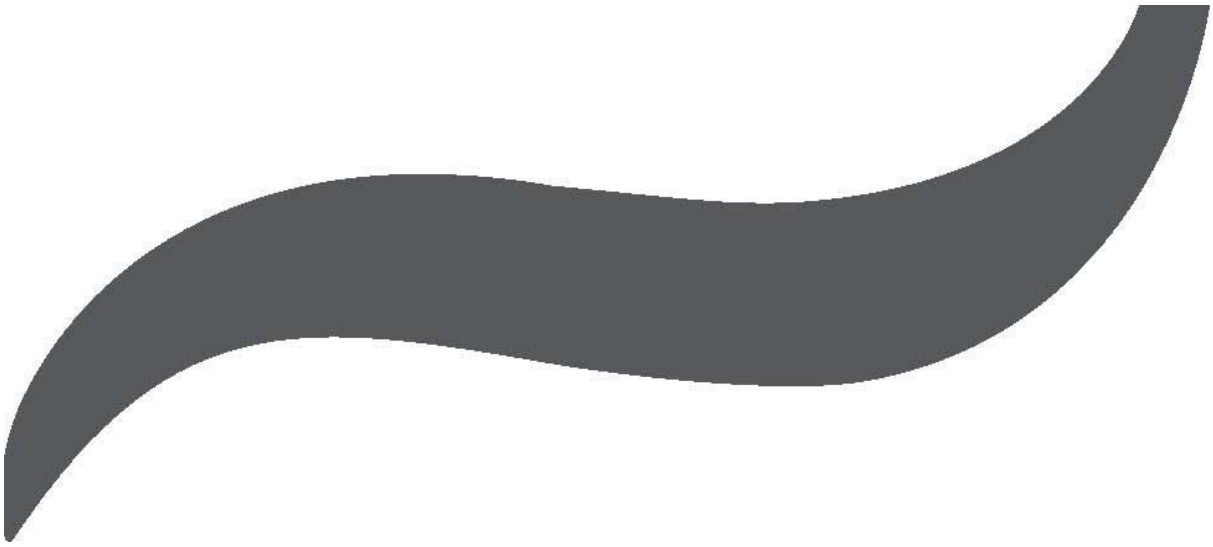
Acute Services Division

NHS
Greater Glasgow and Clyde

Laboratory User Manual

Histocompatibility & Immunogenetics Service



Contents

Contacting the Laboratory

Postal Address for correspondence and samples:
Histocompatibility and Immunogenetics Laboratory,
Gartnavel General Hospital,

Level 1, Laboratory Medicine Building,
21 Shelley Road, Glasgow, G12 0ZD

Tel: 0141 301 7755

Website: https://www.nhsggc.scot/staff-recruitment/staff-resources/laboratory-medicine/histocompatibility-and-immunogenetics/

Other ways to contact the laboratory

Email: ggc.histocompatibilityandimmunogenetics@nhs.scot

The email account is monitored daily, and is suitable for the receipt of patient identifiable (PID) information from secure accounts (including scot.nhs.uk, nhs.scot, nhs.net).

NOTE: PID information should not be added to the subject line.

Laboratory Staff

Head of Service

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Laboratory enquiries / Secretary

Joan Hagen

Tel: 0141-301-7755

E-mail: ggc.histocompatibilityandimmunogenetics@nhs.scot

On Call Scientist

Tel: 0141 211 3000 and ask for on-call tissue-typist

Introduction

This user manual is intended as a guide for users of the services provided by the Greater Glasgow and Clyde (GGC) Histocompatibility and Immunogenetics (H&I) Service.

a) Laboratory scope and location

The H&I laboratory is located on Level 1 of the Laboratory Medicine Building at Gartnavel General Hospital (GGH), Glasgow. It offers a comprehensive range of molecular, serological and cellular tests which support solid organ transplantation (kidney and heart), haematopoietic progenitor cell (HPC) transplantation, disease association testing and pharmacogenetic testing. Tests performed in support of these services are detailed in Appendix 1.

