Standard Operating Procedure:

Food and Nutritional Components

# Purpose

This standard operating procedure (SOP) describes the procedures for sourcing, storage, preparation and administration of food and/or nutritional components to participants. It includes repackaging and labelling of any bulk supplies, and the disposal of excess product.

# Scope

This SOP is applicable to all University of Birmingham (UoB) sponsored clinical research where food and/or nutritional components are sourced, stored, prepared and/or administered to participants. Where clinical research is (co-)sponsored by another institution, this procedure should be followed as far as possible, and in line with the contractual agreement between the UoB and the other institution. This SOP also applies to clinical research approved by UoB Research Ethics Committee (REC) that are required to follow the UoB Principles of Good Clinical Practice (GCP) for Clinical Research (UoB-GCP-POL-001). This SOP may be used as a guidance document in all other cases.

# Implementation plan

This SOP will be implemented directly after the effective date for any clinical research that is still in the set- up phase. For existing clinical research that has already been set up and is in the recruitment phase (or further) at the time of implementation, this SOP will be implemented within 12 months of the effective date.

# Stakeholders

Note that where a clinical trials unit (CTU) is involved, the CTU may take on responsibility for aspects of the procedures relating to food and nutritional components. The CTU may delegate these duties further to their trials team(s). All delegation of duties will be documented e.g. using the Clinical Trials Task Delegation Log (UoB-SPO-QCD-001).

* Chief investigator (CI): the CI may delegate activities to members of their research team, although evidence of CI involvement and approval is still expected and may not be delegated where ‘no delegation allowed’ is indicated. The SOP will state where delegation is possible. For clinical research approved by UoB REC, the role of CI may be termed the principal investigator, or the supervisor for the postgraduate research student.
* Authorised healthcare professional (i.e. doctor, dentist, nurse or pharmacist). This may be the CI where they are an authorised healthcare professional.

# Background and rationale

The purpose of this document is to explain the procedures for the sourcing, preparation, handling and storage of food and nutritional components intended for human consumption as part of a clinical research project. Robust procedures are required for the use of food and nutritional components to ensure the safety and well-being of the participant (see UoB Principles of GCP for Clinical Research (UoB-GCP-POL-001)).

Nutritional components include macronutrients (e.g. carbohydrates and/or protein supplements) and micronutrients (e.g. vitamin and/or minimal supplements).

In this document, preparation of nutritional components may include: (i) the manufacture of components in combination with other reagents; (ii) encapsulation of a supplement; (iii) preparation of components incorporating stable isotope tracers for oral ingestion or intra-venous infusion; (iv) addition of a component(s) to a liquid prior to administration and; (v) repackaging of a product from bulk supply. The preparation of food products includes any processing/cooking of the food products, and repackaging of the food if it is to be consumed at a later time.

Where the product(s) will be parenterally administrated (i.e. administrated by non-oral means), additional safety measures must be incorporated into the research processes, see ‘Parenteral administration’ section below.

In the event of an adverse event, whether related or not to the food and/or nutritional component, see the Adverse Event Reporting SOP (UoB-AES-SOP-001) for reporting requirements.

For deviation and serious breach reporting, see the Deviations and Serious Breach Reporting SOP (UoB-DSB-SOP-001).

# Procedure

## Project classification

1. For use of nutritional components, the CI (or delegate) will determine whether the nutritional component is an investigational medicinal product (IMP) and therefore the clinical research project is classified as a clinical trial of an investigational medicinal product (CTIMP). Refer to the UoB Clinical Research Definitions (UoB-CRG-POL-002).

## Training and facilities

1. The CI (or delegate) will ensure and evidence that relevant staff are appropriately trained in the handling of food and/or nutritional components, and informed of their roles within the project before undertaking their respective tasks. See the Training SOP (UoB-TRN-SOP-001).

* It is expected that staff are trained to at least a Level 2 Food Safety and Hygiene standard.

1. The CI (or delegate) will ensure, as far as is practicable, that staff affected by an infectious disease or who have open lesions on exposed surfaces of the body (that cannot be covered by waterproof dressing) do not engage in activities relating to the handling of food and/or nutritional components.
2. Where relevant, the CI (or delegate) will ensure equipment used is maintained and that servicing and calibration checks are performed (see the Equipment Maintenance Schedule (UoB-CRL-QCD-010). Note that this QCD is intended for clinical trials but could also be utilised for studies to support best practice. See also the Laboratory Facilities SOP (UoB-CRL-SOP-002) for more information.

* Is it expected that defective equipment is removed (if possible), or clearly labelled as defective.

1. The CI (or delegate) will document the appropriate facilities and personal protective equipment (PPE) to be used for the handling and storage of food and/or nutritional components, ensuring the following:

* there is access to hand-washing facilities
* gloves are used to prevent direct contact with the product, or any equipment that comes in contact with the product
* no eating, drinking, chewing or smoking, or the storage of any personal food, drink, smoking materials or medication in the facilities
* storage facilities are capable of maintaining the product(s) at the appropriate temperatures and allow those temperatures to be monitored (where required).

