**Operational Policy NBT SIHMDS - Bristol Haemato-Oncology Diagnostic Service (BHODS)**

**13-1D-101h Background to Service**

Bristol Haemato-Oncology Diagnostic Service (BHODS) was developed within Pathology Services at North Bristol NHS Trust (NBT) to provide an integrated diagnostic process for investigation and reporting blood, bone marrow, lymph node and other tissue samples investigated for the presence of haematological malignancy. This Specialist Integrated Haematological Malignancy Diagnostic Service (SIHMDS) is supported by haematologists, haematopathologists and laboratory scientists with expertise in haematological malignancy. The service uses HiLIS software (also used in Leeds HMDS and UCL) to manage samples, assign tests, records results and correlate investigation into an integrated report. A diagnostic opinion is given based upon the current WHO classification of haematological malignancies coded to ICD-03.

The service core laboratory is a collaboration between the department of Haematology, Immunology, Cellular Pathology and Genetics (termed BHODS). The collaboration is integral to provision of an efficient and robust integrated diagnostic and reporting service for leukaemia, lymphoma and other haematological neoplasms.

The Service has developed a network model for providing SIHMDS across the South West. This has been developed recognising the strength of network pathology solutions to deliver effective service and a belief that local reporting of samples supported by centralised specialist testing offers a number of financial, safety and logistical advantages over a centralised model. Assurance of this model is provided by competency assessment and regular audit.

BHODS was formed in 2010 to support the diagnosis of Haematological malignancy in patients presenting at NBT and Bristol Children’s Hospital. From an initial 50 requests per month the service now receives an average 450 requests per month from a wide range of requestors across the SW.

The service meets or exceeds the criteria outlined in the NICE Improving Outcomes Guidance for Haematological Cancers, 2004. The service will accept samples for initial diagnosis, assessment of prognostic factors, assessment of relapse and assessment of minimal residual disease.

The service will develop to provide the following components:

1. Networked SIHMDS service supporting local diagnostic reporting meetings
2. Centralised specialist services
3. Single request form
4. Integrated report
5. Specialized IT system to link diagnostic sections and integrate reports
6. SOP for systematic testing defining order and choice of tests
7. SOP for standardised reporting terminology
8. Website to provide information about the service

A steering group is configured to manage and direct the development of the service with an expert scientific group providing support to diagnostic review meeting and clinical MDTs. This group provides advice on developing new investigations and investigative pathways and investigative modalities.

The service will support education of scientific and medical staff and laboratory and clinical research projects.

**13-1D-101h Organisation and Leadership of the Specialist Integrated Haematological Malignancy Service (SIHMDS)**

BHODS is a networked SIHMDS consisting of a core laboratory (based at NBT site) and a series of network partners (defined below). The core laboratory service is led by Dr Alastair Whiteway, Consultant Haematologist who fulfils the role of Head of SIHMDS. Under his leadership core laboratory responsibilities are:

* Overall management of BHODS SIHMDS network
* Design of investigational algorithms, in consultation with network partners and the Network Site Specific Group (NSSG)
* Defining strategy for SIHMDS in consultation with network partners and the NSSG
* Use of resources
* Reporting Standards, KPIs
* Coordination of relationships with users
* Ensuring service compliance with Peer Review and NICE Improving Outcome Guidance.
* Reporting of metrics to network partners
* Ensuring effectiveness of service
* Ensuring ongoing competency of all individuals with reporting responsibilities within BHODS
* Provision of MDT support
* Error reporting/Incident management
* Maintain UKAS accreditation

