



A Guide to the Histocompatibility and Immunogenetics Services Provided to Support Kidney, Pancreas and Islet Cell Transplantation



This guide outlines the Histocompatibility and Immunogenetics (H&I) services provided by the Transplantation Laboratory, Manchester Royal Infirmary in support of renal, pancreas and islet cell transplant programmes. The guide is of use to clinical and support staff in renal dialysis units, diabetes centre and renal transplant units.

**Revised by Dr Judith Worthington,
Prof Kay Poulton & Julie Johnson.**

Valid until December 2025

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Introduction

The Transplantation Laboratory is a regional specialty pathology service and as such offers a wide range of high quality, efficient and cost-effective services using state of the art technologies to Manchester University NHS Foundation Trust, other regional Trusts, and healthcare providers. The main services provided by the Transplantation Laboratory are described below:

a) Solid Organ Transplantation

The laboratory provides H&I support for:

- Kidney, kidney and pancreas, pancreas and islet cell transplantation programmes at Manchester Royal Infirmary.
- Cardiothoracic organ transplantation at Wythenshawe Hospital
- There is a 24 hour on-call service for kidney / kidney and pancreas / pancreas only / islet transplantation and all thoracic organ transplants.

b) Haematopoietic Progenitor Stem Cell Transplantation

The Transplantation Laboratory provides Histocompatibility & Immunogenetics (H&I) support for the haematopoietic progenitor stem cell transplantation programmes at Manchester University NHS Foundation Trust (MRI and RMCH) and other regional trusts. The laboratory utilises state of the art molecular HLA typing technologies for patients and their potential donors who may need a stem cell or bone marrow transplant. The laboratory is one of the leading laboratories in the country in the application of chimaerism monitoring using short tandem repeats post progenitor stem cell transplantation. The laboratory provides additional KIR typing and interpretation of results for haploidentical stem cell transplants.

The laboratory offers a rapid and professional Graft Information and Advisory Service (GIAS) to undertake donor selection. This service is delivered by highly qualified and experienced HCPC registered staff and is led by RCPATH qualified H&I Consultant Clinical Scientists.

c) Immunogenetics testing

The Transplantation Laboratory provides testing to support disease diagnosis and management for the Manchester University NHS Foundation Trust, Primary Care Centres and hospitals. A range of tests is provided, including HLA-B*27 and HLA-B*57:01 determination and HLA typing to support the diagnosis of Actinic Prurigo, Uveitis, Birdshot Retinopathy, Narcolepsy and Coeliac Disease. On request the laboratory can perform additional HLA typing to aid disease diagnosis and drug hypersensitivity investigations for tests in addition to those outlined.



d) Research and Innovation

The Transplantation Laboratory participates in research and innovation relevant to the clinical services provided to ensure that we continually improve our service provision in line

with the current clinical evidence base. Projects are closely tailored to local clinical practice to ensure the most appropriate services are provided for the patients.

The Transplantation Laboratory is part of a network, which is cross-directorate and is known as the Manchester Institute of Nephrology and Transplantation (MINT). MINT is a multi-professional body of physicians, surgeons, nursing staff, scientists, other professions allied to medicine and managers. Its aim is to improve and develop the research and educational activities of the transplantation, nephrology and dialysis services to achieve the best possible care for transplant patients.

e) Audit

The Transplantation Laboratory is actively involved in audit related to laboratory activities as well as clinical audit in conjunction with the services we support. The process of clinical audit directly relates to the Trust's Clinical Effectiveness Strategy that aims to improve the quality and outcome of patient care. The laboratory also has an internal audit cycle against ISO 15189:2012 and European Federation for Immunogenetics standards to ensure continual compliance and continual improvement in transplant outcome.

f) Quality assurance



7878



The Transplantation Laboratory is a UKAS accredited medical laboratory No.7878 and has European Federation of Immunogenetics accreditation (EFI No: 03-GB-009.991).

The laboratory has a well-established quality management system in operation which allows the laboratory to be focused on continual improvement in line with needs and requirements of our users. The QMS provides a structured framework for the laboratory and is monitored and maintained by the Laboratory Operations and Quality Manager. The Quality Policy which is reviewed annually describes the aims of the services.

Any test performed in the laboratory is subject to a variety of factors that may influence the outcome of the result. Some of these factors include the sample itself, the test method, reagents used and different operators carrying out the same process. Variations can also be caused by procedures that involve the measurement of analytes and reagents whereby environmental factors such as temperature and humidity may affect results. Any equipment used in the process will further introduce the opportunity for variation. To provide a measure of confidence in results produced it is necessary to identify all factors which may contribute to variation in a process and assess their potential to influence uncertainty. Once identified these factors must be reduced or controlled to an acceptable level and a value for the range of acceptable uncertainty assigned where possible.

The Transplantation Laboratory has chosen, where possible, to utilise internal Quality Control material and data to establish Uncertainty of Measurement where applicable. Upon request the laboratory shall make its estimates of measurement of uncertainty available to laboratory users.

Participation in external quality assurance programmes such as UK NEQAS and UCLA schemes, together with continual internal quality assessment monitoring of our tests, ensures that the laboratory's high quality standards are maintained.

UK NEQAS schemes conform to high standards of professionalism, impartiality, clinical relevance and strict financial accountability across all disciplines and specialities, so that all concerned with the quality of laboratory investigations may have confidence in the service provided.

A highly experienced consultant team offers support to clinicians and service users 24 hours a day, seven days a week. The team provides information related to using the service, interpretation of test results and clinical advice. Reviews and changes to the service provision will be in consultation with our users and will be clearly defined in revised Service Level Agreements (SLAs), where applicable.

The Transplantation Laboratory actively supports and encourages staff training and continual professional development. It is recognised by both the Royal College of Pathologists, the National School for Healthcare Scientists and the British Society for Histocompatibility and Immunogenetics as a training laboratory in Histocompatibility and Immunogenetics. Where appropriate, staff members are registered with the Health and Care Professions Council (HCPC).



Details of our accreditation, including current certificates and performance data, are available upon request from the Laboratory Operations and Quality Manager (julie.johnson2@mft.nhs.uk).

In order to help us improve our service, you may be asked to complete a questionnaire. We greatly appreciate and value your input and would like to thank you for your assistance and suggestions.

g) Complaint Procedure

The Transplantation Laboratory is continually aware of, and takes into consideration the requirements of its users and staff, whilst striving to create the best standards of professional care. According to Trust policy, any complainants are referred to the Patient Advice and Liaison Service (PALS) who can support staff and patients to achieve speedy solutions. Also, complaints can be directed to the Laboratory Director, a Consultant Clinical Scientist or any Transplantation Laboratory representatives at Multidisciplinary Team meetings. Please make any concerns you have about the quality of the service known to us as soon as possible; we take your complaints seriously.

Any suggestions from users regarding any aspect of our service provision, or indeed how the User Guide could be improved, are very welcome. Please forward any suggestions to the Laboratory Operations & Quality Manager (julie.johnson2@mft.nhs.uk).

h) Clinical Liaison and Advice



A Consultant Clinical Scientist or deputy will always be available to attend multi-disciplinary team meetings as required in order to ensure optimum communication between the laboratory and clinical teams and provide advice relating to Cardiothoracic Transplant Service provision.

A 24-hour, 365-day on-call service is provided for deceased donor HLA typing and crossmatching. The Clinical Advice Scientist on call rota is staffed by experienced Clinical Scientists who hold FRCPath and who have been trained to offer clinical advice out of hours in support of transplantation.

I) Confidentiality and Personal Information

The Transplantation Laboratory adheres to Manchester University NHS Foundation Trust's policies on data protection and disclosure.

