profiles. A TPP outlines the desirable characteristics and minimally acceptable specifications of a product that is needed to address a well-defined clinical problem. In the event of a future infectious disease outbreak, TPPs should be used to drive the development of IVDs.

Develop common specifications. Common specifications are clinical and technical requirements – other than a standard – that provide a means of complying with legal obligations applicable to a device, process, or system. They are useful in situations where standards do not exist or are insufficient. Key stakeholders should consider developing common specifications to help guide IVD developers for use in the event of a future infectious disease outbreak when standards are unlikely to exist.

Make routine health data more readily available. Access to health data may be of a value when developing and validating a test. Making routine health data more readily available to IVD developers in the event of a future infectious disease outbreak would facilitate the development and validation process.

Digitise the regulatory approval process. Paper-based systems may be associated with delay and are less flexible when responding to a need to conduct audits and review virtually. Digitising the regulatory approval process would speed up the process and overcome potential challenges that may be posed during a future pandemic.

Ensure continued access to laboratory-developed tests. An LDT is a non-commercial IVD that is designed, manufactured, and used within a single laboratory. At the start of the COVID-19 pandemic, when no commercial tests were available on the market, it was LDTs that were initially used to diagnose patients with COVID-19. It is essential that future IVD regulation continues to ensure patient and public access to these tests, which will invariably play an important role in the event of a future infectious disease outbreak.

Ensure access to pathogen-specific reference materials. Efforts should be made to ensure effective distribution of pathogen-specific reference materials in the event of a future infectious disease as they are essential for the development and validation of tests. In the UK, the Medicines and Healthcare products Regulatory Agency and the National Institute for Biological Standards and Control would be well placed to organise and oversee this process.

Increase the emphasis placed on post-market surveillance. In the event of a future infectious disease outbreak, increasing the emphasis placed on post-market surveillance will ensure early access to essential tests, whilst enabling effective real-world evaluation of test performance.

Dissemination of information

Provide patients and the public with accessible, clear, timely, and understandable information. The COVID-19 pandemic demonstrated the importance of high-quality, test-related information and highlighted how hard communicating this kind of information to patients and the public can be. Authorities should invest in developing best practice guidance for communication about tests and ensure it is employed in the event of a future infectious disease outbreak. Online shops selling direct-to-consumer home testing kits should be made to present test-related information in a standardised manner.

Promote the use of standardised reporting guidelines for studies involving IVDs. The Standards for Reporting of Diagnostic Accuracy Studies (STARD) reporting guidelines specify the minimum content needed when reporting a diagnostic accuracy study. The use of STARD reporting guidelines should be promoted, as their use helps to improve the design, delivery, and evaluation of such studies.

Abbreviations

BHP	Birmingham Health Partners
CRSI	Centre for Regulatory Science and Innovation
COVID 19	Coronavirus disease
EU	European Union
EU IVDD	European Union In Vitro Diagnostic Directive (98/79/EC)
EUA	Emergency Use Authorization
IVD	In vitro diagnostic
LDT	Laboratory-developed test
RHC	Regulatory Horizons Council
SARS CoV 2	Severe acute respiratory syndrome coronavirus 2
STARD	Standards for Reporting of Diagnostic Accuracy Studies
TPP	Target product profile
UK	United Kingdom of Great Britain and Northern Ireland
US	United States

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Disclaimers

While this report was commissioned by the Regulatory Horizons Council, Birmingham Health Partners Centre for Regulatory Science and Innovation retained full editorial control of the report's content. The views expressed in this research reflect research findings and not necessarily of Government. None of this represents government policy.

This report reflects the views of a range of stakeholders and should not be attributed to specific individuals or organisations unless explicitly stated.

Drs Han and Ibrahim contributed equally to this report and are recognised as joint first authors.

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*Advisory board members

APPENDIX 1: Methods

Qualitative methods were used to collate the views of stakeholders from across the medical device sector.

1. Data Collection

Data were collected from four sources:

Figure 1. Data Sources.

1.1. Literature Review

A literature review was conducted on 08 January 2021. PubMed and Google Scholar were used to search published literature and Google Search Engine was used to search grey literature. Only the first 100 citations from Google Scholar and Google Search Engine were screened due to time constraints. Citations were independently screened by two co-investigators (DH and HI) according to predefined inclusion and exclusion criteria. Disagreements were resolved via consensus. A total of 38 citations were included in the literature review.