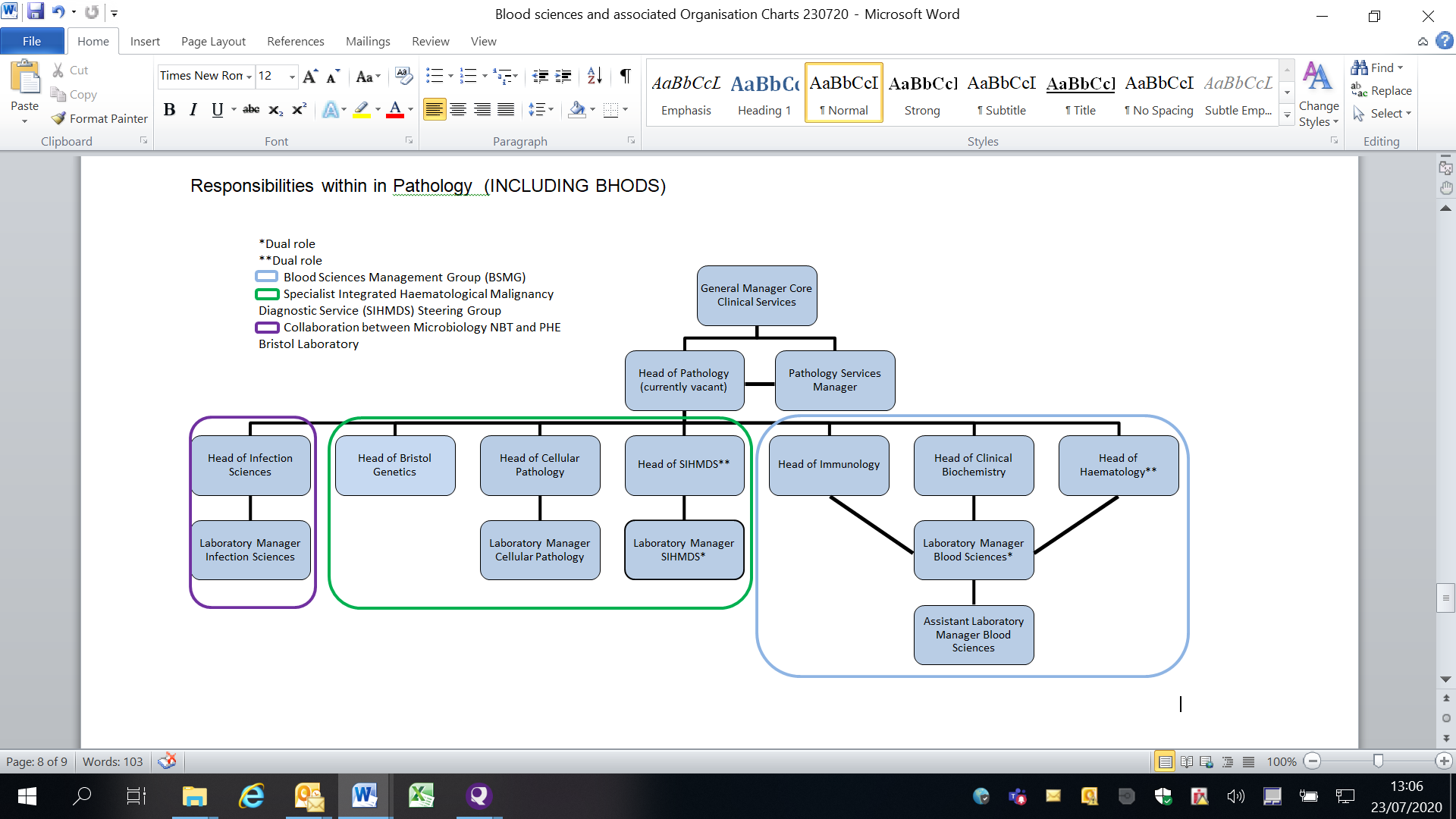
Each network partner is led by a lead Clinician. These are:

* Bristol Children’s Hospital (BCH) – Dr John Moppett, Consultant Haematologist
* North Bristol NHS Trust – Dr Alastair Whiteway, Consultant Haematologist
* Royal Devon and Exeter (RD+E) – Dr Jason Coppell, Consultant Haematologist
* Royal United Hospital Bath (RUH) - Dr Sally Moore, Consultant Haematologist
* Torbay Hospital –Dr Rui Zhao, Consultant Haematologist