2. General Information

2.1 Postal Address

Transplantation Laboratory
2nd Floor, Purple Zone
Manchester Royal Infirmary
Oxford Road
Manchester
M13 9WL



Tel: 0161 276 6397

Fax: 0161 276 6148

2.2 Business Hours

Opening Hours for routine work:

08.30 – 17.00 hrs

Out of hours, weekends and Bank holidays:

On call staff & Clinical Advice
Scientist can be paged via
MFT switch Tel: 0161 276
1234

2.3 Laboratory Key Personnel

Laboratory Director

Prof Kay Poulton PhD, FRCPath
Consultant Clinical Scientist,
0161 276 6397
Email: kay.poulton@mft.nhs.uk

Consultant Clinical Scientists

Mr Stephen Sheldon, FRCPath
Tel: 0161 276 6397
Email: stephen.sheldon@mft.nhs.uk

Ms Natalia Diaz Burlinson, FRCPath
Tel: 0161 276 6397
Email: Natalia.DiazBurlinson@mft.nhs.uk

Dr Helena Lee PhD, FRCPath
Tel: 0161 276 6397
Email: Helena.Lee@mft.nhs.uk

Kidney Pancreas Support Services Enquires

Dr Judith Worthington PhD FRCPATH

Principal Clinical Scientist

0161 276 7988

Email: judith.worthington@mft.nhs.uk

Laboratory Operations and Quality Manager

Julie Johnson MSc. HCPC

Principal Clinical Scientist

0161 276 6424

Email: julie.johnson2@mft.nhs.uk

General Enquiries

Business and Administration Manager

Judith Spencer

Tel: 0161 276 6397

Fax: 0161 276 6148

Email: judith.spencer@mft.nhs.uk

2.4 Essential Telephone Numbers

Specimen Reception:	0161 276 6471
Admin office:	0161 276 6397
Histocompatibility Team – General Enquiries	0161 276 7988 / 7919 / 6651 / 6656

2.5 Essential Email Addresses

Transplantation Laboratory (general enquiries)	: TransplantLab@mft.nhs.uk
Cardiothoracic Patient Listings	: OnCall.TLab@mft.nhs.uk
Solid Organ Enquiries	: mft.histocompatibility@nhs.net

2.6 Internet page

<https://mft.nhs.uk/mri/services/transplantation-laboratory>

3. Use of the Laboratory

3.1 Service Availability

The laboratory is open for receipt of routine specimens from 08:30 to 17:00 between Monday to Friday. Internal on site samples may be sent directly to the laboratory using the pneumatic pod system (Transplantation Pod No 805).

There is an on-call service provision available outside normal working hours provided by an on call team consisting of a HCPC registered Clinical Scientist, a technologist and a Clinical Advice Scientist. This service is generally restricted to the solid organ transplant programme.



The on-call team can be contacted through the paging service provided by PageOne or directly via the MRI Switchboard (0161 276 1234).

Using the PageOne paging service

There are a number of ways to send messages via PageOne.

Web-Send

- Go to www.pageone.co.uk/web-send.
- Enter the pager number of the person you are trying to contact in the “Number” field.
- Enter the message, including the telephone number that you wish to be contacted on, in the “Message” field.
- Click the “Send” button.

Email

- Send an email to PagerNumber.pageone@p1c.net
- Replace *PagerNumber* with the pager number of the person you are trying to contact.
- Enter your message in the main body of the email, make sure there is no signature in the text and click “Send”.

Via SMS Text Message

- Send a text to either 07860023039 or 07860023040.
- In the message, first type the pager number of the person you are trying to contact, then a space, then the message.

DDI (numeric) or Call-Centre (message)

- Dial the pager number of the person you are trying to contact.
- Follow the voice prompt to either:
 - Enter a numeric message via your telephone keypad (the number you wish to be contacted on).
 - Wait for the operator to answer and dictate your message when asked. The operator should confirm that your message has been sent.

3.2 Labelling of sample containers

The Transplantation Laboratory will make every effort to ensure requests are processed in a safe and timely manner but it is essential that request forms and samples are labelled appropriately and legibly. The minimum acceptance criteria for request are normally **3 key identifiers** that should include at least:

- Patient's name (forename and surname)
- Date of birth
- Hospital number and or MRI District number
- NHS number
- Home Address of the patient.

These are all identifiers specific to the patient which help us to confirm identity and are essential.

It is also important to clearly identify the investigations required when completing the request card, please only select the test required and send only the appropriate sample tube.

If you have any concerns regarding this please ring 0161 276 6471 / 6397 for further advice.

Specimens will not be accepted for analysis if:

- There are insufficient unique identifiers for the patient as specified.
- Incorrect sample type or tube
- Incorrect transportation conditions mean that the sample is not viable for testing
- Sample is received in a hazardous condition e.g. leaking or sharps attached.
- Mismatch of details between the form and sample(s)
- The information provided is illegible

Samples that fail to meet the above criteria will be discarded as unsuitable for analysis, and the sender will be informed. The only exception to this is for patients whose identity is anonymous and they have their own unique identifier, for example patient samples from Genitourinary Medical Centres or potential stem cell donors. In other circumstances samples may be accepted without the 3 key identifiers at the discretion of the laboratory.

3.3 Transportation of routine samples to the laboratory

All users are advised to refer to P650 Packaging Instruction which applies to UN No. 3373 (Diagnostic Specimens) for information on the correct procedures for packaging and transporting samples. When sending samples to the laboratory it is important to follow the correct courier and postal procedures and ensure the specimens are appropriately packaged. (**See Appendix 2**)

All specimens should be transported at room temperature (**approximately 22°C - 25°C**), unless otherwise instructed, avoiding where possible prolonged over exposure to heat. The samples should be transported directly to the laboratory as quickly as possible after collection to maintain the integrity of the sample and avoid compromising the results.

Internal on site specimens may be transported directly to the Transplantation laboratory via the porter's rounds during the normal working day or by pneumatic pod system to Pod No 805. Samples should be placed in a specimen bag with the request for transportation around the trust.

Please contact the laboratory on 0161 276 6471 / 6397 if there are specific questions regarding transportation of specimens.

3.4 Urgent samples

If a result is required urgently and the sample will arrive during working hours the laboratory MUST be notified by telephone so that we can prioritise your request.

All samples should be packaged and transported as above. If you need to submit a sample out of normal working hours for testing on-call please contact the Clinical Scientist on-call via the hospital switchboard (0161 276 1234) or via the paging service provided by PageOne (see 3.1 Service Availability for instructions)

3.5 Acceptance time limit after sample drawing

Time limits and storage temperature requirements are imposed to maintain the integrity of the sample, to ensure accuracy and reliability of the testing and reduce the need for repeat samples. For all tests complete the request card or an ICE request for users within MFT. See **Appendix 4** for a full list of tests and samples required.

HLA genotyping

Whole blood – minimum 3 ml EDTA blood	No time limit
Buccal swab	No time limit
Dried Blood Spot	No time limit

(See pages 13-14 for instruction on how to take buccal swabs/ dried blood spot samples).

HLA antibody/ donor specific antibody (DSA) testing

5 ml Clotted blood (no anticoagulant)	Up to 48 hours
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Crossmatching

EDTA/ Heparinised blood for crossmatching	Up to 24 hours
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Storage conditions prior to sending






Clotted samples can be kept overnight at 4°C but sent immediately the next morning to the laboratory for testing.

EDTA blood samples should be kept at room temperature whilst waiting and during transport to the laboratory, avoiding any excessive heat exposure.

Request cards can be obtained from the Transplantation Laboratory, please call on 0161 276 6397 or email TransplantLab@mft.nhs.uk . These request cards are also available in electronic format upon request.

3.6 Instructions for the collection of a Sample using a Buccal Swab

INSTRUCTIONS FOR COLLECTION OF BUCCAL CELL SAMPLES USING SWAB TECHNIQUE

<p>Preparation:</p> <ul style="list-style-type: none"> • Do not use swab within 1 hour of eating, drinking or cleaning your teeth. • Wash your hands thoroughly. • Rinse your mouth out with water immediately before collecting sample • Complete sticker label included in the pack with the individual's Forename, Surname and Date of Birth. • Complete the sample card with the individual's surname, forename, date of birth and date of specimen collection. 	
<p>1</p> 	<p>1. Pull the swab package open from one end.</p>
<p>2</p> 	<p>2. Remove the swab from the tube, taking care not to touch the white pad head.</p>
<p>3</p> 	<p>3. Insert the swab into your mouth. Using firm pressure, repeatedly rub against the inside of your cheek for 1 minute.</p>
<p>4</p> 	<p>4. Place the swab back into the tube, taking care not to touch the white pad head.</p>
<p>5</p> 	<p>5. With the swab head in the tube, place your thumbnail in the small groove set in the swab handle (approximately 1 inch from swab head), then snap the handle in two by bending to one side. Let the swab head fall into the tube.</p> <ol style="list-style-type: none"> a. Seal the tube with the cap provided. Affix the completed label to the tube, ensuring the excess sticker from both sides of the label stick together to form a flag-like formation - this will ensure the entirety of the label is visible. b. Put the tube in an envelope and send to the address stated on the accompanying letter.
<p>Send the collected sample to the Transplantation Laboratory (address overleaf) by first class in approved packaging.</p>	

3.7 Instructions for the collection of a Sample using a Blood Spot



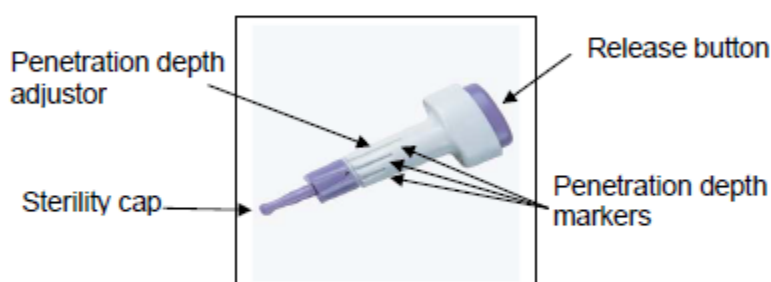
Manchester University
NHS Foundation Trust

