UK Health Security Agency

Title: UK Health Security Agency (UKHSA) Framework Protocol for Clinical Evaluation Studies of the Performance of In-vitro Diagnostic Devices (IVDD) in Detecting Covid-19 and Other Infectious Diseases

Short Title: UKHSA IVDD Clinical Evaluation Framework Protocol

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ACRONYMS AND ABREVIATIONS

Abbreviation	Definition
CAG	Confidentiality Advisory Group
CAPA	Corrective and preventative Action Plan
CI	Chief Investigator
DPIA	Data Processing Impact Assessments
EDC	Electronic Data Capture
ESAG	Evaluations Scientific Advisory Group
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HRA	Health Research Authority
ICF	Informed Consent Form
IVDD	In-Vitro Diagnostic Device
MHRA	Medicines and Healthcare products Regulatory Agency
ONS	Office for National Statistics
PIS	Patient Information Sheet
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedures
STARD	Standards for Reporting Diagnostic Accuracy
UKHSA	UK Health Security Agency
VoC	Variant of Concern

1. LAY SUMMARY

During the early stages of the SARS-CoV-2 pandemic, the UK Health Security Agency (UKHSA) introduced a national Covid-19 testing programme. This involved the UKHSA directly delivering Covid-19 testing across the UK population. At the beginning there were no licensed tests for Covid-19 and therefore, UKHSA worked with manufacturers of test kit components to manufacture new testing devices. Since then, UKHSA has worked in collaboration with the UK biotechnology industry to develop national diagnostics manufacturing capabilities. The aim of which was to ensure that the UK had a continuous supply of high-quality in-vitro diagnostic tests to meet the demands of a national pandemic.

The rapid development of tests in response to an urgent public health threat may mean that new tests need to be developed quickly. As such, the tests do not have the normal checks/studies to confirm the degree of accuracy of the tests in larger populations or over longer periods of time, and those studies that are conducted by manufacturers may be based on small numbers of samples. Therefore, it is important to confirm that they perform adequately when used in larger populations and as diseases change or mutate over time. It is also essential to ensure that we have the capability to rapidly develop and validate tests for public use in future infectious disease outbreaks where there are no suitable commercially available tests.

We aim to ensure that the tests used in national infectious diseases testing programmes are of a high standard of diagnostic accuracy and that UK resources are used wisely. We will do this by studying:

- The accuracy of the tests used, or planned to be used, within national testing programmes.
- The effectiveness of the ways in which we deliver testing.
- Whether the tests, or where relevant sample collection kits, are safe and relatively easy for people to use.

This framework protocol will ensure that these studies can be delivered quickly and safely, under one standardised ethical and governance framework, to inform key policy decisions, support the development of improved testing approaches and to provide assurance of the clinical effectiveness of UKHSA testing programmes.

2. SYNOPSIS

Title	UKHSA Framework Protocol for Clinical Evaluation Studies of the Performance of In-vitro Diagnostic Devices (IVDD) in Detecting Covid-19 and Other Infectious Diseases	
Short Title	UKHSA IVDD Clinical Evaluation Framework Protocol	
Description and scope	This framework protocol provides the standardised approach to clinical studies evaluating IVDD technologies, methodologies and testing regimens selected by UKHSA for diagnosing and managing Covid-19, or other infectious diseases, as part of the national infectious disease testing programme.	
Sponsor	UK Health Security Agency	
Funder	UK Health Security Agency	
Aim / Objectives	<u>Aims</u>	<u>Objective</u>
	- To explore the performance of IVDDs to inform potential implementation or required adjustments within the	To gather new evidence on:

	UKHSA's national infectious diseases testing programmes. - To generate generalisable new evidence to inform broader testing policy decisions. - To provide evidence of IVDD performance to the Medicines and Healthcare products Regulatory Agency (MHRA) in support of UKHSA's Emergency Use Authorisation and CE/UKCA marking applications.	- The clinical performance of chosen testing technology, and/or sampling methodology. - The effectiveness of current or future planned testing regimens or approaches - The appropriateness and ease of use of testing service within chosen use-cases / settings.
Outcome Measures	Primary	Secondary
	Standard diagnostic accuracy of IVDD's relative to the relevant reference or comparator test (e.g. sensitivity, specificity, void rate).	Sensitivity stratified by covariates including viral load, symptom status, symptom duration, demography (gender, ethnicity, age, region). Usability data including surveys, questionnaires, observations or photographs/audio/video recordings
Intervention(s)	IVDD kits/ testing technologies / methodologies/regimen used for diagnosing and managing SARS-CoV-2, or other infectious diseases.	
Sample types	Sample types may include various swab types including: saliva, shallow nasal, breath condensate or sputum; skin or lesion swabs; scab collection or scrapings; finger pinprick samples; urine, faecal, vomit or semen samples; biopsy, blood or serum samples (where routinely collected).	
Comparator	To allow comparison across all methods and technologies, participants will provide a sample for a diagnostic standard test for analysis as the comparator (e.g. a primary diagnostic method). This may be self-test/sample collection or professionally administered.	
Participants	Individuals known, or suspected, to have an infectious disease which is the subject of a UKHSA National Testing Programme (or equivalent health protection initiative), contacts of such individuals, or any individual who is at risk of contracting the disease in question (e.g. healthcare workers, hospital inpatients, etc).	
Planned Review Period	Approval will be sought at least every 5 years. The framework protocol, Patient Information Sheet (PIS), Informed Consent Form (ICF) and other supporting documents will be reviewed annually, and any minor amendments submitted for approvals as appropriate. Substantial amendments shall be submitted where a new population, device, testing method, or sampling technique is planned for inclusion which is outside of standard of care and not listed in this framework protocol.	

3. BACKGROUND AND RATIONALE

The unprecedented SARS-CoV-2 pandemic has required the UKHSA to assume new responsibilities in governing and implementing the creation of a new national diagnostic testing infrastructure. This was in part

due to the scale at which globally all countries were required to rely on national diagnostic capabilities and the major UK pharmaceutical and biotechnology companies not having a tradition in diagnostics techniques and technologies, outside of leading UK research institutes and small biotech companies.

These circumstances, coupled with the urgent need for effective interventions, led the UKHSA to become the responsible body accountable for overseeing and scaling many technologies and techniques aimed at drastically increasing the national testing capability, all whilst safeguarding testing accuracy (sensitivity and specificity) standards and public safety.

As a result, during the early stages of the SARS-CoV-2 pandemic, The UK Health Security Agency (UKHSA) assumed responsibility for governing and implementing a new national diagnostic testing infrastructure for infectious diseases. This involved the UKHSA directly delivering point-of-care testing across the UK population, manufacturing novel IVDDs and facilitating the development of a national diagnostics manufacturing capability, scaled to meet the demands of a national pandemic.

Critical to this undertaking was the need to generate urgent evidence of the clinical performance of the devices deployed and the efficacy of the national testing programme to support regulatory and policy decisions.

