WORK INSTRUCTION

WI48–Process for starting/restarting RD&E-sponsored and hosted non-pandemic studies during pandemics

Version	1
Effective Date	15 October 2020
Review Date	15 October 2023
Author & Position	Alison Kerridge, Assistant R&D Manager
Signature	
Date	3/12/2021
Approver & Position	Helen Quinn Director Joint Research Office
Signature	
Date	01-12-2020

Controlled document

This document has been created following the Royal Devon and Exeter NHS Foundation Trust Policy for the Development, Ratification & Management of Procedural Documents. It should not be altered in any way without the express permission of the author or their representative.

It is the responsibility of all users of this Work Instruction to ensure that the correct version is being used. If you are reading this in a paper format please go on-line to confirm you have the latest version.

DISCLAIMER

This generic R&D Work Instruction (WI) must be followed unless a study specific SOP/WI exists.

Once printed this is an uncontrolled document

Full History			
Version	**Date**	**Author**	**Reason**
1			New procedure introduced to enable sponsor safety and viability assessment and site capacity and readiness assessment of RD&E research during the Covid-19 pandemic as per NIHR Covid guidelines

Associated Trust Policies/ Procedural documents:	
Key Words:	COVID-19 Sponsor Host Restart safety and viability capacity and readiness
In consultation with: Governance Oversight Group (August 2020)	

Contents

1 INTRODUCTION

In response to the COVID-19 pandemic, Department of Health and Social Care asked NHS Trusts to suspend clinical research which was not directly related to COVID-19 or was providing urgent treatment only available in a trial protocol and to prioritise the set-up and delivery of designated Urgent Public Health studies. As COVID-19 treatment and other trials were rapidly set up and prioritised for support there was, as expected, a rapid and significant reduction in non-COVID National Institute for Health Research (NIHR) and other commercial and non-commercial research activity. At the Royal Devon & Exeter NHS Foundation Trust (RD&E) recruitment was paused and the vast majority of patients already enrolled in trials had their follow-up care provided remotely and medication delivered to their home addresses.

In response to the reduction in the pressures on the NHS, the NIHR has issued a framework to support the re-start of research activity; Urgent Public Health studies are still prioritised, all other studies are expected to be assessed for continued viability and safety, including the potential effect of a further surge in COVID-19 cases and the need to consider the 'deliverability' of research taking in to account measures to minimise COVID-19 transmission https://www.nihr.ac.uk/documents/restart-framework/24886

The responsibility for assessing the overall viability and safety of a particular study lies with the study 'Sponsor' (the institution with overall responsibility for the study) and Chief Investigator (CI) who is the clinician leading the study. If the decision is made that a study is viable and safe, the sponsor will then need to liaise with the clinical sites delivering the study to assess if the site still has the capacity and capability and readiness to deliver that study.

2. PURPOSE

This document describes the procedures required to ensure that any RD&E-sponsored non-COVID study that is 'paused', remained 'open' or was 'open and in follow up' during the COVID-19 pandemic is assessed for overall safety and viability. In addition, this document describes the site assessment process for ensuring RD&E, when acting as a site (both in sponsored & hosting trials), has the capacity and readiness to start/restart the research.

This process should be used in conjunction with any Trust restart policies.

3. SCOPE

This Work Instruction (WI) is applicable to all non-COVID research sponsored and hosted by the Trust delivered on behalf of external sponsor organisations.

This WI is applicable to all RD&E research that has been submitted to the Health Research Authority (HRA) for approval and the research that is generated from tissue bank and biobanks. However, it is not applicable to the tissue bank and biobank collections which are covered by their own committees.

The WI is applicable to Chief Investigators (CI), Principal Investigators (PI), delegated trial team members involved in Trust-sponsored studies and Research & Development (R&D) team members undertaking sponsor and hosted activities on behalf of the Trust.

