

Performance in Initiating and Delivering Clinical Trials

UH Bristol research targets introduced through NIHR contracts:

What they are and how researchers can help us meet them

About the targets

For **performance on initiating clinical research**, UH Bristol must now measure and publish data on the days elapsing between the time we receive a valid research application (see page 3) for a clinical trial and the time when the first patient is recruited to the trial, for all clinical trials we host. This applies for all clinical trials irrespective of the funder. Wherever the duration exceeds 70 days, we will be expected to explain the reason for the delay to the NIHR in writing.

For **performance on delivering clinical research**, the initial focus is on commercial contract trials. For this, we will need to publish:

- a) the Target Number of patients we have agreed to recruit to that trial;
- b) the time that we have agreed we would take to recruit the Target Number of patients;
- c) whether trial recruitment here is ongoing or finished; and
- d) if trial recruitment has finished, whether or not the agreed Target Number of patients was recruited within the agreed time.

NIHR has provided some **FAQs**, which I have transcribed below in this document for your information.

Question

Why is the initial focus on data for trial delivery of commercial contract clinical trials?

Answer

There is a perception within industry and other stakeholders, backed up by data, that recruitment to and conduct of clinical trials in the UK is slower, less reliable, and more costly than in many other countries within and outside Europe. This detracts from the undoubted strengths that do exist within the NHS for efficiently conducting high quality research. This perception discourages industry from using the NHS as a setting for undertaking research and indirectly makes the UK a less competitive location for life sciences research. It can deny patients the opportunity of participating in trials of novel interventions.

When will we be expected to publish the first performance data?

NIHR will start requiring quarterly returns to be submitted by this trust, because we have signed new NIHR contracts, from the end of the 1st quarter of the contractual period. The data on clinical trial initiation to be included in each return must include data for every clinical trial for which we have given NHS permission during the previous 12 months. The data on clinical trial delivery must include every commercial contract trial for which we have given NHS permission during the previous 12 months. NIHR will publish further guidance about the requirements for us shortly, and will work with us on improving data quality.

UH Bristol, the contractual period commences 1 April 2012. The reporting period for UH Bristol is 1 July 2011 to 30 June 2012; the first report was submitted on 30 July 2012.

When will NIHR funding to providers of NHS services be affected?

NIHR is making performance in initiating and delivering clinical research a condition in all relevant new contracts issued from December 2011. Performance will not affect NIHR funding to these providers of NHS services until 2013.

What are the financial consequences of not meeting benchmarks?

There may be legitimate reasons why it takes longer than 70 days to recruit the first patient to a trial, for example in the case of an extremely rare disease. Subject to this, from 2013, a provider of NHS services which does not meet the NIHR 70-day benchmark for trial initiation for two successive quarters, and which is unable to provide satisfactory explanations, will find the Department of Health suspends payments due on the research contract. In addition, performance against benchmarks will be taken into account when NIHR considers further applications from the provider for new research contracts.

What explanations for not meeting benchmarks will be taken into account?

The Department will act in a reasonable and fair way, taking into consideration any factors outside our control that have contributed to the delay. This information will also help NIHR understand better the factors that inhibit the successful initiation and delivery of clinical studies. See Table 1 at the end of this document for list of options provided by DH.

How will providers of NHS services seek review of NIHR decisions?

Any disputes around performance and initiating clinical research will be resolved according to the clauses in the contract for all dispute resolution. Disputes will be resolved by negotiation in the first instance and whenever possible. If the matter cannot be resolved by negotiation, then the parties must attempt to resolve through an agreed alternative dispute resolution (ADR) procedure. If not resolved by an agreed ADR, then final and binding arbitration will apply – clause 30 refers.

What is a valid research application?

A complete research application that has been received by the trust’s research management office following its submission via the Integrated Research Application System (IRAS) that enables regulatory reviews by other agencies (including but not limited to Research Ethics Committee and MHRA approval) to be conducted in parallel with the work on NHS permission by the research management office (see later section ‘R&D application for NHS permission’).

What is a clinical trial?

