University Hospitals Bristol and Weston NHS Foundation Trust

Specialist Integrated Haematological Malignancy Diagnostic Service (SIHMDS)

User guide

Contact Information

Key Contacts		
Clinical Lead	Dr Andrew Stewart	Andrew.Stewart@nhs.net
Operational Lead	Dr Ulrika Johansson	Ulrika.Johansson@UHBW.nhs.uk
Quality Manager	Mrs Natalia Casey	Natalia.Casey @UHBW.nhs.uk
Laboratory Head of Sections		
SI-HMDS Reception	Dr Ulrika Johansson	Ulrika.Johansson@UHBristol.nhs.uk
Morphology	Dr Andrew Stewart	Andrew.Stewart@nhs.net
Flow Cytometry (FC)	Dr Ulrika Johansson	Ulrika.Johansson@UHBristol.nhs.uk
Molecular Genetics	Mr Tim Clench	Tim.Clench@ nbt.nhs.uk
Cytogenetics	Dr Chris Wragg	Chris.Wragg@nbt.nhs.uk
Haematopathology	Dr Joya Pawade	Joya.Pawade@nbt.nhs.uk
Laboratories		
SI-HMDS reception	0117 342 2596	
Flow Cytometry	0117 342 2596/0779	Natasha.Futhee@UHBW.nhs.uk; Ulrika.Johansson@UHBristol.nhs.uk
Molecular Genetics	0117 414 6174	nbn-tr.haematooncology@nhs.net
Molecular Genetics, MRD service	0117 414 6173	nbn-tr.haematooncology@nhs.net
Cytogenetics	0117 414 6174	nbn-tr.haematooncology@nhs.net
Histopathology	0117 414 9875	Simon.Florio@nbt.nhs.uk; Mark.Orrell@nbt.nhs.uk
Urgent referrals		
Urgent clinical queries	**Bleep 2455** (Laboratory Duty SpR)	
Urgent samples	Alert reception on 0117 34**2 2596**	
Unexpected urgent samples	**Haematology on call service on bleep**	
Postal and Visiting Address		**Laboratory hours:**
UHBW SI-HMDS Level 8, Queen's Building Bristol Royal Infirmary Upper Maudlin Street Bristol BS2 8HW		**Monday - Friday, 09.00 - 17.00** Out of hours service may be pre-arranged for urgent samples: Contact reception on ext. 22596

Specimen Requirements

Request samples on ICE or Medway. Alternatively use print version of request form (last page of this document). All specimens must be labelled with patient name, date of birth and hospital or NHS number.

Send samples for urgent attention to SI-HMDS reception, Department of Haematology, Level 8, Queen's Building, Bristol Royal Infirmary, Upper Maudlin Street, Bristol BS2 8HW.

Blood and bone marrow samples must be received within 24 hours of sampling.

Cerebrospinal must arrive within hours and absolutely on the same day. If this is not possible: Place CSF for flow analysis in transfix (contact SI-HMDS reception to arrange a specimen vial containing the transfix preservative).) Cell count and cytospin samples must not be placed in transfix**.**

Fine needle aspirates must be received in tissue culture media Contact SI-HMDS reception to arrange delivery of media bottles for FNA sampling.

Investigation	**Sample type**	**Samples required** (volumes for pediatric samples may be reduced)
Leukaemia, Lymphoma	FNA / core biopsy (non-marrow tissue)	**FNA for Cytology**: Place the FNA in a 20ml universal tube **FNA for flow cytometry and genetics:** Place the FNA in tissue transport media* **Core:** Place in formalin
	Open biopsy (non-marrow tissue)	**For flow cytometry and genetics:** Place in transport media* or as last resort, saline. **For histology:** Place in formalin.
Leukaemia, Lymphoma, Marrow failure, Non-haemato-poietic malignancies	Bone Marrow Always send a 1× EDTA peripheral blood sample with any bone marrow request	**Aspirate** **Morphology and Perl stain**: Bedside smears, minimum 4 **Flow**: EDTA (1×purple top, minimum 1 ml) **Molecular genetics**: EDTA (1×purple top, minimum 1 ml) **Cytogenetics/FISH**: Heparin (1×green top, minimum 2 ml); or cytogenetic transport media **Trephine biopsy** **Histology**: Formalin **Flow/molecular genetics**: transport media* or as last resort, saline. **FISH** may be carried out on
Leukaemia, Lymphoma	Peripheral Blood	**Film and Flow**: EDTA (1×purple top) **Molecular genetics**: EDTA (1×purple top) **Cytogenetics/FISH**: Heparin (1×green top) or cytogenetic transport media
	Cerebrospinal Fluid	**Cell count and cytospin**: 10 drops **Flow:** Minimum 10 drops, preferably 20 drops
	Other Fluid Samples	Please send for cell count and cytology, no anticoagulants required. Contact HMDS for further advice and discussion.
	Post treatment monitoring	This depends on type of disease and investigations required. The laboratory will provide information.
PNH	Peripheral Blood	**Flow**: EDTA (1×purple top)
Other	Contact the HMDS office on 0117 342 0779	

*Transport media: For urgent unexpected sampling: Contact reception on 0117 342 2596.