Under their leadership site responsibilities are:

* Site Operational Management
* Governance Reporting on SIHMDS issues
* SIHMDS Reporting as defined in Operational Policy GP/PPP/0017.
* Convening a diagnostic review meeting (supported by SIHMDS core lab)

**Organogram Describing Relationship of BHODS Networked SIHMDS to Parent Organisation NBT**



**Organogram Describing Relationship and Responsibilities of Core Laboratory and Network Partners**

**Site Responsibilities**

Compliance (UKAS)

Site Operational Management

Governance Reporting on SIHMDS issues

SIHMDS Reporting as defined in Operational Policy

Diagnostic Review Meeting (supported by SIHMDS core lab)

Torbay Site

RUH Site

BCH Site

NBT Site

RD+E Site

SIHMDS Director

SIHMDS Manager

**Core Lab Responsibilities**

Strategy

Governance

Compliance (Peer Review)

Effectiveness

Operational Policy

Metrics

Competency

**13-1D-102h Provision of Investigational Modalities**

The NBT Core Laboratory provides the following investigational techniques:

1. morphology and cytopathology of bone marrow aspirates, trephine biopsies and tissue biopsies;
2. flow cytometry
3. immunocytochemistry;
4. molecular techniques for detection of clonality, chromosomal translocations and mutations

Flow cytometry, molecular testing, cytogenetics and FISH are provided from the core laboratory for the entire network.

Cellular Pathology Services are centralised for NBT and Bristol Children’s services at NBT.

BHODS SIHMDS supports local morphology reporting at sites as this provides an important safety cross check (patient/specimen identity) and allows early definition of case urgency e.g. APML. In addition, local reporting maintains professional, educational and training value for senior colleagues and trainees, allowing retention of important skills in all network hospitals. These skills are vital for the recognition of cases that require referral in the first place.

The process of multidisciplinary investigation of Haematological Malignancy will result in a small number of cases where either diagnostic modalities or reporting clinicians are unable to define a single unifying diagnosis. These cases are subject to multi-disciplinary review within NBT SIHMDS Diagnostic Review Meeting. Where there is significant diagnostic doubt within a case an urgent NBT SIHMDS Diagnostic Review should be sought prior to release of interim/final report. Where MDT decision is different from one stated in the final report, the responsibility lies with the MDT lead to request diagnostic review.

NBT SIHMDS Diagnostic Review Composition/Quoracy

Consultant Haematologist

Flow Cytometry Senior Scientist

Genetics Senior Scientist

Haematopathologist

**13-1D-103h The QA System for the SIHMDS**

BHODS uses HILIS as its IT system for network SIHMDS service. This records data which provides an audit trail showing the pathway for each sample. This is available in HILIS allowing effective logging and tracing of samples, actions and reports providing on-going quality assurance and audit of the service.

HILIS has a number of workload management features (worklists and dashboards) that graphically display status of all requests. Request urgency and length of time since receipt of sample are clearly identified.

Competency and Consistency of those performing integrated reporting is assessed by quarterly distribution of “blinded” reports to all reporters. Consensus against the original SIHMDS is assessed. The results of these exercises will be evaluated by the SIHMDS Manager and feedback to participants.

Document control for authorised protocols and policies are in line with requirements of ISO 15189:2012 and in compliance with site document control policies.

Modality testing subsection/sites within BHODS participate in all relevant NEQAS schemes. All are CPA/UKAS accredited.

**13-1D-104h The IT System for the SIHMDS**

HILIS is the primary IT system for BHODS networked SIHMDS. This is available to all network partners via secure N3 connection. Integrated reports from HILIS can be exported via HL7 links to network partners order communications systems (e.g. Sunquest ICE) such that the integrated haematopathology report forms part of the patient’s pathology records.

**Key HILIS Features**

**Access**

System access is provided with each individual user having a unique ID and password. Access levels are defined based on role within SIHMDS.

