Royal Brompton & Harefield NHS
NHS Foundation Trust

Guidance for monitoring of clinical research during pandemic

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1. BACKGROUND

The COVID-19 pandemic has rapidly escalated, putting the National Health Service (NHS) under enormous pressure to deliver clinical services, whilst still maintaining regulatory compliance to ensure safety of patient in clinical trials. Royal Brompton and Harefield NHS Foundation Trust (RB&HFT) is a research active organisation that recognizes the impact of COVID-19 on delivery and management of clinical research. Consequently, most research studies were suspended due to COVID-19, to allow delivery of critical clinical care.

Following recent implementation of extraordinary measures, to support adjustment to clinical trials due to limited access to public places to minimise risks of spreading infection, interruptions to the IMP supply chain, participants self-isolation or mandatory quarantine *etc.* some research activities are now being reactivated in accordance with Research Office COVID 19 guidance can be found here: https://www2.rbht.nhs.uk/services/research/covid-19/.

In order to minimise risks of COVID-19 exposure and transmission to patients, research staff, other hospital staff, external staff, and contractors, the RB&HFT has recently issued a guidance document for undertaking research procedures on site.

Measures that have been introduced to manage COVID-19 exposure have resulted in amendments to research study protocols and early closure of many research studies. One measure that has been introduced is limiting external visitors to RB&HFT sites. External Sponsors are increasingly requesting access to the Trust to enable resumption of study monitoring activities. This guidance is drafted to ensure compliance with the UK Policy for Health and Social Care Research and the UK Medicines for Human Use (Clinical Trials) Regulation 2004 (as amended), Good Clinical Practice (GCP), General Data Protection Regulation (GDPR) and any other applicable regulation.

2. SCOPE and PURPOSE

This guidance outlines interim arrangements for remote and/or onsite monitoring of research studies in response to the impact of COVID-19 on research in the coming months.

This document provides guidance for Principal Investigators (PIs) hosting clinical research monitoring visits at Royal Brompton and Harefield NHS Foundation Trust (RB&HFT), to support continuance of these studies in compliance with Good Clinical Practice (GCP) while ensuring health, safety and wellbeing of study participants and minimizing risks to study data integrity.

This guidance document applies to all clinical research and it is applicable to external Sponsors, Clinical Research Organizations (CROs), Clinical Trial Units (CTUs) *etc.* wishing to conduct on site and/or remote monitoring and Source Data Verification (SDV).

Given the nature of monitoring visits, the Research Office liaised closely with support departments (*e.g.* Pharmacy, Clinical Research Facility (CRF), Information Governance) to ensure awareness of this guidance along with their support in allocating time necessary to host monitoring visits as requested.

3. RESEARCH OFFICE POLICY

All procedures and guidance documents produced approved by the Research Office must be used in conjunction with other Royal Brompton and Harefield NHS Foundation Trust (RB&FHT) policies and procedures.

Research Office acts as the representative of RB&HFT and as such will be the official name on all procedures to represent RB&HFT acting as Sponsor and/or a site hosting externally sponsored research.

4. DEFINITIONS

4.1 Clinical Trial of Investigational Medicinal Product (CTIMP) - Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any Adverse Reactions (ARs) to an investigational product(s), and/or study absorption, distribution, metabolism and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

4.2 Substantial amendment is defined as an amendment to the terms of the application, or to the protocol or any other supporting documentation, that is likely to affect to a significant degree:

a) the safety or physical or mental integrity of the subject of that trial;
b) the scientific value of the trial;
c) the conduct or management of the trial; or
d) the quality or safety of any Investigational Medicinal Product (IMP) used in the trial.

4.3 Urgent Safety Measure – An Urgent Safety Measure is a procedure that is necessary, not defined in the protocol but has to be taken without any authorisation from the REC, in order to protect the trial subjects from any immediate hazard to their health and safety. The Investigator/Lab undertaking such procedure will need to report this to RO to enable reporting to the main REC immediately.

5. PROCEDURE

The following procedure was drafted in accordance with information provided by the MHRA and HRA specific guidance on research conduct, management and oversight during the COVID-19 pandemic. RB&HFT acknowledges temporary measures

implemented by clinical research Sponsors to ensure appropriate oversight of research activities at site. It is recommended that study sponsors take a risk-based approach to study monitoring, prioritising the safety, rights and well-being of study participants while also ensuring integrity of the study data.

5.1 Requesting access to RB&HFT for monitoring

Research sponsors should contact the PI and/or the research team to discuss arrangements for monitoring visits on a study by study basis. The Sponsor must ensure that the PI is informed of any necessary amendment to the study protocol to facilitate alternative monitoring arrangements.

The PI and the research team should consider any requirement for additional consent that may be required for some of the arrangement proposed below (*e.g.* sharing data *via* video link, providing patient identifiable information outside of the Trust).

While it is the responsibility of the Sponsor to ensure appropriate submission and approvals of study documentation, the PI should always review any changes and discuss this with the Research Office if deemed necessary: research@rbht.nhs.uk.

