Academic and Clinical Central Office for Research and Development

COVID-19 Clinical Research Plan and Guidance

1. Purpose

- Provide clear guidance to researchers about how to manage their investigator-led research during the COVID19 pandemic, including restart of studies.
- Provide researchers with information about how ACCORD manages investigator-led research activities during the COVID-19 pandemic.
- Provide guidance on research activity and the required response that is consistent with NHS Lothian (NHSL), other regulatory bodies, and Scottish/UK government.

2. COVID-19 Related Research Prioritisation

- The NIHR launched a national process to prioritise COVID-19 research – this applies to multicentre/UK wide studies https://www.nihr.ac.uk/covid-19/. An NIHR Urgent Public Health (UPH) Group review all new submissions for research which have been approved by the Chief Medical Officers. This is being coordinated and fed back through the CSO for prioritisation of projects in Scotland.
- The NIHR has also released guidance for a 'second wave' of COVID-19 activity. The guidance instructs that the deployment of NIHR funded staff to frontline duties should only occur in exceptional circumstances. The guidance also reiterates that decisions around restarting NIHR research activities should be led locally and the NIHR will continue to encourage non-COVID-19 research to restart, although this may change if NHS priorities change.
- Information on the Health Research Authority (HRA) process for fast track Research Ethics Committee (REC) review of COVID-19 research studies (including timelines) is available on the HRA website; https://www.hra.nhs.uk/covid-19-research/fast-track-review-guidance-covid-19-studies/.
- Researchers who have a COVID-19 study that they would like to be considered for fast-track REC review should contact the HRA at this address: fast.track@hra.nhs.uk.
- The Medicines and Healthcare product Regulatory Agency (MHRA) have procedures for rapid scientific advice, reviews and approvals in relation to COVID-19 clinical trials. An informal regulatory advice meeting with the MHRA can be arranged by contacting CTU.advicemeetings@mhra.gov.uk with a list of questions and an outline of the proposal.
- New COVID-19 clinical trial applications should be submitted to the MHRA clinical trial helpline clintrialhelpline@mhra.gov.uk, as well as through the normal CESP route. A pre-assessment service is available, enabling a 2-way communication, rolling review of the submission and this can be arranged via the aforementioned helpline email address. MHRA advice can also be obtained by calling 02030806456. Please ensure that the WHO official acronym – COVID-19 – is entered in the title field of the trial registration data set (Annex 1XML). This will facilitate finding and extracting clinical trials related to COVID-19 from public databases.
- ACCORD will apply the 3 levels of study prioritisation in accordance with the NIHR 'Framework for Restart' (https://www.nihr.ac.uk/documents/restart-framework/24886). This will be adopted for sponsorship reviews and for R&D Governance reviews. The updated prioritisation levels, supported by the Chief Scientist Office (CSO) are as follows;

- **Level 1A (Top Priority) - COVID-19 UPH vaccine and prophylactic studies (as prioritised by the Vaccines Task Force and agreed by Jonathan Van-Tam, deputy CMO) and platform therapeutics trials (currently RECOVERY/RECOVERY +; PRINCIPLE; REMAP CAP).**
- **Level 1B - Other COVID-19 UPH 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 COVID-19 studies not in Level 1A or 1B).**

3. Obtaining Advice

- Should you need to seek advice on COVID-19 or non-COVID-19 related research then please send your enquiry to the appropriate ACCORD mailbox as detailed below;

ENQUIRY	ACCORD MAILBOX
Return of COVID-19 restart risk assessments for monitored studies and queries relating to authorisation to restart monitored studies	monitors@accord.scot
Other queries related to COVID-19 research Sponsored by University of Edinburgh (UoE) and/or NHSL	resgov@accord.scot
Query related to COVID-19 research hosted by NHSL (Sponsored by another organisation)	accord@nhslothian.scot.nhs.uk
COVID-19 research study (Sponsored or Hosted) seeking review by the NHSL COVID-19 Oversight Committee	accord@nhslothian.scot.nhs.uk
COVID-19 research study (Sponsored or Hosted) submitting to the CMVM COVID-19 Committee	CMVM-Covid19.Research@ed.ac.uk
COVID-19 research feasibility query	accord@nhslothian.scot.nhs.uk

4. New Research Proposals

4.1 Grant Deadlines/Milestones

- All grant applications (COVID-19 or non-COVID-19 related research) will be progressed and supported by ACCORD, following normal processes, within the capacity available within the team. The Edinburgh Research Office (ERO) is implementing a policy to provide adequate notice to ACCORD for approval and NHS costing of grants, which should be respected by applicants and the ERO team.

- Researchers are advised to check existing deadlines with funders, as these may be altered or postponed during the COVID-19 pandemic.
- Researchers are advised to provide at least 10 days warning before any deadline if review is required. During the pandemic there can be no guarantee that ACCORD review and sign-off will be possible.