A framework protocol was developed to ensure that critical evidence of the performance of novel UKHSA-selected test testing technologies (point of care IVDDs) and practices (sampling methodologies and service designs) was generated at pace to support the rapid development of diagnostic tests and the urgent need for these to be deployed and scaled nationally. This original framework delivered the real-world research evidence needed to safely deploy IVDD self-testing nationally and to introduce a range of novel lateral flow devices, ensuring the UK had a robust supply chain of safe and effective devices and the capacity and capability to deliver mass testing.

As the pandemic progresses, this framework continues to play a critical role in which urgent studies can be delivered rapidly, under one standardised ethical and governance framework. Such studies include evaluations of the impacts of new or emerging health threats (e.g. new infectious diseases or variants of concern [VOCs]), different testing methodologies (e.g. new devices, different swabbing procedures or sample types) or testing regimens upon the performance of the national infectious diseases programme. The original framework has been modified to reflect a change in approach needed due to the ending of universal Covid-19 testing in the general population, ramping down of in-person-testing and closing of NHS Test and Trace Sites. This new framework adopts the same scientific and methodological approaches but is delivered through new operational delivery models which have been adapted to reflect the enduring UKHSA service delivery models.

4. AIMS AND OBJECTIVES

The aim is to provide the framework for rapidly exploring the 'real-world' performance of UKHSA's IVDD technologies, methodologies and regimens, in response to urgent public health evidence needs, to inform potential implementation or required adjustments within the UKHSA's national infectious diseases testing programmes.

Such evaluation studies may therefore be in response to new SARS-COV-2 VoCs, a concern over the performance of current testing technology, or a need to develop new capabilities to control infectious disease outbreaks/new health protection threats in the UK.

Evidence generated from this programme will also support pre- and post- market clinical performance evidence in support of regulatory submissions and in delivery of UKHSAs obligations as a manufacturer of IVDD under the UK Medical Devices Regulations 2002[1] (including the Medical Devices [Coronavirus Test Device Approvals) (Amendment] Regulations 2021[2]).

Its platform design will allow for rapid deployment and flexibility in which IVDDs are evaluated or changes in UKHSA choice of reference standard.

The framework protocol, PIS, ICF and other supporting documents will be reviewed annually, and any minor amendments submitted for approvals as appropriate. Substantial amendments shall be submitted where a new population, device, testing method, or sampling technique is planned for inclusion which is outside of standard of care and not listed in this framework protocol.

5. DESIGN

This framework incorporates both prospective observational cohort studies and performance evaluation studies of IVDD's, methodologies or testing regimens for SARS-CoV-2 and other infectious diseases.

Fundamentally, studies will be designed to either evaluate a different testing option within a standardised process (new device, new testing regimen), or to explore the use of a standardised test in a new context (e.g. a new sampling technique, a new variant of concern, or a new infectious disease).

IVDD's, sampling methods or testing regimens under evaluation used may be randomly allocated to individuals, organisations or test sites through computerised randomisation procedure. This approach will only be used where there is a requirement to control other confounding factors which may affect study validity. Examples of which include swabbing order, geographical location, and sociodemographic factors. However, all participants will receive standard of care diagnostic testing appropriate for the use-case/setting.

Potential designs falling within the scope of this framework also include:

a) Participants doing two or three tests simultaneously or within a few hours of each other.
b) Participants doing daily, regular or follow up testing for a set period (e.g. the incubation period)
c) Participants using different sample collection methods or materials (e.g. saliva versus nose and throat swab, viral inactivation versus viral transport medium).
d) Participants providing samples to be used for in-vitro validation of IVDDs in the laboratory or other service-based functions (such as viral characterisation) as part of the health protection response.

If a proposed study requires the introduction of new requirements beyond the scope of this protocol, amendments may be submitted describing these additional requirements which may include informed consent procedures, safety characteristics, and any other relevant considerations.

5.1 Choice of IVDD and Testing Procedure

Where possible, studies will involve CE marked IVDD's which are used or planned for use in the UKHSA national testing programme in accordance with their approved Instructions For Use (IFU) (i.e. used 'On-Label'). IFU's provided by the manufacturer may be edited for the purposes of the evaluation if deemed necessary by UKHSA without altering the approved use of the device.

UKHSA may be required, as part of an urgent public health response and in close collaboration with MHRA, to put into use CE marked products outside of their instructions for use, or new devices which are not yet CE marked. Where this occurs, a clinical evaluation shall be undertaken to generate evidence to provide clinical assurance of the device performance and to provide clinical evaluation evidence in support of an emergency use authorisation and/or CE marking application. Such evaluations will be within scope of the IVDD Clinical Evaluation Framework protocol and will be subject to Clinical Evaluation or Performance Evaluation notification to MHRA prior to implementation.

Such evaluation studies will be registered via the MHRA DORS process prior to initiation and will be delivered in accordance with applicable UK Medical Devices Regulations[1]. The approach has been agreed with Suzanne Fuller, Interim Head of Approved Bodies and Market Surveillance, Medical Devices Audit and Compliance, MHRA.

5.2 Inclusion Criteria

- Individuals able to give consent to participate in the evaluation, or
    - a minor (<16 years), who's parent/person with parental responsibility is willing to consent on their behalf, or
    - an adult who lacks capacity, who's identified personal or nominated consultee advises that they would be willing to participate.

- Individuals who are known, or suspected, to have an infectious disease which is the subject of a UKHSA National Testing Programme, contacts of such individuals, or any individual who is at risk of contracting the disease in question (e.g. healthcare workers, hospital inpatients, etc.).

5.3 Exclusion Criteria

Rationale for excluding participants may include the below:

- Individuals for whom obtaining informed consent/consultee declaration to participate is not possible.
- Individuals for whom their caregiver, healthcare worker or physician stipulate that the process of sample collection is clinically unsuitable.

5.4 Participant Identification

UKHSA testing is deployed in a variety of settings and to a range of different user groups ('use-cases'). Where possible, IVDD evaluation studies will complement these deployment channels, ensuring that study design maximises opportunities for the participants standard diagnostic test to also serve as the reference / comparator test in the evaluation study. This approach minimises both the likelihood of requiring duplicate testing and any additional time or inconvenience for participants.

Participants will typically be recruited from UKHSA testing service users who receive testing via post, via their health or social care provider or other organisation participating in UKHSA national infectious diseases testing programmes/health protection responses, or those who attend UKHSA test sites.

In certain circumstances, it may be necessary to contact other non-service users to ask them to participate in a UKHSA evaluation study. Such circumstances may include populations not currently served but who are identified as eligible due to being:

- A member of a cohort planned for inclusion in future testing policy
- International passengers arriving into the UK who have indicated, via a passenger locator form (or similar tool), that they have recently travelled from or via a country with a higher prevalence of an infectious disease or VOC specified by UKHSA.
- An individual who is participating in surveillance activities via UKHSA, Office for National Statistics (ONS) or other government agencies.
- An individual who is not yet a service user, but who is eligible for testing as part of a UKHSA National Testing Programme.
- A participant in another ethically approved infectious disease research study or survey.

