Clinical Trials Involving Investigational Medicinal Products and Medical Devices
Policy

For use in: All areas of the Trust
For use by: All Trust staff
For use for: Setting up and running Clinical Trials Involving Investigational Medicinal Products (IMP) and Medical Devices within the Trust
Document owner: Research and Development
Status: Approved

Purpose of this document
This policy provides guidance for all staff within the West Suffolk NHS Foundation Trust about the requirements and processes for opening a clinical trial involving a medicinal product, and for prescribing, storing, manufacturing/preparing, dispensing, administration, return and destruction of IMPs / Medical Devices for use in clinical trials.

Contents

1. Introduction 1
2. General Principles of conducting clinical trials at WSFT 2
3. Opening a Clinical Trial 3
4. Manufacturing and Preparation of IMPs 4
5. Storage of IMPs 5
6. Prescribing of IMPs 5
7. Prescription forms for IMPs 5
8. Dispensing of IMPs 5
9. Labelling of IMPs 5
10. Administration of IMPs 6
11. Return and Destruction of IMPs 6
12. Code Breaks and Unblinding 6
13. Glossary 7
Appendix 1. Duties and Responsibilities 11
Appendix 2. What is manufacture? 12

1. Introduction

This policy sets out the standards required for the management of Clinical Trials involving investigational medicinal products (CTIMPs) and medical devices at the West Suffolk NHS Foundation Trust in order to comply with the UK Policy Framework for Health and Social Care Research v3.2. It is applicable to both non-commercial and commercially sponsored studies and all phases of clinical research. While some clinical trials will involve the use of existing marketed products within their licensed indications, others will use new medicines or devices, formulations or methods of administration / use unfamiliar to the staff handling them. Therefore extra precautions need to be taken to ensure safety and security in their use.
Each clinical trial must have a sponsor responsible for the initiation, management and financial arrangements of the trial. The sponsor may be a pharmaceutical company, a medical device manufacturer, a research organisation, a NHS Trust, an academic institution, or a combination of these.

2: General Principles of conducting clinical trials at WSFT.

2.1 Sponsorship
The Trust does not currently act as sponsor for any clinical trials of either Medical Devices or IMPs. If a clinician has a study where the Trust could potentially be the sponsor, then they should contact the R&D office as early as possible to discuss this. The decision to act as sponsor will be determined by risk assessment of the protocol. This may require the protocol being discussed at the Clinical Safety and Effectiveness Committee (CSEC).

2.2. Excluded Clinical Trials
The Trust does not have the facilities to safely conduct the following types of clinical trial.
Phase 1 – CTIMP trials
Any Phase ATIMP trials (Advanced Therapy Products e.g. Gene Therapy).
Any trials of Radiopharmaceuticals EXCEPT where the Radiopharmaceutical is supplied in a ready to use form by the Sponsor.

2.3. Radiopharmaceutical Trials
The trust is rarely involved in trials involving radiopharmaceuticals. Due to the licensing requirements we are only able to participate in trials of radiopharmaceuticals where the radiopharmaceutical is supplied “ready to use” by the sponsor. This limits us to trials involving radiopharmaceuticals based on longer half-life isotopes as there are no radiopharmacies which hold an MIA (Manufacturer Authorisation for IMPs) (IMP) within the Eastern region.

In addition to the usual authorisations, R&D must be in receipt of copies of the following before the R&D approval letter can be issued;

- The PI’s ARSAC License (Research) for the trial.
- Confirmation that our Radioactive Waste License has been amended to cover the isotopes involved.
- Agreement from the Trust’s Radiation Protection Officer.

2.4. Continued Supply of Clinical Trial Medication.
The Trust cannot guarantee the continued supply of clinical trial medication following the closure of any clinical trial. This must be made clear to the patient when consent is taken. Continued supply may be possible if discussed with the relevant commissioners.

2.5. Annual Reports
Principal investigators are required to submit annual report in accordance with regulatory, ethical and R&D reporting requirements.