Reports

All results are reported on the Laboratory Information System (LIS) and visible on Medway. *Standard* Turnaround times for Peripheral blood and CSF samples: 7 days; Fine needle aspirates& core: 24-48 hours for flow and cytology, 5 days for core biopsy; Bone marrow: 24-72 hours for interim (morphology and flow) and up to 3-5 weeks for final, including extended genomics tests. Turnaround times are guided by clinical urgency.

Urgent reports are issued for treatment-guiding results, where treatment is required promptly.

Urgent results may be telephoned prior to being issued on the Laboratory Information System.

Tests provided

The table below outlines the general strategy. SI-HMDS diagnostics deals with rare and unusual diseases: full diagnostic information may be found in the World Health Organization (WHO) classification system for tumors of the hematopoietic and lymphoid tissues (Swerdlow SH, editor. WHO classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th edn. Lyon, France: International Agency for Research on Cancer; 2017). A copy is available in the Morphology room. Genomics testing must follow the NHS England national test directory. This may be found on NHS England » National Genomic Test Directory. As of 2021, the details of strategies are still under regional and national evaluation.

For full details of each test and for a complete description of diagnostic pathway: Please contact the office and/or relevant section.

Disease	Flow cytometry	Immunohistochemistry	Molecular genetics	FISH	Karyotyping
?CML Diagnostic sample	Myeloid progenitor quantification	MPN panel	Qualitative and quantitative BCR-ABL on blood	t(9;22)	Yes if diagnosed
CML FU samples		MPN panel	Quantitative BCR-ABL on blood Monitoring 3 monthly	t(9;22) Until negative or suspected relapse	
? MPN	Myeloid progenitor quantification If ? Mastocytosis: Mast cell panel	MPN panel	JAK-2 V617F, JAK-2 exon12 MPL515 MPL Baltimore (special request) BCR-ABL FIP1L1-PDGFRa Familial ET: EPOR. NGS panel if relevant If ? Mastocytosis: KIT D816V	Not unless target suspected or identified by karyotyping	Yes if diagnosed
? MDS	Myeloid progenitor quantification; MDS score	MDS panel	NGS panel if clinically relevant	Not unless target suspected or identified by karyotyping	Yes
? AML	Acute leukaemia panel	MDS panel	Qualitative PML-Rara, t(8;21), inv16, Flt-3 NPM1, Guided by interim diagnosis and may need urgent activating	If ? APML: t(15;17) If ? Monomyeloid with eosinophilia: inv 16 If ? With maturation: t(8;21); Guided by interim diagnosis and FISH need urgent activating	Yes
AML Follow-up	MRD where available	MDS panel	MRD where available	If target identified at Dx: Until negative or suspected relapse	

samples					
APML Follow-up samples	Until cytogenetic remission and at suspected relapse	MDS panel	Quantitative PML-Rara	t(15;17) post each course until negative	
? CLL/SLL	B-LPD panel Clonal B cell quantification MRD analysis on follow-up samples	lymphoma panel	IgVH (<60 years) p53 mutation, NGS panel as indicated	Trisomy 12, Del 13q, Del 11q, del 17p P53 as indicated	
? MCL	B-LPD panel Clonal B cell quantification	lymphoma panel		t(11;14) as indicated	
? FL	B-LPD panel Clonal B cell quantification	lymphoma panel		t(14;14) if diagnostic uncertainty	
? HCL	B-LPD panel Clonal B cell quantification	lymphoma panel	BRAF V600E		
? NHL	LPD panel, T/B panel as required Clonal B/T cell quantification	lymphoma panel	Guided by interim diagnosis (note for T-LGLL, STAT3 and STAT5 may be requested)	Guided by interim diagnosis	Guided by interim diagnosis
? HG NHL	LPD panel T/B panel as required; TdT/Partial AL panel if required; KI-67; Clonal B/T cell quantification	High grade lymphoma panel		t(8;14) if Burkitt's needs excluding, High grade panel	Guided by interim diagnosis
?CTLC	LPD panel, Sezary panel; T-cell clonality and quantification	lymphoma panel	Guided by interim diagnosis		
? HL		Hodgkin Lymphoma panels			
? Burkitt's Lymphoma	LPD panel TdT/Partial AL panel	High grade B cell lymphoma panel		t(8;14) , High grade panel	
? ALL	Acute leukaemia panel	ALL panel	BCR-ABL	If suspected or if identified by karyotyping t(9;22), t(11;23), TEL/AML-1 . t(8;14) if Burkitt's needs excluding	Yes
ALL Follow-up samples	MRD		If target identified	If target identified	
? Myeloma/PCD	LPD panel, Plasma cell Panel	CD138, CD20, CD3, CD56		If diagnosed: Del 13q, t(11;14), t(4;14), del 17p	
Myeloma/PCD Follow-up samples	Plasma cell Panel, MRD	CD138, CD20, CD3, CD56			

Accreditation and Quality Assurance

UHB SI-HMDS is a NICE compliant networked SI-HMDS.
Reception, morphology, flow cytometry, and final integrated reporting are all located at UHB and are accredited to the ISO 15189:2012 standards by the United Kingdom Accreditation Service (UKAS) (reference number 8227).
The NHS England Genomics service is provided by Bristol Genetics Laboratory; and are accredited to the ISO 15189:2012 standards (reference number 9307)
The Histology service is located at NBT NHS Trust, Histology Department; and are CPA accredited (reference number 36)

Multidisciplinary team meetings (MDTs) are held on Thursdays and leads for respective laboratories usually participates.