Participant identification and approach may take place in a number of different ways dependent upon the specific evaluation study. Possible scenarios include the following:

Scenario 1 (most typical scenario): Evaluation to be conducted within a cohort of existing service users.
Recipients of UKHSA IVDD testing kits may be invited to participate in a new evaluation study via an option to express interest in participation when registering as a new service user, during their routine test kit ordering process or when returning a completed test/result. They may also be contacted via post/email/text or telephone by a member of the study team and invited to participate, subject to meeting the eligibility criteria. Contact details of registered users may be used for this activity in accordance with UKHSA Testing Privacy Notice[6] (see section 15.5 for further details on data privacy).

Scenario 2: Outbreak of a new VoC identified internationally but not yet prevalent within the domestic population.
Where a VoC is not yet seen in significant numbers within the domestic UK population, it may be necessary to urgently evaluate the performance of the UKHSA IVDD in detecting the variant in those entering the UK from high-risk countries. In collaboration with the ONS International Passenger Survey team, and with support from port officials, ONS personnel shall undertake participant identification and approach on behalf of the research team. They will obtain verbal agreement from eligible individuals to take a participant information leaflet and test kit pack away with them. Once they have considered the information provided, and decided to take part, consent will be confirmed digitally via the return of completed online questionnaire and submission of samples back to the lab. Participant facing materials will be made available in the appropriate languages for the target population and onsite or telephone translation services are provided via ONS or the NHS translation service.

Scenario 3: **Outbreak of a new VoC in a specific UK region**
Where a new variant is identified within a specific region of the UK but has not yet spread to other areas in significant numbers, it may be necessary to widen recruitment outside of the existing service users in that area, in order to generate urgent evidence of the performance of UKHSA IVDD in detecting the variant. This may be achieved by recruiting participants via another research or public health surveillance programme or via their healthcare provider. In such circumstances, the identification and approach will be made by their current study or surveillance programme team (in accordance with appropriate consent and ethical approval) or healthcare provider. In such circumstances, generic ethically approved advertisements may be posted via regionally targeted social media campaigns, GP waiting room or pharmacy adverts or adverts via other public areas/platforms such as patient support group / charity / research newsletters, community notice boards and social venues, or other appropriate channels. Such adverts will be generic in nature and will not contain

details of any specific evaluation. Volunteers would be invited to register their interest via text, email or telephone call to the evaluation study recruitment team, or in-person to a UKHSA test operative or member of the study team during their attendance at a test site, who would then enrol them into the study.

Scenario 4: Deployment of a new UKHSA infectious disease national testing programme.
Where UKHSA instigates a new national testing programme in response to a new UK health security threat, there may be a requirement to identify and approach cases suspected of having the disease, their close contacts, or others at high risk of infection (e.g. healthcare workers). Where possible such approaches will be made by the Health Protection Team or healthcare provider who will invite eligible individuals to take part.

Scenario 5: Participant testing for enrolment via other research programme in the same population (e.g. infectious disease surveillance, therapeutic or vaccine study.
Eligible individuals may be invited to take part in a UKHSA evaluation study in parallel with their enrolment into other infectious disease studies. Individuals who are identified and approached to take part in other ethically approved infectious disease research studies may also be offered the opportunity to participate in a UKHSA evaluation study where they are suspected to have the disease of interest, and this does not conflict with their study participation or standard care pathways. In such circumstances, eligible individuals will be informed by their healthcare provider or their study team about the option to take part in a UKHSA evaluation. This option may be used where there is a public health need to demonstrate the performance of devices in populations not currently served by UKHSA or to identify future service users.

5.5 Informed consent

Data subject consent is not requested for evaluation studies limited to the secondary use of routinely collected data which is subject to the UKHSA Testing Privacy Notice[6]. However, all such participants are required to confirm that they have read the UKHSA Testing Privacy Notice and that they agree to the use of their data as detailed in the notice when registering as a service user, ordering test kits, or returning completed tests/results.

For all studies which involve modifications to standard testing protocols, explicit consent (or consultee declaration) is required.

Written information will be available in the form of posters at participating sites, printed or digital adverts, invitation letters and PIS. All information provided will be based on the generic advert/poster, Invitation Letter, PIS and ICF. If any substantial amendment is required to these items to accommodate the requirements of a specific study, then this will be submitted for approval.

Participants will be provided as much time as they require to consider taking part and to discuss with others if needed. They will be provided with contact information to discuss the study with a member of the study recruitment team. Informed consent will be obtained in line with Good Clinical Practice (GCP) guidelines. Appropriate consent training will be provided to members of the study recruitment team and to any UKHSA test site operative involved in this activity.

5.5.1 Assessing capacity and seeking participation of adults lacking capacity

Participation in evaluation studies will take place simultaneously with, or closely following, routine testing. All adults will be assumed to have capacity, unless proven otherwise.

Where consent is required for participation in interventional studies within this framework, this will typically take place within a health or social care setting or as part of a coordinated public health response. Assessment of capacity in accordance with the Mental Capacity Act 2005 will be routinely undertaken by the healthcare professional responsible for assessing capacity to consent to routine testing (e.g. the individuals GP or attending physician, or appropriately trained nurse, or, exceptionally, a member of the health protection team or local authority public health team). The healthcare professional responsible for assessing capacity will identify an appropriate consultee to give an opinion on the individuals participation.

The UKHSA testing programme also provides postal testing services where test kits are sent via the post to members of the public for them to perform at home. For Covid-19 this has been in the past critical to scaling a population level public health response and continue to deliver home-based testing services to vulnerable members of society such as those eligible for anti-viral therapies.

Due to the low risk of self-administered IVDDs this home-based testing takes place without any health professional oversight, and as such, a clinical assessment of capacity prior to consent to routine testing is not undertaken at that time. Adults who have previously been clinically determined as lacking capacity and who routinely test at home will be under the regular care of another person, whether that is a family member, friend, or professional carer (or 'caregiver'). The caregiver will be aware of their relative/friend/client's capacity and any arrangements in place for healthcare decisions to be made on their behalf. Arrangements for informed consent to participate in an evaluation in the home setting will follow those for consent to routine testing.

Individuals who are invited to participate in home-based evaluation studies shall be sent the generic participant invitation letter by post together with the information leaflet and consent/consultee declaration form. The invite letter provides caregivers appropriate guidance and information on who may act as a consultee on behalf of an incapacitated adult and what the role entails.

5.5.2 Consent approach for minors (<16 years)

For children and young adults under 16 years of age, consent is required from a person with parental responsibility. Where this is not possible, consent may be sought from a personal legal representative. This may be a person not connected with the conduct of the evaluation who is suitable to act as the legal representative by virtue of their relationship with the child / young person, and is available and willing to do so.or a legal representative.

Those consenting on behalf of a minor, will be encouraged to discuss participation with the minor and reminded that their wishes should be respected. Weblinks to additional age-appropriate information sheets will be provided in the Participant Information Sheet for adults. These can be used to support discussions with minors to accommodate different competency levels.