4.2 New COVID-19 Research Proposals

- Those wishing to establish a new COVID-19 related research study (or implement an amendment to an existing study), where funding is in place, should send a short proposal to resgov@accord.scot (sponsored) or accord@nhslothian.scot.nhs.uk (hosted). If the proposal involves UoE resources (e.g. facilities and/or staff members), a Microsoft Form (https://forms.office.com/Pages/ResponsePage.aspx?id=sAafLmkWiUWHiRCgaTTcYU7lg63zEgdBpQ0KDrEnzD9UM0JGUEo3SlJUWUhZV0QwUU5aMFJPSUJNTCQlQCN0PWcu) must be completed, capturing a summary for COVID-19 research proposals for assessment by the CMVM COVID-19 Priority Research Committee. If an Investigator is unsure whether UoE resources will be utilised in their research, they can contact the CMVM committee (CMVM-Covid19.Research@ed.ac.uk) to seek clarification before preparing a form/proposal. Investigators will be notified of the outcome as soon as the assessments are complete. The target time to complete assessments is 48 hours. Any questions about this process can be submitted to CMVM-Covid19.Research@ed.ac.uk. The outcome of the assessment must then be provided to ACCORD (to resgov@accord.scot) for sponsor review.
- Proposals involving the NHS will also be forwarded by the CMVM COVID-19 Priority Research Committee to the NHSL COVID-19 Clinical Oversight Committee to assess logistics, feasibility and capacity within NHSL and competition with existing research.
- Proposals received not involving UoE resources/staff but involving NHS will be forwarded by ACCORD to the NHSL COVID-19 Clinical Oversight Committee for assessment of clinical capacity.
- If the new study does not yet have funding and the proposal includes a grant application for review, this must be submitted to ACCORD (resgov@accord.scot). The outcome of the assessment by the CMVM Committee, if known, must then be provided to ACCORD (resgov@accord.scot) prior to submission of the grant application to the funder.

5. New Research Study Review in ACCORD (COVID-19 & NON-COVID-19)

5.1 Sponsorship Review (UoE and/or NHSL)

- All eligibly funded COVID-19 research (UPH and/or CSO supported) that has received support from the NHSL COVID-19 Clinical Research Oversight Committee will be expedited for sponsorship review/approval, and be prioritised over any non-COVID-19 work. COVID-19 research that is not UPH badged/CSO supported will not be prioritised.
- All research, whether relating to COVID-19 or not, will undergo UoE/NHSL sponsor review and will be progressed for ethics, MHRA, and other relevant non-NHS approvals as usual within the

capacity of the ACCORD UoE Research Governance team, with due consideration of clinical and pharmacy capacity to provide input to sponsor review processes.

- Due to the large volume of proposals at this time, please be aware that sponsor reviews may not progress according to the usual timelines.
- For UoE and/or NHSL sponsored studies, onsite monitoring visits (including Site Initiation Visits (SIVs)) may be arranged on a per study basis, dependent on COVID-19 risk assessment, capacity within the ACCORD monitoring team and the ability of the study team to accommodate a visit, only where compliance with local and national government policy can be ensured.
- Researchers are strongly advised to adjust their study timelines and only plan to progress new studies after COVID-19 pandemic pressures decrease.
- Researchers are advised to inform their funders that timelines will need to take account of the impact of COVID-19.

5.2 R&D Review (sponsored & hosted studies)

- Eligibly funded COVID-19 research (UPH and/or CSO supported) that has received support from the NHSL COVID-19 Clinical Research Oversight Committee will be expedited for NHSL R&D approval to start, and be prioritised over other research. COVID-19 research that is not UPH badged/CSO supported will not be prioritised.
- For non-COVID-19 studies currently under review by NHSL R&D (not yet received R&D management approval):
    - Where there is evidence from the sponsor (commercial or non-commercial) that sponsor set-up is ongoing and progressing AND it is considered feasible that the study will commence recruitment during the pandemic, every effort will be made to progress local NHSL R&D approval.
    - ACCORD will accept new applications to set-up and give local R&D approval for COVID-19 and non-COVID-19 hosted research (commercial and non-commercial) in NHSL . Capacity within the R&D Governance team will remain under regular review throughout the pandemic, and any changes in the prioritisation strategy will be published in revised versions of this document.
    - **Applications for R&D approval for non-commercial studies (sponsored or hosted) that do not have an eligible source of funding are the lowest priority for review and are unlikely to be processed for many months. The CSO list of eligible funders can be seen by following this link;** http://www.nhsresearchscotland.org.uk/uploads/tinymce/NRS%20Funding%20Guidance%20-%20Annex%202%20-%20Eligible%20Funders%2029%20June.pdf
    - Where the PI of a non-commercial, non-eligibly funded study considers there is a strong case to progress NHSL R&D review sooner than may be possible based on the priority level of the study, and the current backlog of work in R&D, an exemption request can be submitted. This request must provide justification as to why the project should be given higher priority for R&D review. This will be reviewed by the COVID-19 Clinical Research Oversight Committee. Any requests for exemption should

be submitted to the following e-mails: Heather.Charles@nhslothian.scot.nhs.uk and Fiona.McArdle@nhslothian.scot.nhs.uk

- The decision of the NHSL COVID-19 Clinical Research Oversight Committee in relation to exemptions will be final. Of note, this committee includes senior members of the ACCORD management team, pharmacy, the CRF, the key research groups delivering COVID research, and several senior independent clinical researchers.

- Due to the large volume of studies under review at this time, please be aware that R&D reviews may not progress according to the usual timelines.
- It should be noted that the NHSL CRFs and EMERGE team, as well as other NHSL support departments, may need to prioritise support for COVID-19 vaccine trials and NIHR UPH COVID-19 research studies in accordance with government guidance.