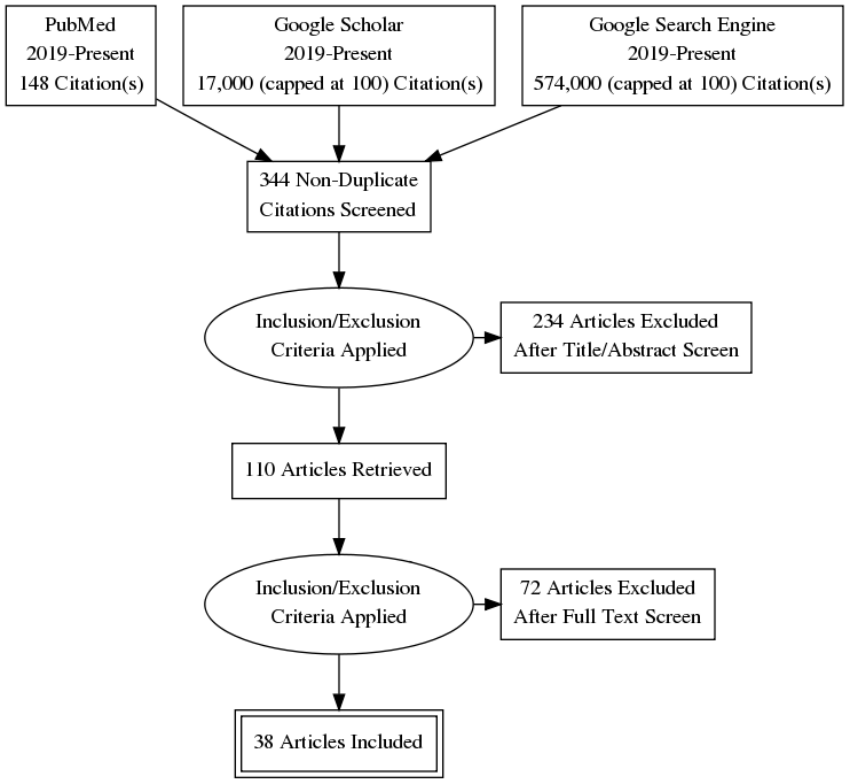
Table 1. Search Terms

PubMed		Google Scholar	Google Search Engine
Search Terms	Record no.	covid-19 "in vitro" medical devices regulation UK	covid-19 "in vitro" medical devices regulation UK
1 (in vitro diagnostic devices) or (in vitro diagnostic device) or (In vitro diagnostic medical device) or (In vitro diagnostic medical devices) or (IVDD) or (IVDDs) or (in vitro device) or (in vitro devices)	164,048		
2 (SARS-CoV-2) or (COVID-19) or (Coronavirus disease)	98,993		
3 ((in vitro diagnostic devices) or (in vitro diagnostic device) or (In vitro diagnostic medical device) or (In vitro diagnostic medical devices) or (IVDD) or (IVDDs) or (in vitro device) or (in vitro devices)) AND ((SARS-CoV-2) or (COVID-19) or (Coronavirus disease))	191		
4 (COVID-19 testing) or (COVID-19 related medical device) or (COVID-19 related medical devices)	8,050		
5 "In vitro"	1,548,996		
6 ((COVID-19 testing) or (COVID-19 related medical device) or (COVID-19 related medical devices)) AND ("In vitro")	106		
7 (((in vitro diagnostic devices) or (in vitro diagnostic device) or (In vitro diagnostic medical device) or (In vitro diagnostic medical devices) or (IVDD) or (IVDDs) or (in vitro device) or (in vitro devices)) AND ((SARS-CoV-2) or (COVID-19) or (Coronavirus disease))) OR (((COVID-19 testing) or (COVID-19 related medical device) or (COVID-19 related medical devices)) AND ("In vitro"))	283		
8 (Legislation) or (Legislations) or (Regulation) or (Regulations) or (regulatory) or (authorization) or (authorisation) or (approval)	5,238,406		
9 ((((in vitro diagnostic devices) or (in vitro diagnostic device) or (In vitro diagnostic medical device) or (In vitro diagnostic medical devices) or (IVDD) or (IVDDs) or (in vitro device) or (in vitro devices)) AND ((SARS-CoV-2) or (COVID-19) or (Coronavirus disease))) OR (((COVID-19 testing) or (COVID-19 related medical device) or (COVID-19 related medical devices)) AND ("In vitro"))) AND ((Legislation) or (Legislations) or (Regulation) or (Regulations) or (regulatory) or (authorization) or (authorisation) or (approval))	148		

Table 2. Inclusion and Exclusion Criteria for Literature Review.

Inclusion criteria	Exclusion criteria
English language	Non-English language
Published on or after 01 December 2019	Published on or before 30 November 2019
In vitro diagnostic medical devices	Does not clearly specify in vitro diagnostic medical devices in title or abstract
Regulation	Does not clearly specify regulation in title or abstract
Debates, discussions, lessons learned, opinions, reflections, and views about application of in vitro diagnostic medical devices regulation	Factual information about about application of in vitro diagnostic medical devices regulation

Figure 2. Flow Diagram for Literature Review.



1.2. Stakeholder Interviews

Stakeholder interviews were conducted online via MS Teams between 04 January 2021 and 02 February 2021. A total of 30 one-on-one, semi-structured interviews were conducted with stakeholders from across the medical device sector: medical device companies (n=7), regulatory consultancies (n=6), UK Government agencies (n=5), product testing or certifying bodies (n=4), academics and clinicians (n=4), trade associations (n=2), and patient and public partners (n=2).

1.3. Stakeholder Workshop

A workshop was conducted online via MS Teams on 09 February 2021. The aim of the workshop was to discuss areas of agreement and disagreement identified after analysis of data from the literature review and stakeholder interviews. A total of 16 stakeholders attended the workshop.

1.4. Post-Workshop Survey

A post-workshop survey was conducted online via Qualtrics Survey Software between 19 February 2021 and 05 March 2021. The survey was designed to further explore areas of contention discussed during the workshop. A total of 9 stakeholders completed the survey.

2. Data Analysis

Data were managed and analysed thematically using the framework approach. This method allows a comprehensive review of collected narratives, that is driven by stakeholders' original accounts and literature review. Raw data from the four sources were analysed by two co-investigators (DH and HI). The interviews were reviewed and coded independently using the stakeholder interview questions as an initial thematic framework. Textual codes were grouped into clusters around similar and interrelated concepts and a matrix of themes were created and analysed within Google Sheets.