5.5.3 Documenting digital or verbal consent

All in-person study procedures, including informed consent, will take place in line with site-specific infection control measures as it is imperative that all non-essential contact between the participants and evaluation team is prevented to minimise the risk of infection transmission. Stringent infection prevention and control procedures are deployed within each test setting to ensure transmission is minimised. As such, we will minimise contact by using a combination of digital consent and/or researcher recorded verbal consent in this framework.

Where informed consent is obtained remotely, the individual (or their consultee) will read and complete the Consent / Consultee Declaration Form provided and record their consent via the online UKHSA portal.

Where no digital confirmation of consent is provided by, or on behalf of, the participant, but where evaluation samples and data are returned to UKHSA, consent for their inclusion in the evaluation will be implied by the act of returning the samples and data.

Where a test site or organisation registers information on the individual's behalf (e.g. in a care home a professional staff member may complete the online registration on the residents behalf), the professional responsible for uploading the data, will be asked to confirm that consent was obtained for all participants prior to submission.

Where informed consent is obtained by a member of the study team or UKHSA testing operative, either in person or via the telephone, it will be done so verbally and documented via the online UKHSA results portal by the person taking consent.

5.6 Translation

It is important to note that we consider accessibility of testing to be a key part of the evaluations, and as such we would not look to exclude an individual from the opportunity to enrol in an evaluation because of language proficiency. The invite letter will direct participants requiring translated copies of information to the government/UKHSA website. This site contains guidance on the national testing programme and instructions for using the tests deployed by UKHSA provided in a number of alternative languages. Welsh translations will also be sent to individuals in Wales. Study information materials will be translated into other languages upon request.

6. STUDY PROCEDURES

This is a platform research protocol that is being set up to evaluate multiple point of care IVDD test kits, technologies and testing methodologies used for diagnosing and managing infectious diseases which are subject to UKHSA National Testing Programmes or other health protection responses.

This may involve participants performing testing or sample collection procedures themselves (self-test); performing self-testing procedures under the observation of a member of the study team, UKHSA testing operative, member of the health protection team or other healthcare professional (observed self-test); or test procedures administered or assisted by a trained professional (professional use)

Participants will receive standard of care testing alongside any evaluation test/method to ensure that participant care is not compromised. Participant's onward care pathway following a diagnostic test will be based on the standard of testing for that setting.

Participants will be provided with a study-specific Step-by-Step Participant Guide. Where they are performing in-person testing, the testing operative or healthcare provider will use this to guide the participant through the study procedures:

Participants (or their parent / care giver) will typically be asked to complete the following study-specific steps

1. Complete two (or more) IVDD tests in accordance with the IFUs provided. Participants will typically be asked to undertake:

   a. one comparator test – performed in accordance with standard care for that use-case/setting in accordance with UKHSA testing policy, and
   b. one (or more) evaluation test(s) - performed either in accordance with standard care for that use-case/setting in accordance with UKHSA testing policy, or performed using an experimental IVD device, method or regimen which is different to standard care (e.g. a new device, a device used off-label, a different number or frequency of tests).

2. Additional samples may be collected from a subset of participants for in-vitro laboratory validation of IVDDs or for other service activities in line with a public health response (e.g. clinical characterisation of a virus). Samples collected for this purpose will not typically be considered to be diagnostic test and will be used only for research or quality assurance purposes subject to participant consent / consultee declaration. Such samples may be collected at the same time as the other tests or following confirmation of the diagnostic test result.
3. Process any rapid point of care tests in accordance with their IFU.
4. Enter the details of any diagnostic tests taken, rapid test results, current health status, demographic and other information (all of which are routinely collected) via the UKHSA web-based portal as described in a study-specific step-by-step guide.
5. Return any PCR (or other laboratory processed) sample for analysis in accordance with study specific instructions as described in a study-specific step-by-step guide.

Participants (or their parent / caregiver) may be asked to provide additional information regarding their observations of the ease of use of the test where this is a new product planned to be or concurrently deployed across UKHSA. Ease of use observations may alternatively be collected from a healthcare professional, a member of the study team or a UKHSA testing operative in scenarios where they are observing or performing in-person testing.

The maximum number of tests/sample collections any participant may be asked to perform on the same day is expected to be three. However, it is anticipated that three tests will not be suitable for some use-cases and may deter participation. Therefore, this will only be considered where it is necessary to answer the research question and extra care will be given to the selection of the appropriate use-cases for inclusion in the study.

Evaluations may be conducted remotely with participants being sent the tests to complete in their homes, in a healthcare setting or in a social care organisation. Participant recruitment and/or other study procedures may also take place within UKHSA mobile testing units, test sites (including organisation led testing sites), participants homes or in other suitable public or commercial setting which are assessed as being suitable for such activities and approved by UKHSA.

6.1 Sample Collection, Processing and Disposal

Biological samples to test for specific infectious diseases will be collected from all participants.

The types of samples collected will be determined by the type of IVDD under evaluation. Sample collection for a respiratory disease typically involves taking a swab sample from the nose and/or throat or collecting a small sample of saliva, breath condensate or sputum. However, other sample types which may be required include, finger pinprick, skin or lesion swabs, scab scrapings or scab collection, vomit, urine, faecal or semen samples. Blood or biopsy samples may also be required. However, these will be limited to diagnostic samples which are routinely collected as part of standard care and collected by trained healthcare professionals.

Samples may be collected using different sampling systems and materials, including transport mediums or methods of transport. All such approaches will be selected as appropriate for the specific requirements of the evaluation and shall be subject to clinical risk assessment by UKHSA, which will be undertaken during study planning.

All samples which require laboratory processing will be sent via courier or, where appropriate, priority post, to national laboratories and processed as part of the national testing programme.

All diagnostic samples will be processed and disposed of in accordance with IVDD manufacturer's instructions and standardised laboratory protocols. This includes, where appropriate, additional viral load analysis and genomic sequencing of positive samples to identify viral mutations.

Samples collected for laboratory-based quality assurance and technical validation of IVDD's will be retained with subject consent / consultee declaration and used only for the purposes for which they have consented. Any residual material which is stored be disposed of upon completion of the activity for which consent was obtained. Disposal will be in accordance with UKHSA laboratory standard operating procedures (SOPs).

6.2 Infection Prevention and Control

All personnel who may be undertaking in-person recruitment or assisting participants with in-person testing (where appropriate) will be required to follow the current UKHSA infection prevention and control guidance regarding the collection and processing of samples.

Any clinical incidents will be handled and reported in accordance with UKHSA incident policy.

6.3 IVDD Result Communication

There are two potential results pathways included in this framework. The first, most typical pathway is the diagnostic tests pathway. The other is the research sample pathway. Both approaches are described below:

A. Diagnostic Tests: Tests which are intended to provide a clinical diagnosis to the participant. This may be their standard of care test, or another test completed in addition to standard of care, which may add some additional diagnostic value to the participant or their healthcare team.

   Participants will be informed of the outcome of their laboratory processed diagnostic tests according to current UKHSA policy and procedures and will be provided with appropriate advice reflecting current UK public health guidelines. They will be advised to follow the appropriate guidance for the result of their diagnostic test(s).