4. DEFINITIONS

DHSC	Department of Health & Social Care
CI	Chief Investigator
CTU	Clinical Trials Unit
HRA	Health Research Authority
GOG	Governance Oversight Group
NIHR	National Institute for Health Research
PI	Principal Investigator
R&D	Research & Development
RD&E	Royal Devon & Exeter NHS Foundation Trust
Sponsor	An individual, company, institution or organisation which takes responsibility for the initiation, management and financing of a clinical trial. Sponsorship activities may be delegated to the Investigator, CTU and/ or other organisations as appropriate
TMF	Trial Master File
WI	Work Instruction

5. DUTIES AND RESPONSIBILITIES OF STAFF

The **Sponsor Panel** is responsible for the assessment and authorisation of the Sponsor Restart Framework (see Appendix 1). This panel is composed of R&D Director, R&D Governance & Quality Manager, Assistant R&D Manager, Clinical Trials Research Nurse.

The Research Site–Level **Re-start Assessment Panel** is responsible for the assessment and authorisation of the Restart Framework to ensure that the Trust can continue to discharge its duties as a research site (see Appendix 2). The panel is composed of R&D Director, R&D Governance & Quality Manager, Lead Clinical Trials Research Nurse, Senior R&D Facilitator. A member of the Delivery Team may attend to provide addition information but will not be involved in decision making.

The **CI** is the Lead Researcher and is responsible for the overall conduct of a research project. They will be responsible for completing the framework assessment with support from their research Trial Team where applicable.

The **PI** is responsible for the safe conduct of the research project at site level. They will be responsible for ensuring that site level activity is safe for research participants and staff.

The **Senior Research** Nurse responsible for the delivery of the study will liaise with the Sponsor of each study to confirm completion of the Sponsor re-start assessment and ensure relevant details are used to inform the site level assessment.

The **Senior Research Nurse** responsible for the delivery for each individual study is responsible for ensuring completion of the restart assessment and will do so in collaboration with the PI and support of the relevant Team Lead as required.

6. PROCEDURES

6.1 Completing the framework

6.1.1 Sponsor framework Safety & Viability Assessment

The R&D team must approach all CIs (and where applicable include the CTU and/or trial manager and/or lead research nurse) of RD&E-sponsored, non-COVID studies where the study status is 'in set up', 'paused to recruitment' or 'in follow up' with a sponsor assessment safety and viability framework to complete (see Appendix 1 for framework).

The framework ensures the CI and team consider such aspects as ongoing trial viability, participant safety, Covid security, the need to revise time frames, funding, consider changes to patient pathways, necessary protocol amendments and individual site feasibility where the study is delivered at more than one research site.

There may be some questions that remain unanswered and will need further clarification. These should be highlighted in the assessment. There is an expectation that the more complex studies may require several updates before approval.

CI and their research team must consider framework and return a draft to R&D within 2 weeks of receipt, providing as much information as possible. If the CI is unable to complete the framework at the time of receipt, for example if there are no plans to resume services in the foreseeable future, the CI should still communicate this to R&D

Once in receipt of framework, R&D will transfer all details via 'RD&E Reviewing Paused Sponsored Studies (v1 Jun20)' workflow onto EDGE on the study wide screen (green level). This will be accessible to the relevant research teams and R&D team members to monitor the progress of the assessment and to ease review of the framework.

6.1.2 Research Site-Level framework

Senior Research Nurse (or research nurse responsible for the delivery of the study) to complete re-start assessment in collaboration with the PI for all non-Covid studies currently in set-up, recruiting or in follow-up. This should include all current studies except PIC activity, including those where activity was paused due to the impact of Covid and those where some activity has continued. This should be documented on the research site screen (red level) of Edge using the 'RD&E Reviewing paused hosted studies (v1 Jun20) re-start workflow template.

The re-start assessment should consider changes to patient pathway due to Covid that may impact on the ability to deliver the study protocol while maintaining patient safety, e.g. outpatient appointments moved from face to face to online or telephone consultations. This should be documented on the workflow.

Any points requiring further clarification or where issues remain e.g. access to service departments, should be highlighted on the workflow for consideration by the Panel.

6.2 Panel Assessment and Sign Off

Completed assessments will be submitted for review by the relevant Review Panel (see Section 5). Regular Panel meetings will be convened to facilitate reviews. Assessments will be scrutinised to ensure that all questions have been considered and appropriately answered.