**Data Input**

Data input to HILIS is via a user friendly requesting function. Patients are entered based on a minimum 3 points of identity (name, date of birth and unique identifying number (ideally NHS number). There is support within the system for entry of trial numbers (where patients are registered on clinical trials) local hospital number (where NHS number is provided) and sample urgency. Data input is predominantly done at the core laboratory however pilots of site data entry have begun to increase the traceability of samples.

**Test Requesting and Diagnostic Pathways**

Test assignment is made via a screening process within HILIS. Design of investigational algorithms (Diagnostic Pathways) are made in consultation with network partners and the NSSG. These are hard coded into HILIS as a screening term. Based on clinical details and initial morphological assessment a screening term is selected that translates within HILIS to the pre-agreed diagnostic pathway for that disease entity.

**Test Tracking**

Real time sample/test tracking to allow:

* Reporters to manage collation of integrated reports via incomplete and unreported worklists.
* Laboratory staff from individual testing modalities to manage workload via section specific outstanding work lists.

**Integrated Report**

The integrated report includes:

* A summary of results of all investigations performed
* The mandatory use of the WHO classification of tumours of haemopoietic and lymphoid tissues 2016 with appropriate ICD- 0-3 codes.
* The mandatory use of the WHO leukaemia/lymphoma classification of diagnostic subtypes
* That it should be authorised by a single pathologist, who should only be from a list of individuals authorised for this purpose by the head of service.
* Reports are sent as a paper copy to original requestor or where required to expedite delivery will be e mailed to a secure nhs.net e mail address.

**Performance Metrics**

HILIS provides the following performance metrics on request:

* Diagnosis Frequency
* Diagnosis Status (new vs. relapsed cases)
* Requests by day/month
* Diagnostic error and updates

Quarterly Reports are provided to Network Partners including:

* Workload/referrals
* Turnaround Time by sample type (marrow/Tissue)
* Diagnostic Error rate report
* Diagnostic Update Report

In addition an annual report will be provided to include:

* Compliance/Governance Report
* Annual Report for Network SIHMDS
* Developmental Plan for SIHMDS

**13-1D-105h Laboratory Investigational Guidelines and Internal Protocols of the SIHMDS**

* Samples are received within the core laboratory sample reception where requests are checked and triaged as required. Fresh tissues are directed to Cellular Pathology for rapid assessment and cut up with distribution to other laboratories as required.
* Sample handling protocols describe procedures for recording patients' demographics and clinical details on receipt, entry into HILIS and screening and distribution of material to relevant laboratories.
* Each laboratory has a series of protocols describing processing and reporting of results for individual diagnostic modalities
* Integrated reports are compiled within HILIS by designated, competent individuals.
* Diagnostic Pathways for Haematological Disorders are coded into HILIS to ensure their application. The appendices below described the stages key disorders.

**Appendix I:** Further information on genetic testing is available from the National Genomics Test Directory (Cancer) <https://www.england.nhs.uk/publication/national-genomic-test-directories/>