   All diagnostic Covid-19 test results are routinely reported to UKHSA testing service users via email and text. Positive results are also reported to their general practitioner via a digital update to the healthcare record delivered by NHS Digital. The exact mechanism of reporting results of other infectious diseases which may in future be subject to a UKHSA Testing Programme may vary in-line with clinical pathways. Appropriate public health guidance and links to further support will be provided in Step-by-Step participant guide. Where an evaluation involves completing multiple tests, the Step-by-Step Guide will include advice to account for a scenario where a person receives two conflicting results. This advice will reflect current public health guidance. This guidance is subject to change to reflect changes to national guidelines, the infectious disease in question and which tests are included in the evaluation. Where the

participant processes a test themselves (e.g. LFD tests or other rapid self-tests), regardless of whether this is for diagnostic or research purposes, the result will be available to the participant at the time of reading the test in accordance with the relevant IFU. Participants will be asked to report this result via the UKHSA online results reporting portal for it to be included in their care record and for the result to be included in the evaluation.

In certain circumstances, participants may be required perform several diagnostic tests which require laboratory processing. Where the IVDD's used in the evaluation are considered to be of equivalent diagnostic value to the standard of care test (e.g. two CE marked PCRs completed, one in accordance with their IFU and another using a different swabbing technique or sample medium) a decision matrix may be deployed to provide a single overall result, rather than the participant receiving each result individually. Where the results are discordant, the matrix will be designed to ensure that any positive test produces an overall positive result which is then communicated to the participant and recorded in their healthcare record.

B. Research Samples: Samples which are not intended to be used for diagnostic purposes, will not be needed to support clinical care and are therefore collected purely for research or quality assurance (QA) purposes.

Where samples are donated for research/QA purposes only (e.g. in-vitro characterisation studies) and do not contribute to the participants clinical diagnosis, the participant will not be send any analytical results arising from these samples. In such cases participants will be informed this via the Participant Information Leaflet and Step-by-Step Participant Guide. This will never be to the detriment of their standard care clinical diagnosis.

6.4 Compliance

Members of the study team may contact participants by phone/email/text to follow-up after receipt of a test kit where the results have not yet been reported, or samples returned, to UKHSA. During this follow up, consent to continue in the evaluation will be confirmed.

Compliance will be explored during data analysis and minimum compliance for inclusion in primary analysis will be specified in the Statistical Analysis Plan (SAP) at the outset where appropriate.

6.5 Early Discontinuation/Withdrawal of Participants

Each participant has the right to withdraw from the study at any time by contacting the study team via the contact details provided in the PIS. If a participant withdraws, their diagnostic samples will be processed and resulted as normal. If any additional study sample has been taken and submitted or data reported by the participant, participants will be informed during the consent process that their study sample and data will still be included as part of the evaluation study but that they will not be asked to participate further.

Withdrawn participants will not be replaced. Participants are not required to give a reason for withdrawing, however this question may be asked to improve the service in the future. The Evaluation team may discontinue a participant from the evaluation at any time if they consider it necessary for any reason including:

- ineligibility (either arising during the evaluation, or retrospectively, having been overlooked at eligibility assessment)
- significant protocol deviation
- withdrawal of consent
- if the participant refuses to do any of the tests required for inclusion in the final dataset.

6.6 Definition of End of Study

The end of an evaluation will be the last data capture point for the last participant for the last test evaluated. This will be decided after enough samples have been captured to satisfy the initial evaluation population threshold which is pre-specified in a SAP prepared for each study and approved by the UKHSA's Evaluations Scientific Advisory Group (ESAG). If a planned Interim analysis suggests that the study will not match the sample size criteria, or that the non-inferiority margin will not be reached upon achieving the pre-specified sample size, then recruitment maybe be stopped earlier upon approval of the ESAG.

7. SAFETY REPORTING

Studies within this framework include minimally invasive sample collection procedures (including nose and throat swabs, skin or lesion swabs, finger pricks) which are known to cause some transient discomfort to participants, but there are no clinically significant risks associated with the procedure. However, to mitigate these minor risks, self-sampling will be supported where appropriate, otherwise these procedures will be carried out by personnel who have received training in these procedures or who carry out these procedures as a routine element of their duties. Other clinically invasive sample types including blood and biopsy samples, will only be collected as part of routine care by trained healthcare professionals. Provision of other potential sample types including saliva, breath condensate, sputum, vomit, urine, faecal or semen samples are unlikely to cause discomfort to any participants.

Clinical incidents will be reported in accordance with UKHSA standard incident reporting protocols. Any incidents reported in relation to an evaluation study within this framework will be monitored by Investigators. The PIS will remind participants to follow the standard processes for reporting any clinical incident via the NHS coronavirus incident service online or by calling 119.

A 'serious adverse event' (SAE) is one which:

1) led to death

2) led to serious deterioration in the health of the subject, that either resulted in;

   a) a life-threatening illness or injury, or

   b) a permanent impairment of a body structure or a body function, or

   c) in-patient or prolonged hospitalization, or

   d) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,

3) led to foetal distress, foetal death or a congenital abnormality or birth defect

An SAE occurring to a participant should be reported to the REC that gave a favourable opinion of the study where in the opinion of the Chief Investigator (CI) and the event was 'related' (resulted from administration of any of the research procedures) and 'unexpected' in relation to those procedures. Reports of related and unexpected SAEs should be submitted within 15 working days of the CI becoming aware of the event, using the HRA report of serious adverse event form (see HRA website). Where the event occurs in a clinical evaluation or clinical investigation, SAE's will also be reported to MHRA with an initial report submitted as soon as possible, followed-up, where appropriate with further information from a full investigation submitted later.

Where these are considered to be unexpected (i.e. not listed in the protocol or IFU as an expected occurrence) and related (i.e. they resulted from administration of any of the evaluation procedures) to the IVDD, this will be reported in the resulting evidence report and in annual safety reports as appropriate in line with HRA requirements.

8. QUALITY ASSURANCE PROCEDURES

Study progress will be monitored weekly by the Evaluation Study Team and any issues or incidents will be managed via a corrective and preventative action plan (CAPA). Data quality and completeness will be monitored during interim analysis and as part of routine data quality control.

Consent confirmation, clinical, laboratory and demographic data are entered directly by the participant (or their parent/care giver) or laboratory official and are not captured in any other source document which would permit source data verification. The UKHSA laboratories are routinely audited as part of their accreditation and all study SOPs are subject to periodic audit and review. Evaluations which involve the generation of performance evaluation data or Post Marketing Clinical Follow-up evidence submitted to regulatory bodies, will be subject to regulatory inspection as required under UK law.

9. RESEARCH GOVERNANCE AND STUDY MANAGEMENT

Evaluation studies delivered under this standardised protocol will be subject to prospective review and approval in accordance with UKHSA research governance frameworks prior to implementation. This includes oversight and approval of new study SAPs and evidence reports by the ESAG.

The ESAG, led by the UKHSA Director for Public Health Testing, comprises key scientific stakeholders within UKHSA and independent academic statistical and clinical advisors with expertise in IVDD performance studies.