6. Active Studies (sponsored & hosted)

6.1 Research Study COVID-19 Risk Assessment

- The priority at all sites is the safety of clinical research participants who are already enrolled in studies.
- Specifically, this includes ongoing collection of study data, protocol compliance, clear documentation of protocol deviations and violations, and reporting AEs, SAEs and SUSARs according to the protocol.
- It is possible that participants may not be able to attend hospital for follow-up appointments or other study-related activities.
- Shortages of research staff as a result of illness, self-isolation, or deployment to clinical duties is a risk.
- For CTIMPs, the supply of IMP is also a potential risk.
- If research involves taking samples (blood, sputum, etc.) it is essential to ascertain whether there is concern that the patient has COVID-19 infection. In patients who are symptomatic but not confirmed positive, an individual risk assessment should be undertaken. Ensuring the safety of staff processing samples is paramount.
- The Potential Impact of COVID-19 Risk Assessment Checklist has been provided to assist PIs to assess the potential impact of the COVID-19 pandemic on study activity at their site, taking account of resources and processes required for safe research.
- **Completion of the Potential Impact of COVID-19 Risk Assessment Checklist is mandatory for CIs or PIs running UoE/NHSL sponsored CTIMPs and studies with ACCORD monitoring plans in place and recommended for other studies.**
- **Each Potential Impact of COVID-19 Risk Assessment Checklist should be updated and re-submitted if described risks are thought to have increased since the previous risk assessment document was submitted to ACCORD.**
- **Please follow the guidance in Table 1.**
- **The Potential Impact of COVID-19 Risk Assessment Checklist should be filed in the Investigator Site File (ISF). Only if your study has an ACCORD monitoring plan in place, a copy should be provided to ACCORD** (monitors@accord.scot).

- PIs should decide whether it is feasible for their site to support their studies during the COVID-19 pandemic.
- CIs for multicentre studies sponsored by UoE and/or NHS Lothian are asked to provide clear guidance to all participating sites using the guidance in this document or in the ACCORD Guidance for Restarting Non-COVID-19 Clinical Research document.

6.2 R&D Amendment Review

- UPH badged COVID-19 studies will receive highest priority in relation to reviewing and approving amendments. These will be expedited as quickly as possible.
- Amendments for non-COVID19 research will only be reviewed by the ACCORD R&D governance team if the study is known to have re-started since June 2020, and ACCORD notified of completion of the re-start checklist (as per ACCORD guidance).
- For locally sponsored research, the UoE governance team will continue to receive and progress amendment proposals for sponsor review and progress those, with due consideration for R&D capacity and clinical/pharmacy resources.
- Due to the large backlog of amendments, please be aware that R&D review of amendments may not progress according to the usual timelines.

7. Restarting Research (sponsored & hosted)

- Before restarting a research study, CIs/PIs **must** contact the relevant NHS support departments (e.g. labs), service providers and essential collaborators (e.g. database providers) before they restart the study.
- In Lothian, where the study (sponsored or hosted) involves Edinburgh Imaging facilities, you must contact Dawn Cardy (dawn.cardy@ed.ac.uk) to establish capacity.
- In Lothian where restarting the study (sponsored or hosted) means that you will require access to a UoE laboratory/building, approval by the Sponsor/CI to restart cannot be given until the UoE has approved access for the study to the UoE laboratory/building. It should be noted that based on Government guidance it may not be possible to access University laboratories at this time. To confirm whether this approval is in place, please contact:
    - Edinburgh BioQuarter: Sharon Hannah (sharon.hannah@ed.ac.uk)
    - IGMM / WGH: Angela Ingram (angela.ingram@igmm.ed.ac.uk)
    - Easter Bush: Val Hughes-White (val.hughes-white@ed.ac.uk)
    - Central Area (Biomedical Sciences) Janet Philp (j.philp@ed.ac.uk)
    - Central Area (Usher) Vivien Smith (vivien.smith@ed.ac.uk)
- A flow chart has been provided in Appendix 1 which summarises what a Chief Investigator (CI) or Principal Investigator (PI) needs to do to restart/commence depending on whether the study is sponsored by the UoE and/or NHSL or another organisation, and depending on the regulatory status of the project. More detailed guidance on each study type is also provided in this document.