When the Panel is satisfied that each question has been addressed, the outcome of the

review will be documented on Edge by completing the workflow.

For Trust sponsored studies, a formal email will be sent to the CI confirming approval from the sponsor perspective that the study is safe and viable to continue/start. EDGE green screen study status will be updated to 'Open'. The CI should retain a copy of the approval email in the Trial Master File (TMF).

For research site (hosted) studies a formal email will be sent to the Sponsor organisation to confirm ongoing capacity and capability to deliver the study protocol. EDGE red screen will be updated appropriately e.g. open, closed in follow-up.

6.3 Panel queries and escalation

In the event that the framework is incomplete or that the Panel has queries, these will be fed back to the, CI or PI and/ or Sponsor for further clarification. The study will continue to be referred back to the Panel until the queries have been resolved/ framework has been completed.

In the event, that the Sponsor deems the study is no longer safe or viable, the study will be closed down as per study and HRA standard early closure procedures.

In the event that the PI and/ or Delivery team raises concerns about safety or viability, these will be raised to the Sponsor.

In the event of disagreement about the ongoing safety or viability of a study or where there are unresolved issues around site capacity and capability, these will be escalated.

6.4 Site communication, RD&E sponsored studies

CIs will communicate the outcome of this assessment to participating sites and sponsor organisations, confirming study restart from a sponsor perspective, any required amendments to protocol, or where necessary, the early termination of the study. Even if RD&E as sponsor and the CI are content the study is viable and safe, it is expected that all participating sites must complete their own assessment for deliverability and readiness to start as some sites may not have the capacity to re-start.

7. DISSEMINATION AND TRAINING

7.1 This WI and associated templates and forms will be uploaded to the RDE Research website shortly after having been released.

7.2 All staff whose activities are subject to this WI should ensure that they take time to read and understand the content of this WI.

8. MONITORING COMPLIANCE AND EFFECTIVENESS OF THIS WI

8.1 In order to monitor compliance with this WI, the auditable standards will be monitored as follows:

No	Minimum Requirements	Evidenced by
1.	(For Trust Sponsored studies) Sponsor assessment safety and viability framework form completed by CI.	R&D file and/or EDGE
2.	(For Trust Sponsored studies) 'RD&E Reviewing Paused Sponsored Studies (v1 Jun20)' workflow entered on EDGE	EDGE
3.	(For hosted studies) Re-start assessment completed by lead research nurse and PI evidenced by 'RD&E Reviewing paused hosted studies (v1 Jun20)' workflow entered on EDGE.	EDGE
4.	Review panel approval received.	EDGE Trial Master File and/or Investigator Site File

8.2 Outcomes from audit will be presented to the R&D Governance Oversight Group (GOG) which will monitor any resulting action plans until all issues have been addressed to satisfaction.

8.3 Issues identified via the audit process which require escalation will be referred to GOG.

9. ARCHIVING ARRANGEMENTS

9.1 The original of this document will remain with the R&D Quality Assurance Coordinator. An electronic copy will be maintained on the R&D section of the Q-Pulse document management system and a pdf copy on the RDE Research website.

9.2 Archive copies must be maintained for any documents which have been superseded. Archive copies in electronic format should be retained indefinitely.

10. REFERENCES

https://www.nihr.ac.uk/documents/restart-framework/24886

Appendix 1: Framework for reviewing paused RD&E sponsored studies

Study Name		IRAS number	
CI		Date completed	

			Comment
1	Is the study NIHR portfolio adopted?	Yes No	
2	Has clinical guidance been issued which has changed the patient pathway e.g. frequency/mode of follow-up and will this affect the deliverability of the protocol?	Yes – comment No	
3	What is the risk of exposure to COVID-19 and what measures will be put in place to mitigate these (e.g. equipment sterilisation)? Is what is being proposed as safe as or safer than the clinical care pathway alternatives?		
4	Are protocol amendments to reduce risk required? For example, combining research assessments with essential clinical reviews /visits or enabling remote assessments. Does this affect the primary outcome measure?	Yes – comment No	i.e. must not have an adverse impact on safety e.g. reducing clinic visits; should map to revised usual care where possible
5	Does the study require participants to been seen on site?	Yes - comment No	
6	Does the study require participants to visit other sites for investigations as part of their follow –up? Do these sites have capacity for these visits to resume?	Yes - comment No	
7	Are you aware of any local site policies in respect of COVID-19 which would affect the deliverability of the study?	Yes – comment No	
8	What guidance about Covid-19 related safety issues and measures for participants and staff are required?		
9	Is there a need for patient testing for COVID-19 and what are the requirements for personal protective equipment (PPE)?	Yes – comment No	Do PPE requirements increase research costs?
10	Is it necessary to include these requirements in the research protocol / procedures, or will local site policies be used?	Yes No Local policy	