1. The CI (or delegate) will set up appropriate housekeeping procedures to ensure facilities are kept in a sufficiently clean and orderly state to protect the product and prevent contamination. See also Housekeeping Schedule (UoB-CRL-QCD-006) (note that this document is intended for laboratories but can be adapted for use in a research kitchen). See also Laboratory Facilities SOP (UoB-CRL-SOP-002) for more information.
2. The CI (or delegate) will document details of the food and and/or nutritional component related procedures within the risk assessment. See also the Project Oversight and Quality Management SOP (UoB-POS-SOP-001) for details on performing a project-specific risk assessment.

## Sourcing, receipt and storage

1. The CI (or delegate) will define and document the source of any food and/or nutritional components that will be administrated to participants. This will include details on shipping requirements (e.g. temperature controls), and a process for monitoring conditions during shipping (if necessary).

* Additional information should be included where relevant e.g. the reason(s) for selecting a particular manufacturer.

1. The CI (or delegate) will document the specific storage instructions for the food and/or nutritional component. This will include procedures for temperature monitoring, dealing with adverse storage conditions and checking for tampering during storage.
2. The CI (or delegate) will define a process for documenting the receipt and storage of the food and/or nutritional component, including any quality checks to be performed on incoming products and dealing with damaged products (e.g. due to tampering). It is expected that the data listed below is recorded in a receipt and storage log (see the Receipt and Storage Record (UoB-FNC-QCD-001) for a template).

* Name of product (and code).
* Manufacturer of product.
* Arrival date of product.
* Quantity received (amount/vials numbers).
* Batch number (where applicable).
* Person who has received and stored the product.
* Expiry date.
* Storage location.
* Temperature of storage.

## Preparation and administration

1. The CI (or delegate) will develop and document a process for ensuring the safe and hygienic preparation and administration of the food and/or nutritional component. This will include the follow items detailed below (where applicable).

* Validating, calculating and authorising any formulas used to determine amounts/doses.
* Product stability/shelf life if it requires repacking prior to administration.
* Packaging instructions (if applicable, see also ‘Repackaging bulk supplies of nutritional components’ section below).
* Recording the identity (initials) of the person(s) performing each process and, where appropriate, the name of any person who checked/authorised the process.

1. The CI (no delegation allowed) will approve the project-specific process for ensuring the safe and hygienic preparation and administration of the food and/or nutritional component.
2. The CI (or delegate) will maintain an appropriate inventory of the food and/or nutritional components used during the project (see the Accountability Log (UoB-FNC-QCD-002) for an example).
3. Where applicable, the CI (or delegate) will document a procedure for the randomisation and/or blinding of food and/or nutritional components. See also the Randomisation and Blinding SOP (UoB-RND-SOP-001). This procedure will include processes for, but not limited to:

* maintaining the integrity of the blind and preventing accidental or deliberate (unauthorised) unblinding
* unblinding in a medical emergency and/or pre-specified protocol indication
* unblinding for analysis purposes.

1. Where administration of the product(s) is at home, the CI (or delegate) will:

* provide relevant information (‘training’) to participants on how, when and where to store and consume the products (e.g. through instructions on the packaging)
* consider procedures for assessing compliance (e.g. participant diaries) and implement as appropriate.

### Repackaging bulk supplies of nutritional components

1. The CI (or delegate) will design a label to be used for repacking the product.

* As a minimum the label will include the information listed below.
* Participant identification number/treatment number and where relevant, the visit number
* Study/trial reference code allowing identification of the research project, site, investigator and sponsor.
* In addition to the minimum label requirements above, for products used off-site (e.g. taken unsupervised by the participant at home) the label will also include the information listed below.
* Name and contact details of the investigator (the main contact for information on the product, clinical research and emergency unblinding as applicable). Note that if the participant has been given a card with the address and telephone number of the investigator and told to keep this in their possession at all times, the label does not need to repeat these contact details.
* Directions for use detailing the dosage form, route of administration, quantity of dosage units, and in the case of open trials, the name/identifier and strength/potency. Note reference may be made to a leaflet or other explanatory document intended for the participant administering the product.
* Batch and/or code number to identify the contents and packaging operation.
* “For clinical research use only” or similar wording.
* The storage requirements for the product.
* Period of use (use-by date, expiry date or re-test date as applicable), in month/year format and in a manner that avoids any ambiguity.
* “Keep out of reach of children” except when the product is for use in projects where the product is not taken home by participants.

## Parenteral administration

1. The CI (or delegate) will follow the [UoB health and safety policies and guidance for biological safety](https://intranet.birmingham.ac.uk/hr/wellbeing/worksafe/biological/index.aspx), including performing a separate risk assessment for work with biological materials.
2. Where the product(s) will be parenterally administrated, the CI (or delegate) will inform the Clinical Research Compliance Team (CRCT) of this work, and seek advice about the Good Manufacturing Practice (GMP) requirements.