Transplantation Laboratory

Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL

Tel: 0161 276 6397, Fax: 0161 276 6148

COLLECTION OF BLOOD SPOT SAMPLES USING THE ACCU-CHEK® SAFE- T-PRO PLUS STERILE SINGLE-USE LANCING DEVICE



1. Ensure the collection paper is fully labelled with **surname, forename, date of birth** and **date of specimen**.
2. Wash hands thoroughly using soap and warm water and dry well to ensure a clean puncture site.
3. Twist the sterility cap and remove it.
4. The penetration adjustor is pre-set to the medium depth (~1.8mm) and is suitable for most adults. For children adjust to the low penetration depth (~1.3mm).
5. Hold the lancing device between the middle and index finger with the thumb on the release button.
6. Press the lancing device firmly against the puncture site, the side of the finger is recommended, and press the release button.
7. Squeeze the finger to encourage blood flow and collect at least 4 blood drops on each of the four circles (labelled 1-4) on the collection card (ensure the whole circle is filled with blood). A second puncture of the finger may be necessary.
8. Cover puncture site(s) with a plaster, dispose of the lance in an appropriate medical waste container and allow the blood spots to dry completely before packaging.

4. General Information regarding services available

4.1 Descriptions of standard tests

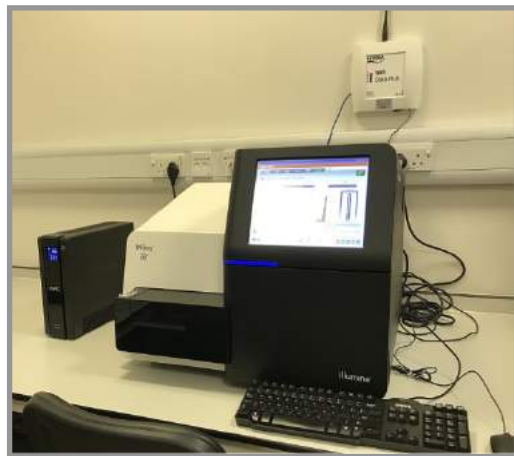
What is HLA typing (Tissue Typing)?

HLA typing is performed predominantly to match a donor and recipient for solid organ or haemopoietic progenitor stem cell transplantation (HPCT). Minimising the number of HLA mismatches between donor and recipient maximises the opportunity for optimal transplant survival.

HLA molecules are crucial to normal immune processes by enabling the cells involved in immune responses to recognise foreign organisms and react against them. Following transplantation the recipient's immune cells can recognise donor HLA molecules as foreign and react against them causing rejection.

HLA typing refers to the series of laboratory tests whereby the HLA molecules expressed on the surface of an individual's body cells are identified. HLA molecules are on the surface of all nucleated cells (i.e in humans, all cells apart from red blood cells) but lymphocytes are routinely used for tests because they can easily be isolated from anti-coagulated peripheral blood.

The technique used for testing varies according to the clinical requirement. For example, a rapid, but intermediate resolution technique (LinkSēq™) may be used to HLA type a potential donor in a solid organ transplant setting.



LABType® SSO offers intermediate level resolution and facilitates rapid batch testing of samples for routine testing. All patients also receive extensive next generation sequence (NGS) based typing analysis to provide a high resolution HLA type. The Transplantation Laboratory employs state of the art NGS HLA typing technology to assist in interpretation of HLA antibodies and thus permit suitable donor identification.

An individual's HLA type defines the combination of HLA molecules on the surface of their body cells. These are determined genetically. The HLA genes are unique in the human genome because of their considerable variability, which results in many different HLA types. The HLA genes are identified by letters (e.g. HLA-A) and the different gene products (specificities) by numbers (e.g. HLA-A2). Each individual inherits one set of HLA molecules from each parent thus they have two HLA-A, two HLA-B types and so on.

What is Antibody Screening?

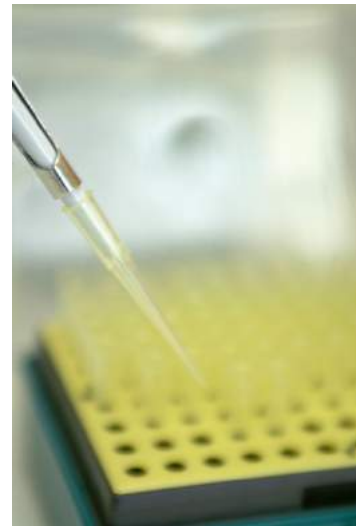
Individuals can produce antibodies directed against HLA specificities that they do not possess. This can happen following exposure to non-self HLA during pregnancy, blood transfusion or transplantation. These antibodies are detected in serum and can potentially react with a donor organ or graft and cause transplant rejection.

It is important that patients are screened for the presence of HLA antibodies and that the specificities of any antibodies detected are defined prior to transplantation. **Samples for antibody screening should be sent to the laboratory every 4-6 weeks from patients on the transplant list and approximately two weeks after a known sensitising events (e.g. blood transfusions).** When a patient is known to have antibodies against a particular HLA specificity, that specificity is listed as an unacceptable donor antigen.

HLA specific antibodies are detected and defined by microbead array techniques, which are highly sensitive and specific. They are referred to as Luminex assays and are semi quantitative.

For sensitised parous female patients being listed for transplantation, it is our policy to HLA type the father of the children or the children themselves in order to fully define pregnancy-related sensitisation where possible.

Some patients have non graft damaging “autoantibodies” that can cause false positive donor crossmatches, the laboratory will request samples to specifically test for these as necessary.



What is Crossmatching?

Crossmatching is a pre-transplant test in which donor lymphocytes are tested against serum samples from the potential recipient(s) to ascertain whether any donor-reactive antibodies are present that would cause transplant rejection. Donor-reactive antibodies that cause a positive crossmatch test are normally a contraindication to transplantation.

- The *cytotoxic crossmatch* is a cell killing test.
- The *flow cytometry crossmatch* is a more sensitive test that uses fluorescence to detect antibody binding to donor cells.
- A “*virtual crossmatch*” assessment is performed pre-transplant for solid organ patients, whereby the donor HLA type is reviewed against the patient’s HLA antibody profile (antibodies are listed as unacceptable antigens) to determine whether the patient has any donor-directed antibodies that could cause a positive crossmatch test result. In cases where all unacceptable antigens have been clearly defined, sensitised patients can be transplanted without the need for a prospective crossmatch as long as all unacceptable antigens are absent from the donor HLA type. This is the basis of the



current solid organ allocation process in the UK and the low frequency of unexpected positive crossmatches for patients suggests that patients who have been rigorously assessed and defined as negative for donor-directed antibodies can safely proceed to transplant before the crossmatch test result is available. The purpose of this approach is to reduce the cold ischaemia time without compromising the safety of transplantation.

Potential recipients will be assessed for their suitability for a “virtual crossmatch” against a particular donor and a “virtual crossmatch negative” report issued if appropriate. The transplant unit must be able to confirm that no potential sensitisation events have occurred since the date of the last patient serum sample tested for HLA antibodies.