7.1 Restarting CTIMPs & Non-CTIMPs with an ACCORD Monitoring Plan (sponsored)

- Completion of the Restart Risk Assessment Checklist (Part A-H) is mandatory for CIs running existing UoE/NHSL sponsored Clinical Trials of Investigational Medicinal Products (CTIMPs) and studies with an ACCORD monitoring plan in place (see exception to this below for studies in follow up).
- The study Restart Risk Assessment Checklist must be submitted to ACCORD (Monitors@accord.scot) to obtain Sponsor approval to restart the study.
- The study Restart Risk Assessment Checklist can cover the NHSL site (Part E-H) as well as the study as a whole (Part A-D).
- On receipt of a valid Restart Risk Assessment Checklist from the CI, the Sponsor will approve restart of the study. The Sponsor will copy NHSL R&D (accord@nhslothian.scot.nhs.uk) when the approval is issued.
- CIs for multicentre studies sponsored by UoE and/or NHSL must provide clear instructions about the resumption of new recruitment to all participating sites based on the guidance in this document. The CI is responsible for informing PIs of the Sponsor approval to restart. The Sponsor will provide a letter to be disseminated to sites by the CI/Trial Manager.
- For multi-centre studies, non-NHSL sites must follow local R&D procedures to restart the study, obtaining R&D approval where this is required. PIs from non-NHSL sites need only complete the ACCORD Restart Risk Assessment Checklist where there are no local R&D procedures in place to restart the study to ensure that they have all the resource required to deliver the project and ensure participant safety. Exceptions to this are detailed below (i.e. the MATCH and SNAP-It trials).
- The Sponsor (UoE/NHSL) is delegating approval to restart at other NHS Boards/Trusts/Sites to the local PI, assuming that all local R&D procedures have been followed.
- It is acknowledged that not all sites will be able to restart at the same time and that this will be based on resource/approval at site.
- The CI or Trial Manager is responsible for confirming that each site PI has confirmed capacity to restart and for obtaining a copy of a local R&D risk assessment/checklist or the ACCORD Restart Risk Assessment Checklist (if used). There is no requirement for the CI or Trial Manager to obtain evidence of local support department or R&D sign off to restart at each site.
- Trial Managers must follow up with sites to confirm if any retraining is required at site and to ensure that any deviations/violations and Adverse Events (AEs) which occurred during periods of low resource are now recorded and reported as required.
- The CI or Trial Manager must inform ACCORD when a site has restarted (Monitors@accord.scot). Non-NHSL site PIs do not need to submit site specific checklists to ACCORD (with the exception of the studies mentioned in the next bullet point).
- **The exception to this are the MATCH and SNAP-IT trials which are categorised as 'C' under the ACCORD Combined Risk Assessment procedure (GS002) and will require Sponsor approval to restart per site. The CI or Trial Managers for these studies should ensure that**

the completed site specific Restart Risk Assessment Checklists are submitted to ACCORD (Monitors@accord.scot) for each site.

- CTIMPs and non-CTIMPs with an ACCORD monitoring plan that are in follow up, and have not halted follow up activities, **do not** need to complete the Restart Risk Assessment Checklist.
- CTIMPs and non-CTIMPs with an ACCORD monitoring plan that are in follow up, and did halt follow up activities, **do not** need to complete Part A-D of the Restart Risk Assessment Checklist. However, for trials in follow up in NHSL, that are restarting previously suspended follow up procedures, Part E-H of the Restart Risk Assessment Checklist should be completed and NHSL R&D notified of the restart (accord@nhslothian.scot.nhs.uk). The PI must send this communication to R&D clearly stating in the e-mail ***'As the Principal Investigator of 'STUDY TITLE', I confirm that I have completed the ACCORD Restart Risk Assessment Checklist and all necessary resources to restart this study have been verified by me. On this basis, I plan to restart this study on DD/MMM/YYYY'***. The NHSL R&D team will acknowledge these e-mails and this acknowledgment should be filed in the study Investigator Site File (ISF). These risk assessments **do not** need to be submitted to the ACCORD Monitoring team for approval. However, please note that the Sponsor may request to see the completed Restart Risk Assessment Checklist should the research team raise any queries regarding restart.
- For trials in follow up at non-NHSL sites, that are restarting previously suspended follow up procedures, site PIs should follow local R&D processes for restarting study specific procedures where these may have been halted and ensure any changes to the COVID-19 Study Specific Risk Assessment (ACCORD COVID-19 Clinical Research Plan and Guidance) are updated and submitted to ACCORD where required.
- Documentation associated with local R&D procedures to restart and the Sponsor approval to restart should be filed in the Investigator Site File (ISF).
- The Restart Risk Assessment Checklist and the Sponsor approval to restart should be filed in the Trial Master File (TMF).
- **For UoE/NHSL sponsored studies, CIs do not have Sponsor approval to restart CTIMPs & studies with an ACCORD Monitoring Plan without submitting the Restart Risk Assessment Checklist to ACCORD for review (Part A-D).**
- CIs/PIs should re-visit the risk assessments based on local or national changes in guidance and local resource issues (for example further COVID-19 waves).
- Studies that received ACCORD approval for an exemption to the recruitment halt during the height of the COVID-19 pandemic, where circumstances have not changed since the initial exemption request, need **not** complete the Restart Risk Assessment Checklist or follow local R&D procedures to restart.
- For UoE and/or NHSL sponsored studies, the halt on remote Site Initiation Visits (SIVs) and Sponsor Authorisation to Open Sites (SATOs) has been lifted. Please be aware that at this time the monitoring team will prioritise restart of already active studies before new studies.
- On-site monitoring visits by ACCORD may be arranged on a per study basis dependent on COVID-19 risk assessment, capacity within the ACCORD monitoring team and the ability of the study team to accommodate a visit, only where compliance with local and national government policy can be ensured.