2.6 Re-imbursement of costs incurred in undertaking Commercially Sponsored Research.
All costs incurred during the course of undertaking commercially sponsored research, must be recovered from the sponsor. In order to facilitate this, the Trust requires the use of the NIHR Industry costing templates for ALL (adopted and non-adopted onto the UKCRN Portfolio) studies. The costs must be included in the Clinical Trials Agreement / Clinical Investigation Agreement.
2.7 Responsibilities
All staff have a responsibility for ensuring the principles outlined within this policy are universally applied. For further information on specific responsibilities see Appendix 1 and R&D SOP006.

2.8 Regulations
Statutory requirements for the conduct of all interventional trials involving medicines are imposed by the Medicines for Human Use (Clinical Trials) Amendment Regulations 2006\(^1\), the Medicines for Human Use (Clinical Trials) Amendment (No. 2) Regulation 2006\(^2\), the Medicines for Human Use (Clinical Trials) and Blood Safety and Quality Amendment Regulations 2008\(^3\) which implement the requirements of EU directives 2001/20/EC\(^4\) and 2005/28/EC\(^5\).

All trials must be run in compliance with these regulations.

3.0 Opening a clinical trial

3.1 Authorisations Required
Prior to a Clinical Trial being opened at the Trust the following regulatory steps must be completed. All information for the regulatory authorisations (Health Research Authority & MHRA) has to be submitted using the Integrated Research Application System (IRAS). The sponsor will complete all of the information required for the regulatory and ethical submissions, and some of the information for the R&D submission with the Principal investigator or their nominee completing the site specific information and gathering the approvals from the relevant support departments within the trust.

Regulatory Authorisation
The use of medicines in a trial must be supported by a Clinical Trials Authorisation (CTA) issued by the MHRA. This will also clarify which medicines are considered IMPs and NIMPs. **All trials not conforming to all of the following conditions are considered to be interventional and will require a CTA.**

A non-interventional study is defined as a study of one or more medicinal products which have an MA (i.e. are licensed products in the UK), where the following conditions are met:

i. The products are prescribed in the usual manner in accordance with the terms of the authorisation.
ii. The assignment of any patient involved in the study to a particular therapeutic strategy is not decided in advance by the protocol but falls within current practice.
iii. The decision to prescribe a particular medicinal product is clearly separated from the decision to include the patient in the study.
iv. No diagnostic or monitoring procedures are applied to patients included in the study, other than those that are normally required in the course of the particular therapeutic strategy in question.
v. Epidemiological methods are to be used for the analysis of the data arising from the study.

The Trust may seek confirmation from the MHRA that the trial falls outside the regulations before Trust approval is granted.

**Ethical “approval”**
Before recruitment to a trial can begin, a study must receive a favourable opinion from a Research Ethics Committee. A comprehensive guide to the application process can be found at [www.hra.nhs.uk](http://www.hra.nhs.uk) and also at [www.myresearchproject.org.uk](http://www.myresearchproject.org.uk). The R&D office is also
available for advice about completing the necessary documentation and processes for applying to regulatory authorities. Please see R&D SOP003

**Trust Research and Development (R&D) Approval**

R&D approval ensures compliance with the Research Governance Framework. The Statement of Activities (SoA) document, along with the Schedule of Events (SoE) document are used to support R&D approval. Acknowledgement of approval from support services where applicable, is required as part of the application process.

The approval process (R&D SOP002) includes:

- feasibility
- review of SoA and SoE study specific documents
- review of the financial considerations of the trial
- review of staffing requirements
- review of facility requirements
- review of Clinical Trial Agreement / Clinical Investigation Agreement
- review of the potential number of patients to be recruited
- pharmaceutical review (all CTIMP trials, and some medical device trials will require this review).
- confirmation necessary regulatory authorisations are in place
- review of risk to Trust (See R&D SOP004)

Please note that NO trial initiation activities can be undertaken until the Trust approval letter has been issued by R&D.

4. Manufacturing and Preparation of IMPs

Manufacturing of IMPs cannot be undertaken in the WSFT Pharmacy as the department does not hold a MIA (IMP) from the MHRA. The pharmacy can however prepare IMPs under an exemption.

Appendix 2 gives details of what activities are considered manufacturing and what activities are considered preparation.

**Aseptic Preparation**

Aseptic preparation of IMPs is either undertaken within the pharmacy production unit or at ward / clinic level. The decision of where an IMP should be prepared is taken by the Senior Pharmacy Technician (Clinical Trials and QA), the Production Pharmacist, and the sponsor (particularly in commercial trials).

