Policy:

UoB Clinical Research Definitions

# Purpose

This policy describes the definitions used by the University of Birmingham (UoB) to distinguish between the different types of projects in clinical research. This document also includes a decision matrix, authored by the Medicines and Healthcare products Regulatory Agency (MHRA), that can be used to determine whether, or not, a clinical research project is a clinical trial of a medicinal product.

Where clarification is needed on whether a project is a clinical trial of a medicinal product, please contact the [Research Ethics, Governance and Integrity Team](mailto:researchgovernance@contacts.bham.ac.uk) (REGI). It is recommended that the REGI are contacted at the initial conceptualisation of the project (e.g. at the grant-application phase) to ensure that the project is adequately resourced.

See the Clinical Research Quality Manual (UoB-CQM-POL-001) for details on the UoB’s framework for conducting clinical research, and the Project Set-up SOP (UoB-SET-SOP-001) for the procedures for setting up a clinical research project with the necessary approvals.

# Scope

This policy applies to all those who work in any UoB clinical research.

# Implementation plan

This policy will be implemented in line with this document’s effective date.

# Stakeholders

* UoB staff members and others working with the UoB quality management system (QMS) for clinical research.

# Clinical Research Definitions

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| --- | --- | --- |
| **Research type** | **Definition** | **Features** |
| Clinical trial of an investigational medicinal product (CTIMP) or advanced therapy (ATIMP) | An investigation of one or more investigational medicinal products (IMPs) in human participants in order to determine their safety, efficacy, clinical effectiveness, or pharmacological or pharmacodynamic effects. *Précised form of EU Clinical Trial Directive 2001/20/EC, Article 2(a).*  Investigational medicinal product: a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorization but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form. *IMP definition EU Clinical Trial Directive 2001/20/EC, Article 2(d).* | Protocol-driven allocation to receive intervention. |
| Clinical trial, non-CTIMP | Prospective interventional biomedical research not involving IMPs in human participants to determine safety, efficacy or effectiveness of the intervention. | Protocol-driven allocation to receive intervention.  Examples include devices, surgery and radiotherapy trials. |
| Clinical studies | Research projects that use human participants or human data to evaluate biomedical or health-related outcomes | May involve an intervention, but solely for the purposes of acquiring biomedical information.  No randomised allocation except for cross-over designs which randomize order of receipt of the intervention and the comparator in observational studies.  This may include UKCA (CE)-marked medical device(s) that are used within its intended purpose.  Analysis of routinely collected data.  Physiology studies involving human volunteers. |
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## MHRA’s Decision Matrix

This algorithm and its endnotes can be used for determining whether a clinical research project is a CTIMP, a non-CTIMP interventional clinical trial, or a non-interventional clinical trial. Please start in column A and follow the instructions. Additional information is provided in the notes at the end of the table. Adopted from the [MHRA’s online algorithm (“Is it a clinical trial of a medicinal product?”)](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/317952/Algothrim.pdf), with permission under the [Open Government Licence v3.0](https://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/).

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| --- | --- | --- | --- | --- |
| **A** | **B** | **C** | **D** | **E** |
| **A CLINICAL TRIAL OF A MEDICINAL PRODUCT?** | | | | **A NON-INTERVENTIONAL CLINICAL TRIAL** |
| **Is it a medicinal product? i** | **Is it not a medicinal product?** | **What effects of medicine are you looking for?** | **Why are you looking for those effects?** | **How are you looking for those effects?** |
| If you answer no to all the questions in column A, the activity is not a clinical trial on a medicinal product.  If you answer yes to any of the questions below go to column B. | If you answer yes to the question below in column B the activity is not a clinical trial on a medicinal product. ……………  If you answer no to the question below go to column C. | If you answer no to all the questions in column C the activity is not a clinical trial under the scope of Directive 2001/20/EC.  If you answer yes to any of the questions below go to column D. | If you answer no to all the questions in column D the activity is not a clinical trial under the scope of Directive 2001/20/EC.  If you answer yes to any of the questions below go to column E. | If you answer yes to all these questions the activity is a non-interventional trial which is outside the scope of Directive 2001/20/EC. If your answers in columns A, B, C & D brought you to column E and you answer no to any of these questions the activity is a clinical trial within the scope of the Directive. |
| A.1 Is it a substance ii or combination of substances presented as having properties for treating or preventing disease in human beings?  A.2 Does the substance function as a medicine? i.e. can it be administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or to making a medical diagnosis or is otherwise administered for a medicinal purpose?  A.3 Is it an active substance in a pharmaceutical form? | B.1 Are you only administering any of the following substances?   * Human whole blood iii * Human blood cells * Human plasma * Tissues except a somatic cell therapy medicinal product iv * A food product v (including dietary supplements) not presented as a medicine * A cosmetic product vi * A medical device | C.1 To discover or verify/compare its clinical effects?  C.2 To discover or verify/compare its pharmacological effects, e.g. pharmacodynamics?  C.3 To identify or verify/compare its adverse reactions?  C.4 To study or verify/compare its absorption, distribution, metabolism or excretion? | D.1 To ascertain or verify/compare the efficacy vii of the medicine?  D.2 To ascertain or verify/compare the safety of the medicine? | E.1 Is this a study of one or more medicinal products, which have a marketing authorisation in the Member State concerned?  E.2 Are the products prescribed in the usual manner in accordance with the terms of that authorisation?  E.3 Does the assignment of any patient involved in the study to a particular therapeutic strategy fall within current practice and is not decided in advance by a clinical trial protocol viii ?  E.4 Is the decision to prescribe a particular medicinal product clearly separated from the decision to include the patient in the study?  E.5 Will no diagnostic or monitoring procedures be applied to the patients included in the study, other than those which are applied in the course of current practice?  E.6 Will epidemiological methods be used for the analysis of the data arising from the study? |