APPENDIX 2: Evidence

Challenges that have arisen around the application of IVD regulations during the COVID-19 pandemic

Key themes	Interview	Workshop	Literature review
Quality of diagnostic tests			
Self-certification meant that many COVID-19 tests were made available on the market without regulatory oversight.	• Under the current EU regulatory framework for IVDs, IVDs can be validated according to the EU IVD Directives (IVDD) or the IVD regulations (IVDR) until 2022, at the earliest. According to the EU IVDD, COVID-19-related test assays qualify as low-risk, "self-certification" class. This meant notified body oversight was only required for about 20% of products under IVDD, allowing a vast majority of IVDs to be placed on the EU market solely under the exclusive responsibility of their manufacturer, without the involvement of any NBs. • The high demand for COVID-19-related diagnostic tests, the paucity of relevant regulatory standards, and the fact that most COVID-19-related IVDs are self-certified contributed to an increased global risk of substandard tests based on falsified claims flooding the market. • A relatively little scrutiny over the reporting standards of test accuracy, safety and comparability has also led to ambiguities for downstream clinical interpretation by healthcare professionals, who had to rely on self-claimed performance results.	• The risk classification of an IVD device cannot change depending on intended use and contextual use (i.e. implications of a result during a pandemic) under current EU IVDD regulation.	• Multiple in vitro RT-qPCR diagnosis kits are available on the market for the detection of SARS-CoV-2. Some of them have received emergency use authorization (EUA) from the U.S. Food & Drug Administration (FDA) while others only report validations made by manufacturers, and in general little is known about their performances using clinical specimens. • It is important to be vigilant about fraudulent commercial claims of test performance. • Part of the problem is a lack of oversight. Manufacturers selling certain products, including medical devices, in the EU must "CE mark" their products, which indicates conformity with health, safety and environmental protection standards. However, manufacturers self-report compliance, and a CE mark is not evidence of third-party testing.
Test characteristic requirements were not reviewed with the implications of inaccurate COVID-19 test results in mind.	• Many companies rushed products onto the market very quickly without adequate testing. This was partly due to unclear evidence requirements and what the cutoff levels were for important metrics such as sensitivity and specificity. • Many companies rushed products onto the market very quickly without adequate testing. This was partly due to unclear evidence requirements and what the cutoff levels were for important metrics such as sensitivity and specificity. • Insufficient importance was placed on the wider implications of an incorrect IVD test result such as the psychological impact of an incorrect IVD test result.	• Many COVID-19 tests have issues with thresholds for sensitivity and specificity and ultimately clinical performance. Many poor tests have been allowed onto the market without sufficient scrutiny.	• Diagnostic sensitivity and specificity of rapid tests and serological assays for COVID-19 in well designed clinical trials is still missing and essential to perform before introducing them into the routine as a standalone test.
Insufficient emphasis was placed on the intended use of different COVID-19 tests.		• The intended purpose of COVID-19 tests and therefore the suitability of their utilisation in different circumstances (e.g. screening, diagnosis) was often unclear.	

Key themes	Interview	Workshop	Literature review
Development and distribution of diagnostic tests			
Regulators have struggled to meet the surge in demand for their services due to the significant numbers of novel diagnostic tests that have been developed during the COVID-19 pandemic.	• The major challenge regulatory bodies have faced is having to evaluate and approve new IVDs as quickly as possible whilst maintaining a focus on safety. • There was no way for the MHRA to assess the vast amounts of information that was being provided to them. The MHRA said to manufacturers that they could not take on and approve additional newer tests even if they were better due to a lack of capacity as the market was too saturated. • The regulators (MHRA) faced operational challenges such as there being a lack of staff being able to signpost, a lack of capacity to be able to duly validate information, and an over-reliance on third-parties.	• There is a lack of IVD-specific regulatory expertise. • There is a lack of IVD-specific clinical expertise i.e. not enough clinical experts who understand the contextual application of IVDs (e.g. how IVDs are used as a part of diagnostic pathway, triage, screening), when classifying devices and making decision around appropriate performance of IVDs.	• The industry response has been unprecedented; by the 17th of July 2020, 746 tests had been developed or are under development. Although this extraordinarily fast development offers hope that the current testing shortfalls can be overcome, this creates a real challenge for diagnostic regulatory bodies. For many years, the conversion of diagnostic innovation from bench to clinical practice has been riddled with problems and is notoriously slow. • A surge in demand for laboratory diagnostic tests inevitably results in insufficient validation of new tests accompanied by lack of resources. • Healthcare professionals are also focused on managing the outbreak. They are no longer available to conduct most clinical studies, nor to advise healthcare authorities, industry or Notified Bodies on IVDR / MDR implementation. • Notified Bodies: Travel restrictions prevent many physical audits from happening as foreseen around the globe. Some audits are continuing remotely, but others are being cancelled or postponed because they are believed necessary to conduct in person. NBs are unavailable, due to lockdowns or self-quarantine. This results in less auditing and certification capacity to meet demand, leading to unexpected delays in conformity assessment for an unknown period. • Auditing a quality management system (QMS) is a key requirement of ISO 13485:2016 certification for medical devices. Audits are a fundamental compliance activity for Quality Assurance to capture non-conformances, address issues and identify opportunities for improvement. Three days after the WHO's announcement of the pandemic, the Association of Certified Bodies (ABCB) called for the immediate suspension of all physical audits in the interests of the safety of auditors. • The wet signature dilemma. The inability to sign paper documents in person (wet sign) – in the context of lockdowns and social distancing – is a key obstacle for quality during COVID-19.
Lack of clear and comprehensive COVID-19-specific guidance for IVD developers.	• There has been a lack of lay information which has meant the public were not able to decide which device is best for them. Being unable to obtain high-quality information to compare test accuracy and potential risks involved, exacerbated confusion among the public and patient.	• People are desperate for information that comes from trusted sources - this point has been magnified throughout the stages of COVID 19 crisis.	• At the point of online purchase of home self-sampling COVID-19 tests, users in the UK are provided with incomplete, and, in some cases, misleading information on test accuracy, intended use, and test interpretation. • We found widespread evidence of websites failing to provide such evidence-based guidance, and some cases of websites actively suggesting unsafe behaviour. • Without adequate and correct information the public may purchase the wrong or a poor test, or use the test in the wrong way or at the wrong point in time. These errors or applications will increase their chances of getting an erroneous test result. Even when used properly, few websites assisted users in interpreting test results and understanding their inherent uncertainty. • The UK's medicines regulator has sounded the alarm over unsafe and unlicensed coronavirus tests, warning that unscrupulous suppliers are seeking to exploit people's desperation to be screened for the disease. The Medicines and Healthcare Products Regulatory Agency, which assesses medicines and medical devices, said it was working urgently to investigate a large number of potential scams and had already taken down several fraudulent websites. The regulator is particularly worried about the marketing of self-testing kits for use at home that would allow people to test for antibodies to see whether they have recovered from coronavirus.
Variable access to crucial SARS-CoV-2 reference materials.			• A major hurdle to validation was the lack of access to SARS-CoV-2 live or inactivated virus. • Several challenges arose for validating this molecular virology assay, including a lack of reference materials