**Precursor Cell + Myeloproliferative Neoplasm – Bone Marrow**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Disorder** | **Morphology** | **Flow Cytometry** | **Cellular Pathology** | **Genomics** | **Other** |
| B Precursor ALL (<30 years) | MGG | Acute Leukaemia Panel | Acute Leukaemia panel | Childhood B-ALL FISH Panel  Targetable kinase panel  SNP array  MRD Target ID [Ig/TCR]  Whole Genome Sequencing (WGS)  Germline *TPMT/NUDT15* | Flow MRD Combination defined for follow up  DNA and RNA banked |
| B Precursor ALL (Adults)  >/=30 years | MGG | Acute Leukaemia Panel | Acute Leukaemia panel | Adult B-ALL FISH Panel Karyotype  MRD Target ID [Ig/TCR]  Whole Genome Sequencing (WGS)  Germline *TPMT/NUDT15* | Flow MRD Combination defined for follow up  Targetable kinase panel (clinician defined)  DNA and RNA banked |
| T Precursor ALL (<30 years) | MGG | Acute Leukaemia Panel | Acute Leukaemia panel | T-ALL FISH Panel  Targetable kinase panel  MRD Target ID [Ig/TCR]  Whole Genome Sequencing (WGS) | Flow MRD Combination defined for follow up of ETP only  DNA and RNA banked |
| T Precursor ALL (Adults)  >/=30 years | MGG | Acute Leukaemia Panel | Acute Leukaemia panel | ALL FISH Panel  Karyotype  MRD Target ID [Ig/TCR]  Whole Genome Sequencing (WGS) | Flow MRD Combination defined for follow up of ETP only  Targetable kinase panel (clinician defined)  DNA and RNA banked |
| ALL Follow-up | ?MGG | Flow MRD | - | ALL MRD [Ig/TCR] |  |
| APL | MGG | Acute Leukaemia Panel Urgent PML Protein | Acute Leukaemia panel | PML/RARA  Karyotype  Whole Genome Sequencing (WGS) | DNA and RNA banked |
| AML for intensive therapy | MGG | Acute Leukaemia Panel + Exclusion/Inclusion of ETP | Acute Leukaemia panel | *FLT3/NPM1*  Karyotype  Whole Genome Sequencing (WGS) | Flow MRD Combination defined for follow up  DNA and RNA banked |
| AML – Non Intensive | MGG | Acute Leukaemia Panel | Acute Leukaemia panel | *FLT3/NPM1*  Karyotype  Whole Genome Sequencing (WGS) | DNA and RNA banked |
| AML Follow-up | ?MGG | Flow MRD | - | Molecular monitoring as required e.g. NPM1 |  |
| CML Diagnosis | MGG | Acute Leukaemia Panel if excess of blasts morphologically | MDS/MPN panel | Karyotype  *BCR-ABL1* PCR if not previously undertaken | Whole Genome Sequencing (WGS) in childhood CML |
| CML Follow Up | MGG |  | Selective markers from MDS/MPN panel as appropriate | Karyotype if Treatment Warning/Failure |  |
| MDS | MGG + iron stain | MDS Panel – Enumeration of Blasts and Monocytes | MDS/MPN panel | Karyotype (MDS FISH if failed)  MDS NGS | Whole Genome Sequencing (WGS) in childhood MDS |
| PV | MGG | Only if excess of blasts on aspirate morphology | MDS/MPN panel | Karyotype  MPN NGSi | DNA/Suspension banked |
| ET/MF | MGG | Only if excess of blasts on aspirate morphology | MDS/MPN panel | Karyotype  MPN NGSi | DNA/Suspension banked |
| MPN | MGG | Only if excess of blasts on aspirate morphology | MDS/MPN panel | Karyotype  MPN NGSi | DNA/Suspension banked |
| Myeloid or Lymphoid Neoplasms with Eosinophilia | MGG | LPD Panel  Others based on Morphology |  | PDGFRA  Karyotype  HES panel (clinician defined) | Clonality, KIT (clinician defined) |
| Histiocytic neoplasms | MGG | None | Histiocytic neoplasm panel | BRAF p.Val600Glu [V600E] in failed first line therapy  Histiocytosis panel |  |

**MPN peripheral blood molecular investigation**

|  |  |  |
| --- | --- | --- |
| **Disorder** | **Genomics** | **Other** |
| CML Diagnosis | RT-PCR (Qualitative): *BCR-ABL1* [t(9;22)] | *BCR-ABL1* FISH if sample >72 hours old |
| CML Follow-Up | RT-PCR (Quantitative): *BCR-ABL1* | Monitoring frequency and AKD mutation testing accordance with ELN guidelines |
| PV | JAK2 p.(Val617Phe) [V617F]  MPN NGSi | JAK2 exon 12 dependent upon EPO (clinician defined) |
| ET/MF | JAK2 p.(Val617Phe) [V617F], CALR [exon 9], MPL [exon 10]  MPN NGSi | CALR/MPL reflex testing if JAK2 negative |
| MPN | JAK2 p.(Val617Phe) [V617F], JAK2 [exon 12], CALR [exon 9], MPL [exon 10]  MPN NGSi |  |
| Myeloid or Lymphoid Neoplasms with Eosinophilia | *PDGFRA* |  |