Risk Assessment Crossmatching

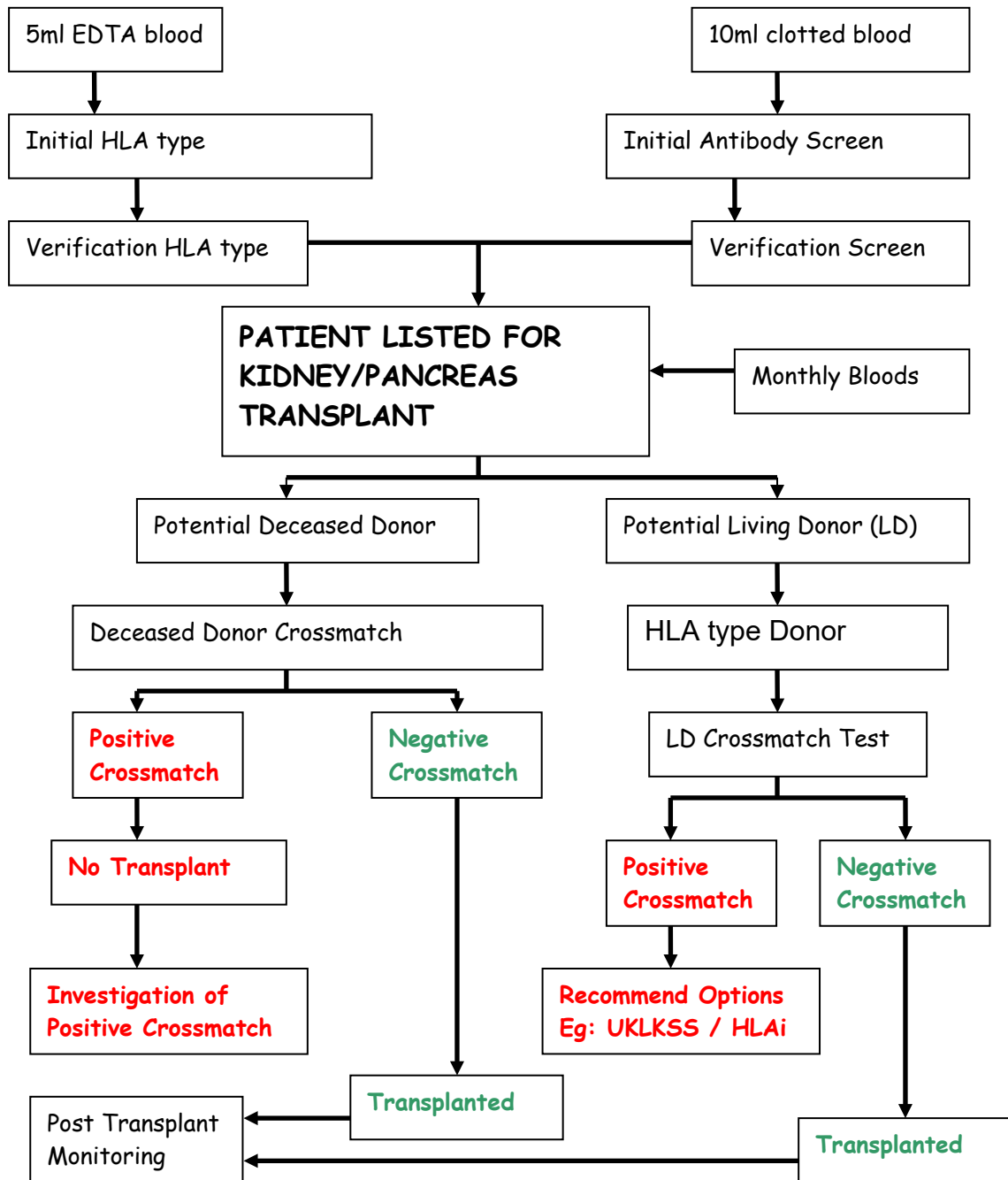
For patients with donor-directed antibodies, a pre-transplant “*risk assessment crossmatch*” can be performed on request. In a “risk assessment crossmatch” the level of immunological risk associated with proceeding to transplant with a particular donor is determined by performing a cytotoxic and flow cytometry crossmatch using both current and historic serum samples for the recipient. Immunological risk is then assigned using the BSHI/BTS guidelines for Detection and Characterisation of Clinically Relevant Antibodies in Allotransplantation.

It must be noted that the validity of virtual and risk assessment crossmatch results for antibody positive patients is dependent on the donor HLA type being correct. In 2021, nationally, discrepancies were detected in 0.34% of donor HLA types after the organs had been allocated.

Post-transplant Donor Specific Antibody (DSA) testing

Post-transplant recipients can produce specific antibodies associated with transplant rejection. A post-transplant antibody monitoring service is available, including testing for donor-directed antibodies. Post-transplant samples for DSA testing to support the diagnosis of rejection should be sent when clinically indicated to support the diagnosis of antibody-mediated rejection.

Overview of Kidney / Pancreas Support Service for Patients with Chronic Renal Failure



5. Requesting Tests/Samples Required

The Transplantation Laboratory has its own distinctive request cards which can be obtained from the Transplantation Laboratory (TransplantLab@mft.nhs.uk). Internal on site requests should be made using the ICE system using the Transplantation Laboratory tab following the MFT standard operating procedure. All other requests should be made using the request cards shown below following the procedure described below for the test required.

Appendix 3 includes a list of laboratory tests and sample requirements

5.1 HLA (Tissue) Typing (Recipient)

Complete the request card – an example is shown in **RED** below

As a minimum requirement, include patient surname, forename, date of birth, hospital number, referring hospital, consultant, person requesting the test and the date sample taken.

It is essential that the patient is clearly identified on the card and on the specimen.

- At initial referral to laboratory (**1st set of bloods**) send 5ml EDTA blood for HLA typing and 10ml clotted blood for antibody screening.
- At surgical referral send 5ml EDTA blood for **verification typing** and 10ml clotted blood for antibody screening.

Recipient samples should be received within 24 hours by the laboratory and by midday on Friday, to allow adequate time for processing, except by prior arrangement.

Send 5ml EDTA blood and 10ml clotted blood

THE TRANSPLANTATION LABORATORY, MANCHESTER ROYAL INFIRMARY TEL: 0161 276 6397 FAX: 0616 276 6148				
SURNAME*	FORE NAME*	DATE OF BIRTH*	SEX	HOSPITAL*
HOSPITAL NUMBER*	NHS NUMBER	REQUESTED BY* (Block Capitals)	WARD	CONSULTANT*
NHS PATIENT YES NO	BLOOD GROUP ABO____ Rh____	BLOOD TRANSFUSION DATE____ No UNITS____	No PREGNANCIES	SAMPLE DRAW DATE*
DIAGNOSIS* RECIPIENT <input checked="" type="checkbox"/> KIDNEY	<input type="checkbox"/> PANCREAS	<input type="checkbox"/> COMBINED K/P	<input type="checkbox"/> ISLETS	DONOR <input type="checkbox"/>
				OTHER <input type="checkbox"/>
TESTS REQUIRED*:		RECIPIENT HLA SPECIFIC ANTIBODIES		
RECIPIENT HLA TYPING <input type="checkbox"/> HLA TYPING (5ml EDTA)		<input type="checkbox"/> HLA SPECIFIC ANTIBODIES (10ml CLOTTED BLOOD)		
LIVING DONOR HLA TYPING <input type="checkbox"/> 5ml EDTA POTENTIAL RECIPIENT_____		LIVING DONOR CROSSMATCH <input type="checkbox"/> 40ml HEPARIN or EDTA (DONOR); 10ml CLOTTED (RECIPIENT) RELATIONSHIP OF DONOR TO RECIPIENT_____		
PREGNANCY RELATED UNACCEPTABLE ANTIGENS <input type="checkbox"/> 5ml EDTA		RECIPIENT_____		
POST TPX DONOR SPECIFIC ANTIBODIES <input type="checkbox"/> 10ml CLOTTED BLOOD		AUTO CROSSMATCH <input type="checkbox"/> 20ml HEPARIN or EDTA		
* ESSENTIAL INFORMATION REQUIRED IN ORDER TO PROCESS REQUEST				

5.2 HLA (Tissue) Typing (Potential Living Donor)

Complete the request card – an example is shown in **RED** below

As a minimum requirement include potential donor surname, forename, date of birth, referring hospital, consultant and person requesting test, date sample taken and name of potential recipient plus relationship. Wherever possible attach a copy of the potential donor's ABO report to the request card.

THE TRANSPLANTATION LABORATORY, MANCHESTER ROYAL INFIRMARY TEL: 0161 276 6397 FAX: 0616 276 6148				
SURNAME*	FORENAME*	DATE OF BIRTH*	SEX	HOSPITAL*
HOSPITAL NUMBER*	NHS NUMBER	REQUESTED BY* (Block Capitals)	WARD	CONSULTANT*
NHS PATIENT	BLOOD GROUP	BLOOD TRANSFUSION	No PREGNANCIES	SAMPLE DRAW DATE*
YES NO	ABO ____ Rh ____	DATE _____ No UNITS ____		
DIAGNOSIS*			DONOR	OTHER
RECIPIENT			<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> KIDNEY	<input type="checkbox"/> PANCREAS <input type="checkbox"/> COMBINED K/P <input type="checkbox"/> ISLETS			
TESTS REQUIRED*:		RECIPIENT HLA SPECIFIC ANTIBODIES		
RECIPIENT HLA TYPING		<input type="checkbox"/> HLA SPECIFIC ANTIBODIES (10ml CLOTTED BLOOD)		
<input type="checkbox"/> HLA TYPING (5ml EDTA)		LIVING DONOR CROSSMATCH		
LIVING DONOR HLA TYPING		<input type="checkbox"/> 40ml HEPARIN or EDTA (DONOR); 10ml CLOTTED (RECIPIENT)		
<input type="checkbox"/> 5ml EDTA				
POTENTIAL RECIPIENT _____		RELATIONSHIP OF DONOR TO RECIPIENT _____		
PREGNANCY RELATED UNACCEPTABLE ANTIGENS		RECIPIENT _____		
<input type="checkbox"/> 5ml EDTA				
POST TPX DONOR SPECIFIC ANTIBODIES		AUTO CROSSMATCH		
<input type="checkbox"/> 10ml CLOTTED BLOOD		<input type="checkbox"/> 20ml HEPARIN or EDTA		
* ESSENTIAL INFORMATION REQUIRED IN ORDER TO PROCESS REQUEST				

5.3 HLA (Tissue) Typing Pregnancy Related Bloods

Complete the request card – an example is shown in **RED** below

As a minimum requirement include the surname, forename, date of birth, referring hospital, consultant and person requesting test, date sample taken and name of potential recipient plus relationship.