Key themes	Interview	Workshop	Literature review
Dissemination of information relating to diagnostic tests			
Lack of accessible, clear, timely, and understandable information about COVID-19 tests for patients and the public.	• There has been a lack of lay information which has meant the public were not able to decide which device is best for them. Being unable to obtain high-quality information to compare test accuracy and potential risks involved, exacerbated confusion among the public and patient.	• People are desperate for information that comes from trusted sources - this point has been magnified throughout the stages of COVID 19 crisis.	• At the point of online purchase of home self-sampling COVID-19 tests, users in the UK are provided with incomplete, and, in some cases, misleading information on test accuracy, intended use, and test interpretation. • We found widespread evidence of websites failing to provide such evidence-based guidance, and some cases of websites actively suggesting unsafe behaviour. • Without adequate and correct information the public may purchase the wrong or a poor test, or use the test in the wrong way or at the wrong point in time. These errors or applications will increase their chances of getting an erroneous test result. Even when used properly, few websites assisted users in interpreting test results and understanding their inherent uncertainty. • The UK's medicines regulator has sounded the alarm over unsafe and unlicensed coronavirus tests, warning that unscrupulous suppliers are seeking to exploit people's desperation to be screened for the disease. The Medicines and Healthcare Products Regulatory Agency, which assesses medicines and medical devices, said it was working urgently to investigate a large number of potential scams and had already taken down several fraudulent websites. The regulator is particularly worried about the marketing of self-testing kits for use at home that would allow people to test for antibodies to see whether they have recovered from coronavirus.
Insufficient emphasis placed on importance of using reporting guidelines for studies involving IVDs.	• It can be difficult for IVD developers to show that their product meets specific requirements and demonstrate that they've gone through certain due processes. This makes it difficult for reviewers as it is harder to compare different IVDs which have been developed and reported differently. More emphasis should be placed on evidence requirements. • There are too many technical specifications (i.e. highly complex information aimed at laboratories) and too few guidance documents (i.e. understandable information on what needs to be assessed in terms of risk before and after a product goes to market).		
Widespread use of preprint servers for sharing IVD-related data before peer review.			• An entirely novel aspect during this outbreak was the widespread use of preprint servers for sharing research data before peer-review (for example, medRxiv or bioRxiv), where studies appeared evaluating the relative performances of different diagnostic technologies.

Strategies that could be adopted to overcome the key challenges in the event of a future infectious disease outbreak