7.2 Restarting Non-CTIMP Studies Sponsored by UoE and/or NHSL

- This applies to non-CTIMPs without an ACCORD monitoring plan only. If the study is a non-CTIMP sponsored by UoE/NHSL and has a monitoring plan, see guidance for restarting above.
- The study Restart Risk Assessment Checklist can cover the NHSL site (Part E-H) as well as the study as a whole (Part A-D).
- Completion of the Restart Risk Assessment Checklist (Part A-H) is required for CIs running UoE/NHSL sponsored non-CTIMP studies that involve NHSL support departments and/or UoE labs. These risk assessments **do not** need to be submitted to ACCORD for approval. However, please note that the Sponsor may request to see the completed Restart Risk Assessment Checklist should the research team raise any queries regarding restart.
- CIs/PIs **must** inform the NHSL R&D department that the study has restarted (accord@nhslothian.scot.nhs.uk). The PI must send this communication to R&D clearly stating in the e-mail ***'As the Principal Investigator of 'STUDY TITLE', I confirm that I have completed the ACCORD Restart Risk Assessment Checklist and all necessary resources to restart this study have been verified by me. On this basis, I plan to restart this study on DD/MMM/YYYY'***. The NHSL R&D team will acknowledge these e-mails and this acknowledgment should be filed in the study Investigator Site File (ISF).
- CIs for multicentre non-CTIMP studies (without a monitoring plan) sponsored by UoE and/or NHSL must provide clear instructions about the resumption of new recruitment to all participating sites based on the guidance in this document. The CI is responsible for informing PIs of the approval to restart.
- For multi-centre studies, non-NHSL sites must follow local R&D procedures to restart the study, obtaining R&D approval where this is required. Non-NHSL PIs need only complete the ACCORD Restart Risk Assessment Checklist where there are no local R&D procedures in place to restart the study. The Sponsor (UoE/NHSL) is delegating approval to restart at other NHS Boards/Trusts/Sites to the local PI, assuming that all local R&D procedures have been followed to ensure that they have all the resource required to deliver the project and ensure participant safety.
- It is acknowledged that not all sites will be able to restart at the same time and that this will be based on resource/approval at site.
- There is no requirement for the CI to obtain evidence of local support department or R&D sign off to restart at each site.
- CIs must follow up with sites to confirm if any retraining is required at site and to ensure that any deviations/violations and Adverse Events (AEs) which occurred during periods of low resource are now recorded and reported as required.
- Non-CTIMPs without an ACCORD monitoring plan, and have not halted follow up activities, **do not** need to complete the Restart Risk Assessment Checklist.
- Non-CTIMPs without an ACCORD monitoring plan that are in follow up, and did halt follow up activities, **do not** need to complete the Restart Risk Assessment Checklist (Part A-D). However, for trials in follow up in NHSL that are re-starting suspended follow up procedures, Part E-H of

the Restart Risk Assessment Checklist should be completed and NHSL R&D notified as above (accord@nhslothian.scot.nhs.uk). The completed checklists **do not** need to be submitted with this notification to R&D. However, please note that the Sponsor may request to see the completed Restart Risk Assessment Checklist (Part E-H) should the research team raise any queries regarding restart.

- For trials in follow up at non-NHSL sites, that are restarting previously suspended follow up procedures, site PIs should follow local R&D processes for restarting study specific procedures where these may have been halted and ensure any changes to the COVID-19 Study Specific Risk Assessment (ACCORD COVID-19 Clinical Research Plan and Guidance) are updated and submitted to ACCORD where required.
- Documentation associated with local R&D procedures to restart and the Sponsor approval to restart should be filed in the Investigator Site File (ISF). These checklists **do not** need to be submitted to ACCORD.
- The overall study Restart Risk Assessment Checklist and the CIs approval to restart should be filed in the Trial Master File (TMF).
- CIs/PIs should re-visit the risk assessment based on local or national changes in guidance and local resource issues (for example further COVID waves).
- Studies that received ACCORD approval for an exemption to the recruitment halt during the height of the COVID-19 pandemic, where circumstances have not changed since the initial exemption request, need **not** complete this risk assessment.

7.3 Restarting Studies Hosted in NHSL

- Completion of this Restart Risk Assessment Checklist (Part E-H) is required for CIs or PIs running studies hosted in Lothian that involves NHSL support departments and/or UoE labs. These restart risk assessments **do not** need to be submitted to ACCORD for approval i.e. by signature of the risk assessment the CI/PI will approve restart of these projects. The CI/PI must send this communication to R&D clearly stating in the e-mail ***'As the Principal Investigator of 'STUDY TITLE', I confirm that I have completed the ACCORD Restart Risk Assessment Checklist and all necessary resources to restart this study have been verified by me. On this basis, I plan to restart this study on DD/MMM/YYYY'***. The NHSL R&D team will acknowledge these e-mails and this acknowledgment should be filed in the study Investigator Site File (ISF).
- CIs/PIs for hosted research projects need to be mindful of any additional information or advice that they have received from the study Sponsor (e.g. requirement to complete a Sponsor restart specific checklist, commercial Sponsors may want to delay re-starting recruitment to their studies if there are supply issues in relation to IMP) and must seek Sponsor approval to restart.
- All CIs/PIs MUST communicate with support departments when completing the Restart Risk Assessment Checklist to ensure that they have all the resources required to deliver their project and ensure patient safety.
- The completed Restart Risk Assessment Checklist should be filed in the Investigator Site File (ISF). These checklists **do not** need to be submitted to ACCORD.

