iMATCH: overview of services in Greater Manchester

Lead Organisation: iMATCH

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Division of Cancer Sciences

Standard Operating Procedure

(Version 1.0)

iMATCH: overview of services in GM
(Adapted from iMATCH WP2.2)

Revision History		
Number	**Date**	**Reason for Change**
1.0	**18/1/22**	

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1. Greater Manchester demographics.

The overall population of Greater Manchester for 2017 was estimated to be 2,798,799 (ONS, 2018). Table 1 breaks down the populations by borough.

Table 1. Population of Greater Manchester by Borough.

Borough	***Population estimate*** *ONS Estimated population of the boroughs of Greater Manchester for 2017.*	***Local Hospital/NHS Trust.***
Manchester	545,501	Manchester University NHS Foundation Trust.
		The Christie NHS Foundation Trust.
		North Manchester General (Pennine Acute Hospitals).
Salford	251,332	Salford Royal NHS Foundation Trust
Trafford	235,493	Manchester University NHS Foundation Trust
Bury	189,628	Fairfield General (Pennine Acute Hospitals).
Wigan	324,650	Royal Albert Edward Infirmary (Wrightington, Wigan and Leigh NHS Foundation Trust).
Rochdale	218,459	Rochdale Infirmary (Pennine Acute Hospitals).
Stockport	291,045	Stepping Hill (Stockport NHS Foundation Trust.
Bolton	284,213	Royal Bolton (Bolton NHS Foundation Trust).
Tameside	224,119	Tameside Hospital (Tameside and Glossop Integrated Care NHS Foundation Trust).

Oldham	233,759	Royal Oldham (Pennine Acute Hospitals).

n.b. Manchester University NHS Foundation Trust consists of the following hospitals: Manchester Royal Infirmary, Royal Manchester Children's Hospital, St Mary's, Royal Eye Hospital (Central Manchester) Wythenshawe Hospital (Wythenshawe, South Manchester) and Trafford General (Davyhulme,, Trafford). It is expected that North Manchester General Hospital will join Manchester University NHS Foundation Trust by April 2019, transferring from Pennine Acute Hospitals.

2. Surgical sites in Greater Manchester.

Oncological surgery is split between The Christie NHS Foundation Trust and Wythenshawe Hospital in South Manchester, Manchester Royal Infirmary in Central Manchester and Salford Royal NHS Foundation Trust in Salford. Table 2 lists the surgical sites and specialities.

Table 2. Surgical sites and specialities.

The Christie – Withington, South Manchester.
Gynaecological- **Endometrial, Cervical cancer, Vulval, Ovarian**
Urological – **Prostate, Bladder, Kidney, Testis, Penile, Retroperitoneal**
Head and Neck
Colorectal
Breast
Sarcoma

Wythenshawe Hospital – Wythenshawe, South Manchester
Lung
Urological- **Prostate, complex open renal surgery,** **Cystectomy, Penile.**
Head and Neck
Colorectal
Breast

Manchester Royal Infirmary – Central Manchester
Gynecological – **Ovarian, Endometrial, cervical vaginal and vulval**
Colorectal
Hepatobillary-

Liver, Pancreatic
Urological
Sarcoma
Head and neck

Salford Royal – Salford.
Breast
Neurological and Spinal
Oesophago-gastric

Chemotherapy.

Chemotherapy for residents of Greater Manchester is carried out at The Christie.

3. What is in place?

3.1 Licencing and ethical requirements for using human tissue in research.

Licences for procurement, storage and use of human tissue in research are authorised by the Human Tissue Authority (HTA), who ensure compliance with the Human Tissue Act and EU legislation. Table 3 describes HTA licence agreements for sites across Greater Manchester.

Table 3. Human Tissue Authority Licences for research, human application and storage for sites across Greater Manchester.

Licence site	Manchester University NHS Foundation Trust
Area Covered	Human Application
Designated Individual	
HTA Licence number	22596
Specifics covered	• Distribution • Processing • Procurement • Storage • Testing • Storage of Relevant Material (Human Tissue Act)

Comments.	Licence amendment needed for distribution of peripheral blood stem cells to other sites- this has been applied for, to be added to licence agreement 22596.

Licence Site	Manchester University NHS Foundation Trust
Area Covered	Research
DI	Nalin Thakker
HTA Licence Number	12552
Specifics Covered	• Storage of Relevant Material
Comments	

Licence Site	Manchester University NHS Foundation Trust
Area Covered	Research (Satellite-main licence holder Liverpool Blood and transfusion)
DI	Ian Bateman
HTA Licence Number	12608
Specifics covered	• Removal of Relevant Material
Comments	

Licence Site	The Manchester Cancer Research Centre Biobank –The Christie
Area covered	Research
DI	Jane Rogan
HTA Licence Number	30004
Specifics covered	• Storage of Relevant Material
Comments	

Licence site	The Christie
Area Covered	Human Application
DI	
HTA Licence Number	11081

Specifics Covered	• Distribution • Processing • Procurement • Storage • Testing • Storage of Relevant Material (Human Tissue Act)
Comments	

Licence Site	Salford Royal NHS Foundation Trust
Area Covered	Research
DI	Rob Oliver
HTA Licence Number	12291
Specifics covered	Storage of relevant material
Comments	

Licence Site	Salford Royal NHS Foundation Trust
Area Covered	Research (Satellite, main licence holder Liverpool Blood and Transfusion
DI	Ian Bateman
HTA Licence Number	12608
Specifics covered	Removal of relevant material
Comments	

Licence site	Immetacyte (Grafton Street, Manchester)
Area covered	Human Application
DI	
HTA Licence number	22657
Specifics Covered	• Procurement • Testing
Comments	• "As part of these authorised activities the establishment processes and expands autologous tumour infiltrating lymphocytes for adoptive cell therapy. Only donor

	selection, procurement of starting material and testing are within the remit of the HTA; all other activities related to manufacture and administration of ATMPs are regulated by the MHRA". *HTA Inspection report(2017)*

Licence Site	Pennine Acute Hospitals
Comments	No Licence on HTA website, however Pennine procure tissue for MCRC biobank.