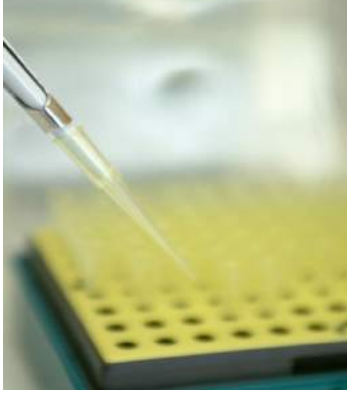
THE TRANSPLANTATION LABORATORY, MANCHESTER ROYAL INFIRMARY TEL: 0161 276 6397 FAX: 0616 276 6148				
SURNAME*	FORENAME*	DATE OF BIRTH*	SEX	HOSPITAL*
HOSPITAL NUMBER*	NHS NUMBER	REQUESTED BY* (Block Capitals)	WARD	CONSULTANT*
NHS PATIENT	BLOOD GROUP	BLOOD TRANSFUSION	No PREGNANCIES	SAMPLE DRAW DATE*
YES NO	ABO ____ Rh ____	DATE ____ No UNITS ____		
DIAGNOSIS*			DONOR	OTHER
RECIPIENT			<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> KIDNEY	<input type="checkbox"/> PANCREAS	<input type="checkbox"/> COMBINED K/P	<input type="checkbox"/> ISLETS	
TESTS REQUIRED*:				
RECIPIENT HLA TYPING		RECIPIENT HLA SPECIFIC ANTIBODIES		
<input type="checkbox"/> HLA TYPING (5ml EDTA)		<input type="checkbox"/> HLA SPECIFIC ANTIBODIES (10ml CLOTTED BLOOD)		
LIVING DONOR HLA TYPING		LIVING DONOR CROSSMATCH		
<input type="checkbox"/> 5ml EDTA		<input type="checkbox"/> 40ml HEPARIN or EDTA (DONOR); 10ml CLOTTED (RECIPIENT)		
POTENTIAL RECIPIENT _____		RELATIONSHIP OF DONOR TO RECIPIENT _____		
PREGNANCY RELATED UNACCEPTABLE ANTIGENS				
<input type="checkbox"/> 5ml EDTA		RECIPIENT _____		
POST TPX DONOR SPECIFIC ANTIBODIES		AUTO CROSSMATCH		
<input type="checkbox"/> 10ml CLOTTED BLOOD		<input type="checkbox"/> 20ml HEPARIN or EDTA		
* ESSENTIAL INFORMATION REQUIRED IN ORDER TO PROCESS REQUEST				

5.4 HLA (Tissue) Typing (Deceased Donor)

The on-call Clinical Scientist should be notified by the Specialist Nurse for Organ Donation (SN-OD) as soon as a potential donor has been identified. Samples must be accompanied by an NHSBT HLA Typing Request form (FRM4279/4) and should be delivered to the Transplant Unit (MRI Ward 10) or the Central Specimen Reception at MRI. Instructions on how to contact the laboratory on-call staff are printed on the specimen box lid. The on-call Clinical Scientist should immediately be notified of their arrival by the reception staff in A&E via switchboard so that collection and delivery to the laboratory can be arranged.

Send 10ml EDTA blood

5.5 HLA Antibody Screening



Routine monthly samples from patients on the transplant list or post-transplant need not be accompanied by a request card although tubes must be clearly labelled with patient name, date of birth, hospital number and date of sample collection.

Samples can be received within 48 hours Monday to Friday and sent by 1st class post in appropriate packaging. (See Appendix 2)

Send 10ml clotted blood

THE TRANSPLANTATION LABORATORY, MANCHESTER ROYAL INFIRMARY TEL: 0161 276 6397 FAX: 0616 276 6148				
SURNAME*	FORENAME*	DATE OF BIRTH*	SEX	HOSPITAL*
HOSPITAL NUMBER*	NHS NUMBER	REQUESTED BY* (Blocked Capitals)	WARD	CONSULTANT*
NHS PATIENT	BLOOD GROUP	BLOOD TRANSFUSION	No PREGNANCIES	SAMPLE DRAW DATE*
YES NO	ABO ___ Rh ___	DATE _____ No UNITS _____		
DIAGNOSIS*				
RECIPIENT				
<input checked="" type="checkbox"/> KIDNEY	<input type="checkbox"/> PANCREAS	DONOR <input type="checkbox"/> COMBINED K/P	OTHER <input type="checkbox"/> ISLETS	<input type="checkbox"/>
TESTS REQUIRED*:				
RECIPIENT HLA TYPING		RECIPIENT HLA SPECIFIC ANTIBODIES		
<input type="checkbox"/> HLA TYPING (5ml EDTA)		<input checked="" type="checkbox"/> HLA SPECIFIC ANTIBODIES (10ml CLOTTED BLOOD)		
LIVING DONOR HLA TYPING		LIVING DONOR CROSSMATCH		
<input type="checkbox"/> 5ml EDTA		<input type="checkbox"/> 40ml HEPARIN or EDTA (DONOR); 10ml CLOTTED (RECIPIENT)		
POTENTIAL RECIPIENT _____		RELATIONSHIP OF DONOR TO RECIPIENT _____		
PREGNANCY RELATED UNACCEPTABLE ANTIGENS				
<input type="checkbox"/> 5ml EDTA		RECIPIENT _____		
POST TPX DONOR SPECIFIC ANTIBODIES		AUTO CROSSMATCH		
<input type="checkbox"/> 10ml CLOTTED BLOOD		<input type="checkbox"/> 20ml HEPARIN or EDTA		
* ESSENTIAL INFORMATION REQUIRED IN ORDER TO PROCESS REQUEST				

5.6 Crossmatching (Deceased Donor)

Deceased organ donor samples

Donor spleen and lymph node specimens should be taken by the organ retrieval team and despatched to the Transplant Unit (MRI Ward 10). The on-call Clinical Scientist must be immediately notified of their arrival by the ward staff so that collection and delivery to the laboratory can be arranged.

Recipient samples

If a sample is requested by the laboratory for crossmatching against a potential kidney donor, send 10ml clotted blood as a matter of urgency.



For patients proceeding to transplant on the basis of a Virtual Crossmatch a “Day of Transplant” sample (10ml clotted blood) should always be sent to the laboratory for retrospective testing.

The Tissue Typer On Call can be contacted through the paging service provided by PageOne or directly via MRI Switchboard (0161 276 1234). Alternatively it may be necessary to contact via their On Call mobile phones.

5.7 Crossmatching (Living Donor)

These tests must be pre-arranged with the laboratory, are time sensitive and must be accompanied by a request card – see an example below.

From the recipient send 10ml clotted blood.

From the donor send 40ml EDTA blood

THE TRANSPLANTATION LABORATORY, MANCHESTER ROYAL INFIRMARY TEL: 0161 276 6397 FAX: 0616 276 6148				
SURNAME*	FORENAME*	DATE OF BIRTH*	SEX	HOSPITAL*
HOSPITAL NUMBER*	NHS NUMBER	REQUESTED BY*	WARD	CONSULTANT*
NHS PATIENT YES NO	BLOOD GROUP ABO____ Rh____	BLOOD TRANSFUSION DATE____ No UNITS____	No PREGNANCIES	SAMPLE DRAW DATE*
DIAGNOSIS*			DONOR	OTHER
RECIPIENT			<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> KIDNEY	<input type="checkbox"/> PANCREAS	<input type="checkbox"/> COMBINED K/P	<input type="checkbox"/> ISLETS	
TESTS REQUIRED*:				
RECIPIENT HLA TYPING		RECIPIENT HLA SPECIFIC ANTIBODIES		
<input type="checkbox"/> HLA TYPING (5ml EDTA)		<input type="checkbox"/> HLA SPECIFIC ANTIBODIES (10ml CLOTTED BLOOD)		
LIVING DONOR HLA TYPING		LIVING DONOR CROSSMATCH		
<input type="checkbox"/> 5ml EDTA		<input type="checkbox"/> 40ml HEPARIN or EDTA (DONOR) 10ml CLOTTED (RECIPIENT)		
POTENTIAL RECIPIENT _____		RELATIONSHIP OF DONOR TO RECIPIENT _____		
PREGNANCY RELATED UNACCEPTABLE ANTIGENS				
<input type="checkbox"/> 5ml EDTA		RECIPIENT _____		
POST TPX DONOR SPECIFIC ANTIBODIES		AUTO CROSSMATCH		
<input type="checkbox"/> 10ml CLOTTED BLOOD		<input type="checkbox"/> 20ml HEPARIN or EDTA		
* ESSENTIAL INFORMATION REQUIRED IN ORDER TO PROCESS REQUEST				

5.8 Donor Specific Antibodies

Post-transplant samples for donor specific antibody testing to support the diagnosis of antibody-mediated rejection must be accompanied by a request card. See example below. Guidelines for the frequency of testing are shown in Appendix 8

Send 10ml clotted blood.