- CIs/PIs should re-visit risk assessment overall based on local or national changes in guidance and local resource issues (for example further COVID waves).
- Studies that received ACCORD approval for an exemption to the recruitment halt during the height of the COVID-19 pandemic, where circumstances have not changed since the initial exemption request, need **not** complete this risk assessment.
- Where local research teams can accommodate them, on-site monitoring visits from other Sponsor organisations can take place on NHSL sites, only where compliance with local and national government policy can be ensured. A remote monitoring facility is provided in NHS Lothian. This should be the default monitoring procedure when government restrictions apply. These activities must comply with organisation and departmental policies e.g. building access rules, PPE and social distancing requirements.
- The NIHR has also released guidance for a 'second wave' of COVID-19 activity. The guidance instructs that the deployment of NIHR funded staff to frontline duties should only occur in exceptional circumstances. The guidance also reiterates that decisions around restarting NIHR research activities should be led locally and the NIHR will continue to encourage non-COVID-19 research to restart, although this may change if NHS priorities change.
- Please be aware that support departments and Heads of Service will not have the capacity to sign off the large number of studies and amendments currently in our system as well as new studies and amendments received in the coming weeks/months. These processes will take longer than usual.
- Amendments relating to hosted non-COVID-19 research that have not re-started since March 2020 will not be reviewed until R&D has received confirmation that the study has restarted (in accordance with the procedure detailed in this document).
- The ACCORD team will continue to progress amendments to studies that have already restarted but there is a significant backlog of work, and delays should be expected.
- CIs/PIs should notify R&D at the earliest opportunity if they do not intend to restart/commence projects that already have R&D management approval or where a local R&D review is in progress i.e. the project will never be restarted or commence. Please contact R&DOffice@nhslothian.scot.nhs.uk.
- **The NHSL Clinical Research Facilities (CRFs) and EMERGE team, as well as other NHSL support departments, may need to prioritise support for COVID-19 vaccine trials and NIHR UPH COVID-19 research studies, in relation to restart/commencement, in accordance with government guidance.**

Table 1: Documentation of Actions

The table below identifies the immediate actions CIs/PIs may need to take in relation to their studies. This table will be kept under regular review by ACCORD and updates issued if changes are needed.

CIs for multicentre studies sponsored by UoE and/or NHS Lothian are asked to provide clear guidance to all participating sites.

Options	Considerations and Documentation
Missed study visit.	Study participants may already be choosing not to attend visits, or sites may be reducing outpatient visits which will impact research visits. **Document each missed visit as a deviation**. More than one missed visit can be recorded on a single deviation report, if the missed visits are within the same study. There is no requirement to report an increase in protocol deviations, as a serious breach, during this period.
Planned reduction in participant checks, deemed to potentially increase risk to participants.	**Submit as a substantial amendment, to REC and R&D only, through the usual email routes, clearly marking with the subject header 'IRAS ref# Amendment – COVID-19' so the amendment can be expedited. Any reduction in participant monitoring visits should be recorded and justified in the each Covid-19 risk assessment however, the MHRA do not need to be notified via substantial amendment.**

Options	Considerations and Documentation
Changes to the nature of the study visit.	Where possible, schedule visits as per the protocol using the flexibility of visit windows. In some cases, participant site visits may be too much burden on site staff/resources. Consider changing participant site visits to phone calls or postal questionnaires. **Handle as a non-substantial amendment.** If home visits are being considered as an option to facilitate safety follow up, consider the following: • Conduct an assessment on the risk of the participant, or family members in the same household being infected with COVID-19. Please refer to the Health Protection Scotland website (or equivalent) for up to date advice on screening questions before confirming the home visit https://www.hps.scot.nhs.uk/a-to-z-of-topics/covid-19/ • Ensure that staff using personal vehicles for business purposes have the appropriate insurance and are registered on the NHSL Grey fleet (or equivalent), to be certain they are insured for work travel and reimbursement of travel expenses Refer to the NHS Lothian intranet - Guidance on the Management and Use of Vehicles Within NHS Lothian (or equivalent). • Loan Working Staff will require a 'buddy' or Guardian Angel' system in place to ensure staff safety: Refer to the NHS Lothian intranet – Lone Working Policy (or equivalent). • If carrying hazardous material or samples, ensure that these are stored and transported safely. When clinic visits become possible again, schedule participants to be seen as soon as possible to complete any missed assessments. **Document out-of-window visits, unplanned missed visits, missed assessments as deviations.**