Key themes	Interview	Workshop	Literature review
Quality of diagnostic tests			
Regulatory oversight should be required for all tests.	• There needs to be an up-to-date classification system that is flexible and responsive to overcome the issue of self-certification. The EU is in the process of producing such a system to be used with IVD-R. The UK could use this system, when it is published, to facilitate production of its own classification system. • More scrutiny on risk element/classification of IVD regulations. For example, class 2/2A IVDs would be classified as low-risk if we looked fundamentally at the risk.	• Although EU IVDR covers various aspects of legislation but effective implementation measures are much needed • There needs to be a rigorous evaluation and more rational basis on determining classification and which types of tests are required for each class. •	
Test characteristic requirements should be reviewed with the implications of inaccurate test results in mind.	• Focus on psychological and pathological impact to look at the realistic risk on the patients & clearer measurement of risks.		
Greater emphasis should be placed on usability testing. =	• Greater emphasis should be placed on usability assessments as these are one of the most important aspects of an IVD that determines whether it will work properly when deployed during a crisis.		• A rapid evaluation pipeline is required to ensure that tests offering real health benefits are integrated into practice within a timeframe that will support international efforts to curtail the transmission of SARS-CoV-2.
Development and distribution of diagnostic tests			
Train and retain IVD regulatory experts.	• Build theoretical and practical IVD-related knowledge and skills using a competency framework.	• Efforts need to be made to improve the experience of IVD experts to decrease dropout and increase retention of expertise in the UK. • There is massive clinical expertise across this country: this expertise could be deputised rather than having a centralised authority.	
Plan for and permit remote auditing.			• The pandemic highlights the need to plan for a remote internal auditing process. • Remote auditing was immediately considered as a potential alternative.
Establish a permanent diagnostic unit with in-house clinical and regulatory expertise.		• It would be useful if there was a diagnostic unit in place within DHSC to support IVD evaluation that could be mobilised when needed (i.e. during future pandemics) rather than having to establish a whole unit from scratch at the start of a pandemic purely for the purposes of a specific disease (i.e. as was done for COVID-19). • The Vaccine Task Force was an important aspect of the vaccine response. We need to set a diagnostic strategy (R+D, manufacturing processes, packaging could be involved much earlier on) to respond more resiliently in future pandemics.	
Provide clear and comprehensive situation-specific guidance for IVD developers.	• Companies should know exactly what is required from regulators. • There needs to be clear guidance from regulators regarding the regulatory approval process. • There should be regular updates from regulators to IVD developers answer IVD-specific questions and provide information.		• The government's message was clear, decisive, and supportive of the companies. • With in-person inspections suspended by many regulators, greater use of reliance mechanisms and full information-sharing among regulators is vital.
Use target product profiles.	• A TPP acts as an interface between healthcare provision and regulation. This kind of thing helps to translate medical devices and IVDs into practice safely. • The use of TPPs would be supported by having a body in place to act as an intermediate who can consult clinical experts and help in that translational process from clinical need through to developing a target product profile.	• TPPs are a key way of acquiring something that is needed urgently i.e. when responding to a public health threat or pandemic. • These should be used in the UK to respond to UK-specific epidemiological needs. Identify which product profiles are required by comparing UK epidemiological data with lists of existing IVDs (e.g. EUDAMED, NBOG Designation Codes) to see where the "gaps" are. • It is important to note that TPPs are also helpful on an international scale, but perhaps should be driven by international organisations (e.g. WHO, FIND) that can respond to wider epidemiological issues.	• In March 2020, the World Health Organization (WHO) outlined a research roadmap recommending the development of Target Product Profiles (TPPs) to drive the research and innovation process around new diagnostic tests for COVID-19. A TPP is a document that summarises in advance the desirable and minimally acceptable specifications for a new test to address a well-defined clinical need. The overarching aim is to ensure that innovation efforts are focused on developing 'fit for purpose' tests. The National Institute for Health and Care Excellence (NICE) have recently begun an economic modeling exercise to help inform TPP specifications for COVID-19 tests. At the core of TPP development is the scoping and definition of unmet clinical needs.

Key themes	Interview	Workshop	Literature review
Development and distribution of diagnostic tests (continued)			
Develop common specifications.		• Implement EU MDR/IVDR's Common Specifications (previous Common Technical Specifications in EU IVDD) or develop a similar criteria to prepare for situations where harmonised standards do not exist or are insufficient; or there is a need to address public health concerns.	
Make routine health data more readily available.	• Manufacturers can utilise routine health data to develop better medical devices and IVDs more quickly. Changes could be made to make NHS health data more available. Not only would this help in normal times, it would be useful to get new/required IVDs tested and onto the market in a timely manner.		
Digitise the regulatory approval process.	• A digital process rather than a paper-based one would be beneficial.		
Ensure continued access to laboratory-developed tests.	• The main concern of colleagues around the EU is the risk that many laboratory-developed tests may cease to be available so we need to protect against that. •	• Many tests are developed in-house by university hospital laboratories and clinical chemistry departments. New regulation says that in house developed tests should only be used if there is no industry or general alternative - this has implications for business and risk of creating monopolies. • Future regulation must enable laboratories (universites, hospitals) to develop and use lab-developed tests to increase capacity to test and improve patient care.	• The exponential growth of COVID-19 infections resulted in the abandonment of diagnostic test guidelines, and the US FDA began to permit laboratory-developed SARS-CoV-2 tests without prior agency approval. • Balancing the increasing use of laboratory-developed tests, the risk of test errors, the need for tests, the burden on healthcare systems, the benefits of early diagnosis, and the risk of unnecessary exposure remain significant challenges. • Scientific organizations such as the European Federation of Laboratory Medicine could play an important role in shaping the future use of LDTs by proposing criteria that could be applied to determine if there is a legitimate rationale for the use of LDT such as better analytical performance allowing broader application of the method (e.g., LC-MSMS method for testosterone that can be used in children, adult men, and post-menopausal women), lower minimum sample volume making it better suitable for pediatric patients or the fact an LDT combines multiple CE-marked assays and there is a need for this combination. There is currently also no provision for a transition period regarding LDTs that were developed before a CE-marked test becomes available. The IVDR requires laboratories to stop immediately performing their LDT without waiting for the verification of the CE-marked test (ISO15189:2012 requirement). In summary,while 97.6% of the results/year were performed with an CE-IVD test, only 41.8% of the laboratory tests were CE-IVD. There is currently no alternative on the market for 71.5% of LDTs performed in our laboratory which do not fall within the scope of the current IVDD. Compliance with the IVDR will require a significant investment of time and effort.
Ensure access to pathogen-specific reference materials.	•	• Effective distribution of reference samples around the country is crucial in future pandemics as access to clinical samples is important. Reference materials need to be made available to IVD developers to help them develop products. It also helps IVD develops perform internal quality control, thereby taking some of the pressure off the regulators. • In the UK, involvement of the National Institute for Biological Standards and Control (NIBSC) would be helpful.	• One way of mitigation is immediate definition of a national reference laboratory to cooperate with the WHO and disseminate related information clearly and unambiguously through the command chain. • As a step forward for optimizing the validations and collecting comparable assays' performance data, the FDA currently offers reference panels for EUA applications which should also assist in different assays' calibrations and on-going monitoring of the performance.
Increase the emphasis placed on post-market surveillance.	• Post-market surveillance makes regulation more efficient, by spreading the risk throughout the regulatory process and allowing products to get to market faster, and more effective, by evaluating devices in the real world.	•	•