THE TRANSPLANTATION LABORATORY, MANCHESTER ROYAL INFIRMARY TEL: 0161 276 6397 FAX: 0616 276 6148				
SURNAME*	FORE NAME*	DATE OF BIRTH*	SEX	HOSPITAL*
HOSPITAL NUMBER*	NHS NUMBER	REQUESTED BY* (Block Capitals)	WARD	CONSULTANT*
NHS PATIENT	BLOOD GROUP	BLOOD TRANSFUSION	No PREGNANCIES	SAMPLE DRAW DATE*
YES NO	ABO____Rh____	DATE____No UNITS____		
DIAGNOSIS*			DONOR	OTHER
RECIPIENT			<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> KIDNEY	<input type="checkbox"/> PANCREAS	<input type="checkbox"/> COMBINED K/P	<input type="checkbox"/> ISLETS	
TESTS REQUIRED*:				
RECIPIENT HLA TYPING		RECIPIENT HLA SPECIFIC ANTIBODIES		
<input type="checkbox"/> HLA TYPING (5ml EDTA)		<input type="checkbox"/> HLA SPECIFIC ANTIBODIES (10ml CLOTTED BLOOD)		
LIVING DONOR HLA TYPING		LIVING DONOR CROSSMATCH		
<input type="checkbox"/> 5ml EDTA		<input type="checkbox"/> 40ml HEPARIN or EDTA (DONOR) 10ml CLOTTED (RECIPIENT)		
POTENTIAL RECIPIENT _____		RELATIONSHIP OF DONOR TO RECIPIENT _____		
PREGNANCY RELATED UNACCEPTABLE ANTIGENS				
<input type="checkbox"/> 5ml EDTA		RECIPIENT _____		
POST TPX DONOR SPECIFIC ANTIBODIES		AUTO CROSSMATCH		
<input type="checkbox"/> 10ml CLOTTED BLOOD		<input type="checkbox"/> 20ml HEPARIN or EDTA		
* ESSENTIAL INFORMATION REQUIRED IN ORDER TO PROCESS REQUEST				

6. Reporting of Results

To maintain patient confidentiality and comply with General Data Protection Regulations (GDPR) and other legal requirements all results are reported via encrypted email or in writing only to an authorised individual. They are signed by a Consultant Clinical Scientist or named deputy. Other results are only reported by telephone after agreement by a Consultant Clinical Scientist. Provision of non-urgent results by email is available on request during office hours and Clinical Advice Scientist is available on a 24hr basis. The Measurement of uncertainty (MoU) shall be considered for all examinations which include a measurement step where it has influence on the reported result. Estimates of the MoU will be made available to users upon request. Users shall be informed of deviations from agreement that may impact on results.

All times are quoted as working days from the receipt of the sample in the Transplantation Laboratory

For **HLA typing results** from renal patients and potential living donors, 90% will be issued **within 10 working days** of correct specimen receipt.

HLA typing results for deceased donors will be reported by emailed to NHSBT-ODT, **within 4 hours of specimen receipt.**

HLA antibody screening results for new patients will be reported when the patient is listed for transplantation, unless specifically requested. For patients on the transplant list data on current antibody status is included on the circulated monthly transplant list. When there is a change in the antibody profile of a listed patient that would change their predicted wait time a *Renal Patient Antibody Profile* will be issued.

Unacceptable antigens resulting from pregnancy related sensitisation will be reported as an HLA Report: *HLA type performed to determine pregnancy-related sensitisation.*

The Transplant Chance gives a measure of the chance of a suitably HLA matched donor becoming available for the patient - the higher the value, the better the chance. It is calculated on the basis of the patient's ABO blood group, HLA type and unacceptable antigens with reference to the ABO blood groups and HLA types of all organ donors recorded locally (over 2000). The Transplant Chance is included on the patient HLA profile for newly listed patients, the Renal Patient Antibody Profile Report and on the monthly transplant list. (See Appendix 5)

Potential Living Donor Compatibility Summary will be issued when all essential information and samples have been received by the laboratory usually **within 15 days of receipt**

Deceased Donor / Recipient Crossmatch results are reported to the transplant team, **within 5 hours of receipt of crossmatch specimens.**

Immediate pre-transplant Living Donor / Recipient Crossmatch. A report will be issued by the day preceding the transplant date.

Donor Specific Antibodies results will be reported as “Renal Transplant Recipient – Post Transplant Antibody Investigations” report **within 15 working days of receipt**. Copy reports are available to view via the Renal Unit IT system Clinical Vision.

Turnaround Time (TAT)

Over 90% of the results are reported within **the specified timescale** from receipt of samples. Special arrangements requiring a shorter turnaround may be established on a user-specific basis, by arrangement with the Consultant Clinical Scientist and subject to the technical limitations of the assays. The turnaround times quoted are supported by audit data.

7. Patient Registration on the Kidney/Pancreas Transplant List

Essential Tests -

- **All patients**

- ABO blood group report
- HLA type (tested on two separate occasions)
- HLA antibody screen

- **IgM alloantibody positive patients**

- Autoantibody test

Recommended Tests -

- **Parous female patients**

- HLA type of partner/father(s) of their children, or
- HLA type of each child

Listing Process -

Refer patients to Transplant Surgeons. The referral letter **must** be accompanied by a completed listing proforma signed by the referring physician, plus a copy of the ABO blood group report. When the patient has been assessed and / or discussed at MDT, the form will then be countersigned by a Consultant Transplant Surgeon and then sent to the Transplantation Laboratory.

The Transplantation Laboratory will acknowledge receipt of the listing proforma and request any outstanding samples. When all necessary testing is complete the patient will be registered on the local and national (NHSBT-ODT) lists.

Each month the laboratory will issue a report to each referring centre to show which patients are pending entry to the list and the outstanding specimens/data/tests.

As soon as the patient is registered on the transplant list a "Notification of Entry to the List" will be issued to the referring physician stating the patient's HLA type, antibody status, unacceptable antigens, transplant chance and transplant category.

In addition a letter is sent to the patient to notify them that they have been registered with NHSBT ODT and whether they are currently "Active" on the list or "Temporarily Suspended".

8. Maintenance on the Transplant List

Laboratory Tests

10ml clotted blood samples from each patient on the transplant waiting list must be sent to the Transplantation Laboratory each month for HLA antibody screening and use in crossmatching.

10ml clotted samples must be sent two weeks post blood transfusion accompanied by a request card which includes transfusion information.

Any other tests will be specifically requested in writing by the laboratory as necessary.

Administration

A copy of the transplant list will be circulated monthly to each referring centre, the transplant unit and other individuals as agreed.

A monthly list will be circulated of all patients from whom clotted samples have not been received within the previous three months. A sample from each patient on the list should be urgently sent to the laboratory.

Requests to amend a patient's status on the transplant list must be notified to the Transplantation Laboratory in writing by FAX (forms available from the Business and Administration Manager) or email (mft.histocompatibility@nhs.net) as soon as patient's suitability for transplantation changes. Local and national lists will be amended Monday to Friday.

Multi-disciplinary team meetings / Clinical Liason / Patient Information

Representatives from the laboratory regularly meet with the clinical teams at the referring dialysis centres. These meetings facilitate the review of current transplant lists and patients in work up for transplant listing. They also include comprehensive reviews of patients with complex immunological profiles and provide advice on Transplant Options for these patients.

In addition the laboratory contributes to patient education events including a monthly meeting organised at Manchester Royal for newly registered patients. The laboratory also offers the opportunity for patients to be referred to Transplant Immunology clinics. These clinics provide the patient with the opportunity meet with members of the transplant team (representatives from the laboratory, nephrology and recipient co-ordinators) to discuss their chance of a transplant offer and strategies to improve their chance of an offer.

9. Transfer of Patients to Other UK Transplant Units

NHSBT-ODT issued guidelines in April 2006 designed to prevent patients being disadvantaged when transferring from one unit to another in terms of their registration on the national list.