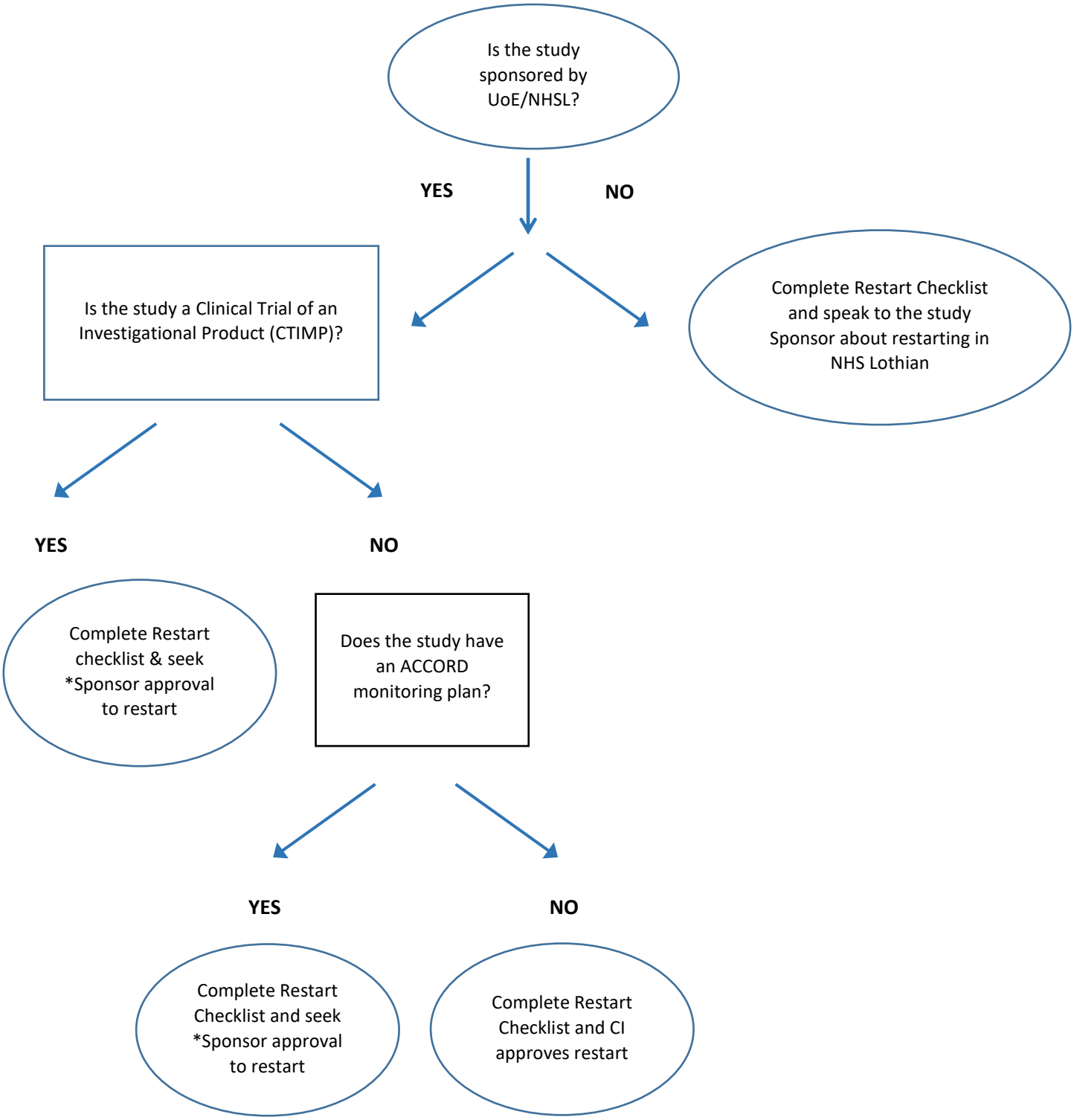
Options	Considerations and Documentation
CTIMPs and regulated device investigations: Changes to site capacity and capability to comply with safety reporting requirements.	As part of the initial completion of a risk assessment, the possible impact of the pandemic on the ability to report Serious Adverse Events (SAEs) to the Sponsor will have been assessed. This initial assessment may change at any time - be aware that any changes potentially impacting an ability to report SAEs and other safety information to ACCORD must be notified to ACCORD as soon as they arise. Revise the Risk Assessment document to reflect any changes in a situation (highlighting the changes), submit to Monitors@accord.scot and await further instructions from ACCORD. Alternatively, if the Restart Risk Assessment Checklist (see ACCORD Guidance on Restarting Non-COVID-19 Clinical Research) can be completed, there is no need to revise the initial risk assessment.
CTIMPs and regulated device investigations: Implement a temporary halt (i.e. site or study wide halt of all trial activity and/or Suspension of recruitment) if required.	If the reason for the halt / suspension of recruitment is due to COVID-19 related capacity or capability reasons, **prepare a file note documenting the reason(s) for the halt and file in the TMF and provide to ACCORD**. If the reason for the halt is due to a participant safety incident, **report as a temporary halt via a substantial amendment to the MHRA and REC in the usual way within 15 days of the halt**. If the reason for the halt is due to an IMP supply issue, **inform the MHRA by email to the clinical trial helpline (to allow them to escalate the issue to DHSC)**. If the study has research sites outside the UK, contact the Competent Authority in each country and seek specific instructions regarding notifications. Ensure sites are informed.
Non-CTIMPs - suspend recruitment only	No amendment is required however inform ACCORD via resgov@accord.scot. Keep a record of this in the study file. Ensure sites are informed.
Non-CTIMPs - Implement a temporary halt (i.e. site or study-wide halt of all trial activity)	**Prepare a non-substantial amendment in accordance with HRA guidance.** Inform ACCORD via resgov@accord.scot. Notify the non-substantial amendment to NHS Lothian R&D if single centre or NRSPCC if multi-centre for their information only. An approval is not required. There is no need to notify the REC. Please keep a record of this in your study file. Ensure sites are informed.
Check sites have sufficient supplies of IMP and other study materials for existing participants.	Check site stock levels.

Options	Considerations and Documentation
IMP Accountability	If COVID-19 related issues affect the ability to perform IMP accountability (including IMP delay/discrepancy), this should be described in the COVID-19 risk assessment and other ways to achieve accountability should be considered. If accountability is not critical, then the drug can be destroyed instead of being returned to minimise exposure to the virus, although the Sponsor and site pharmacies must be involved in this decision. If accountability is important, you (in consultation with the Sponsor and site pharmacies) should consider whether there are other ways this can be achieved whilst mitigating risks to virus exposure. The risks and mitigation for performing drug accountability checks should be documented e.g. ACCORD Study Specific Risk Assessment Potential Impact of COVID-19 v5.0. <u>NHS Lothian Only:</u> • IMP should not be returned to an NHS Lothian pharmacy from an inpatient ward and should instead be destroyed on the ward, except in the RECOVERY trial, where IMP can be moved to another COVID-19 treatment ward. • Used vials should not be returned to an NHS Lothian pharmacy in any circumstances. • IMP returns, from a research team, to an NHS Lothian pharmacy will bagged, labelled and stored for 9 days (minimum) before reconciliation tasks begin. • Participants should not be instructed to return IMP, by post, to an NHS Lothian pharmacy. Participants should instead keep IMP at home and return packs at their next clinic visit, whenever that may be.