Key themes	Interview	Workshop	Literature review
Dissemination of information relating to diagnostic tests			
Provide patients and the public with accessible, clear, timely, and understandable information.	•Regulatory agencies need to produce a plain language summary of their IVD work as high-quality lay information will help people work out what is best for them as a patient. •There should be regular updates from regulators to patients and the public to answer IVD-specific questions and provide information.	•Communication to patients must be timely and clear – plain language summaries important for this reason – so patients can understand exactly what they're getting. Communication should be timely, intentional, and meaningful. •Communication with patients is important but is not easy: you cannot simply put an expert in front of a bunch of people and be confident that the audience will receive the information well; for this reason, it is important to invest in programmes to communicate better. •There will be many opportunities for patient education about IVDs after the COVID-19 pandemic. Patient organisations often have conferences. Never previously seen a presentation at a conference about IVDs. Would be well received and important.	•Best practice guidance for communication about tests to the public should be developed and enforced for online sales of COVID-19 tests. •It is essential that companies selling tests identify the type of test, and the situations in which it is appropriate to order such a test. While websites were clear whether they were selling molecular or antibody tests, they also need to indicate the situations when it is appropriate to order a molecular "swab" test or an antibody "blood" test in order to select the correct one. •Websites must also describe the full testing process and clearly indicate what is required of users to complete testing. For example, two antibody websites currently indicate that purchasers will need to identify individuals qualified to take venous blood samples, which is impractical for most people. •We identified five key communication issues with websites selling direct to consumer home-sampling COVID-19 tests. All five of these issues may be improved by developing a basic framework of what information should be provided, and standard ways to present such information. This would also facilitate comparison between websites.
Promote the use of STARD reporting guidelines for studies involving IVDs.			•Still, caution should be exercised with interpretation of non-peer-reviewed manuscripts..... comply with Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines.