Notes

1. MPNP panel inclusion criteria:
   1. Patients who are triple negative thrombocytosis or myelofibrosis
   2. Intermediate 1 MF and a potential allogenic transplant candidate
   3. Post PV progression and potential allogenic transplant candidate
   4. Accelerated phase (10-20% blasts) and a potential allogenic transplant candidate
   5. All patients requiring molecular studies to determine long term prognosis and management

**Lymphoproliferative Disorder – Bone Marrow**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Disorder** | **Morphology** | **Flow Cytometry** | **Cellular Pathology** | **Genomics** | **Other** |
| B LPD | MGG | LPD Panel | Low Grade B lymphoma panel (marrow) | As indicated if >20% infiltration |  |
| HCL | MGG | LPD Panel + CD11c, CD25, CD103, CD123 | CD20, CD3, Cyclin D1, CD123, DBA44, Annexin A1 – not in-house) and other Low grade B lymphoma markers as appropriate | *BRAF* p.Val600Glu [V600E] |  |
| Myeloma | MGG | Myeloma panel | MGUS/Myeloma panel | Myeloma FISH panel (<5%Pc on aspirate morphology) | Flow to Exclude Clonal B Cells if Plasma Cell panel negative |
| MGUS | MGG | Myeloma panel | MGUS/myeloma panel | Plasma Cell Enriched material stored |  |
| T LPD | MGG | LPD Panel + TCR Vβ repertoire by flow cytometry as required | Selective High grade T lymphoma markers as appropriate | Clonality assessment | Reticulin, CD3 + CD20 immunostain on trephine |
| ?LPL |  |  |  | *MYD88/CXCR4* |  |

**Lymphoproliferative Disorder Blood**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Disorder** | **Morphology** | **Flow Cytometry** | **Genomics** | **Other** |
| B LPD | MGG | LPD Panel | TP53 deletion/mutation | IgVH (clinician defined) |
| ?Mantle Cell |  |  | IGH/CCND1 FISH  TP53 deletion/mutation |  |

**Lymphoproliferative Disorder Solid Tissue**

**Pathway defined by review of H+E**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Disorder** | **Flow Cytometry** | **Cellular Pathology** | **Genomics** | **Other** |
| High Grade B-NHL | If fresh tissue available | High grade B lymphoma panel | High Grade NHL FISH panel as required | PCR for B-Clonality as required |
| Low Grade B-NHL | If fresh tissue available | Low grade B lymphoma panel | FISH as required as per [National Genomics Test Directory](https://www.england.nhs.uk/publication/national-genomic-test-directories/) | PCR for B-Clonality as required |
| T-NHL | If fresh tissue available | T lymphoma panel | FISH as required | PCR for T-Clonality as required |
| Hodgkin | ND | Hodgkin Lymphoma panel | ND |  |

**Other Diseases – Bone Marrow**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Disorder** | **Morphology** | **Flow Cytometry** | **Cellular Pathology** | **Genomics** | **Other** |
| Marrow aplasia / hypoplasia | MGG | PNH clone analysis peripheral Blood. Flow on Marrow based on morphology | MDS/MPN panel | As per [National Genomics Test Directory](https://www.england.nhs.uk/publication/national-genomic-test-directories/) (Rare Disease) | Fanconi/DKC Screen as required (clinician defined) |
| Non-haem malignancy in marrow | MGG |  | Differentiated tumours – markers as required  Undifferentiated tumours – PanCK, S100, CD45, CD20, CD3 and other markers as required | As per [National Genomics Test Directory](https://www.england.nhs.uk/publication/national-genomic-test-directories/) (Rare Disease) |  |
| Non-haem malignancy in lymph node | **Morphology** |  | Differentiated tumours – markers as required.  Undifferentiated tumours – PanCK, S100, CD45, CD3, CD20 and other markers as required. Discussion at MDT for clinical correlation, and consider bone marrow. | As per [National Genomics Test Directory](https://www.england.nhs.uk/publication/national-genomic-test-directories/) (Rare Disease) |  |