It is recommended that all research Sponsors should consider the extent and nature of monitoring that would be proportionate to each specific research study, in these exceptional circumstances, while striking a balance between appropriate oversight and the capacity of the trial site to avoid any extra burden alternative measures it may present.

5.1.1 Contacting support departments

RB&HFT Pharmacy Department can be contacted directly, and this should be done on a study by study basis, in parallel to contacting the PI and the research team, via Email: pharmacytrials@rbht.nhs.uk.

All other support departments will be contacted by the PI and their research team, upon receipt of a monitoring request.

5.2 Monitoring procedures

RB&HFT fully recognizes the impact of reduced monitoring on Sponsor oversight. The following alternative measures are therefore acceptable until the current situation is normalized:

a) On site monitoring

On-site monitoring may be possible in some departments in the Trust. It will only be considered, where the Sponsor provides written confirmation of the necessity for such visits to take place to prevent putting patient safety and study data integrity at risk.

It is the responsibility of the PI to ensure availability of the research team and that appropriate arrangements are put in place in line with government guidance to maintain social distancing to prevent exposure and spread of infection. Monitors are advised to consider traveling arrangements to RB&HFT. The research team and the PI will not be able to guarantee parking at site.

All visitors to the Trust are expected to comply with the RB&HFT COVID-19 guidance and associated local screening procedures.

It is the responsibility of the PI and the research team, hosting an on-site monitoring visit, to ensure that the **Guidance for management of research participant visits at RBHT** is fully implemented prior to hosting the visit.
Sponsor representatives and research teams must also adhere to the Trust local arrangements for pre-screening of any visitors prior to being allowed to access Trust premises. Please see Appendix 1 of this guidance document for further details.

Receiving **external visitors from outside the UK**, will be subject to the Trust local policy, and the research team should contact the Research Office prior to agreeing to host such on-site visit.

In absence of on-site monitoring, RB&HFT strongly encourages research Sponsors to consider alternative arrangements outlined below.

It is important to note that study participants must consent to any sharing of their identifiable personal data outside of RB&HFT. This should always be discussed with the Research Office and Information Governance, and appropriate arrangements for receiving consent should be approved by the REC/HRA.

b) Centralized monitoring

RB&HFT research teams fully support temporary replacement of on-site monitoring with centralized monitoring of Electronic Data Capture (EDC) system and will endeavour to contribute to completeness of such data, in response to Sponsor queries in a timely manner.

c) Off-site monitoring

Off-site monitoring visits including phone calls, video links, emails *etc.* to enable the Sponsor to discuss the study (*i.e.* study progress, any potential issues, changes to the protocol, trial participant status *etc.*) with the PI and the research team are currently feasible at RB&HFT.

It is the responsibility of the PI and the research team to ensure appropriate arrangements, outlined below are in place to facilitate off-site monitoring:

i. Video conferencing should be conducted *via* MS Teams. This is currently approved system and use of any other system requires additional approvals for RB&HFT IT and Information Governance Department (Email: informationgovernance@rbht.nhs.uk) and might delay off-site monitoring.

ii. The Sponsor should provide a copy of an appropriate procedure (*e.g.* Sponsor SOP) to support off-site monitoring and its associated activities. Any queries regarding this process should be directed to the Research Office (Email: research@rbht.nhs.uk).
iii. The monitor responsible for the conduct of the visit is known to the research team and the PI. Alternatively, you must ensure that all requests for such visits are received from a source know to you.
iv. Ensure that off-site monitoring is conducted in a safe and private location.
v. Ensure that any correspondence/documents generated as a result of this visit are appropriately filed in the ISF.

It is the responsibility of the Sponsor to confirm in writing (*e.g.* email) compliance with the following rules of the visit prior to the off-site visit taking place (*i.e.* 'I, insert name of the person, agree to comply with Section 5.2c of the 'RB&FHT monitoring guidance during pandemic', specifically in relation to Sponsor responsibilities for the duration of this off-site monitoring visit'.):

i. Taking screen shots, printing, emailing or downloading of any records during screen sharing is not permitted
ii. Video recording is no permitted
iii. The monitor will inform the research team/PI of any other personnel present in the room during off-site monitoring. Any personnel present at the time, must be familiar with the study, and fully trained in GCP to ensure compliance with regulatory requirements, and patient confidentiality.
iv. The PC used during this activity must be password protected, with adequate security in place (*e.g.* firewall)
v. The PC will not be left unattended and accessible by anyone other than the monitor during this monitoring activity.

It is the responsibility of the PI to ensure with the above arrangements is in place.

d) Remote review of source data

Remote source data verification (SDV) will only be considered for current studies where patients have consented for sharing of their personal information outside of the Trust. Remote SDV should only be considered in exceptional circumstance (*e.g.* COVID-19 pandemic), focusing specifically on the quality control of critical data (*e.g.* primary end point) and important safety data. It is recommended that any other data is monitored simultaneously, while ensure that it does not present extra burden on the study personnel.

Review of electronic patient's medical records *via* any of the Trust Electronic Health Records (EHR) is not possible and it cannot be approved.