In line with Trust policy all parenteral dosage forms of cytotoxic medicines will be prepared in the Pharmacy Aseptic Production Unit. This is with exception of certain Monoclonal Antibodies for use in Rheumatology.

The Pharmacy department is not in the position to prepare parenteral dosage forms of non-cytotoxic medicines. Therefore these will be prepared by appropriately trained staff within the clinical area.

**Non-aseptic preparation**

Non-aseptic preparation of IMPs that does not involve manufacturing can be conducted within the pharmacy department.
**Blinding procedures.**
The blinding of IMPs using processes that do not involve manufacturing can be conducted within the pharmacy department as detailed in the trial protocol.

**Record keeping**
All records of aseptic production, non-aseptic preparation, and blinding of IMPs must be kept within the pharmacy file, and/or where appropriate the investigator site file.

5. **Storage of IMPs**
Wherever possible all IMPs will be stored in the WSFT pharmacy department until the point of dispensing. In very exceptional circumstances IMPs may be stored in other designated clinical areas, for instance in an emergency care trial. In these circumstances this storage area must be approved by the Chief Pharmacist and the Sponsor.

All areas used to store must at a minimum have their temperatures recorded once a day using a calibrated max/min digital thermometer. Any excursions outside of the designated temperature range will be dealt with in accordance with trial procedures and departmental SOPs.

6. **Prescribing of IMPs**
Clinical trial prescriptions can be written by any medical prescriber*, dental prescriber, or non-medical prescriber provided that they:
- Have been included on the delegation log for the trial and have been signed off by the principal investigator.
- Have suitable training, qualifications and experience to prescribe IMPs. This should be documented in the form of a current CV.

* Whilst potentially any medical prescriber can prescribe IMPs this is normally restricted within the Trust to medical staff at Registrar level or above.

7. **Prescription forms for IMPs**
IMPs may be prescribed as inpatient, outpatient or TTA prescriptions. Where available a specific clinical trial prescription provided by the sponsor should be used.

When a specific clinical trial prescription form is not available or is inappropriate then the Senior Pharmacy Technician (Clinical Trials and QA) will provide a suitable prescription. This prescription requires approval of both the sponsor and the PI before use.

Oncology and Haematology trials will usually be prescribed using the ARIA electronic prescribing system.

8. **Dispensing of IMPs**
IMPs will normally be dispensed in by the Pharmacy department in accordance with departmental SOPs. If an IMP is stored outside of the Pharmacy department, then the Senior Pharmacy Technician (Clinical Trials and QA) will provide advice to the trial team to ensure that there is a robust dispensing procedure in place.
9. Labelling of IMPs
All IMPs must be labelled in accordance with annex 13 of GMP guidelines (appendix 2). In addition to the manufacturer's label a Pharmacy label produced on the pharmacy JAC dispensing system will be attached. The JAC label will:
- Show where the IMP was dispensed from.
- Clearly state IMP name e.g. IMP / Placebo (For use in trial x only).
- Clearly specify who the IMP was dispensed to (patient name)
- Clearly indicate the date of dispensing.
- State the instructions for use.

10. Administration of IMPs
Ward and Clinic staff must be given reasonable notice of pending studies and provided with copies of all relevant documentation, including a protocol summary, information on IMP administration, study specific medication administration records, if applicable and any available information concerning possible adverse drug reactions. Ward staff must also be informed of their responsibilities with respect to the confidentiality of study information.

Administration of IMPs is subject to the requirements of WSFT Policy for the use of medicines. In most cases the IMP will be an unlicensed preparation or a licensed product administered outside of the licensed indications.

Staff administering unlicensed or off-label medicines should be aware of their unlicensed status.

11. Return and Destruction of IMPs

Return of used and unused IMPs to Pharmacy
All used and unused study medications or their containers and immediate packaging must be returned to the study team in a safe and timely manner to ensure full accountability is undertaken. All medication must be promptly returned to the pharmacy clinical trials staff. Please note empty infusion bags, syringes, and pump reservoirs MUST not be returned but disposed of into an appropriate sharpsmart immediately after administration.

Disposal of IMPs
It is the responsibility of the PI and local study team to ensure that the disposal of IMPs is in accordance with the study protocol.