11	How will the Government guidance on social distancing be addressed?		
12	Special consideration should be given to participants who are 'clinically extremely vulnerable' who are 'shielded' including consultation with their GP and/or Specialist and only essential visits to the research site, does this guidance need to be considered?	Yes – comment No	
13	How will participants concerns about COVID including the need to feel safe and reassured about the research process be addressed?		
14	Are there any key improvements which could be included which would improve the re-start/completion of the study?	e.g. review recruitment processes	
15	If the study protocol needs to be amended will this require additional research costs and is it possible to secure these?	Yes – comment No	e.g. study extension
16	Does the SoECAT need to be revised?	Yes – Comment No	e.g. additional costs / savings
17	If the study protocol needs to be amended will this require additional Excess Treatment Costs and has this been recorded?	Yes No	
18	If the study protocol needs to be amended and is not NIHR portfolio adopted will this require additional costs?	Yes - comment No	
19	How will site compliance with the protocol and regulatory requirements be monitored?		
20	Can study monitors/visits/meetings be undertaken remotely or minimised?	Yes - comment No - comment	
21	Has capacity to continue to support the study been confirmed from other collaborators e.g. CTU?	Yes No NA	
22	What would be the effect if the study had to be re-paused?		
23	Does the study need to close?	Yes – comment No	Agree close out plan, site and enrolled participant communication

Study Priority			
24	Level 1: Essential studies providing evidence for pandemic management, i.e. nationally prioritised COVID-19 Urgent Public Health (UPH) Research studies.		
25	Level 2: Studies where the research protocol includes an urgent treatment or intervention without which patients could come to harm. These might be studies that provide access to potentially life preserving or life-extending treatment not otherwise available to the patient.		
26	Level 3: All other studies (including new COVID-19 studies not in Level 1).		

RDE as sponsor have reviewed this study and agree it can re-start; *please note site agreement to re-start is also required*	Yes / No	Date	Comment:

Appendix 2: Framework for reviewing hosted studies

Study Name		IRAS number	
CI		Date completed	

		Comment
1	Sponsor request to restart study	Q: Has the sponsor advised they have considered the studies viability and safety and are content for recruitment to continue? P: If yes, enter the date the request was made Also applies to studies which were not paused; has sponsor been asked to confirm If no, please comment Select the tick box and enter the current date on the day you complete the task
2	Participant visits	Q: Does the study require participants to be seen on site? P: If yes, comment required. Which site will patients be seen at? Select the tick box and enter the current date on the day you complete the task.
3	Clinical service	Q: Has the clinical service in which the patient would enter a study/trial been restored and the patient would be attending the site as part of their care? P: If yes, enter the date the request was made. Select the tick box and enter the current date on the day you complete the task
4	Visits to site	Q: Would the trial protocol require visits to the site over and above those required for usual clinical care? P: If yes, enter the date the request was made, and enter a reason for the justification. Select the tick box and enter the current date on the day you complete the task.
5	Covid-19 minimisation	Q: What mitigation will be put in place to provide assurance to research participants that their risk to exposure of COVID-19 has been minimised? P: Consider the place the patient will be seen; the staff they will be in contact with; will they be exposed to other patients. Enter details in comments box. Select the tick box and enter the current date on the day you complete the task.
6	Consultation with patient's GP/ Specialist	Q: Have arrangements to consult with the patients GP and/or Specialist been put in place? P: People considered 'clinically extremely vulnerable' who are 'shielded' and who have participated in a paused study or are considered for a new study require special considerations and their GP and/or specialist should be consulted to ensure they continue to receive the appropriate care with only essential visits to the research site, does this guidance need to be considered? If yes, enter the date the request was made. Select the tick box and enter the current date on the day you complete the task.
7	Protocol deviation expected?	Q: Can the study/trial protocol be delivered without protocol deviations and adhering to the Trusts IPC measures including patient testing? P: If yes, enter the date the request was made.