APPENDIX 3: References

3.1. Literature Review

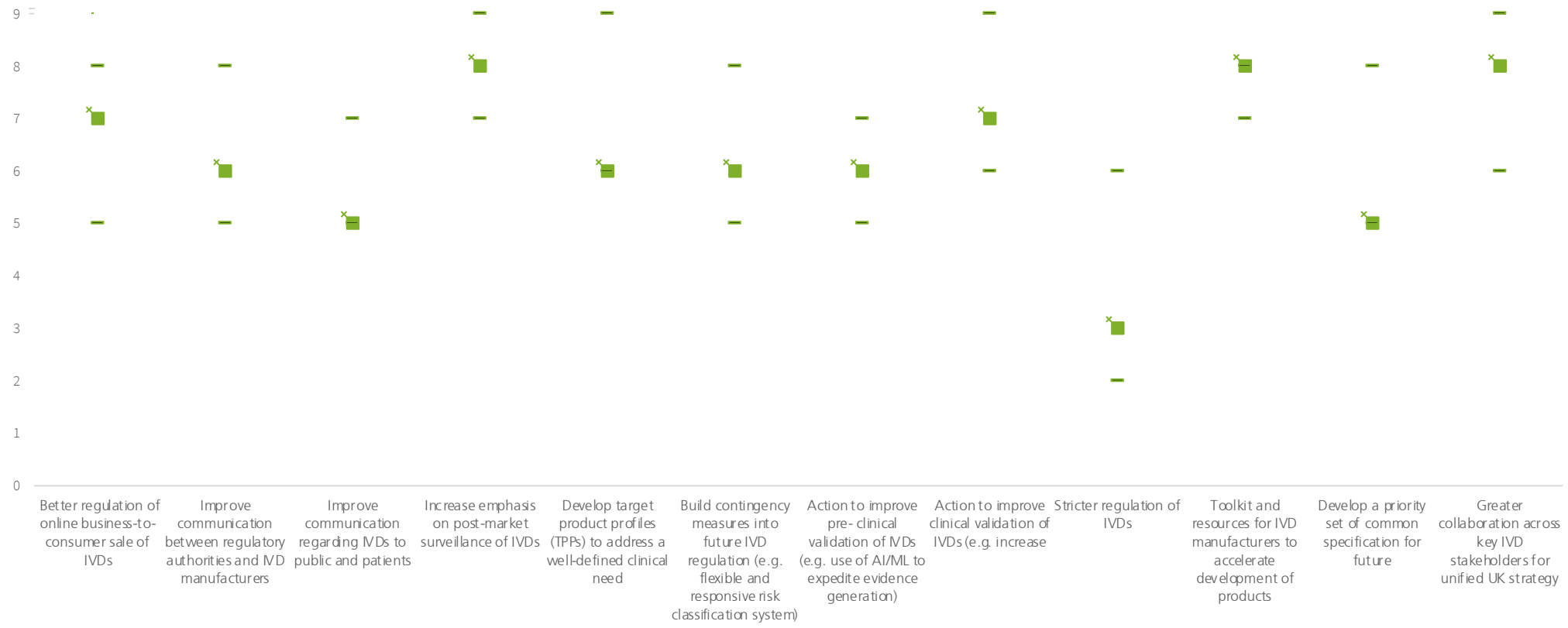
1. A guide to quality and regulatory compliance during COVID-19 | Cambridge Network. Accessed February 5, 2021. https://www.cambridgenetwork.co.uk/news/guide-quality-and-regulatory-compliance-during-covid-19
2. Additive manufacturing for COVID-19: devices, materials, prospects, and challenges | MRS Communications | Cambridge Core. Accessed February 5, 2021. https://www.cambridge.org/core/journals/mrs-communications/article/additive-manufacturing-for-covid19-devices-materials-prospects-and-challenges/4264A7924F4AACA8ED45C99976A3ADD4
3. Covid-19 coronavirus: regulatory flexibility and the importance of collaboration in the UK. A&O Life Sciences Hub. Published April 28, 2020. Accessed February 5, 2021. https://www.aolifescienceshub.com/covid-19-regulatory-flexibility-and-the-importance-of-collaboration/
4. COVID-19: Free EU Standards & MD/IVD Registration | Obelis. Obelis — Your Consultant on EU Regulation. Published March 26, 2020. Accessed February 5, 2021. https://www.obelis.net/news/covid-19-free-european-standards-and-easier-md-ivd-registration/
5. COVID-19: New MHRA guidance and processes. Hill Dickinson. Published March 27, 2020. Accessed February 5, 2021. https://www.hilldickinson.com/insights/articles/covid-19-new-mhra-guidance-and-processes
6. covid-19-rapid-risk-assessment-coronavirus-disease-2019-ninth-update-23-april-2020.pdf. Accessed February 5, 2021. https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-rapid-risk-assessment-coronavirus-disease-2019-ninth-update-23-april-2020.pdf
7. EU device regulations, COVID-19 response and global regulatory strategy. Accessed February 5, 2021. https://www.raps.org/news-and-articles/news-articles/2020/5/eu-device-regulations-covid-19-response-and-global
8. Information given by websites selling home self-sampling COVID-19 tests: an analysis of accuracy and completeness | BMJ Open. Accessed February 5, 2021. https://bmjopen.bmj.com/content/10/11/e042453
9. Medical Device and IVD Emergency Use Routes in Europe. Emergo. Published April 1, 2020. Accessed February 5, 2021. https://www.emergobyul.com/services/europe/medical-device-and-ivd-emergency-use-routes-europe
10. Mitigating the Impact of COVID-19 on Healthcare Systems Urgent Need to Pause the new Medical Technology Regulations Implementation. Accessed February 5, 2021. https://www.advamed.org/sites/default/files/resource/mitigating_the_impact_of_covid-19_-_need_to_pause_the_medtech_regulations.pdf
11. The European Commission postpones Medical Devices Regulation. Accessed February 5, 2021. https://www.penningtonslaw.com/news-publications/latest-news/2020/the-european-commission-postpones-medical-devices-regulation
12. UK medicines watchdog warns over unsafe coronavirus tests | Financial Times. Accessed February 5, 2021. https://www.ft.com/content/166fb1d5-8763-4091-8f7e-59714452a077
13. Badnjević A, Pokvić LG, Džemić Z, Bečić F. Risks of emergency use authorizations for medical products during outbreak situations: a COVID-19 case study. Biomed Eng Online. 2020;19(1):75. doi:10/ghzh7m
14. Bhalla N, Pan Y, Yang Z, Payam AF. Opportunities and Challenges for Biosensors and Nanoscale Analytical Tools for Pandemics: COVID-19. ACS Nano. 2020;14(7):7783-7807. doi:10/gg8kvj
15. CDC. COVID-19 and Your Health. Centers for Disease Control and Prevention. Published February 11, 2020. Accessed February 5, 2021. https://www.cdc.gov/coronavirus/2019-ncov/testing/diagnostic-testing.html
16. Ching L, Chang SP, Nerurkar VR. COVID-19 Special Column: Principles Behind the Technology for Detecting SARS-CoV-2, the Cause of COVID-19. Hawaii J Health Soc Welf. 2020;79(5):136-142.
17. Fraser AG, Szymański P, Macintyre E, Landray M. Regulating drugs, medical devices, and diagnostic tests in the European Union: early lessons from the COVID-19 pandemic? Eur Heart J. 2020;41(23):2140-2144. doi:10/ghzh7n
18. Freire-Paspuel B, Vega-Mariño P, Velez A, Castillo P, Cruz M, Garcia-Bereguiain MA. Evaluation of nCoV-QS (MiCo BioMed) for RT-qPCR detection of SARS-CoV-2 from nasopharyngeal samples using CDC FDA EUA qPCR kit as a gold standard: An example of the need of validation studies. J Clin Virol. 2020;128:104454. doi:10/ghzh7p
19. Freire-Paspuel B, Garcia-Bereguiain MA. Poor sensitivity of "AccuPower SARS-CoV-2 real time RT-PCR kit (Bioneer, South Korea)." Virol J. 2020;17(1):178. doi:10/ghzh7d
20. Graziadio S, Urwin SG, Cocco P, et al. Unmet clinical needs for COVID-19 tests in UK health and social care settings. Sapra A, ed. PLOS ONE. 2020;15(11):e0242125. doi:10/ghzh7g
21. H S, Mg H, Ck Y, et al. Nationwide External Quality Assessment of SARS-CoV-2 Molecular Testing, South Korea. Emerg Infect Dis. 2020;26(10):2353-2360. doi:10/gg6wjr
22. Kubina R, Dziedzic A. Molecular and Serological Tests for COVID-19. A Comparative Review of SARS-CoV-2 Coronavirus Laboratory and Point-of-Care Diagnostics. Diagnostics. 2020;10(6). doi:10/ghw2hw
23. Kyhlstedt M, Andersson SW. Diagnostic and digital solutions to address the COVID-19 pandemic: The need for international collaboration to close the gap. Health Policy Technol. 2020;9(2):126-128. doi:10/ggx3dh
24. Lai C-C, Wang C-Y, Ko W-C, Hsueh P-R. In vitro diagnostics of coronavirus disease 2019: Technologies and application. J Microbiol Immunol Infect. Published online June 5, 2020. doi:10.1016/j.jmii.2020.05.016
25. Lee S. Steering the Private Sector in COVID-19 Diagnostic Test Kit Development in South Korea. Front Public Health. 2020;8. doi:10/ghzh7c
26. Lee YJ, Lim Y, Hur KW, Sung H, Kim M-N. Quality of Ribonucleic Acid Extraction for Real-Time Reverse Transcription-PCR (rRT-PCR) of SARS-CoV-2: Importance of Internal Control Monitoring. Ann Lab Med. 2020;40(6):490-492. doi:10/ghc5dw
27. Mascuch SJ, Fakhretaha-Aval S, Bowman JC, et al. A blueprint for academic laboratories to produce SARS-CoV-2 quantitative RT-PCR test kits. J Biol Chem. 2020;295(46):15438-15453. doi:10/ghzh7f
28. McDermott A. Inner Workings: Researchers race to develop in-home testing for COVID-19, a potential game changer. Proc Natl Acad Sci. 2020;117(42):25956-25959. doi:10/ghf6qf