Evaluations Scientific Advisory Group (ESAG) membership: Dr Tom Fowler (Chair / CI), Dr Sarah Tunkel (Deputy Chair), Prof Tim Peto, Prof Any Vail, Dr Iftekhar Khan, Mrs Carolyn Lewis (Operational Lead).

10. INDEPENDENT PEER REVIEW

Expert peer review of the framework protocol, SAPs and final reports are critically assessed by independent experts from other external government agencies (MHRA, ONS) and several leading UK universities with expertise in infectious diseases and IVDD technology (including professors from University of Oxford, Cambridge, Liverpool, LSHTM and The Alan Turing Institute) and research councils (MRC) who are unconnected to both the decision-making body and those who have prepared the material being assessed.

11. PROTOCOL DEVIATIONS

A study related deviation is a departure from the ethically approved study protocol or other study document or process (e.g. consent process or administration of study intervention) or from GCP or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the study master file.

12. SERIOUS BREACHES

A "serious breach" is a breach of the protocol or of the conditions or principles of GCP which is likely to affect to a significant degree – (a) the safety or physical or mental integrity of the trial participants; or (b) the scientific value of the research. In the event that a serious breach is suspected the Sponsor must be contacted within 1 working day. In collaboration with the CI, the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the approving REC committee and any relevant NHS host organisation within seven calendar days.

13. DATA COLLECTION AND MANAGEMENT

13.1 Data Collection

Most study data will be obtained from the secondary use of routinely collected UKHSA testing information. Where additional information is required in relation to any user feedback or additional clinical or demographic information, required to address the specific study requirements, participants may be contacted by the study team and asked to provide the additional information via a short web-form or during a telephone call and will be kept to a minimum. Participants may also be asked to report ease of use by uploading a photograph of the completed test or a video of them performing the test.

If required, NHS Digital records may be accessed for any future sub-studies in order to perform a subset analysis for effectiveness of in-vitro Diagnostic Devices (IVDDs).

The four primary data sources include:

- Self-reported demographic and clinical symptom data provided by participants.
- Lab reported test outcomes.
- Self-reported test outcomes.
- Self-reported user feedback providing insights into the ease of use or acceptability of test or testing approach.

The following data may be captured or accessed, depending on the requirements of the specific study objectives.

Type	Item	Reason for collection
Contact details	Name	Routinely collected as part of UKHSA service user registration process. This data is required to communicate laboratory results to participants and permits follow-up by phone/text/email.
	Address	
	Telephone/mobile number	
	Email address	
Demographics	Gender	Routinely collected as part of UKHSA service user registration process. Required to monitor the representativeness of study sample to wider UK population.
	Age or age group	
	Ethnicity	
Clinical Details	Use Case / reason for testing	

	Symptom status (e.g., symptomatic / asymptomatic)	Routinely collected as part of UKHSA service user registration process. Testing performance is expected to be affected by these variables and therefore are typically included as secondary outcome measures in statistical analysis.
	Symptom type	
	Duration between symptom onset and taking the test	
	Person performing test (self/ healthcare professional / caregiver)	
Test Data	Test Type	Routinely collected as part of UKHSA laboratory analysis and reporting process.
	Test ID / barcode	
	Test Results (positive/negative/void/missing, variant type, CT values / viral load)	
	Test processing data (date/time processed/reported, laboratory)	
User Feedback	Self-reported test acceptability score (Likert scale)	Only collected where the study is evaluating a new device to capture end-user experience.
	Self-reported problems with completing the test (e.g. process errors / indeterminate results / not done/ etc)	
	Self-reported or observed test usability feedback (free text)	
	Images or media files provided by the participant.	
Other	Other demographic, clinical, test or qualitative data which is required for a specific evaluation study. Where appropriate this will be derived from routinely collected pseudo-anonymised and linked data (e.g. demographics) held within government information management systems or volunteered by participants.	

13.2 Data Security, Access, and Data Sharing

Data will be pseudo-anonymised as soon as possible following collection and once participants have completed study procedures. Please see section 15.5 for further detail on pseudonymisation, data storage and data access.

Only data required to interpret and assess evaluation objectives will be communicated to the evaluation Data Management and Statistics Team, this will include pseudo-anonymised data only. Typically, a test barcode is used as a unique identifier for this purpose, however it may be necessary to use other unique identifiers such as the UKHSA assigned Electronic Record Number. Only a very limited number of authorised members of the study team will be able to link this identifier back to an individual participant for quality assurance and incident reporting purposes only.

Contact details will be shared securely with members of the Evaluation Study Recruitment and Compliance Team for the purposes of sending out test kits and performing compliance follow-up communication activities. This data will be used only in accordance with UKHSA's Testing Data Privacy Notice[6] and for the purposes of the evaluation study. No other data (i.e. clinical, test result or qualitative data) will be shared with the recruitment team, other than information volunteered by the participant with their consent during any direct communications.

Once cleaned by the Data Management Team the pseudo-anonymised data will be transferred to named individuals on the Statistical Team for analysis. Transfer of data will be encrypted and only between named individuals on the Evaluation Team via a UKHSA approved and General Data Protection Regulation (GDPR) compliant data sharing platform. The data will then be stored on UKHSA and NHS IT infrastructure. This will be held in a location with named access only.

The data management plan has been developed to comply with the GDPR and Data Protection Act 2018. As such, the UKHSA, as the data controller, will create and then manage the systems required for data collection, handling, sharing and storage. This includes electronic data capture (EDC) systems and the evaluation database. NHS Digital will remain the responsible organisation for managing individual level and treatment pathway data.

Due to the bespoke nature of the requirements, the evaluation data management solutions in place have undergone substantial review and have been approved by a consortium of relevant stakeholders. Including, but not limited to, the Confidentiality Advisory Group (CAG), UKHSA Data Protection Office, NHS Digital, NHS Information Governance, and NHS Clinical Assurance, with review considering technologies implemented and considerations on GDPR, the NHS Data Protection and Security Toolkit, and ISO 27001.

Data collection is done through methods and technologies that have been through a full review process with NHS Digital, NHS Information Governance, and NHS Clinical Assurance. The UKHSA are responsible for providing access to this data and following UKHSA data privacy processes.

Aggregate level summaries of the data may be circulated outside of the study team as part of report and publication of evaluation outcomes. All anonymised data will be checked for reidentification risk (e.g. small n sample sizes) prior to publication.

Anonymised data may be passed to third parties to support regulatory submissions for exceptional use and appropriate certification where required. Pseudo-anonymised or anonymised data may be subject to reanalysis to answer additional questions or to conduct pooled or meta-analysis across several studies delivered within this framework.

14. STATISTICS AND ANALYSIS

The overall approach for statistical analysis of an IVDD evaluation study is described below.

14.1 Questions to be Explored

What is the performance of the index IVDD; **a)** test kit/technology, **b)** testing methodology, or **c)** testing regimen, when compared to a relevant comparator / the current standard of care (where applicable)?