Options	Considerations and Documentation
Check study participants have sufficient supplies.	Consider if study supplies e.g. IMP can be delivered directly to participants' homes if it is not feasible for a relative or carer to collect from the hospital on their behalf. This should be described in the COVID-19 risk assessments described in this document, with site pharmacies involved in the assessment. It should also consider if training is required for IMP administration. **Prepare a non-substantial amendment.** Inform ACCORD via regov@accord.scot. Notify the non-substantial amendment to NHS Lothian if single centre or NRSPCC if multicentre for their information only. Approvals are not required. There is no need to notify the REC. **Prepare study specific and/or site specific Work Instructions**. Work Instructions should include the method and conditions of delivery and site specific risk assessments should be considered if methods involve deviating from local pharmacy polices. Consideration should be made to any temperature specific storage and stability profile for the IMP. Any items requiring refrigeration or freezer storage must be transported appropriately. Participants must consent verbally (this should be documented in their notes) to providing contact details for shipping purposes. If the participant does not want to sign for the delivery due to self-isolation, then a follow-up phone call should be used to confirm they have received the package - a process for confirming shipment and delivery must be in place. Where posting medicines to the participant is the only option, Royal Mail Signed For™ is the minimum recommended level of traceability acceptable for posting of medicines, subject to any public health requirements around individuals being able to accept a package and sign for the delivery. Any potential delays to delivery should be considered.
Check ability to store study samples if shipments are not possible.	Review storage capabilities.
If participants are infected with COVID-19 or may have undiagnosed COVID-19 based on clinical symptoms ensure that any samples are dealt with appropriately.	If research involves taking samples (blood, sputum, etc.) it is essential to ask the COVID-19 status of participants. In patients who are symptomatic but not confirmed positive an individual risk assessment should be undertaken. Ensuring the safety of staff processing samples is paramount. Assume that samples should NOT be taken for research purposes from infected or possibly infected patients unless SOPs guaranteeing safety are agreed. For samples used for safety monitoring in NHS local laboratories check with local laboratories to clarify procedures for research participants. **If it is considered necessary to add testing for SARS-CoV-2 to the protocol, follow procedures for an Urgent Safety Measure. The substantial amendment, describing the USM, can be deferred for 28 days after the measures have been taken and email notification.**

Options	Considerations and Documentation
Check ability to identify, document and, where applicable, onward report SAEs to ACCORD.	Consider if timely SAE identification could be compromised by missed/changed visits. **Ensure all SAE reports are sent by email to Safety.Accord@ed.ac.uk. We cannot accept submission by fax or in person for the foreseeable future.**
Check procedures for emergency unblinding procedures can be fulfilled at sites.	Where trials are being adapted, consideration should be given to continuing support for trial critical electronic systems such as Interactive Response Systems used for code-breaking and randomisation activities or safety reporting systems. Where these cannot be supported adequately, consider whether to continue to run the trial or put in place alternative mechanisms, following discussion with ACCORD and the sponsor.
Signatures	If your processes require wet-ink signatures, consider alternative methods of demonstrating approvals, such as email confirmation.
Arrange for all TSC and DMC meetings to be held virtually.	
Drug Safety Reporting	Follow the MHRA advice and procedures in regards to COVID-19 specific drug safety reporting to the MHRA: https://content.govdelivery.com/accounts/UKMHRA/bulletins/28cb65a
ACCORD may postpone/cancel scheduled monitoring visits and Site Initiation Visits.	ACCORD monitoring plans have been reviewed and considerations made around remote monitoring and remote SIVs, where possible. There are no current plans for ACCORD Clinical Trial Monitors to perform on-site monitoring visits and SIVs at this time. This is likely to change in line with the evolving guidance from the Scottish/UK Government.
On-site monitoring visits from other Sponsor organisations	Where local research teams can accommodate them, on-site monitoring visits from other Sponsor organisations can take place, only where compliance with local and national government policy can be ensured. These activities must comply with organisation and departmental policies e.g. building access rules, PPE and social distancing requirements. NHSL has procedures in place to aid remote monitoring.
Where PI is taken off a study	If the absence will be greater than one month, notify the REC. If the absence will be greater than 3 months, alternative arrangements should be put in place.
Equipment maintenance & calibration	During the COVID-19 pandemic, it may not be possible to maintain equipment according to a planned schedule. If you intend to use equipment that has fallen out with its calibration/preventative maintenance dates, before doing so you must assess the risk on patient safety and data integrity. Please discuss with your Sponsor and document rationale and risk mitigation in the Study Specific Risk Assessment. Use of equipment out with calibration/preventative maintenance dates must be recorded as a deviation or violation.

Appendix 1: WHAT TO DO TO RESTART THE RESEARCH PROJECT?



*To obtain Sponsor (UoE and/or NHSL) approval to restart, e-mail your completed and CI/PI signed Restart Risk Assessment Checklist to Monitors@accord.scot.