The laboratory is currently accredited by the United Kingdom Accreditation Service (UKAS), 9010 Medical Single (ukas.com) and by the European Federation for Immunogenetics (EFI).

The terminology used for HLA alleles and antigens will confirm to the latest report of the WHO Committee on Nomenclature (EFI F1.1)

The H&I laboratory is committed to providing the highest quality and standard of service. In order to accomplish this, the laboratory:

- operates a Quality Management System
- upholds professional codes and values
- implements and complies with standards set out by local, national and international regulatory bodies
- reports examination results in a manner that is timely, confidential, accurate and clinically useful
- undertakes approved research and development projects in collaboration with other specialities
- performs duties as would befit a centre of excellence in H&I
- complies with local, national and international standards on confidentiality and data protection

b) Opening hours

Normal working hours

Monday - Friday 8.00 – 16.30

24 hour transplant on-call service

An on call service is provided to facilitate kidney and heart transplantation. Contact can be made via the GGH switchboard. Please ask for the on-call tissue typist.

A one in four on-call Consultant / Principal Clinical Scientist rota is shared with the H&I service in Edinburgh. Scientists are contacted directly for virtual crossmatch queries, and indirectly via the on-call tissue-typist.

c) Deliveries and visitors

Deliveries

Routine samples are delivered to the H&I laboratory. Out of hours, urgent samples must be delivered to the sample drop box located at the front door to 21 Shelley Road when agreed in advance with the on call scientist.

Entrance to the building for deliveries is obtained via intercom. Small goods may be delivered via the side entrance. If lift access is required, this must be requested via the laboratory.

Parking

Parking is accessible in the nearby NHS car park (maximum 4 hours) or at a charged parking facility at the hotel situated directly across from the laboratory entrance.

Visitors

Visitors are seen by appointment only.

d) Sample collection, documentation and test requesting

Test request forms are available on request by emailing ggc.histocompatibilityandimmunogenetics@nhs.scot or calling the laboratory on 0141 301 7755.

TrakCare tests can also be requested using TrakCare (Histocompatibility and Immunogenetics catalogue)

1. Request Forms

Request forms must be legible and contain:

*Patient's Surname and Forename

*Date of birth

*CHI number (for samples originating in Scotland)

*Address

*Hospital and ward

*Consultant/requester to whom the report is to be issued

*Clinical details

*Date of sample acquisition

2. Sample labelling (multiple samples from the same patient must all be labelled as below)

*Name

*DOB / CHI number (for samples originating in Scotland)

*Date of sample acquisition

PLEASE NOTE:

Sample labelling must ensure unequivocal identification of the patient, in particular when multiple samples are taken from the same patient.

The information supplied must match the request form. If not, the sample will be rejected.

Samples received without a request form will be rejected.

Labels must be attached the correct way so the vial contents are still visible. This impacts downstream processing and is a health and safety risk to staff if label has to be removed.

3. Additional Documentation

- **Renal patient for activation**

  *Fully completed activation form

- **HPC transplant patient for volunteer unrelated donor (VUD) search**

  * Completed VUD referral form

  Please note that as soon as a patient presents with a condition that may require HPC transplant, an EDTA (buccal or saliva may be sent from patients with low cell counts, or circulating blast cells) and clotted sample should be forwarded to the laboratory. This will prevent unnecessary delay at a later date

- **Local deceased donors**

  * HLA Typing Request Form (FRM4279/2) completed by donor coordinator.

e) Primary sample collection and handling

1. Pre collection activities

There are no specific instructions or requirements for preparing the patient prior to collection of sample.

There are no specific timings for sample collection required except when patient is undergoing antibody reduction treatment and timings must be agreed with laboratory.

The laboratory must be informed if patients have a low lymphocyte count.

