Information document

| Title: Types of Clinical Studies (inc. NIHR Portfolio) | |
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## 1. Scope

This document explores the categories of clinical studies and the additional requirements and procedures that may apply to certain project types. It is important to note that what is considered research at Bournemouth University, may not be considered research within the NHS.

## 2. Responsibilities

The *Chief Investigator (CI)/Researcher* is responsible for ensuring that s/he secures Bournemouth University (BU) sponsorship before making any applications for NHS REC and HRA approval[1], via the Integrated Research Application System (IRAS). The CI/Researcher is also responsible for ascertaining (with the assistance of the Clinical Governance Advisor, and Wessex Clinical Research Network), whether their project is eligible for National Institute for Health Research (NIHR) portfolio adoption.

If no application for portfolio adoption will be made, then the CI/Researcher must ensure that s/he corresponds with their participating sites' R&D departments as early as possible, in order to confirm their ongoing interest to open the study.

The CI in the case of Clinical Trials of Medicinal Investigational Products (CTIMPs), or device studies, is responsible for ensuring that s/he is aware of, and implements the additional requirements as laid out in the Statutory Instrument 2004/1031. Similarly, they must categorise their project according to the MHRA definitions of –

- **Type A** = No higher than the risk of standard medical care;
- **Type B** = Somewhat higher than the risk of standard medical care;
- **Type C** = Markedly higher than the risk of standard medical care.
  (Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products, 2011)

*See BU RDS SOP 017.*

The *Clinical Governance Advisor* (CGA) is responsible for liaising with BU staff in establishing the category of their research study, and advising as to which approval bodies

[1] Please note, as of June 2018, HRA approval is now HRA and Health and Care Research Wales (HCRW) approval

they will need to apply. The CGA will also act as a reference to study staff at BU with regard to the NIHR portfolio, and the requirements and implications of running a study that has portfolio status.

## 3. Procedure

3.1 There a multiple factors that will influence the way a research project is categorised, in turn determining the approvals required. Additionally, with the existence of the NIHR Clinical Research Network (CRN) portfolio, there are further implications to consider.

3.2 *Clinical Trials* (that is, studies where treatment(s) are being investigated), fall into *phases*:

- A phase I trial is when an Investigational Medicinal Product (IMP) is being tested for the first time in human beings (Health Research Authority, 2018). These trials look at how the drug behaves in a human participant, in comparison with how it behaved in laboratory studies. The trial will also look into the safe dosing of the drug and its side effects. Only accredited units may run phase I studies.

- A phase II trial is larger than phase I, and often look at a new treatment in comparison to a treatment already in use in the given population. Phase II trials may identify additional side effects, and will enhance understanding of the best dose to use. If the results show that the new treatment is just as effective as the existing treatment then it will move into phase III. Some phase II trials are *randomised* (defined in point 3.6)

- Phase III trials compare new treatments with the best currently available treatment (standard treatment). These trials may also look into different doses or ways of administering standard treatment, and will involve a significantly larger participant population than phase I and II trials. Most phase III trials are randomised.

- Phase IV trials take place once a drug has been granted marketing authorisation, and look into the side effects of the drug, alongside the long term risks and benefits. Phase IV also investigate how well the drug will work if used more widely (for conditions other than what it is licensed for, for example).

3.3 Although most commonly, *interventional* studies are thought of as investigations through the use of drug products, there are also studies using devices, such a knee replacements, which are likewise identified as *interventional.* Similarly, interventions such as technology (e.g. text messaging), exercise, and new diagnostic testing (e.g. collecting samples via a new bowel screening kit) will mean that a study is classed as such.

Any study intervening in the patient's care will be categorised as interventional.

3.4 As alluded to above, within the research landscape *interventional* studies are mostly associated with investigations of new drugs or drugs being used for a new indication. Researchers should check when embarking on an interventional project as to whether the intervention they are using is CE marked, as this can affect the level of involvement required by the MHRA.

In addition, some products, although not 'drugs' can be identified as investigational products, for example in the past few years, a study looking at *chewing gum* vs. ibuprofen for orthodontic pain, required MHRA Clinical Trial Authorisation. Similarly studies using herbal products such as ginseng, have been categorised the same. Further information on this may be found here and at the end of this document.

In order to reduce bias in a given study, the Investigator may decide to introduce *randomisation* to their study. Randomisation is when study participants are allocated to one of the trial groups at random.

For example, participants are randomised in a study investigating one type of bandage vs. another, post-surgery or patients are randomised to receiving the investigational drug vs. the standard care or placebo. In order to further reduce bias, the Investigator may decide to introduce blinding. There are four categories of blinding:

- Un-blinded – all parties are aware of the treatment participants are receiving;
- Single-blind – only the participant is unaware of the treatment they are receiving;
- Double-blind – the participant and clinicians/study staff are unaware of the treatment the participant is receiving;

Triple-blind – the participant, clinicians/study staff *and* the trial statisticians are unaware of the participant's treatment.