The definition being used for the purposes of this exercise is “A clinical trial is a set of medical research procedures conducted on human participants to allow safety and adverse effects of interventions, their efficacy, or their effectiveness to be established, often by comparison with alternative or placebo/sham interventions. Interventions may be drugs, diagnostics, prophylactics, surgery, devices, non-invasive therapies, screening or other healthcare procedures or technologies”.

How do the data requirements differ from the NIHR Clinical Research Network’s High Level Objectives relating to reduction in time to achieve NHS permission, reduction in time to recruit the first patient to NIHR CRN Portfolio studies, and delivery to recruitment time and target?

The collection of our data on initiating and delivering clinical research is a separate exercise from the collection of performance data by the NIHR Clinical Research Network (CRN) against the CRN High Level Objectives. However both exercises have, as overall aims, increasing the number of patients able to participate in research, and enhancing the nation’s attractiveness as a host for research. Some specific differences are that this exercise relates to all clinical trials, regardless of funder and NIHR CRN Portfolio status (rather than to NIHR CRN Portfolio studies only), and that data are collected on an individual NHS provider basis (rather than on an individual study basis).

How are we collecting the

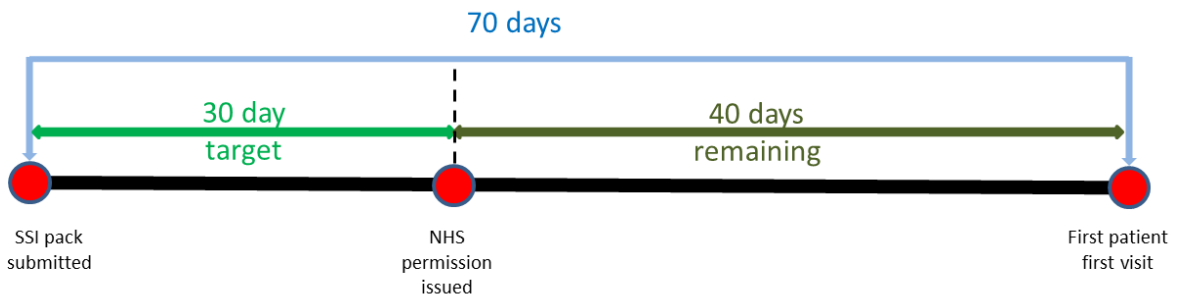
We are running reports on data entered into EDGE.

data in UH Bristol?