The laboratory must be informed if patients are receiving therapeutic antibody treatment

e.g. rituximab, ATG

2. Primary sample volume and additive requirements

Test	Specimen Requirement [5]	Minimum Volume /ml	Target Turnaround Time from sample receipt to test result authorisation
Disease association testing	EDTA[4]	4	21 days except B*57:01 (7 days)
HLA-A*02:01 testing for tebentafusp	EDTA[4]	4	14 days
HLA typing (recipient)	EDTA[4]	4	21 days
HLA typing (potential living donor)	EDTA[4]	4	21 days
HLA typing (local deceased donor)	EDTA	8	4 hours from receipt of sample 8 hours from sample bleed time
HLA antibody testing Unsensitised patient	Clot	6	14 days
HLA antibody testing sensitised	Clot	6	28 days
URGENT HLA antibody testing[1]	Clot	6	4 hours
Living donor crossmatches[2] (i) vXM	Donor EDTA Recipient EDTA Recipient Clot	4 4 6	21 days
(ii) Flow XM	Donor EDTA Recipient EDTA Recipient Clot[6]	30 30 6	5 days[3]
Deceased donor crossmatches Flow[3]	Donor EDTA or spleen/ lymph node Recipient EDTA Recipient Clot[6]	30 30 6	6 hours

[1]Urgent HLA antibody testing is available in exceptional circumstances and this requires agreement between the requester and senior laboratory staff. Urgent requests must be followed up with a phone call or email. Contacting the laboratory is an essential step – merely selecting the "Urgent" box in Trakcare/request form will not cause your sample to be handled urgently.

[2]All living donor crossmatches must be pre-arranged with the laboratory.

[3]All deceased donor typing must be pre-arranged with the on-call scientist.

[3]Assuming donor and recipient HLA type is known and recipient HLA antibody testing is up-to-date. If not, reports will take longer.

[4]Buccal or saliva samples may also be received. Please contact the laboratory to request a sampling kit and instructions (LIMOL159).

[5]Samples in the wrong container will be rejected

[6]Sample must be collected within 48 hours pre transplant

3. Sensitising events

Additional samples are required for patients that have had a sensitising event.

For renal patients, please send a sample 14 days after the event (with a clear description on the request form).

For cardiac patients, the laboratory must be notified to establish a testing schedule.

f) Sample packaging and transportation

Samples that arrive in an unsuitable condition will not be processed. Conditions include samples collected in the wrong container, significantly delays in transport and broken sample tubes. Repeat specimens will be requested in these cases.

HLA typing (EDTA) samples are stable at ambient (22˚C) temperature for 4 days.

Antibody analysis (clotted) samples are stable at ambient (22˚C) temperature for 4 days. Samples received after this time will be rejected.

Crossmatching samples (EDTA) These must not be refrigerated and should be received within 24 hours of venesection. All crossmatches must be booked in the lab diary in advance by contacting the laboratory.

Urgent deceased donor samples (EDTA, peripheral blood, spleen, lymph node) from deceased donors must be sent directly to the laboratory. The laboratory/ on-call scientist must be notified in advance of the expected arrival time.

Delivery notification forms to attach to the packaging are made available to transplant coordinators and the transplant unit.

Packaging of samples

All samples must be packaged in containers compliant with UN packaging instruction P650 Packaging and transport requirements for patient samples – UN3373 - GOV.UK (www.gov.uk) and labelled as shown below. Information with regard to high risk specimens must be clearly displayed on both sample and request form.

Biological Substance Category B

Transport of samples

Samples should be transported in

1) the sealable bag attached to the yellow H&I request form (or any sealable bag).
2) Outer packaging which should be rigid e.g a cardboard box
3) Labelled UN3373, Biological Substance Category B, as above

Specimens from the GGH site are delivered via local arrangements. All other specimens must be transported by van, courier or taxi or sent by post (observing postal regulations). Arrangements should be confirmed within your local organisation.

g) Reporting of results

Reports are computer generated from the laboratory patient management system.

Reports generated from this system are valid without a signature for electronic transmission and in this format will be sent to the requester by secure email.