14.2 Statistical Analysis Plan

Study-specific SAPs will be developed and reviewed prior to commencement. The SAPs will focus on key aspects listed below:

1. Descriptive statistics for the baseline demographic and clinical characteristics of participants, presented in tables and graphs.
2. Index test results (e.g. viral load, void samples) compared with reference test
3. Index test performance (e.g. sensitivity, specificity, predictive values) compared with reference tests.

Inferential analyses will be presented with point estimates and 95% confidence intervals. P-values will also be used where appropriate. Comparisons may be made overall and stratified by pre-specified factors including calendar time; test site and laboratory; symptom status; and viral load.

Both participant characteristics and test result information will be analysed in line with the Standards for Reporting Diagnostic Accuracy (STARD) guidelines' result reporting section.

14.3 Sample Size

Typically, IVDD evaluation studies are designed to identify a pre-specified threshold of non-inferiority of test sensitivity compared with the standard reference test. Sample sizes are calculated for each evaluation study, based on current prevalence levels of the target disease/variant, to achieve pre-specified power and confidence interval thresholds. These are typically 80% power and 95% confidence intervals.

14.4 Interim Analysis

Any planned interim analyses will be pre-specified with clear objectives (e.g. verification of prevalence estimate used in sample size calculation, futility) and progression rules. Where there is evidence to recommend alteration of the study design, the ESAG will assess the data and determine progress.

15. ETHICAL AND REGULATORY CONSIDERATIONS

15.1 Declaration of Helsinki, Relevant Regulations, and Guidelines

The Investigator will ensure that evaluations are conducted in accordance with the principles of the Declaration of Helsinki[4] and, where appropriate, the UK Medical Devices Regulations 2002[1] (as amended) (UK MDR 2002), The Medical Devices (Coronavirus Test Device Approvals) (Amendment) Regulations 2021[2,] the MHRA In-vitro Diagnostic Devices Guidelines (2021)[5] and the Data Protect Act 2018[3].

15.2 Approvals

Following Sponsor approval, the protocol, PIS and any proposed advertising material will be submitted to an appropriate REC, and HRA (where required) and host institutions for written approval. Approval from HMPPS will be sought to permit involvement of detained populations where appropriate. The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents. Any relevant evaluation materials relating to usability may be submitted separately for review if required.

Advice has been obtained from the UKHSA Data Protection Office and the CAG for the secondary use of routinely collected data for the purpose of conducting the Evaluations within this Framework. They have confirmed that there is no breach in confidence which requires their approval under section 251 of the Health Service (Control of Patient Information) Regulations 2002.

Separate study-specific SAP, SOPs and step-by-step participant guides will be developed to detail the requirements for each study delivered under this framework. These will not be submitted for approval where they fall within the scope of the framework protocol, but will be subject to internal review and approval within UKHSA.

Where an evaluation study is intended to generate new evidence to support a marketing authorisation or changes to existing authorisations, this will be notified to MHRA as a performance evaluation prior to commencement.

The standardised framework protocol, PIS and other supporting documents will be resubmitted for approval every 5 years and reviewed annually prospectively. Any non-substantial amendments will also be submitted annually to the above parties where required.

15.3 Reporting

Reporting The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC, HRA (where required) host organisation, Sponsor, and funder (where required). In addition, an End of Study notification and final report will be submitted to the same parties.

15.4 Transparency in Research

Prior to the recruitment of the first participant, the study will have been registered on a publicly accessible database.

15.5 Participant Confidentiality

All data are captured and stored by or on behalf of UKHSA as data controller. All systems and applications used in this process are subject to a security review as part of the request to include them in the UKHSA testing programme, including input to or review of designs from the security architects, privacy, and identity teams.

All data shared with data processors on UKHSAs behalf is done so within the terms of established data sharing agreements and in accordance with UKHSA policy. Data processing impact assessments (DPIA's) are maintained throughout this activity and any amendment to processes or parties is formally documented, risk assessed, reviewed, and approved by UKHSA cyber security and data protection teams.

Data will be pseudo-anonymised as soon as possible following collection and once participants have completed study procedures. Data used for research purposes will be minimised and only data required to interpret and assess study objectives will be included in the analysis. All identifiable information will be processed within the secure UKHSA IT infrastructure, using UKHSA hardware, user credentials and with access restricted to only those who require access for the delivery of their role and who have undergone security clearances (including senior UKHSA managers and Data Managers).

All members of the study team are trained in patient level data management in accordance with GDPR upon joining the programme. The training is in place to ensure compliance with the most recent existing data protection regulations. The specifics of the training include understanding personal and special category data, roles of data controllers and processors, the importance of data security and privacy and regulatory guidance. The training also deals with potential project risks, such as breaches in data protection, and how these are to be handled and escalated should they arise.

Any level of access to personal data is heavily vetted and only a restricted number of study team members are allowed access to this. Access to UKHSA systems and software solutions containing personal information

require additional BPSS security clearances, mandatory Information Governance training and internal approval

Processing of personal data will be in accordance with UKHSA Testing for Coronavirus Privacy notice[6] and subject to CAG approval, or consent.

Contact details of testing service users may be used by the study recruitment team to contact individuals to invite them to participate in an evaluation study or to confirm they have received the testing kits. When registering for testing with UKHSA all service users are required to confirm that they have read and agree to the UKHSA Testing Privacy Notice. This is also a requirement for ordering test kits, submitting test results or registering the return of a completed sample prior to sending to the UKHSA laboratory.

The privacy notice informs users that UKHSA 'will only share personal information with researchers who have approval from a medical ethics committee and have obtained either your consent or special permission from the Secretary of State for Health and Social Care or the HRA's CAG to use confidential information. It advises them that this information may be used to invite them to participate in a research study but that they are under no obligation to do so. The notice further details how participants can opt-out of sharing information for research and planning purposes.

Advice has been obtained from the UKHSA Data Protection Office and the CAG regarding the secondary use of routinely collected data for the purpose of conducting the Evaluations within this Framework. They have confirmed that, because the data processing undertaken within the IVDD Evaluation framework is primarily for public health management purposes, those involved in the delivery of these evaluations are permitted to access the data in question for the delivery of these activities, as authorised by Secretary of State. Therefore, their access to this information for broader research purposes does not constitute a breach in confidentiality.

Pseudo-anonymised or anonymised data may be subject to reanalysis to answer additional questions or to conduct pooled or meta-analysis across several studies delivered within this framework. Anonymised data may be passed to third parties to support other research or in support of regulatory submissions where required.

15.6 Expenses and Benefits

While it is anticipated that participation in an IVDD evaluation study will incur minimal inconvenience, UKHSA reserves the option to offer compensation to participants for their time where this is perceived to be a barrier to participation. Although this is not expected to be provided routinely, there may be circumstances where the inconvenience associated with the collection of additional samples or undertaking additional testing as part of an evaluation study is a barrier to participation. In such circumstances a small reimbursement may be made to participants. This will be assessed on a case-by-case basis for each study in the planning phase and included in the participant information leaflets, where appropriate.