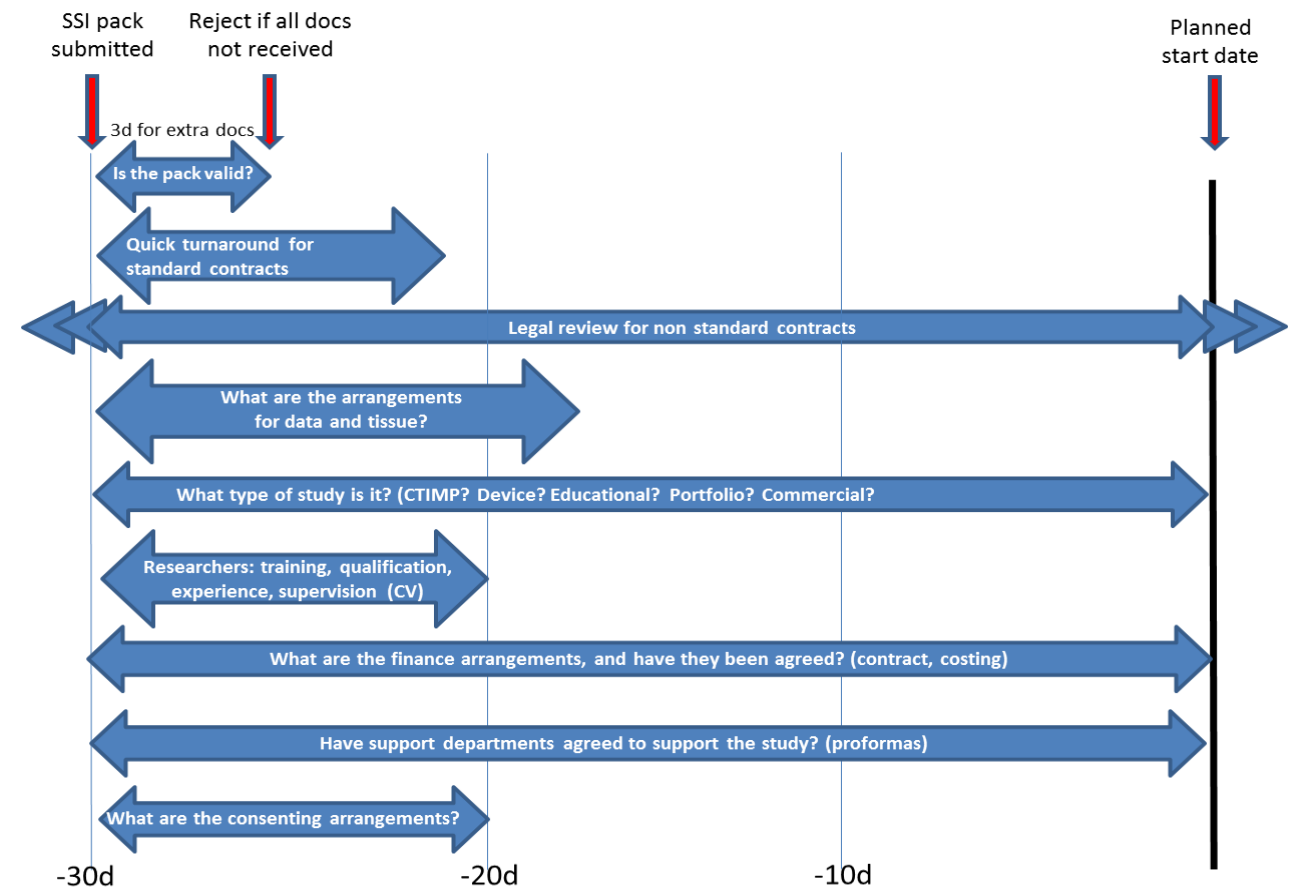
This is why it is important that you enter information about recruitment of patients in real time. You will be contacted by a member of the R&D team if we cannot see data in EDGE for your studies.

How can researchers help meet the targets?

Our target is to recruit the first patient into a clinical trial within 70 days of submitting for R&D approval. Our target for issuing NHS permission (R&D approval) is 30 days after submission.



If we can reduce the time to NHS permission, then we have more chance of meeting the 70 day target. When we receive an application for NHS permission (R&D approval) we have to carry out certain checks, which are illustrated here:



You can help us reduce time to NHS permission (R&D approval) by doing the following things.

Contracts

If there are any contractual arrangements to put in place, discuss these with the research management team as early as possible, before you are ready to submit for NHS permission (R&D approval) through IRAS.

Support departments

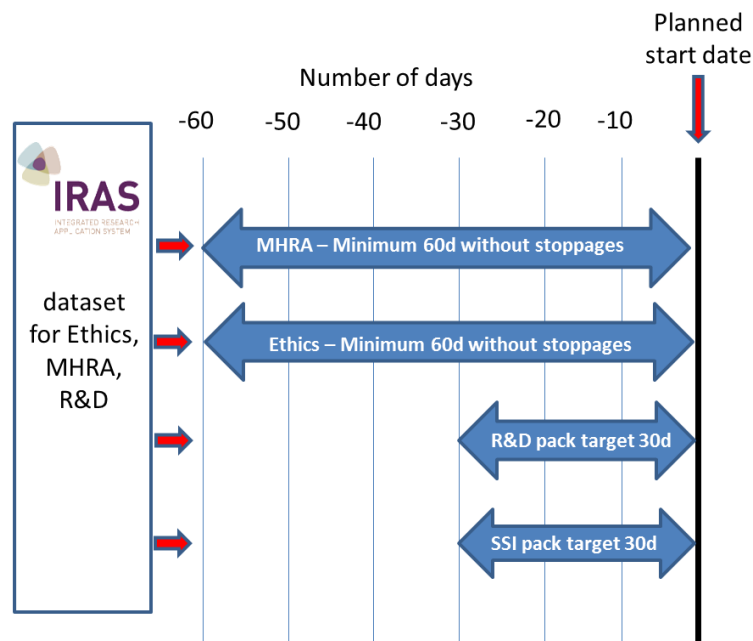
Talk to all support departments about your study – pharmacy, radiology, cardiology, laboratory medicine - and make sure you have documented their agreement to support it. See <http://www.uhbristol.nhs.uk/research-innovation/are-you-a-researcher/information-for-researchers/forms-and-templates/> for proformas and contact details.