Clinical Portal

Reports for the majority of GG&C referrals are issued using Clinical Portal (if a record exists).

Email

Reports for GG&C referrals are issued by email to the requestor in addition to issue on clinical portal. Requests from other health boards are issued via secure email.

Reports will only be sent between secure email addresses as per NHS GGC Email Usage policy.

Postal

If a secure email address is unavailable, reports are printed, signed by authorised staff and dispatched by internal hospital mail.

Other

In order to prevent sensitive or incorrect information being released to inappropriate individuals, verbal reporting is actively discouraged. A verbal report may be issued in an emergency by a senior member of staff to a suitably qualified person. A hard copy report will follow as soon as possible.

Faxing of reports that include patient name and personal information has been prohibited by The Scottish Government.

Clinical advice

Senior laboratory staff may be contacted during working hours (contact details on Page 3).

Out with normal hours, there is an on call Consultant / Principal Clinical Scientist available for advice who can be contacted via the on call tissue typist. The on-call Consultant /

Principal Clinical Scientist rota is served by CCS from SNBTS Edinburgh (UKAS and EFI accredited laboratory) and NHS GG&C. An annual review of CPD to ensure competency is maintained is undertaken.

The laboratory utilises published guidelines to aid definition of clinical decision limits including:

Little et al., BSHI guideline: HLA matching and donor selection for haematopoietic progenitor cell transplantation. Int J Immunogenet 2021;48:75-109

Battle et al., BSHI and BTS UK guideline on the detection of alloantibodies in solid organ (and islet) transplantation. Int J Immunogenet 2023;50 (Suppl 2):3-63

Measurement Uncertainty

Measurement uncertainties have been assessed for relevant examination procedures and these are available to users upon request.

(h) Referral of samples for additional testing

HPC transplant patient and donor serum samples are referred for CMV testing to The West of Scotland Specialist Virology Centre (WoSSVC) based at Glasgow Royal Infirmary. This laboratory is UKAS accredited (UKAS Ref No: 9319).

The WoSSVC's ongoing accreditation status and performance in external proficiency testing is reviewed biannually.

Professional opinion on the results generated by the WoSSVC will be sought from the Consultant in Charge.

(i) Consent & Confidentiality

Each request accepted by the laboratory for examination(s) will be considered an agreement.

All testing requests should be undertaken with the consent of the patient when obtaining samples. The laboratory assumes that when sending a sample consent has been obtained by the requesting clinician.

All patient and donor details, including test results, will be handled in compliance with NHSGGC policies, GDPR and the principles of the Data Protection Act.

The laboratory receives samples collected by venepuncture and buccal / saliva swabs and therefore consent for testing is inferred. For deceased donor sampling, consent is managed by the Organ Donation and Transplantation Directorate of NHS BT. The laboratory shares patient data with NHS BT Organ Donation and Transplantation for the purposes of listing patients for renal transplantation. Patient consent is documented by the transplant coordinator and indicated on the referral to activate form (LFXM087). The laboratory shares patient data with the Anthony Nolan Register for the purposes of undertaking an unrelated donor search. Patient consent is documented on the 'VUD' form (LFRA042).

J) Service Agreements

Service agreements detailing responsibilities of the H&I laboratory and the transplant service users have been issued. These agreements are reviewed every two years by the H&I laboratory director and the director of the transplant service (adult cardiac, adult renal, adult HPC, paediatric renal and paediatric HPC).

(j) Complaints procedure

The H&I laboratory endeavours to provide the best service possible to its users. If there has been a shortfall in expectations or an identified problem with the service, please contact the Quality Manager. Formal complaints must be made in writing. All complaints are recorded, reviewed and acted upon to improve the overall service.

Appendix 1: Laboratory services

1. **Renal transplantation**

The H&I laboratory supports the renal transplant programme in Glasgow which serves adults in the West of Scotland and all children nationally.