The Trust will not routinely dispose of IMPs as we are unable to produce a full audit trail for destruction. However if the sponsor requires the Trust to dispose of IMPs, then the Senior Pharmacy Technician (Clinical Trials and QA) will supply the sponsor with the necessary information regarding our waste policy and procedures.

Disposal of Radioactive IMPs
The above does NOT cover the safe disposal of Radioactive IMPs. These are subject to separate regulations, Nuclear Medicine will provide guidance as and when necessary.

12. Code Breaks / Unblinding
For all blinded trials emergency code break / unblinding information must be accessible 24 hours a day. Unblinding can only occur in accordance with the procedures set out in the trial protocol.

During normal working hours contact the PI directly or if they are unavailable or unknown please contact the Senior Pharmacy Technician (Clinical Trials and QA).

Outside of normal working hours contact the On-Call Pharmacist via switchboard. They will then contact the Senior Pharmacy Technician (Clinical Trials and QA).

In the event of an un-blinding, whether accidental or deliberate e.g. due to a serious adverse event, the investigator must document the action taken and promptly notify the sponsor.

13. Glossary

**Advanced Therapy Investigational Medicinal Products (ATIMP)**
Means an ATMP which is tested or used in a clinical trial.

**Advanced Therapy Medicinal Products (ATMP)**
Means any of the following medicinal products for human use:
- a gene therapy medicinal product
- a somatic cell therapy medicinal product
- a tissue engineered product.

**Administration of Radioactive Substances Advisory Committee (ARSAC)**
This committee oversees the safe administration of radioactive substances to humans and advises Health Ministers with respect to the grant, renewal, suspension, revocation and variation of certificates allowing medical staff to administer radioactive substances to humans.

**Clinical Trial of an Investigational Medicinal Product (CTIMP)**
Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and or other pharmacodynamics effects of an investigational product(s), and/or study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

**Clinical Trial Authorisation (CTA)**
Authorisation given by the competent authority (MHRA in UK) to conduct a Clinical Trial.

**Clinical Trial Agreement (CTA)**
This is the contract between the sponsor and the Trust which lays out the legal obligations of parties, the details with regards to liability and indemnity, and also any financial issues.

**Disposal**
The removal of investigational products from the research either by return to the trial sponsor or by destruction according to local procedures. Destruction is usually performed by an external waste contractor.

**Good Clinical Practice (GCP)**
In clinical trials GCP refers to the ICH GCP E6 document, which is a set of standards for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials. These provide assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.
Good Manufacturing Practice (GMP)
The part of quality assurance which ensures that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use, and as required by the marketing authorisation (MA) or product specification. GMP is concerned with both production and quality control.

Health Research Authority (HRA)
The HRA was established in December 2011. Its main purposes now, in accordance with the Care Act 2014, are to protect and promote the interest of patients and the public in health and social care research, co-ordinate and standardise practices relating to regulation, recognise and establish Research Ethics Committees (RECs), be a member of UK Ethics Committee Authority (UKECA), promote transparency in research and provide approvals for the processing of confidential information relating to patients.

Integrated Research Application System (IRAS)
The online application system used to apply for most permissions and approvals for research in health and social care within the UK (includes MHRA, Ethics, HRA and NHS R&D).

Investigational Medicinal Product (IMP)
A pharmaceutical form of an active substance or placebo being tested, or to be tested, or used, or to be used, as a reference in a Clinical Trial, and includes a medicinal product, which has a marketing authorisation but is, for the purposes of the trial -
  a) used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,
  b) used for an indication not included in the summary of product characteristics under the authorisation for that product, or
  c) used to gain further information about the form of that product as authorised under the authorisation.

Medical Device
Any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap
- investigation, replacement or modification of the anatomy or of a physiological process
- control of conception.

And which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means. Please note that some medical devices are supplied by the Pharmacy department.

Medicines and Healthcare products Regulatory Agency (MHRA)
The government agency which is responsible for ensuring that all medicines and medical devices in the UK work and are acceptably safe.
It is also the competent authority for the UK in relation to the Directive 2001/20/EC and the Clinical Trials Regulations, and for Medical Devices, the competent authority in relation to the Medical Devices Regulations 2002.