As part of the maintenance of the transplant list the Transplantation Laboratory will notify NHSBT-ODT when a patient is transferring to another transplant centre. In order to do this the referring dialysis centre must supply in writing to the Transplantation Laboratory the name of the patient transferring, the unit to which the patient is transferring and if possible the name of the clinician who will assume responsibility at the receiving unit. In all cases a date from which the transfer is to be effective must be included.

Until the transfer process is completed the patient remains on the referring unit's transplant list. This is to ensure that the patient does not lose any accrued wait time points on the national list.

10. Deceased Donor Crossmatching and Transplantation

Potential recipients for a kidney/pancreas/islets from a deceased donor are identified by NHSBT-ODT under the National Allocation Schemes.

Crossmatching

This is an essential pre-transplant procedure which must be carried out to ensure that the recipient has no donor-directed antibodies that would result in early transplant failure.

Potential recipients will be assessed for their suitability for “virtual crossmatching” and a “Virtual Crossmatch Negative” report issued when appropriate. For patient proceeding to transplant on the basis of a Virtual Crossmatch a “Day of Transplant” sample must be taken for retrospective testing.

Where a patient is NOT eligible for a Virtual Crossmatch the crossmatching requirements for that donor / recipient pair will be assessed and samples requested as appropriate via the recipient co-ordinators. All testing will be performed in parallel where possible to avoid delays which may lead to prolonged cold ischaemia time.

If a current recipient sample is requested by the laboratory for crossmatching against a potential donor, a 10ml clotted blood sample should be sent *to the laboratory as a matter of urgency*.

All crossmatch results are reported to the transplant team verbally and in writing by email.



11. Living Donor Programme

Initial donor selection

Laboratory tests: patients

ABO blood group – Copy results must be sent to the Transplantation Laboratory

HLA type

HLA specific antibody test

For parous female patients - HLA type father(s) of children or HLA type of each child.

Laboratory tests: donor

ABO blood group – Copy results must be sent to the Transplantation Laboratory

HLA Type

Compatibility Summary

For unsensitised recipients, potential donors will be typed for HLA-A, B, DR. For sensitised recipients, potential donors will be typed for HLA-A, B, C, DR, DQ (DP). An HLA report and a Living Donor Compatibility Summary will be issued within three weeks of specimen receipt. The Living Donor Compatibility Summary will indicate the risk factors associated with each potential donor and their potential transplant options

Crossmatching

HLA antibody positive patients: Samples for crossmatching may be requested to assess the clinical significance of donor directed antibodies. They will be crossmatched by flow cytometry and cytotoxicity if indicated.

If the crossmatch is negative, then work up can proceed, an immediate pre-transplant crossmatch and antibody screen is also performed.

If the crossmatch is positive, a positive crossmatch report will be issued and the pair may be referred for paired/pooled registration or HLA antibody reduction.

HLA antibody negative patients or patients with fully defined antibody profiles:

If patients fulfil the criteria for a “virtual crossmatch” as described previously, then a Virtual Crossmatch Report will be issued when the preliminary crossmatch test is requested. For patients who do not fulfil the criteria a flow cytometry crossmatch and antibody screen will be carried out. A final flow cytometry crossmatch test will be carried out in the week preceding the transplant.

United Kingdom Living Kidney Sharing Scheme (UKLKSS) Registration Process

ABO incompatible and / or HLA incompatible donor / recipient pairs can be registered with NHSBT-ODT for Paired / Pooled donation. Compatible donor-recipient pairs who may seek a better HLA or age match may also be registered in the scheme.

The forms are completed by the Living Donor Co-ordinator at the referring centre and are then sent to the Transplantation Laboratory for the completion of the H&I data.

Essential tests and information for donor registration

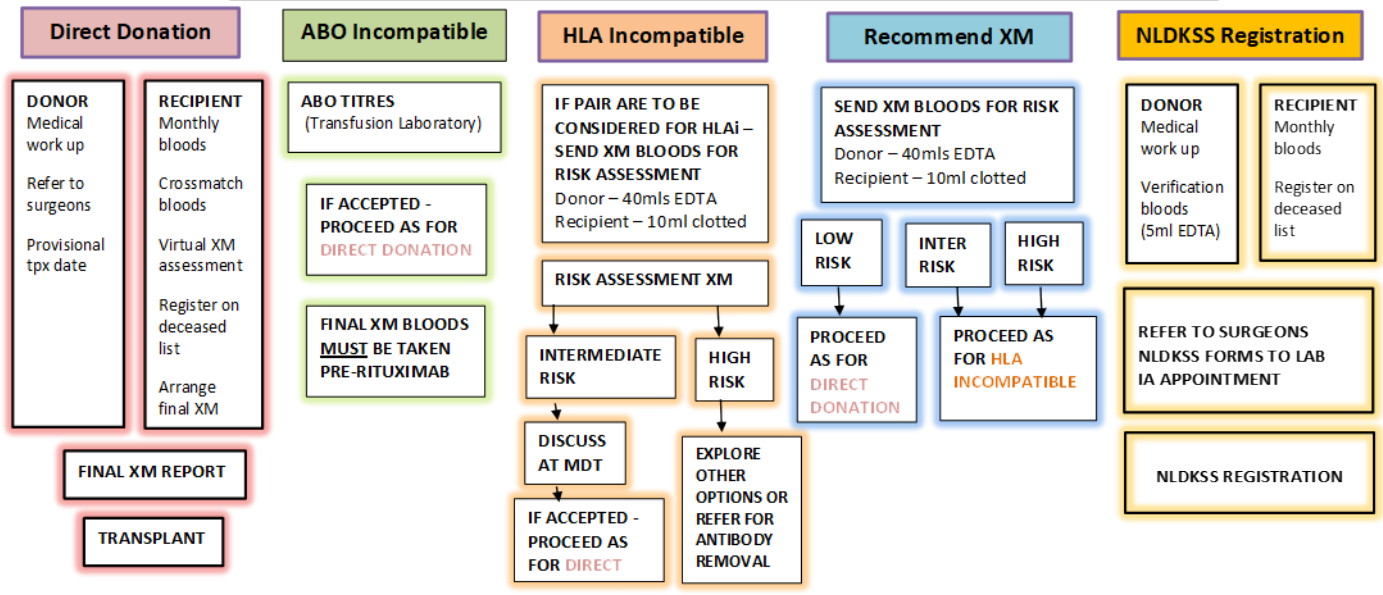
- Donor HLA type (tested on 2 separate occasions)
- Donor ABO blood group
- Surgical review of donor and recipient
- Recipient registration with NHSBT-ODT on deceased donor list

Once all tests are completed and information available the forms are emailed, by the Transplantation Laboratory, to NHSBT-ODT and copied to the Living Donor Co-ordinator for their records.

Living Donation Pathway



INTERPRETIVE MATCHING REPORT and TRANSPLANT OPTIONS



12. Post-Transplant Follow-up

Transplant recipients may produce HLA specific antibodies associated with transplant rejection.

10ml clotted blood samples should be sent from kidney/pancreas transplant recipients to the Transplantation Laboratory **weekly** while the patient is on the Transplant Unit and then **when a transplant patient attends the follow-up clinic****. Antibody production can then be monitored to identify humoral rejection. Also, a comprehensive immunological profile will be established should the patient require repeat transplantation.

** 10ml clotted blood samples accompanied by a request card must also be sent to the Transplantation Laboratory whenever a diagnostic transplant biopsy is performed.

Islet cell transplant recipients receive Basiliximab as part of the immunosuppressive protocol. Serum samples should be sent to the Laboratory 48hours, 7, 14 and 28 days post first infusion.

13. Standards

All aspects of the services provided for the renal / pancreas transplant programme are compliant with the relevant standards/guidelines.

BSHI BTS: Guidelines for the detection and characterisation of clinically relevant antibodies in allotransplantation.

Standards for Histocompatibility Testing Version 8.0 European Federation for Immunogenetics (EFI). January 2020

ISO 15189:2012(en) *Medical laboratories — Requirements for quality and competence*

Appendix 1: Effect of Rituximab on Laboratory Assays

As you will be aware, Rituximab is an IgG monoclonal antibody directed against CD20 which is expressed on B lymphocytes. It is therefore an anti-B cell agent and one of the main routes of action is thought to be by complement activation.

In the cytotoxic crossmatch test, donor lymphocytes are incubated with recipient serum. If donor directed HLA specific antibodies are present then the donor cells are killed and this positive result is a contraindication to transplantation.

If a patient is treated with Rituximab then that will be present in their serum and will also cause cell killing in the crossmatch test. That false positive result will deny a patient a transplant that might actually have been compatible. This situation arose recently when a patient's current serum sample was unexpectedly crossmatch positive. In the absence of information to identify this as a false result, transplantation had to be denied pending further investigation. It transpired that there were no HLA specific antibodies in that sample but the patient had been treated with Rituximab four months previously.

