YORKSHIRE & HUMBERSIDE HAEMATOLOGY NETWORK

Data Collection Manual

Version 10 - September 2020

Contents

Appendices

Confidential Information and data protection

The **Data Protection Act** (DPA 2018) and **General Data Protection Regulation** (GDPR) must be adhered to at all times. More information about these laws can be found here: https://ico.org.uk/for-organisations/guide-to-data-protection/

The **Caldicott Principles** (2013) provide the following guidance for use of confidential data:

Principle 1 - Justify the purpose(s) for using confidential information
Every proposed use or transfer of personal confidential data within or from an organisation should be clearly defined, scrutinised and documented, with continuing uses regularly reviewed, by an appropriate guardian.

Principle 2 - Don't use personal confidential data unless it is absolutely necessary
Personal confidential data items should not be included unless it is essential for the specified purpose(s) of that flow. The need for patients to be identified should be considered at each stage of satisfying the purpose(s).

Principle 3 - Use the minimum necessary personal confidential data
Where use of personal confidential data is considered to be essential, the inclusion of each individual item of data should be considered and justified so that the minimum amount of personal confidential data is transferred or accessible as is necessary for a given function to be carried out.

Principle 4 - Access to personal confidential data should be on a strict need-to-know basis
Only those individuals who need access to personal confidential data should have access to it, and they should only have access to the data items that they need to see. This may mean introducing access controls or splitting data flows where one data flow is used for several purposes.

Principle 5 - Everyone with access to personal confidential data should be aware of their responsibilities
Action should be taken to ensure that those handling personal confidential data - both clinical and non-clinical staff - are made fully aware of their responsibilities and obligations to respect patient confidentiality.

Principle 6 - Comply with the law
Every use of personal confidential data must be lawful. Someone in each organisation handling personal confidential data should be responsible for ensuring that the organisation complies with legal requirements.

Further information can be found here: https://www.igt.hscic.gov.uk/Caldicott2Principles.aspx

Transport and storage of data collection forms
Sealed, lockable bags are provided for the storage and transportation of data collection forms. Each bag should contain contact details of the nurse it belongs to. Identifiable information should not be left unattended, particularly overnight (e.g. in a car boot), and should be returned to the ECSG office at the earliest possible opportunity.

Anonymization of identifiable information
Identifiable information (name, address, date of birth, NHS number) should be removed from printed material (e.g. scans, other test results) wherever possible, using the redacting equipment provided for this purpose. This can be replaced with the patient's unique HMRN Study ID.

Email communication with hospital contacts
NHS accounts (i.e. ending in nhs.net) should be used when emailing patient-identifiable information from ECSG to hospital contacts. Identifiable information should not be sent via an ECSG/university email account.

1.0 Inclusion/exclusion criteria

Decisions about inclusion/exclusion are based on diagnosis, date of diagnosis, address at diagnosis and treating hospital. Medical records should be used to determine inclusion/exclusion status. The exception to this is non-UK patients on clinical trials in the study area, who can be made ineligible without their notes being seen.

If a decision is made to exclude a patient, a comment should be written on the form explaining the reason, to create an audit trail. All ineligible patient-forms should be given to the HMRN manager to be checked/actioned.

Further information on which groups to include, along with examples, can be found in **Appendix I**.

Diagnostic criteria: included

- All patients with a new, confirmed ICD-03 coded haematological malignancy, diagnosed by the Haematological Malignancy Diagnostic Service (HMDS: www.HMDS.info), after 1st September 2004, should be included. A confirmed HMDS diagnosis is required to generate a data collection form and allow data input. This includes people who may have had a different type of haematological malignancy or a precursor condition before 1 September 2004.

  One example is patients newly diagnosed with myeloma after 2004, but with a previous MGUS before 2004 (confirmed by HMDS or 'clinical diagnosis'), who should be included. In this example, data should be abstracted on the form generated from the myeloma diagnosis, beginning at the time of myeloma diagnosis. A comment can then be made about the previous MGUS, if information is available. Another example is CLL diagnosed before 2004 and DLBCL diagnosed after.