**Manufacturers Authorisation for Investigational Medicinal Products (MIA(IMP))**
This has replaced the old Manufacturers Specials (IMP) License, and is issued by the MHRA. It allows the license holder to undertake those activities listed as manufacture in Appendix 1.

**Non Investigational Medicinal Product (NIMP)**
A Non Investigational Medicinal Product (NIMP) is a medicinal product which is not classed as an IMP in a trial, but may be taken by subjects during the trial. Examples include concomitant or rescue/escape medication used for preventive, diagnostic or therapeutic reasons and/or medication given to ensure that adequate medical care is provided for the subject during a trial.

**Phase 1 Studies**
A Phase 1 (Human Pharmacology) Studies are also commonly known as Healthy Volunteer Studies as the majority use health volunteers to study the effect of a new drug entity on a healthy human before moving into using it therapeutically. For some medicines the use of healthy volunteers is unethical, so must be tested in patients with the disease being studied.

**Radiopharmaceutical**
A radioactive drug used in the diagnosis and treatment of disease.

**Research Ethics Committee (REC)**
An independent body, constituted of medical/scientific professionals and non-medical/non-scientific (lay) members, whose responsibility it is to ensure the protection of the rights, safety, and wellbeing of human subjects involved in a clinical trial by, among other things, reviewing and providing a favourable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

**Research Operational and Governance Committee (ROC)**
This is the Trust committee which reviews all research prior to the issuing of Trust Research and Development Approval.

**Sponsor**
An individual, company, institution or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.

**Standard Operating Procedures (SOPs)**
Detailed written instructions to achieve uniformity in the performance of a specific function.

**UKCRN Portfolio**
This is a database of high-quality (peer reviewed) clinical research studies that are eligible for support from the Clinical Research Network in England.
### Review and Monitoring
This policy is reviewed by the Research Operational Committee, and compliance monitored by the Research and Development

<table>
<thead>
<tr>
<th>Author(s):</th>
<th>James Curtis (Senior Pharmacy Technician) R&amp;D Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other contributors:</td>
<td>R&amp;D Manager, Lead Research Nurse and Research Facilitator</td>
</tr>
<tr>
<td>Approvals and endorsements:</td>
<td>Research Operational Committee</td>
</tr>
<tr>
<td>Consultation:</td>
<td>Research and Development Office Research Operational Committee Members</td>
</tr>
<tr>
<td>Issue no:</td>
<td>2</td>
</tr>
<tr>
<td>File name:</td>
<td>O:\Research &amp; Development\Trust Policy\PP(14)313 Clinical Trials Policy v2.doc October 2017 to October 2010</td>
</tr>
<tr>
<td>Supercedes:</td>
<td>Policy\PP(14)313 Clinical Trials Policy v1.doc March 2014 to October 2017</td>
</tr>
<tr>
<td>Equality Assessed</td>
<td>N/a</td>
</tr>
<tr>
<td>Implementation</td>
<td>Via Research Operational Committee</td>
</tr>
<tr>
<td>Monitoring: (give brief details how this will be done)</td>
<td>Policy implementation is monitored by the Research Operational Committee</td>
</tr>
<tr>
<td>Other relevant policies/documents &amp; references:</td>
<td>R&amp;D SOPs Pharmacy SOPs Medicines for Human Use (Clinical Trials) Regulations 2004 ICH-GCP E6 Document – Good Clinical Practice for Clinical Trials. UK policy framework for health and social care research v3.2</td>
</tr>
<tr>
<td>Additional Information:</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 1

Investigator responsibilities.

These are fully detailed in the GCP regulations. Particular vigilance is required when undertaking protocols in which the Trust is acting as sponsor.