**Other Diseases – Peripheral Blood**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Disorder** | **Morphology** | **Flow Cytometry** | **Genomics** | **Other** |
| Marrow aplasia / hypoplasia | MGG | PNH clone analysis peripheral Blood. | As per [National Genomics Test Directory](https://www.england.nhs.uk/publication/national-genomic-test-directories/) (Rare Disease) | Fanconi/DKC Screen as required (clinician defined) |

**Appendix II – Panels**

|  |  |  |
| --- | --- | --- |
| **Disorder** | **Modality** | **Tests** |
| **Acute Leukaemia** | Flow | cCD3, CD7, CD10, CD19, cCD79a, Tdt, CIgM, CD34, CD177, CD33 – Others as indicated based on initial screen |
| Cellular Pathology | CD10, CD117, CD15, CD3, CD34, CD56, CD61, glycophorin A, MPO, PAX-5, TDT, CD123, CD4, CD14 |
| AML FISH | CBFB [inv(16)], RUNX1/RUNX1T1 [t(8;21)] |
| AML NGS | NPM1, CEBPA, RUNX1, FLT3, IDH1, IDH2, KIT, WT1, ASXL1, SRSF2, STAG2, RAD21, TP53, KRAS, NRAS, KMT2A, SF3B1, TET2, DNMT3A, EZH2, BCOR, PTPN11, JAK2, SETBP1 |
| Childhood B-ALL FISH | ETV6/RUNX1 [t(12;21)], BCR/ABL1 [t(9;22)], KMT2A (MLL [t(v;11q23)], E2A (TCF3) [t(1;19)/t(17;19)] |
| Adult B-ALL FISH | BCR/ABL1 [t(9;22)], KMT2A (MLL [t(v;11q23)] |
| Targetable ABL class FISH | ABL1, ABL2, PDGFRA, PDGFRBb |
| T-ALL FISH | BCR/ABL1 [t(9;22)], KMT2A (MLL [t(v;11q23)] |
| **MPN/ET** | Flow | Only if excess of blasts on aspirate morphology |
| Cellular Pathology | Glycophorin A, MPO, CD34, CD117, CD61, CD14, p53, CD123, CD3, CD20, CD138, reticulin c |
| Genetics | JAK2 p.(Val617Phe) [V617F], CALR, MPL |
| MPN NGS | KRAS, NRAS, TP53, JAK2, CALR, MPL, ASXL1, CBL, CHEK2, CSF3R, CUX1, DNMT3A, EZH2, IDH1, IDH2, IKZF1, KIT, SF3B1, SH2B3, SRSF2, TET2, U2AF1, HRAS, RUNX1, SETBP1, ZRSR2 |
| Myeloid or Lymphoid Neoplasms with Eosinophilia | HES FISH | PDGFRA, PDGFRB, JAK2, FGFR1, ETV6 |
| **MDS** | Flow | CD11b, CD13, CD16, CD14, CD34, CD117, CD38, HLA-DR, CD36, CD71, CD235a. |
| Cellular Pathology | Glycophorin A, MPO, CD34, CD117, CD61, CD14, p53, CD123, CD3, CD20, CD138, reticulin c |
| MDS FISH | MDS FISH panel -5/del5, -7/del7 |
| MDS NGS | SF3B1, IDH1, IDH2, NRAS, KRAS, TET2, SRSF2, ASXL1, DNMT3A, RUNX1, U2AF1, TP53, EZH2, BCOR, PTPN11, JAK2, SETBP1 |
| **MDS/MPN** | Flow | CD11b, CD13, CD16, CD14, CD34, CD117, CD38, HLA-DR, CD36, CD71, CD235a. |
| Cellular Pathology | Glycophorin A, MPO, CD34, CD117, CD61, CD14, p53, CD123, CD3, CD20, CD138, reticulin c |
| MDS/MPN NGS |  |
| **Low grade LPD** | Flow | CD3, CD5, CD4, CD8, CD19, CD20, CD79B, Cd43, CD200, kappa, lambda – Others as indicated based on initial screen |