* It is recommended that advice is sought after the initial conceptualisation of a project (e.g. at the grant application phase) to ensure appropriate costs are accounted for.
* The starting material is expected to meet the criteria for manufacturing to GMP standards (typically manufactures refer to this as a ‘Clinical Trial Materials (CTM)’ grade or ‘GMP’ grade).
* Starting material from an unproven source may be used on a recorded/justified risk/benefit analysis with written approval from the Clinical Trial Oversight Committee (CTOC). As a minimum the product will be of microbiological and pyrogen tested (MPT) quality, and a risk assessment will be performed. However, alternative sources should always be considered in the first instance.

1. Following receipt of the product, the CI (or delegate) will ensure the appropriate steps in the ‘Preparation and Administration’ section above are followed.
2. Where additional production steps are required following receipt of the product, the CI (or delegate) will ensure the production process is conducted at an appropriate GMP facility.
3. The CI (or delegate) will ensure oversight is provided by an authorised healthcare professional, with evidence of all calculations/formulas used to determine amounts/doses approved by the authorised healthcare professional.

## Disposal

1. The CI (or delegate) will define procedures for the disposal of surplus products.
2. The CI (or delegate) will seek guidance from the local health and safety officer to ensure that the product and/or its constituents are disposed in accordance with local policy after the expiry date or at the end of the project.
3. The CI (or delegate) will file evidence of the disposal, including the individual responsible for disposing the product and the date of disposal (see Accountability Log (UoB-FNC-QCD-002)).

## Archiving

1. The CI (or delegate) will archive documentation relating to the food and/or nutritional component processes within the study/trial master file at the end of the project. See Archiving SOP (UoB-ARC-SOP-001) for further information on archiving requirements.

# List of expected outputs

* A documented procedure for the sourcing, receipt, storage, handling and disposal of food and/or nutritional components, with evidence of its implementation.
* Evidence of a risk assessment.
* Housekeeping schedule in place and documented evidence of its implementation.
* Where applicable, evidence of:
* equipment maintenance
* a documented randomisation and/or blinding process
* correct labelling of repackaged nutritional components.
* For parenteral administration:
* evidence of the CRCT reviewing processes
* use of an appropriate GMP facility (where appropriate)
* evidence of oversight by an authorised healthcare professional.

# Related documents

* UoB-AES-SOP-001 Adverse Event Reporting
* UoB-ARC-SOP-001 Archiving
* UoB-CRG-POL-002 UoB Clinical Research Definitions
* UoB-CRL-QCD-006 Housekeeping Schedule
* UoB-CRL-QCD-010 Equipment Maintenance Schedule
* UoB-CRL-SOP-002 Laboratory Facilities
* UoB-DSB-SOP-001 Deviations and Serious Breach Reporting
* UoB-FNC-QCD-001 Receipt and Storage Record
* UoB-FNC-QCD-002 Accountability Log
* UoB-GCP-POL-001 UoB Principles of GCP for Clinical Research
* UoB-POS-SOP-001 Project Oversight and Quality Management
* UoB-RND-SOP-001 Randomisation and Blinding
* UoB-SPO-QCD-001 Clinical Trials Task Delegation Log
* UoB-TRN-SOP-001 Training

UoB QMS documents can be found on the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx). Internal work instructions can be obtained from the CRCT ([crct@contacts.bham.ac.uk](mailto:crct@contacts.bham.ac.uk)) and/or from the Research Governance Team (RGT) ([researchgovernance@contacts.bham.ac.uk](mailto:researchgovernance@contacts.bham.ac.uk)).

# References and frameworks

* Food Safety Act 1990: <http://www.legislation.gov.uk/ukpga/1990/16/contents>
* Rules and Guidance for Pharmaceutical Manufacturers and Distributors complied by the Medicines and Healthcare products Regulatory Agency (MHRA). Tenth edition published in 2017. UK: Pharmaceutical Press
* The Food Safety And Hygiene (England) Regulations 2013: <http://www.legislation.gov.uk/uksi/2013/2996/made>
* UoB health and safety policies and guidance for biological safety: <https://intranet.birmingham.ac.uk/hr/wellbeing/worksafe/biological/index.aspx>

# Abbreviations and definitions

| Term | Description |
| --- | --- |
| Authorised healthcare professional | An authorised healthcare professional is defined as a doctor, dentist, nurse or pharmacist. |
| CI | Chief investigator |
| Clinical study | Any health related research study on humans. This includes a study:   * administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology * involving qualitative methods only * limited to working with human tissue samples (or other human biological samples) and data (specific project only) * limited to working with data (specific project only). |
| Clinical trial | For clinical trials using an investigational medicinal product:  Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy.  For all other clinical trials:  Prospective biomedical research on human subjects that are conducted to allow safety (or more specifically, information about adverse drug reactions and adverse effects of other treatments) and efficacy data to be collected for health interventions. Examples include devices, surgery and radiotherapy trials. |
| CRCT | Clinical Research Compliance Team |
| CTOC | Clinical Trial Oversight Committee |
| CTU | Clinical trials unit |
| GCP | Good Clinical Practice |
| GMP | Good Manufacturing Practice |
| MPT | Microbiological and pyrogen tested |
| PPE | Personal protective equipment |
| QMS | Quality management system |
| REC | Research ethics committee |
| SOP | Standard operating procedure |
| 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).