In absence of remote access to EHR, the PI should determine if current situation at site allows sharing of pseudo anonymised copies of trial related source documents with the Sponsor. The PI and the research team must ensure that:

i. the Sponsor has provided an appropriate procedure to outline the extent and nature of remote monitoring proportionate to extra burden for the research team and the type of study and to describe the destruction process

ii. determine if the current situation at site allows extra time and resources needed to comply with the Sponsor request (i.e. scanning of source documents will create a significant administrative burden on the research team)
iii. Patient identifiable data must not be shared electronically without explicit patient consent to proceed. The PI must ensure that any changes to the study consent are clearly documented and approved by the REC/HRA (where applicable).
iv. When agreeing to provide anonymized source data, the PI must consider if this is appropriate, and the research team must ensure that all patient identifiable data is redacted.
v. Monitors agree in writing that adequate measures will be put in place to maintain patient confidentiality at all times, and that reviewing of patient records is conducted in private, and not public places.
vi. Data sharing platform is adequate and secure.
vii. Any requests to provide data by post or courier must be resourced by the Sponsor and assurance given that confirmation of receipt of data will be issued by the Sponsor.
viii. There is an up to date site agreement with the Sponsor to allow monitoring.

5.3 Alternative Arrangements

RB&HFT acknowledges that remote monitoring might not be possible where any or some of the above conditions cannot be guaranteed by the Sponsor. It is recommended that in such cases the Sponsor contacts the Research Office *via* Email: research@rbht.nhs.uk, clearly marking the email with 'Alternative monitoring arrangement' to:

i. Postpone monitoring activities until the site monitoring is allowed
ii. Provide a proposal for any alternative arrangements to be reviewed and approved by the Research Office. These requests will be reviewed in liaison with support departments.

Sponsors are strongly encouraged to frequently visit the Trust website for any future updates regarding guidance on conduct and management of research at RB&HFT during the pandemic.

6. REFERENCES

1. https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/covid-19-guidance-sponsors-sites-and-researchers/

2. https://mhrainspectorate.blog.gov.uk/2020/03/12/advice-for-management-of-clinical-trials-in-relation-to-coronavirus

7. Guidance Appendices

Appendix 1 – Management of sponsor visits

Guidance Revision Chronology:			
Version History (SOP ID and Version number):	**Effective Date:**	**Reason for Change:**	**Author:**
Version 1.0	29th July 2020	Original Version	Ira Jakupovic
Version 2.0	21st August 2020	Appendix 1 added to clarify pre-screening arrangements for on-site monitoring visits.	Ira Jakupovic

Appendix 1

Management of Sponsor Site Visit

Please ensure the any current Trust guidance is reviewed prior to conducting any visit.

Sponsor representatives may attend on-site only if necessary, as outlined in Section 5.2a of this guidance document. Please ensure all arrangements are discussed with the sponsor representative prior to any site visit.

Pre-screening:

If sponsor representatives are required to attend RB&HFT for **essential research purposes only** the pre-screening will be performed by the host research team. This pre-screening will comprise of the following steps:

- Completion of COVID 19 questionnaire (QN) *via* telephone

- If the visitor reports any COVID 19 symptoms, they will be told not to attend RB&HFT and given appropriate advice for further management of their symptoms (*i.e.* call NHS 111 or visit NHS 111 website). This should be documented in the site file.

- Visitors attending Royal Brompton and Harefield sites will adhere to current guidelines regarding staff temperature checks on entering clinical areas and wearing of personal protective equipment (PPE) as appropriate to the area they are visiting.

Arrangements during visit:

The steps to take for managing a visit by a Sponsor representative are as follows:

- Visitors will be given a scheduled time slot for arrival and asked not to arrive early. They will be instructed to contact the host research team by phone on arrival at the hospital.

- A member of the research team wearing appropriate PPE (surgical mask), will meet the visitor at the hospital entrance where they will be provided with a face mask, if they are not already wearing one, and asked to sanitise their hands, and then have their temperature checked.

- If the temperature is above 37.8c, the visitor will be refused access to the hospital and asked to contact NHS 111 or 111.nhs.uk for further advice. If the visitor's temperature is <37.8c the COVID 19 patient questionnaire may then be completed. If the visitor answers yes to any of the questions, they will be asked to return home and contact NHS 111 or 111.nhs.uk for further advice. Visitor temperature checks and QN completion should be documented in the local site file

- If there are no issues with the temperature checks or COVID 19 questionnaire(s), the visitor will be escorted to the designated area.

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- The visitor will be escorted to the designated area by member of host research team wearing appropriate PPE (surgical mask).

- Sponsor representatives attending the Trust must be considerate of all hospital users and maintain required social distancing at all times.

- Specific work areas within the hospital site will be identified by the host research team for use by the sponsor representative. All social distancing and workplace risk assessments will be adhered to, to ensure maintenance of a safe working environment

- Upon completion of the visit a member of the host research team wearing appropriate PPE (surgical mask), will escort the visitor to the hospital exit.

- Cleaning of the area, equipment and frequently touched areas such as door handles will be undertaken by the host research staff at the end of the visit to ensure infection control procedures are adhered to.