| Cellular Pathology | CD20, CD3, CD5, CD10, BCL6, BCL2, CD21, CD23, MUM-1, Cyclin D1, Ki67, CD138. (Other markers not part of panel but used as required: kappa, lambda, pancytokeratin, CD25, annexin-1, DBA-44 (UCL), SOX-11) |
| Genetics | TP53, ATM  Extended panel: 13q14, 12 centromere |
| **High Grade B-NHL** | Flow |  |
| Genetics | Sequential MYC, BCL2, BCL6 |
| Cellular Pathology | CD20, CD3, CD5, CD10, BCL6, BCL2, CD21, CD23, MUM-1, Cyclin D1, Ki67, CD138, CD30, EBER-ISH, c-MYC. (Other markers not part of panel but used as required: kappa, lambda, HHV-8, ALK-1, SOX-11) |
| **T-NHL** | Flow |  |
| Cellular Pathology | CD2, CD3, CD4, CD5, CD7, CD8, CD20, CD10, ALK-1, CD21, CD30, CD56, EBER-ISH, Granzyme B, Ki67, PAX-5, PD1, TIA-1, CD25 |
| Genetics |  |
| **Myeloma** | Flow | CD38, CD138, CD45, CD19, CD117, CD81, CD27, CD56. |
| Cellular Pathology | CD138, CD20, CD3, Congo Red. Further immunohistochemistry as required: p53, Ki67, cyclin D1, CD56, CD117, kappa, lambda |
| Genetics | 1q21 gain, TP53, IGH/FGFR3 [t(4;14)], IGH/MAF [t(14;16)]  On request: IGH/MAFB [t(14;20)], IGH/CCND1 [t(11;14)]  Undertaken on CD138 enriched material |
| **Classical Hodgkin Lymphoma Panel** | Cellular Pathology | CD30, CD15, PAX-5, CD20, CD3, CD45, EBER-ISH, Ki67, MUM-1, CD23, ALK-1, EMA |
| **NLPHL panel** | Cellular pathology | CD20, CD10, CD21, CD23, CD30, BCL2, BCL6, OCT-2, BOB-1, CD45, CD4, EBER-ISH, PAX-5, PD-1, Ki67, |
| **Histiocytic neoplasm** | Cellular pathology | S100, CD68, CD1a, CD14, P53, ALK-1, CD4, CD56, CD123, CD117  +/- mALK |
|  | Genetics | BRAFV600E if failed first line therapy |

**Notes:**

1. All trephines receive a reticulin stain as standard

**Appendix III – Criteria for initiating genomic testing on paraffin sections**

|  |  |  |
| --- | --- | --- |
| **Disorder** | **Criteria** | **Genomics** |
| DLBCL | Germinal centre phenotype, >40% c-MYC immunohistochemistry | MYC, BCL2, BCL6 |
| Large B cell lymphoma with IRF4 rearrangement | Strong MUM-1 staining, waldeyer ring/cervical nodes, low stage, young patients | IRF4 (DUSP22) |
| Lymphoma (LPL, MZL) vs plasma cell neoplasm | For distinction between B NHL and myeloma | MYD88 |
| Anaplastic large cell lymphoma | ALK-1 negative by IHC | ALK, DUSP22 (IRF4)  TP63 |
| Burkitt lymphoma | Typical morphology and immunoprofile | MYC |
| Follicular lymphoma | For confirmation in difficult cases | BCL2 |
| Mantle cell lymphoma | Typical morphology and immunoprofile, and in difficult cases | IGH-CCND1 |