		Select the tick box and enter the current date on the day you complete the task.
8	Protocol deviation required?	Q: If protocol deviation would be required is the sponsor happy to make an amendment or accept the deviation? P: If yes, enter the date the request was made and add a comment. Select the tick box and enter the current date on the day you complete the task.
9	NIHR study?	Q: Is this an NIHR portfolio adopted study? P: Select the tick box and enter the current date on the day you complete the task.
10	Changes to the protocol by Sponsor	Q: Has the sponsor introduced any changes to the protocol resulting in a change to the study schedule e.g. change to visit length, removal of interventions? P: If yes, please comment and enter the date the request was made. Research team to comment on change – R&D to review for cost implications and ensure additional funds where required have been secured and also where there are new ETC that these have been agreed and uploaded to NIHR. Select the tick box and enter the current date on the day you complete the task.
11	Non NIHR study costs	Q: If the study is not NIHR adopted and amendments to the study protocol require additional research, ETC and service support costs have these been agreed by the sponsor? P: If yes, enter the date the request was made. Select the tick box and enter the current date on the day you complete the task.
12	Patient safety	Q: Do the proposed mitigating actions and flexible arrangements to restart a study still ensure patient safety (e.g. reduced clinic visits still ensure critical safety checks to be completed) P: If yes, enter the date the request was made. Select the tick box and enter the current date on the day you complete the task.
13	On-site monitoring	Q: Will on-site monitoring be required by external auditors and to what level? P: If yes, enter the date the request was made and the level of monitoring required. Select the tick box and enter the current date on the day you complete the task
14	Remote monitoring requests	Q: What has the sponsor requested to support remote monitoring? P: Enter details of request. Select the tick box and enter the current date on the day you complete the task.
15	Management of enrolled participants	Q: How would enrolled participants be managed if it were necessary to pause this study/trial in response to a surge in COVID-19? P: Enter comment. Select the tick box and enter the current date on the day you complete the task.
16	Other considerations	Q: Are there any other considerations/comments? P: Please enter comment and tick box to complete task.

17	Directorate review	Q: Has Directorate reviewed and agreed re-start? P: If yes, enter the date the request was made, date and CD who agreed. Select the tick box and enter the current date on the day you complete the task.
18	Pharmacy involvement	Q: Does delivery of the study protocol require pharmacy? P: If yes, select the tick box and enter the current date on the day you complete the task
19	Imaging involvement	Q: Does delivery of the study protocol require imaging? P: If yes, select the tick box and enter the current date on the day you complete the task.
20	Pathology involvement	Q: Does delivery of the study protocol require pathology? P: If yes, select the tick box and enter the current date on the day you complete the task.
21	Other support department involvement	Q: Does delivery of the study protocol require other support services P: If yes, enter support department required. Select the tick box and enter the current date on the day you complete the task.
22	Clinical research delivery staff	Q: Is there sufficient clinical research delivery staff capacity to deliver the study/trial? To be agreed with Lead Research Nurse for Clinical Trials P: If yes, select the tick box and enter the current date on the day you complete the task.
23	Study priority	P: Level 1: Essential studies providing evidence for pandemic management, i.e. nationally prioritised COVID-19 Urgent Public Health (UPH) Research studies. Level 2: Studies where the research protocol includes an urgent treatment or intervention without which patients could come to harm. These might be studies that provide access to potentially life preserving or life-extending treatment not otherwise available to the patient. Level 3: All other studies (including new COVID-19 studies not in Level 1). Please choose level. Select the tick box and enter the current date on the day you complete the task.
24	Re-start confirmed with R&D department?	Q: Has R&D reviewed the study and agree it can restart? P: Select the tick box and enter the current date on the day you complete the task.