In summary the investigator should

- Be qualified by education, training and experience, including up to date GCP training, to assume responsibility for the proper conduct of a trial.
- Demonstrate appropriate resources e.g. time, support staff and facilities to conduct the trial properly and safely within an agreed time period.
- Ensure that the study does not begin until all appropriate regulatory approvals are in place.
- Obtain and document informed consent from each patient, or if the patient is unable to provide informed consent, the patient’s legally acceptable representative, before any trial related activities are performed. Patients and /or their representatives should have a clear understanding of proposed treatments, the potential for harmful effects, and any other available treatments. Written information and instructions which has been approved by the Ethics committee must be provided and the patient must have ample time to ask questions and decide whether to participate or not.
- Ensure that all staff assisting with the trial are suitably informed about the protocol, IMPs, and their related duties and functions.
- Are responsible for reporting serious adverse events to the sponsor in accordance with the protocol and GCP (R&D SOP027).
- Are responsible for all trial related medicinal decisions during and following a patient's participation in a trial.
- Are responsible for IMP accountability at the trial site and delegate this responsibility to the pharmacy department, unless otherwise specified at trial start-up.
- Follow the trial randomisation procedure if applicable and ensure that in blinded trials, the blinding is only broken in accordance with the protocol.
- Ensure the accuracy, completeness, legibility and timeliness of trial data and ensure that all other persons who have been delegate responsibility for data collection are appropriately trained in trial procedures and are aware of their responsibilities.

Pharmacy Responsibilities

- A designated member of pharmacy staff has overall responsibility for the pharmacy clinical trial service. At WSFT this is the Senior Pharmacy Technician (Clinical Trials and Quality Assurance).
- In summary they will
- Before the commencement of a clinical trial involving IMPs or medical devices requiring pharmacy input ensure that the pharmacy has copies of all essential regulatory and technical documents, a copy of the protocol, an investigator brochure or SmPC, if applicable and randomisation codes (if relevant) from the trials team responsible for the study.
- Carry out a review and risk assessment of each clinical trial, and put in place procedures to minimise predictable risks from the trial medication to patients and staff.
- Ensure that all medicines provided or procured for use in non-commercial clinical trials are manufactured in accordance with GMP, if necessary by a holder of a Manufacturers “Specials” License for IMPs, and are of a suitable quality and for purpose.
- Ensure that the packaging and labelling of clinical trial medication is acceptable for use within the Trust and complies with legislation.
- Is responsible for the management of IMP stock, including IMP accountability and any other duties as delegated by the investigator,
**Appendix 2: What is manufacture?**

This table is based on information supplied by the NHS Pharmaceutical Quality Assurance Committee.

<table>
<thead>
<tr>
<th>Description of Process</th>
<th>Classification</th>
<th>MIA(IMP) License required.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filling of capsules with powder</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Over-encapsulation of tablets or capsules</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Dilution of powder with water, with no additional labelling</td>
<td>Reconstitution</td>
<td>No</td>
</tr>
<tr>
<td>Weighing of IMP powder, addition of water and adjustment of pH</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Mixing of IMP powder with other powders and dispensing into unit doses</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Preparation of liquids for oral use</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Filling of ampoules/vials</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Filling large volume parenteral and irrigation solutions</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Filling / Preparation of Ophthalmic dosage forms</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Filling of aerosols</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Production of Tablets, lozenges, pastilles</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Production of Boogies, Pessaries, and Suppositories</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Medical Gases</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Production of batches of Pre-filled Syringes</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Reconstitution of a commercial radiopharmaceutical kit with a radio-isotope solution</td>
<td>Manufacture</td>
<td>Yes</td>
</tr>
<tr>
<td>Reconstitute vial / withdraw from ampoule and transfer into unlabelled syringe for</td>
<td>Reconstitution</td>
<td>No</td>
</tr>
<tr>
<td>immediate dosing on ward</td>
<td>and dispensing</td>
<td></td>
</tr>
<tr>
<td>Reconstitute vial / withdraw from ampoule and transfer into syringe / IV bag etc. for</td>
<td>Reconstitution</td>
<td>No</td>
</tr>
<tr>
<td>dosing (syringe/bag requires annex 13 labelling).</td>
<td>and assembly</td>
<td></td>
</tr>
<tr>
<td>Dispensing from bulk containers for prescription into individual subject pack and</td>
<td>Assembly</td>
<td>No</td>
</tr>
<tr>
<td>labelled according to annex 13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dispensing from bulk containers into batch of subject specific bottles and labelled</td>
<td>Assembly</td>
<td>No</td>
</tr>
<tr>
<td>according to annex 13.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dispensing from bulk containers into batch of non-subject specific bottles, labelled</td>
<td>Assembly</td>
<td>No</td>
</tr>
<tr>
<td>according to annex 13 for bulk storage. Subject specific information added at time of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dispensing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>