i Article 1.2 of Directive 2001/83/EC is replaced by Article 1.1 of Directive 2004/27/EC which provides the definition of "medicinal product" which applies for the purposes of Directive 2001/20/EC.

ii Substance is any matter irrespective of origin e.g. human, animal, vegetable or chemical that is being administered to a human being.

iii This does not include derivatives of human whole blood, human blood cells and human plasma that involve a manufacturing process.

iv Somatic cell therapy medicinal products use somatic living cells of human (or animal) origin, the biological characteristics of which have been substantially altered as a result of their manipulation to obtain a therapeutic, diagnostic or preventative effect (in humans) through metabolic, pharmacological and immunological means.

v Any ingested product which is not a medicine is regarded as a food. A food is unlikely to be classified as a medicine unless it contains one or more ingredients generally regarded as medicinal and indicative of a medicinal purpose.

vi The Cosmetic Directive 76/768/EC, as amended harmonises the requirements for cosmetics in the European Community. A "cosmetic product "means any substance or preparation intended for placing in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and mucous membranes of the oral cavity with the view exclusively or principally to cleaning them, perfuming them or protecting them in order to keep them in good condition, change their appearance or correct body odours.

vii Efficacy is the concept of demonstrating scientifically whether and to what extent a medicine is capable of diagnosing, preventing or treating a disease and derives from EU pharmaceutical legislation.

viii Assignment of patients to a treatment group by randomisation planned by a clinical trial protocol cannot be considered as current practice

# Related documents

* UoB-CQM-POL-001 Clinical Research Quality Manual
* UoB-SET-SOP-001 Project Set-up

Access to the full UoB QMS for clinical research is available via the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx).

# References and frameworks

* Applying for clinical trial authorisation in the UK: <https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk>
* EC Clinical Trial Directive 2001/20/EC (4 April 2001): <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02001L0020-20090807&from=EN>
* Health Research Authority (HRA) guidance on approvals and decisions required: <https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/>
* HRA guidance on whether a study is ‘research’: <https://www.hra-decisiontools.org.uk/research/>
* Integrated Research Application System (IRAS): <https://www.myresearchproject.org.uk/>
* MHRA’s decision matrix for determining whether a clinical research project is a CTIMP, a non-CTIMP interventional clinical trial, or a non-interventional clinical trial: <https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/317952/Algothrim.pdf>
* MHRA – Regulatory guidance for medical devices: <https://www.gov.uk/government/collections/regulatory-guidance-for-medical-devices>
* Open Government Licence for public sector information: <https://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/>
* UoB Code of Practice for Research: <http://www.birmingham.ac.uk/Documents/university/legal/research.pdf>
* UoB REGI: [researchgovernance@contacts.bham.ac.uk](mailto:researchgovernance@contacts.bham.ac.uk)
* UoB sponsorship process: <https://intranet.birmingham.ac.uk/finance/RSS/Research-Support-Group/Research-Governance/How-to-apply-for-UoB-Sponsorship.aspx>

# Abbreviations and definitions

| Term | Description |
| --- | --- |
| ATIMP | Advanced therapy investigational medicinal products |
| CRCT | Clinical Research Compliance Team |
| CTIMP | Clinical trial of an investigational medicinal product |
| HRA | Health Research Authority |
| IRAS | Integrated Research Application System |
| IMP | Investigational medicinal product |
| MHRA | Medicines and Healthcare products Regulatory Agency |
| QMS | Quality management system |
| UoB | University of Birmingham |

See also the [Glossary of Terms](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/Glossary-of-Terms.aspx).