(i) Recipient work up for transplant listing

Prior to registration on the national transplant list, the following H&I testing is performed:

- HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 typing at intermediate or higher resolution. HLA antibody screening on two independent serum samples
- HLA type is verified on a second independently drawn blood sample

The H&I laboratory collates this data and other relevant clinical information before activating the patient on the UK transplant list.

(ii) Patients listed for renal transplantation

For listed patients, the H&I laboratory:

- undertakes HLA antibody screening and identification on serum samples acquired minimally at 3 monthly intervals
- stores serum samples
- suspends and reactivates patients as necessary

(iii) Transplantation with a deceased donor kidney

The H&I laboratory will:

- provide a 24 hour, 365 day on call service
- HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 typing at low/intermediate or higher resolution for deceased donors.

- perform a prospective or retrospective (in the case of virtual crossmatch) crossmatch for recipients receiving a transplant
- crossmatch historic and current recipient serum samples against donor T and B-cells using the flow cytometry crossmatch.
- report results to the transplant surgeon with Consultant Clinical Scientist advice as required

(iv) Post-transplant HLA antibody testing

The H&I laboratory will provide this service annually as routine and at any time it is clinically indicated.

(v) Potential live donor work up

This will not commence until the recipient has completed work up (section i). The H&I laboratory will:

- undertake HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 typing at intermediate or higher resolution. Additional HLA loci may be defined as required.
- perform a virtual crossmatch
- crossmatch, a selection of patient serum samples against donor T and B-cells by flow cytometry.
- report results to the live donor transplant coordinator and the requesting clinician
- perform verification HLA typing on selected living donors

(vi) Local deceased donors

The H&I laboratory:

- undertake HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 typing at low/intermediate resolution meeting the minimum requirements for deceased donor typing
- reports HLA types to NHSBT within 4 hours of receipt of donor material

2. **Cardiac transplantation**

The H&I laboratory supports the national cardiac transplantation programme based at the Golden Jubilee National Hospital, Clydebank.

(i) Recipient work up

Prior to registration on the national transplant list, the following H&I testing is performed:

- HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 typing at intermediate or higher resolution.
- HLA antibody screening on two independent serum samples
- HLA type is verified on a second independently drawn blood sample

The results are reported to the cardiac transplant coordinator for listing on the national cardiac transplant list.

(ii) Patients listed for cardiac transplantation

For listed patients, the H&I laboratory:

- undertakes HLA antibody screening and identification on serum samples acquired at 3 monthly intervals (minimally)
- store serum samples

(iii) Transplantation

The H&I laboratory will:

- provide a 24 hour, 365 day on call service
- HLA-A, B, C, DRB1, DRB3, DRB4, DRB5 DQA1, DQB1, DPA1 and DPB1 typing at low/intermediate resolution for deceased donors
- perform a prospective or retrospective (in the case of virtual crossmatch) crossmatch for recipients receiving a transplant
- crossmatch historic and current recipient serum samples against donor T and B-cells using flow cytometry crossmatch

- report results to the transplant surgeon with Consultant Clinical Scientist advice as required

3. **Haematopoietic Progenitor Cell transplantation**

The H&I laboratory supports the national HPC transplant units at the Queen Elizabeth University Hospital (QEUH), Glasgow and the Royal Hospital for Children, Glasgow.

High resolution typing is defined as the identification of HLA alleles that encode the same protein sequence within the antigen binding site. HLA alleles must be identified at the level of resolution which defines the first and second fields according to WHO nomenclature by at least resolving all ambiguities: Resulting from polymorphisms located within exons 2 and 3 for HLA class I loci, and exon 2 for HLA class II loci. That encompass a null allele, wherever the polymorphism is located, unless it can be demonstrated that an expressed antigen is present on the cells.