29. Mitchell SL, George KS, Rhoads DD, et al. Understanding, Verifying, and Implementing Emergency Use Authorization Molecular Diagnostics for the Detection of SARS-CoV-2 RNA. J Clin Microbiol. 2020;58(8). doi:10.1128/JCM.00796-20
30. Mostafa HH, Hardick J, Morehead E, Miller J-A, Gaydos CA, Manabe YC. Comparison of the analytical sensitivity of seven commonly used commercial SARS-CoV-2 automated molecular assays. J Clin Virol. 2020;130:104578. doi:10/gg7m8d
31. Moulahoum H, Ghorbanizamani F, Zihnioglu F, Turhan K, Timur S. How should diagnostic kits development adapt quickly in COVID 19-like pandemic models? Pros and cons of sensory platforms used in COVID-19 sensing. Talanta. 2021;222:121534. doi:10/gg72sg
32. Nagarajan A. The impact of Covid-19 on the European medical device market. Medical Plastics News. Published May 5, 2020. Accessed February 5, 2021. https://www.medicalplasticsnews.com/api/content/29edc2cc-8e16-11ea-b90e-1244d5f7c7c6/
33. Newton PN, Bond KC, Adeyeye M, et al. COVID-19 and risks to the supply and quality of tests, drugs, and vaccines. Lancet Glob Health. 2020;8(6):e754-e755. doi:10/ggr26z
34. Park J, Chung E. Learning from past pandemic governance: Early response and Public-Private Partnerships in testing of COVID-19 in South Korea. World Dev. 2021;137:105198. doi:10/ghh5nx
35. Ravi N, Cortade DL, Ng E, Wang SX. Diagnostics for SARS-CoV-2 detection: A comprehensive review of the FDA-EUA COVID-19 testing landscape. Biosens Bioelectron. 2020;165:112454. doi:10/gg5khq
36. Sharifi M, Hasan A, Haghighat S, et al. Rapid diagnostics of coronavirus disease 2019 in early stages using nanobiosensors: Challenges and opportunities. Talanta. 2021;223:121704. doi:10/ghzh69
37. SoRelle JA, Frame I, Falcon A, et al. Clinical Validation of a SARS-CoV-2 Real-Time Reverse Transcription PCR Assay Targeting the Nucleocapsid Gene. J Appl Lab Med. 2020;5(5):889-896. doi:10/ghzh7b
38. Tsuchida N, Nakamura F, Matsuda K, Saikawa T, Okumura T. Strategies for the efficient use of diagnostic resource under constraints: a model-based study on overflow of patients and insufficient diagnostic kits. Sci Rep. 2020;10(1):20740. doi:10/ghzh7k

3.2. Others

1. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, LijmerJG Moher D, Rennie D, de Vet HCW, Kressel HY, Rifai N, Golub RM, Altman DG, Hooft L, Korevaar DA, Cohen JF, For the STARD Group. STARD 2015: An Updated List of Essential Items for Reporting Diagnostic Accuracy Studies.
2. Pope C, Ziebland S, Mays N. Qualitative research in health care. Analysing qualitative data. BMJ. 2000;320(7227):114-116. doi:10.1136/bmj.320.7227.114
3. Ritchie J, Lewis J. Qualitative research practice: a guide for social science students and researchers. 2003, London: Sage.

After the COVID-19 pandemic, which strategies should the UK Government prioritise to ensure that IVDs are available on the market in an efficient and timely manner whilst maintaining or improving on high safety standards?



**In each plot, the box is the median, the whiskers on the top and the bottom are lower and upper quartiles. (n=9)*