3.5 When a study is not classed as interventional, then it will be classed as *observational*. These studies do not include any intervention, but the Investigator wishes to observe a particular group of participants or staff.

Examples of observational studies may be where participants with a certain condition or illness receive quality of life questionnaires during their standard care treatment, or when a certain group of patients have a blood sample taken for further analysis and clinical data collected on their comorbidities. Studies conducting interviews/focus groups or handing out simple surveys or questionnaires are classes as observational studies.

3.6 In place of participant randomisation, a study may be *cluster randomised.* This is when the *sites* participating in the study are randomised themselves, so that *groups* of participants are randomised, rather than on an individual basis. The study may be investigating the service within healthcare, or may be investigating treatments. For example, sites are randomised to administering one of two treatments to all its participants, e.g. Poole Hospital was randomised to plan A (aspirin), whereas Bournemouth Hospital was randomised to plan B (ibuprofen).

3.7 Alongside the newly introduced HRA approval process (April 2016), the concept of *Non-Capacity & Capability studies* was likewise introduced. These projects require HRA approval only, and the HRA may assess these as not requiring a capacity and capability review by NHS sites. These may be studies for example where
In this instance, projects are sent to the generic Trust R&D email (for sites listed in Part C of

the IRAS form). Within this email the Sponsor will confirm whether the research can be implemented immediately at site or whether a 35 day review for 'no objection' is required. If the NHS site does not respond, then you may assume that the project will go ahead at site and you may approach whoever is required for the purposes of the research.

Useful links

3.8 If unsure as to whether a study is classed as a CTIMP, then the MHRA have provided the following algorithm (see references).

Likewise, the following document is available to ascertain whether a given project is *research* within the NHS setting (see references).

NIHR CRN portfolio projects

3.9 Whether a study is identified as interventional or observational, if it is adopted onto the NIHR CRN portfolio, then it will be further categorised as either: band 1, band 2, band 3, or band 4.

This table (NIHR CRN, 2017) shows how many 'points' per patient a site recruiting to the portfolio study, is awarded, determined by the banding of the project. The 'points' also carry funding, depending on the NIHR budget for the given year, identified as *Activity Based Funding (ABF points)*. Recruiting NHS sites will report a forecast of their recruitment, and therefore the points they are expecting to gain, to the NIHR each year.

Depending on the nature of the research study, and the activities required in order for the site to meet the protocol requirements, Trust R&D may need to make an application to their local Clinical Research Network (CRN) in order to secure Excess Treatment Costs (ETCs). ETCs are identified in the HRA Schedule of Events Cost Attribution Tool document, for non-commercial studies.

According to AcoRD (Attributing the costs of health and social care Research and Development), costs associated with a research study are categorised as either a research cost, service support cost or a treatment cost. There is a funding attribution document as an appendix document to this SOP. The Study Support team at the local CRN may be contacted for advice and guidance with regard to ETCs.

By successfully obtaining portfolio adoption for your study, the research gains the support of the local CRN, who can advertise the study to additional sites within the network. The local CRN likewise supports the researcher throughout the lifecycle of the project.
The NHS Trusts conducting the study likewise benefit, as they receive points and are awarded funding from the CRN, in receipt of adopting portfolio research. By virtue of portfolio status, the Trust may then provide the support of their own staff such as Research Nurses and Data Managers to assist you in the conduct of your study.

## 4. Abbreviations and definitions

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| ABF | Activity Based Funding |
| CGA | Clinical Governance Advisor |

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| CI | Chief Investigator |
| CRN | Clinical Research Network |
| CTIMP | Clinical Trial of an Investigational Medicinal Product |
| HRA | Health Research Authority |
| IMP | Investigational Medicinal Product |
| IRAS | Integrated Research Application System |
| MHRA | Medicines and Healthcare products Regulatory Agency |
| NIHR | National Institute for Health Research |
| PI | Principal Investigator |
| REC | Research Ethics Committee |

## 5. Related documentation and references


BU RDS SOP 017 - Sponsorship Role

Defining Research. (2017). [PDF] Health Research Authority. Available at: http://www.hra-decisiontools.org.uk/research/docs/DefiningResearchTable_Oct2017-1.pdf [Accessed 13 Apr. 2018].

GOV.UK. (2013). *Decide if your product is a medicine or a medical device*. [online] Available at: https://www.gov.uk/guidance/decide-if-your-product-is-a-medicine-or-a-medical-device#borderline-medicines [Accessed 4 Jan. 2019].

Health Research Authority. (2018). *Phase 1 clinical trials*. [online] Available at: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/phase-1-clinical-trials/ [Accessed 4 Jan. 2019]

MHRA - Is It A Clinical Trial of A Medicinal Product? https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/317952/Algothrim.pdf

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The Medicines for Human Use (Clinical Trials) Regulations 2004 - Statutory Instrument 2004/1031. (2004). pp.10-11 - http://www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf [accessed 13th April 2018]