EQA participation
Morphology: UKNEQAS blood films and bone marrow interpretation.
Flow Cytometry: UKNEQAS Leucocyte Immunophenotyping part I, PNH, CD34, Immune monitoring, CLL MRD*, AML MRD*, ALL MRD*, Plasma cell MRD*. The European Society for Clinical Cytometry (ESCCA) EILCP scheme (non-accredited; covers all haematological malignancies flow cytometry testing).
Integrated diagnosis: UKNEQAS Leucocyte Immunophenotyping part II.
Additionally, informal and semi-formal sample share schemes (non-accredited) are also in place for morphology, flow cytometry and integrated diagnosis.
For histology and genomics EQA participation, please contact respective laboratory.
** Accreditation pending*

Referral of investigations

1. Tissue biopsies with non haematological malignancies are forwarded to relevant histopathologist/pathology team.
2. Bone marrow aspirate samples from patients with acute promyelocytic leukaemia have a sample of cDNA sent to Department of Haematology, Guy's and St. Thomas's Hospital, London (national reference centre) , via the NHS England genomics hub

General Enquires

Contact operational lead / office on
0117 342 0779

If there are problems or complaints about the service please call us. We aim to resolve most problems immediately and informally

Referral form

See next page (use only if ICE/Medway requesting is not possible)

Address/Send samples to:
SI-HMDS
Queen's Building, Level 8
Bristol Royal Infirmary
Bristol, BS2 8HW

Contact Details:
Office Tel: 0117 342 0779
Laboratory Tel: 0117 342 2596
Fax: 0117 342 2531

SI-HMDS Referral Form

Hospital No:
Patient Name:
Gender: M / F
DOB:
NHS No:
(Use Label if available)

New Patient / Follow-up

Previously investigated by UHB HMDS: Yes / No
Post-Transplant: Auto / Sib / VUD / Cord / Haplo
Donor: Male/Female BMT Date: _____

Clinical Details / Suspected Diagnosis:
(If diagnosis known, please specify)

(On GCSF: Y / N / unknown)
(Recent Chemotherapy? Y / N/ unknown)

Blood count:
Hb: .....
WBC: .....
Ne: .....
Ly: .....
Plts: .....
Other
.....

Organomegaly:
Spleen Y / N
Liver Y / N
Lymph Nodes Y / N

Paraprotein: Y / N
G / A / M / D / E κ / λ
Quantitation: .....g/l

Specimen taken by (FULL NAME REQUIRED IN ALL CASES):

.....

Contact details:.....

Date / Time of sample: .....

Referring Consultant:.....

Referring Hospital:.....

Infection Risk? Yes / No **If yes, specify:**

Specimens Referred:
Peripheral blood (EDTA)
Peripheral blood air-dried slide
Bone marrow (BM) aspirate (EDTA/heparin)
BM unstained air-dried slides
BM Trephine
Lymph Node
FNA / Core
Other (specify):

Indicate Required Tests

- ☐ **Urgent** Full ? Acute Leukaemia work-up / ? APML
- ☐ Flow Immunophenotyping
- ☐ PNH (Peripheral blood only)
- ☐ Cytogenetics (Heparinised sample)
  - ☐ Store
  - Karyotype: ☐ Myeloid ☐ Lymphoid
- ☐ FISH (Heparinised sample)
  - ☐ CLL: Full CLL Panel / p53del only
  - ☐ Myeloma FISH
  - ☐ BCR/ABL
  - ☐ FGFR1, FIP1L1/PDGFRA, PDGFRB
  - ☐ Urgent PML-Rara
  - ☐ Other: Please specify
- ☐ Histology/Cytopathology and Immunohistochemistry
- ☐ Molecular genetics (EDTA sample)
  - ☐ Store
  - ☐ T/ B cell clonality
  - ☐ MyD 88
  - ☐ BRAF V600E
  - ☐ IgVH mutation ☐ p53 mutation
  - ☐ BCR ABL p190 / p210
  - ☐ ABL Kinase mutations for non-response to TKIs
  - ☐ JAK2 V617F

  will proceed to: Exon 12 variants for PRV if JAK2 neg
  will proceed to: CALR/MPL for ET/MF if JAK2 neg
  - ☐ SFSR2 ☐ KIT mutation ☐ Myeloid NGS panel

UHBW SI-HMDS Request Form Ed4