(i) Recipient work up

The H&I laboratory:

- performs high resolution HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 typing
- performs verification HLA typing on an independent blood sample
- tests recipient sera for HLA specific alloantibodies
- requests and records CMV testing results
- reports results to the transplant centre

(ii) Potential related donor work up

The H&I laboratory:

- undertakes, minimally, intermediate resolution HLA-A, B and DRB1 typing for all potential related donors
- undertakes high resolution HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 typing for selected potential related donors
- requests CMV testing results
- performs verification HLA typing on an independent blood sample from the selected donor
- reports results to the clinical apheresis unit (adults) and the transplant unit

- initiates a search of the UK and international unrelated adult donor registries upon receipt of a volunteer unrelated donor (VUD) form
- selects and requests blood samples from potential matching donors
- performs high resolution HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 typing on shortlisted donors
- requests and collates CMV testing results
- confirms the absence of HLA mismatches between donor and recipient
- performs verification HLA typing on blood received from the donor at the time of medical examination
- informs the transplant centre on the search and donor identification process
- provides written reports of HLA results and compatibility

(iii) Cord blood search

The H&I Laboratory:

- initiates a search of cord blood banks when appropriate
- prepares a shortlist of cords according to pre-defined criteria
- requests unit reports for shortlisted cords
- requests verification HLA typing for shortlisted cords
- acquires a DNA sample from selected cords and performs high resolution verification HLA typing
- performs verification HLA typing on DNA extracted from the infused product
- informs the transplant centre on the search and cord blood unit identification process
- provides written reports of HLA results and compatibility

4. Disease association testing and pharmacogenetics

The H&I laboratory:

- provides HLA typing to assist in the diagnosis of ankylosing spondylitis, Behçet's disease, Birdshot chorioretinopathy, coeliac disease and narcolepsy
- tests for HLA-B*57:01 to identify individuals at risk of hypersensitivity to abacavir
- tests for HLA-A*02:01 to identify individuals with uveal melanoma suitable for treatment with tebentafusp
- will perform other HLA typing tests when requested as agreed with the consultant clinical scientist where there is clinical evidence to support HLA typing as a useful tool in diagnosis and/or patient management. Please contact the laboratory in these cases.

5. Research studies

The H&I laboratory will undertake histocompatibility and immunogenetics testing to support appropriately funded and ethically approved research studies. Agreement must be made with the laboratory prior to the commencement of testing.

Appendix 2: Laboratory request form

NHS
Greater Glasgow and Clyde

Histocompatibility & Immunogenetics
(Tissue-Typing) Service,
Gartnavel General Hospital
21 Shelley Road, Glasgow, G12 0ZD
Tel: 0141-301-7755 Fax: 0141-301-7761

PERSON DETAILS

Hospital No: | CHI No: | DoB: | ☐ Male ☐ Female

Surname: | Forename: | Consultant: | Requester:

Hospital / Ward / Address for Results:

Clinical Details:

Priority:

Category: ☐ Patient - ☐ Renal ☐ Cardiac ☐ Haematology ☐ Auto ☐ Allo ☐ Other:_____

☐ Relative of:_____
CHI / DOB:_____
Relationship:_____

SPECIMEN DETAILS

Date & Time of Collection:

Type (if not blood):

Contact No:

TEST DETAILS

Pre Transplant
☐ HLA Typing (4ml EDTA)
☐ HLA Antibodies (6ml Clot)
☐ Crossmatch (30ml EDTA + Clot)
Post Transplant
☐ DSA Monitoring (6ml Clot)
☐ Routine or ☐ Urgent (give clinical details)

HLA ASSOCIATION (4ml EDTA)

☐ Ankylosing Spondylitis and Related Disorders (HLA-B27)
☐ Abacavir Hypersensitivity (HLA-B*5701)
☐ Coeliac Disease (HLA-DQ2/DQ8)
☐ Narcolepsy (HLA-DQB1*0602)
☐ Other Disease/Disorder - please give details

Lab Use Only

HLA No:

TISSUE TYPING

PRESS FIRMLY ON EACH END
TO ENSURE A LEAKPROOF
SPECIMEN CARRIER

BIOHAZARD

06/2021