A high street retail voucher up to a maximum of £10 may be issued to participants on completion of all study activities (following the receipt of any data and samples required). E-vouchers will typically be sent via email to the address provided by the participant on registration. However, printed vouchers may be posted to their nominated postal address upon request. This process will be administered by the study team and monitored

by UKHSA. The issuing of these vouchers will be administered by the appointed contract research organisation and overseen by UKHSA.

15.7 Other Ethical Considerations

The main study-specific ethical consideration is the inclusion of vulnerable participants and participants who are unable to consent for themselves.

15.7.1 Adults lacking capacity to consent

Members of the population who are most clinically at risk of adverse outcomes to contracting infectious diseases include the elderly, NHS patients, Adult Social Care residents and individuals identified as clinically vulnerable. These groups are more likely to include adults who lack capacity to consent for themselves but who are most likely to benefit from safe and effective IVDDs which help to control these diseases in the community and identify those who would benefit from therapeutic interventions. And therefore, for whom the performance of UKHSA testing programmes is most critical.

Administering IVDD testing within these groups involves additional challenges associated with their diverse range of care needs. National testing programmes must be developed to be inclusive of the whole population and particularly to those whom the service is designed to protect.

The IVDD evaluation studies seek to understand the performance of these devices when used in the 'real world', outside of controlled laboratory conditions where sampling and/or processing activities are undertaken by trained professionals. It is therefore important to ensure that these devices perform appropriately in the use-cases which reflect the 'real world' challenges of correctly administering IVDDs and for whom the performance of these devices is most critical. As such, we do not feel it is possible or appropriate to extrapolate findings from other populations.

Feedback on the proposed research activities has been sought from UKHSA adult social care testing operations leads, from the NIHR ENRICH team, a care home manager and from other research teams who have undertaken comprehensive stakeholder engagement with care home staff and residents.

This feedback has indicated that the resource burden on adult social care homes to appropriately consent residents, in addition to their pre-existing consent for testing responsibilities, poses a significant barrier to participation. As such, the choice of studies undertaken within this cohort will be carefully considered and where possible, restricted to observational studies limited to secondary use of routinely collected testing data. The secondary use of this data for research purposes is explicitly stated in the UKHSA Testing Privacy Notice[6] which each service user is required to confirm agreement with when participating in a testing programme.

15.7.2 Children and teenagers aged <16 years

It may also be appropriate to include children and young adults <16years of age where there is a specific requirement to study the performance of an IVDD device/method/regimen in this group which cannot be extrapolated from other adult populations. For example, a study which seeks to explore the performance of IVDD testing regimens in a school setting. They will also not be unnecessarily excluded from participating in any study involving their wider use-case (e.g. clinically vulnerable service users).

This approach is consistent with the ONS Covid Infection Survey approach which includes household members of all ages. We have adopted and adapted the paediatric consent documents used in this programme which have been developed in collaboration with patient and public involvement and have been used extensively across the UK.

15.7.3 Prisoners

UKHSA infectious disease testing use-cases/cohorts include 'enclosed' populations where large numbers of people live in close-proximity increasing risks of transmission of infectious diseases. These use-cases include prisoners and prison staff.

Prisoners are particularly vulnerable given their reduced level of personal freedom. However, they represent a UKHSA testing use-case who are at an increased risk of transmission of infectious diseases due to living in close proximity to others within a prison setting. It is recognised that there are significant operational challenges to delivering an interventional study within this cohort and where it would not be appropriate for UKHSA testing operatives or study team members to directly communicate with the individuals. They will not be excluded from participating in future studies. However, their involvement will be limited to observational studies which do not deviate from standard care. The secondary use of this data for research purposes is explicitly stated in the UKHSA Testing Privacy Notice[6] which each service user is required to confirm agreement with when participating in a testing programme.

The inclusion of these vulnerable groups is essential to ensuring that the testing technology and methods deployed by UKHSA meet the diverse requirements of the service users. While participation itself carries minimal risk, enrolment procedures have been designed to ensure that adults or children unable to consent for themselves are not excluded and caregivers are able to consent on the participants behalf.

The researchers do not have a direct relationship with any vulnerable group within this framework and testing organisations have no obligation to participate or perform study activities.

There is no possibility that the testing will result in incidental findings that would be serious and medically actionable, as only SARS-CoV-2 or other specified infectious disease antibodies will be analysed in the samples provided and all participants will continue to receive standard of care diagnostic testing as part of the study.

16. FINANCE AND INSURANCE

16.1 Funding

Funding for these evaluations will be provided by the UKHSA. Where support in recruiting participants is required within NHS institutions, this will be funded via NIHR Service Support Costs via local participating Clinical Research Networks and NHS R&D departments.

16.2 Insurance

The UKHSA indemnifies UKHSA Investigators against any loss incurred by the Investigator whilst undertaking the research study. This cover is provided by NHS Resolutions and all staff benefit from the full scope of the cover under NHS Resolution's principal clinical negligence and non-clinical employers' and public liability schemes. This includes unlimited value clinical and non-clinical professional indemnity cover, and cover for the personal liabilities of employees, including non-executive directors.

17. PUBLICATION POLICY

Where possible, all outputs from this programme will be published online in government publications and via peer reviewed journals. The Investigators are responsible for reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from evaluations. Authors would acknowledge funding was secured by the UKHSA. Freedom of information requests will be processed under current UKHSA guidelines.

18. ARCHIVING

All study data required for regulatory purposes (i.e. in the case of clinical investigation or evaluation) shall be retained in accordance with the requirements of the medical device and IVDD regulations. The required retention period is currently 5 years after the end of the completion of the evaluation/investigation. Testing data constitute General Medical Records, as such, they will be retained by UKHSA in accordance with the Records Management Code of Practice for Health and Social Care 2021, currently 8 years. Following the end of a study, digital records will be electronically archived, and a copy of the final evidence report will be submitted to the UKHSA Public Health and Clinical Oversight Evidence Vault.

19. AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
1	1	15/09/2022	C Lewis	Clarifications in response to REC feedback.
2	2	19/10/2022	E Blandford	Clarifications in response to REC feedback.

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC committee and HRA (where required).

20. REFERENCES

[1] UK Medical Devices Regulations 2002. Available at: https://www.legislation.gov.uk/uksi/2002/618/contents/made

[2] Medical Devices (Coronavirus Test Device Approvals) (Amendment) Regulations 2021. Available at: https://www.legislation.gov.uk/uksi/2021/910/contents/made

[3] Data Protection Act, 2018. Available at: Data Protection Act 2018 (legislation.gov.uk)

[4] WMA Declaration of Helsinki – Ethical Principles For Medical Research Involving Human Subjects, 1964 (updated 2013)

[5] MHRA In-vitro Diagnostic Devices Guidelines (2021). Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/946260/IVDD_legislation_guidance_-_PDF.pdf

[6] UKHSA Testing for Coronavirus Privacy notice. Available at: https://www.gov.uk/government/publications/coronavirus-covid-19-testing-privacy-information/testing-for-coronavirus-privacy-information--2