With this in mind, please notify the Transplantation Laboratory when a patient is treated with Rituximab. The solid phase HLA antibody detection and definition tests we employ are not affected by Rituximab. It is possible to increase the frequency of these tests and to use the results alongside information on the patient's treatment in the interpretation of a crossmatch result. In that way, patients will not be denied a compatible transplant.

Many thanks for your support,

Kay Poulton

Consultant Clinical Scientist

Appendix 2

Requirements for sending specimens by post:-

In order to comply with UN code number UN3373 there should be three layers of packaging.

1. The primary container containing the specimen
2. Secondary packaging e.g. a sealable plastic bag that contains enough absorbent material to contain the entire contents of the primary container without leakage occurring.
3. Outer packaging, to be labelled with the destination address, the name of the sending department and address, and be clearly marked "Diagnostic Specimen"

Appropriate packaging is available from suppliers including the Royal Mail, Royal Mail Safebox, FREEPOST, SWC1 143, Ross-on-Wye, HR9 7ZB.

Appendix 3 List of Tests and Samples Required

Test	Sample Required
Recipient HLA Typing (Initial HLA type)	5ml EDTA and 10ml clotted blood
Recipient HLA Typing (Verification HLA type)	5 ml EDTA and 10ml clotted blood
Recipient HLA-Specific Antibody Screen	10ml clotted blood
Recipient Autoantibody test	20ml EDTA and 10ml clotted blood
Potential Living Donor HLA Typing	5ml EDTA blood
Deceased Donor HLA Typing	10ml EDTA blood
Crossmatching (Deceased Donor)	Donor: spleen and lymph node samples Recipient: 10ml clotted blood
Crossmatching (Living Donor)	Donor: 40ml EDTA blood Recipient: 10ml clotted blood
Recipient Post-Transplant Monitoring	10ml clotted blood

Appendix 4 Renal Transplant Chance Calculation and Estimated Wait Times

The Transplant Chance calculation was introduced to give an indication of the percentage of deceased donors on our database that would fulfil matching criteria for a particular patient. The criteria include ABO identity and 3 or fewer mismatches at HLA-A and HLA-B and no mismatch at HLA-DR. The number of patients on the transplant list continues to increase and consequently there has been an increase in the average wait times.

A review of the transplant list in April 2014 showed that:

Median % Chance	Predicted Waiting time (years)
0.1 - 0	>10
0.2 – 0.1	Up to 10
0.2 – 0.4	Up to 9
0.4 – 0.8	Up to 7
0.8 – 1.0	Up to 5
> 1.0	Up to 4

The above calculation is based on local data. NHS BT ODT have built an on-line calculator called NHSBT Kidney Risk Communication Tool (Kidney-RCT). It was designed to aid discussions between patients and clinicians. The calculator asks for some details about the patient and presents the results in the form of graphs and bar charts based on these details.

Currently the results presented for kidney patients are: waiting time (from point of listing) and chance of getting a transplant whilst acknowledging the risk of death on the list or removal from the list. To create the results presented, data about patients in the past were used to build statistical models and extract results based on what happened to people “like this”.

The Kidney-RCT has been designed to be used by clinicians with patients. It is a communication tool and should not be used by itself to make decisions. The Kidney-RCT can be found on the NHS BT ODT clinical website (<https://odt.nhs.uk/transplantation/tools-policies-and-guidance>).

Appendix 5

Crossmatching for Deceased Donor Renal Transplantation

The purpose of the crossmatch test is to determine whether a patient has antibodies which indicate sensitisation against the specific donor. The cytotoxic crossmatch test has long been established as the definitive pre-transplantation test to prevent hyperacute rejection.

Cytotoxic crossmatching

Patient serum samples are added to donor lymphocytes and incubated. If the serum contains donor-specific HLA antibodies these bind to the donor lymphocytes and cause cell death. This can be visualised using a microscope.

Flow cytometry crossmatching

Flow cytometry crossmatching is a more sensitive method of crossmatching and is used as an additional test for patients deemed to be at "higher risk" eg: those with complex HLA specific antibody profiles.

A flow cytometer detects antibody binding to donor lymphocytes using fluorescence. Software is used to calculate whether the result is positive or negative. This test, when required, is **conducted in parallel** with the cytotoxic crossmatch test.

Patient serum samples are chosen carefully to represent the patient's screening history. A **clotted blood** sample from the patient taken **within 6 weeks** of the crossmatch test must be included and a day of transplant sample.

These tests take on average **3 hours** from receipt of donor material or, if required, a clotted sample from the recipient.

Virtual crossmatching

A virtual crossmatch report may be issued **before crossmatch testing takes place** for some eligible patients. This is followed up by a retrospective cytotoxic crossmatch test which is subsequently also reported.

Patients eligible for a virtual crossmatch are those who have been rigorously assessed and defined as **having no donor-directed sensitisation**.

In some instances HLA antibody positive patients may be considered as suitable for virtual crossmatch. However, these patients are assessed on a case by case basis and may require HLA antibody specificity definition testing prior to a report being issued.

The virtual crossmatch report states that it is essential that the patient has experienced no sensitising events (e.g. transfusion of blood products, infection or pregnancy) since the date of the most recent HLA antibody test result. It is also noted that in 2021, nationally, discrepancies were detected in 0.34% of donor HLA types after organs had been allocated. This poses a risk for sensitised patients progressing to transplant on the basis of a negative virtual crossmatch.

Samples required for deceased donation crossmatching

Recipient

Serum samples stored by the laboratory are used for crossmatching. A **clotted blood** sample taken from the recipient taken on the day of transplant is required for the crossmatch test.

Deceased Donors

Spleen (or lymph node) for crossmatch and confirmatory HLA type.

Appendix 6

Transplantation Laboratory
Guidelines for Email Communication with the Transplantation Laboratory

Request to List Forms

Judith Spencer
judith.spencer@mft.nhs.uk

Donna Whiteoak
donna.whiteoak@mft.nhs.uk

Marcus Lowe
marcus.lowe@mft.nhs.uk

Letters Relating to Patient Listings

TransplantLab@mft.nhs.uk

Activations/Suspensions

Histo Team Generic email
-mft.histocompatibility@nhs.net

Specific Patient Queries
(Re: samples required /DSAs / status on list etc)

Histo Team Generic email
-mft.histocompatibility@nhs.net

or telephone
67988/67919/6 6656/66651

Compiled by Judith Spencer/Judith Worthington April 2018



Appendix 7

Guidelines for DSA testing

Background

Donor-Specific HLA-Antibodies (DSA) are associated with allograft rejection and graft failure of transplanted organs. By systematic post-transplant monitoring in kidney, or simultaneous pancreas and kidney transplant recipients, it is possible not only to identify patients at highest risk of immune-mediated graft loss, but also to initiate early intervention strategies to prevent this. In this policy, we aim to provide guidelines for monitoring all recipients post-transplant for the presence of DSA, with recommended additional measures should the clinical post-transplant profile indicate that the patient is at high risk of graft loss. These recommendations have been adapted from Tait et al, 2013 *Transplantation Volume 95, Number 1, January 15, 2013* and *BSHI BTS: Guidelines for the detection and characterisation of clinically relevant antibodies in allotransplantation*

1. During the First 12 months

a. Standard Risk Patients (No pre-transplant donor directed antibody)

Screen for the presence of DSA under the following circumstances:

- i. 12 months after transplantation, unless there is cause for concern. eg
 1. Whenever a significant change in immunosuppression is considered (eg reduction/withdrawal/conversion)
 2. Suspected non-compliance
 3. Graft dysfunction
 4. Before transfer of care to another transplant centre.

b. Standard Risk Patients (Pre-transplant donor directed antibody detectable by Luminex only)

- i. Monitor for DSA at one month, unless there is cause for concern. eg
 1. Whenever a significant change in immunosuppression is considered (eg reduction/withdrawal/conversion)
 2. Suspected non-compliance
 3. Graft dysfunction
 4. Before transfer of care to another transplant centre.

c. Intermediate risk Patients (Pre-transplant donor directed antibody detectable by flow cytometry crossmatch)

- i. Monitor DSA weekly for first month. If there is additional cause for concern:
 1. Send samples to the Transplant Laboratory daily during period of concern for accurate monitoring of DSA fluctuations. All samples will be stored and testing will be performed as appropriate after discussion with the laboratory and clinical teams to assess appropriate frequency of testing.
- ii. Monitor monthly if all is well until Month 6

d. High Risk Patients (Pre-transplant donor directed antibody detectable by complement dependent cytotoxicity)

These patients are recognised to be at very high risk of early clinical rejection and AMR in the first three months.

- i. Monitor daily for the first three weeks
- ii. Monitor weekly after that until Month 2
- iii. Monitor monthly if all is well until Month 6

2. After 12 months

Monitor annually upon the anniversary of the transplant, unless there is cause for concern as outlined above.