- Please note the following:

  - Sometimes a patient has an HMDS ICD-O3 diagnosis, but at abstraction there is evidence the diagnosis was made weeks, months or years earlier by the local hospital, and observation/treatment started at this time. This is common in MGUS, CLL and some skin lymphomas and is known as 'clinical diagnosis'. Such patients can only be identified after HMDS diagnosis. If the 'clinical diagnosis' is made after September 2004, the patient should be included, with abstraction starting from the 'clinical diagnosis' at the original hospital. Presentation data from the HMDS date of diagnosis should also be recorded using an additional data sheet (**Appendix II**). Sometimes, an earlier 'clinical diagnosis' of a different cell lineage to that confirmed by HMDS is identified. If post-September 2004, abstraction should still take place from this 'clinical diagnosis'; if before, it should be documented as an antecedent event, with abstraction focusing on the new HMDS diagnosis.

  - Sometimes a patient will have an HMDS report with an ICD-O3 code, then earlier HMDS report(s) will be found without an ICD-03 code, often stating "see comments" because the subtype was unclear, and further tests were required to confirm this. Occasionally, such patients are treated after the "see comments" report, without a formal HMDS ICD-O3 diagnosis. The patient is only eligible for inclusion after HMDS diagnosis, and data should be collected using the form generated from the diagnostic sample. The abstraction can, however, start from the "see comments" report date if appropriate (i.e. it is clear they had a haematological malignancy, and had been followed up – observed or treated – since the date the first sample was taken).

Address at diagnosis: included

- Some YHHN hospitals treat patients who live on the border of the study area (e.g. patients at Airedale Hospital may have a Lancashire address or patients treated at Scunthorpe Hospital may live in Doncaster). If these patients are under the care of a YHHN hospital, then they are included in the study.

- YHHN patients living in the area when newly diagnosed may be treated (first line or subsequent) at a non-YHHN hospital, usually because they have moved house, or another hospital is closer to them. In this case they are eligible for inclusion, but as we can't access information from non-YHHN hospitals, their treatment data may be limited. Abstract available data from the notes/letters. Use the hospital where the HMDS sample was taken as the 'centre' and add the actual treating hospital in brackets. Write a comment explaining the pathway and add 'lost to hospital' as a treatment episode where necessary (see section 2.12).

- A patient may live in the YHHN area, but be diagnosed and start treatment elsewhere, e.g. if they are diagnosed while on holiday, or studying at university. These patients are eligible and will be registered by YHHN when they have a HMDS diagnosis. Abstract data from the original diagnosis date, however, and use the YHHN hospital as the 'centre', where necessary, with the actual diagnosing hospital in brackets. Write a comment explaining the pathway.

Private patients: included

Patients who are diagnosed via a Private hospital in the HMRN area are eligible for inclusion, as long as their diagnosis originated from HMDS and they meet other inclusion criteria (Section 1.0). Private patients' medical records cannot be accessed by study nurses until the patient returns within the NHS to receive care. For some patients, this occurs immediately on diagnosis (e.g. more aggressive disease); for others this takes longer or does not occur at all (e.g. precursor/indolent diseases).

Newly diagnosed private patients are added to the HMRN database. When data collection is due, the HMRN study administrator checks HILIS for indications that the patient has returned into the NHS. If so, data collection occurs as normal at whichever NHS hospital the patients is attending.

If not, the 'Data Collection' section of the log is amended and 'Private Patient' selected from the dropdown in 'Reason Form Not Completed'. The form is, however, printed by the HMRN study administrator and kept in a box-file, which is periodically checked to determine whether patients are still receiving private care or have returned to the NHS. Those who return to the NHS have their data collection completed as soon as this is known. Sometimes NHS letters may be available in the notes summarising the patient's private care; as much information should be taken from such letters as possible (e.g. results, treatments etc.) at the time of diagnosis and after. A comment should be written to explain the reason for any missing data.

Diagnostic criteria: excluded

- All patients who were diagnosed with a haematological malignancy before 1 September 2004 that is identical to the 'new diagnosis' after 2004 (recurrence/ relapse).

Address at diagnosis: excluded

- Patients are generally ineligible if they live outside the YHHN area at diagnosis. Exceptions are shown in the "Address at diagnosis - included" section above.

- One-off specimens are sometimes sent to HMDS for assessment, even if the patient does not live in the YHHN area. This may be because a second opinion is required; because patients live elsewhere but are being treated in the YHHN area as part of a trial not available where they live; or if a diagnosis was made in the area but the patient lives and will be treated elsewhere (i.e. diagnosed whilst on holiday). In such cases the patient is ineligible.

Private patients: excluded

Patients diagnosed via a private hospital in the HMRN area are only excluded if they do not meet other inclusion criteria (Section 1.0), not solely because they are being treated in the private setting.

Please check with a senior researcher if you are unsure about eligibility criteria.

2.0 Completion of data record sheet

Ensure all data are abstracted from primary sources where possible (i.e. original laboratory and scan reports).