Licence Site	Stepping Hill Hospital
Comments	Only HTA licenced for post mortems. No HTA Licences for Stockport FT

Licence site	Bolton FT
Comments	No Licences on HTA site

Licence Site	Tameside General hospital
Comments	Only HTA licenced for post mortems.

3.2 Regulatory requirements for Adoptive Cell Therapy.

Use of human tissue in the manufacture, clinical trial and distribution is regulated by the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK. They grant Manufacturing Authorisation for investigational medicinal products (MIA IMP) and for clinical use post trial (MA). For authorisation to be granted, manufacturers must employ as Qualified Person to certify the products. The MHRA also grants medicinal product distribution licences.

Table 4 Manufacturers Agreements and distribution licences granted by the MRHA.

	Immetacyte
Licence type	• MHRA Manufacturers Authorisation for Investigational Medicinal Products. • Manufacturing Special (MS) Authorisation
Qualified Person	Gillian Lewis

Licence Site	The Christie
Licence Type	WDA(H) – Wholesale Distribution Authorisation (Human) (DoH MHRA, 2018) • *1.1 WITH A MARKETING AUTHORISATION IN EEA MEMBER STATE(S)* • *1.2 WITHOUT A MARKETING AUTHORISATION IN THE EEA AND INTENDED FOR EEA MARKET* • *2.1 PROCUREMENT* • *2.2 HOLDING* • *2.3 SUPPLY* • *3.1.1 NARCOTIC OR PSYCHOTROPIC PRODUCTS 3.3 COLD CHAIN PRODUCTS (REQUIRING LOW TEMPERATURE HANDLING)* • *4.1 PRESCRIPTION ONLY MEDICINES* • *4.4 PHARMACY*

3.3 Ethics.

Demands on the tumour and risks.

1. Whole genome screening will be implemented from 2019 for sporadic cancer patients in England. It is expected to add pressure on the tumour sample in terms of the increased demands on its diagnostic and therapeutic value. Particularly with smaller tumour types, there risks a dilemma over appropriate use of a finite resource.
    - When in the pathway would a decision be made as to what the tumour will be used for? Can patients be screened out through prior knowledge that TIL therapy will not be possible due to lack of sample, avoiding unnecessary confusion for the patient?

2. A benefit of WGS is the identification of the most effective treatment for patients. This may indicate adoptive cell therapy is not the most appropriate treatment. In this instance;
- What would happen to the stored sample? Would it need to be destroyed or is there justification in maintaining its storage?
- How often is this likely to happen?

3. Risks of unknown environmental changes on the TIL prior to infusion.

Could harmless differences in the TIL be magnified and become pathological as a result of expanding that difference? What do patients need to know of these potential risks?

Consenting.

4. Need to assess patient understanding of adoptive cell therapies; what they already understand and what they want to understand. This ensures the PIS and consent process is relevant and comprehensive from the patient perspective. PPI groups can be utilised for this - Salma Hashmi and Anne Lowry on board and happy for us to approach their PPI groups.
5. Consultees may be required - PIS/consent needs to be made for them. Would be beneficial to include family members in PPI to assess understanding and approval of adoptive cell therapy compared with patients.
6. Consent needs to be reconfirmed wherever possible, particularly in light of the time lag between procuring the sample and infusion. The patient's care team need to be educated on the project for this to occur. This will need to be an ongoing process, integrated into training for new staff to ensure this process is not lost to staff turn-over.

4. Further requirements.

4.1 MHRA. "A clinical trial authorisation application including a description of the IMPs has to have been submitted to the MHRA. When granted a QP (Qualified Person) certification against that clinical trial authorisation is required. (Moon, 2016).

There is no requirement within the legislation for any MHRA licence to carry out storage and distribution of IMPs. In this respect, the legislation differs from that for medicinal products. However, you will need to be named within the appropriate annex of your client's MIA(IMP) as a site of storage and distribution. Therefore any clients who wish to make use of your services will need to vary their MIA(IMP) accordingly.

Note that the storage and distribution of a licensed medicinal product must remain in the licensed distribution chain until it is supplied to the Sponsor for use in a trial".

4.2 Local and national REC approval.

4.3 Consideration needs to be taken on both eligibility and ineligibility. How will ineligible patients enquiring about TIL therapy be managed?

4.4 Eligible patient will need to understand success rates of TIL therapy, to manage expectations.

4.5 C.V.'s of all staff involved in the project for the site file.

4.6 Prediction of cellular behaviour after infusion back to the patient. Can this be monitored (cell tracking)?

4.7 Risk of amplifying infective component during culture?

4.8 Data storage for traceability requirements.

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