R&D application for NHS permission

Submit a valid application for review by the research management team. If you're not sure what this consists of, please refer to the relevant IRAS checklist for your study (see <https://www.myresearchproject.org.uk/Help/IrasCheckLists.aspx>); if you are still unsure, contact the research management team for help before you submit. If there are no contractual difficulties and we receive a valid application, we expect to be able to approve your study within 30 days of receipt.

Other approvals – Ethics and MHRA

Your R&D application, MHRA and ethics applications are each submitted out of the single data set held in IRAS ('www.myresearchproject.org.uk').



It is possible to submit MHRA, Ethics and R&D all at once. However, if you **submit your R&D pack and SSI pack after MHRA and ethics, you can dovetail approval time with other approvals.**

Recruiting your first patient	Carefully plan the logistics of the study and what needs to be in place before you can recruit your first patient. You must do this before submitting your application for NHS permission (R&D approval) through IRAS. Your divisional research unit should be able to support you in this. Please contact R&I for contact details if you need them.
Staff	Before you submit your application for NHS permission (R&D approval) make sure that you have the necessary staff in place to run the study and recruit patients, if staff are required,. Don't forget to request letters of access or honorary research contracts if you need them.
Patients	Think about where you will recruit your patients from. Carry out feasibility checks to ensure that your patient population can really be recruited from the centres/clinics which you have access to. Try to identify in advance a list of patients who might be suitable for the study. Tell your colleagues and other staff who might see eligible patients about the study, and ask them to recruit into the study. Consider what the patient pathway for the whole study will be, and how you can make this straightforward for your patients to take part.
Targets	Agree realistic targets for the study, based on feasibility checks and experience, and in conjunction with a review of the inclusion and exclusion criteria. Never agree to an unrealistic target that you cannot meet. Ensure the agreed target is clear and consistent throughout your submission for NHS permission and contract (if applicable). The agreed recruitment period should also be clearly defined.
Taking part	Only agree to do a study if you think you can deliver on it.
Reasons for not recruiting	Document why you are having problems with recruiting to a study. It might be helpful if you can base these on the reason codes, which are attached at the end of this document.

Please contact someone in the R&I office if you would like more information or support:
research@uhbristol.nhs.uk or 0117 342 0223.

Table 1: POSSIBLE REASONS FOR NOT MEETING THE 70 DAY BENCHMARK

In order to facilitate data collection and analysis, a number of possible reasons for not meeting the 70 day benchmark have been provided on the template:

- a) **Relevant permissions have not yet been granted**
 - Study-wide review not yet completed
 - Local review not yet completed
 - NHS Research Ethics Committee review not yet completed
 - Medicines and Healthcare products Regulatory Agency (MHRA) review not yet completed
 - Other regulatory reviews not yet completed
 - NHS permission letter not yet issued
- b) **Relevant permissions have been refused**
 - Study-wide review unsuccessful
 - Local review unsuccessful
 - Favourable ethical opinion not granted
 - MHRA approval not granted
 - Other regulatory approvals not granted
- c) **Study suspended by sponsor**
 - Study suspended at all sites
 - Study suspended at this site
- d) **Study closed by sponsor**
 - Safety reasons
 - Lack of clinical equipoise, as defined by the sponsor
 - Change in development pipeline within sponsor company
 - Strategic/financial reasons within sponsor company
- e) **Study-wide recruitment completed**
- f) **Staff availability issues at site**
- g) **Delayed site initiation visit**
- h) **Delayed confirmation from sponsor of study open to recruitment at site** (*i.e.* delays in receiving “Green Light”)
- i) **No eligible patients seen during the reported period**
- j) **Eligible patients seen during the relevant period but did not consent to participate in the trial**
- k) **Contracting delays**
 - Within NHS provider
 - Within sponsor company
- l) **Other** (please describe)

Please note that the inclusion of a possible reason for non-compliance on this list does **not** necessarily mean that this reason will be deemed to be acceptable.