Presentation data should be recorded from results that are as close as possible to the time of diagnosis, and prior to the start of any treatment. Some patients do not have follow-up appointments for several months following diagnosis. Blood results can be collected from such appointments, if necessary (and if no treatment has been given), but make a comment explaining this.

Complete the abstraction using black ink, unless it is a follow-up in which case red ink should be used. If for any reason the form is being completed at follow-up for the first time, black ink should be used.

Record the abstraction date and your initials in the bottom right hand corner of the form.

Any complex issues and difficulties relating to data collection should be discussed and resolved with the study coordinator. Such issues and their resolution, including any changes to practice will also be discussed and circulated at the scheduled study meetings.

Follow-up data collection

Follow-up is where further data on treatment/response is recorded from the medical records, subsequent to first abstraction. More information on this process can be found in **Appendix III**.

Follow-up takes place for all patients who have died since the original data collection. It is important to ensure all relevant data are abstracted at this time, as deceased records are stored for a limited time before being destroyed, so there may not be another opportunity to revisit the notes. Follow-up also takes place for specific groups, often targeted by diagnosis/diagnostic interval (year of diagnosis).

During follow-up it is important to verify that baseline data abstraction was correct. Incomplete or new fields should be completed. Discrepancies or difficulties that cannot be resolved should be discussed with the study coordinator.

Follow-ups may need to be prioritised ahead of routine data collection, along with their inputting and scanning. This will be clarified by the study coordinator for each follow-up initiated.

2.1 Missing data

If a value cannot be found in the medical records, it should be recorded as ‘unknown’ or ‘not done’. ‘Unknown’ means it is known the test was done but results cannot be found. ‘Not done’ means it is known the test was not done, or there is no evidence it was done.

Occasionally, a patient is not referred to haematology (e.g. they died pre-HMDS diagnosis, or are being monitored by their GP, often for CLL or MGUS). Demographic sections, available blood results and reason the patient was not seen should be documented. ‘Not seen’ should be written in the ‘1st appointment’ box.

If information is unavailable make sure the reason is stated rather than leaving a blank field.

2.2 Demographics

Gender

Circle as appropriate.

Date of Diagnosis

Occasionally, this will pre-date the date printed on the form. For example, a diagnosis of LPD NOS may be made, followed by a more accurate diagnosis. The form with the latter diagnosis should be printed, but the date of diagnosis should be that of the original LPD NOS report.

Address at Diagnosis

Use hospital sticker if possible. Do not amend this if the address has changed at follow-up.

GP Address

Record GP name and practice name/ address at diagnosis.

Date of Death

If the patient has died, record the date of death as documented in notes.

Date first seen

Use the date the patient is first seen in-person by the haematology team even if the patient is diagnosed via a pathway for non-specific symptoms such as a Multidisciplinary Diagnostic Centre (MDC). There may have been prior telephone contact between the haematologist and GP before this, but do not use such dates. If there is a gap (months) between first haematology appointment and diagnosis, still use the first-seen date. If there is a longer gap (years), a lapse in follow-up or re-referral, use the first haematology appointment date relating to the recent diagnosis. In both cases, write an explanation.

Palliative Date

Record date of first referral to the Specialist Palliative Care team (hospital or community), regardless of whether the patient is seen.

2.3 Antecedent/concurrent event

Record if the patient has:

- Immunodeficiency (HIV positive)
- Had a solid organ transplant
- Down syndrome

Solid organ transplant and Down syndrome should be recorded regardless of whether the patient has received chemotherapy or radiotherapy. Otherwise, write ‘none’, unless the patient has received chemotherapy or radiotherapy (at the same time or before their blood cancer diagnosis), in which case chemotherapy, radiotherapy or both should be circled as appropriate, and the reason for this treatment (i.e. event) documented from the following list:

- Non-haematological malignancy
- Haematological malignancy
- Non-haematological malignancy and haematological malignancy
- Autoimmune disorder
- Other

In all cases, add a brief comment about the type of disease (except HIV), date of diagnosis and treatment.

2.4 Treatment history

Ensure all haematological malignancy treatments are recorded from diagnosis onwards, consecutively (if possible), or numbered for clarity. Treatment type should be selected from section 2.5.2, with further information given in sections 2.5 - 2.19.

Gaps between treatments are expected between appointments, or when awaiting tests to guide further therapy decisions. Comment on particularly prolonged gaps (e.g. over 2 months) and delays within planned treatment courses (e.g. due to neutropenic sepsis).

If another haematological malignancy is diagnosed, record treatments for both diseases on the same form, consecutively. Comment on the second diagnosis, giving the HMDS report number and date. Presentation data for the subsequent disease should be recorded using the additional sheet (**Appendix II**).

If a patient has CLL and autoimmune haemolytic anaemia (AIHA), or has plasma cell myeloma/ MGUS and amyloid light-chain (AL) amyloidosis, treatments for these associated diseases should be added to the data collection form, in chronological order. Comment to indicate which disease each treatment relates to (if possible).

New treatments are released on license by the manufacturing company and cannot be made by others until the original patent expires, at which time almost identical copies can be made/used. One example is the immunotherapy Rituximab (trade name MabThera), which is now available as Rixathon or Truxima. These biosimilars should be recorded in the same way as other treatments, but new drugs may need to be added to the HILIS Treatment List.

2.5 Recording treatment episodes

2.5.1 Centre

Record the treating hospital. This is usually within the YHHN area, but may be outside. Some of the more common non-YHHN hospitals can be input (see **Appendix IV**), otherwise write the name of the associated YHHN hospital, then document the actual hospital beside in brackets and the reason for use of this hospital. If treatment starts in one hospital and continues in another, only record the treatment once, using the place most of the treatment was given and document the name of the second hospital in brackets.

2.5.2 Treatment - regimen/trial/agent

Choose the appropriate treatment from the list below:

Bisphosphonates*
Care of the dying pathway
Chemotherapy (record regimen)*
Clinical trial (record trial name, see section 2.8)*
Community monitoring (see section 2.9)
Died before treatment/diagnosis
Discharged to GP (see section 2.10)
Discharged from haematology (see section 2.11)
End of life care pathway
Erythropoeitin
Helicobacter eradication therapy
Immunosuppressive*
Liverpool care pathway
Lost to hospital (this also covers lost to follow-up, see section 2.12)
Non-haematological for co-morbidites (see section 2.13)
Observation (see section 2.14)
Orchidectomy (see section 2.15)
Palliative (see section 2.16)
Radiotherapy (see section 2.17)*
Refused treatment
Resection (see section 2.18)
Splenectomy
Stem cell harvest (see section 2.19)
Stem cell transplant (priming, conditioning, harvest - see section 2.19)*
Steroids*
Supportive care*
Venesection
Vertebroplasty

*Refer to current HILIS treatment list to select specific treatment type

Additional details should be given for some categories, including bisphosphonates, chemotherapy, clinical trials, stem cell transplants, steroids and supportive care (marked with an asterisk*). These should be selected from the HILIS treatment list, and recorded exactly as they appear, as this is how they will be identified at inputting.

The HILIS treatment list is updated regularly, so a current version should be carried at all times. If a new treatment is identified, the name, as well as whether it is part of a clinical trial (and if so details of treatment arm) should be checked via the internet or hospital contacts. Any details should be added to the 'New Treatments' box file in the YHHN nurses office. Information on large new trials (e.g. UKALL) are summarised, based on the protocol, and circulated by a member of the YHHN study team. Treatment arms may need to be added/changed as more data are collected. A data manager should be asked to add new treatments to HILIS, so these can be input. A monthly email is dispatched to all study staff with information about additions/changes to the list.

Record chemotherapy regimens as originally prescribed (e.g. 'CHOP/Rituximab'), even if part is subsequently omitted, in which case comment on the drug omitted and the reason.

If chemotherapy is reduced/attenuated, comment on the reason for this; whether the dose was attenuated from the outset, and if not, the date the change was made.

If chemotherapy is stopped early, comment on the reason (e.g. toxicity, intolerance or a good response).

Some treatments are started by the GP (e.g. aspirin for MPDs). These should be recorded, with an 'unknown' start date and a comment.

2.5.3 Cycles

If treatment is complete at the time of abstraction, enter the number of cycles received; if the patient is still receiving the treatment, leave blank until follow-up. This is irrelevant for some treatments (e.g. aspirin, imatinib etc.).

2.5.4 Start date

Record the date of the first cycle/day of treatment. If possible try to estimate this date if it is unknown and put (est.) beside the date. Alternatively, add 'Unknown' if there is absolutely no information available to help estimate the date. If the start of chemotherapy is delayed whilst a patient recovers from surgery (e.g. tissue biopsy/resection), write a comment explaining this, so it is clear this is not an administrative delay or error.

2.5.5 End date

If treatment is completed at the time of abstraction, then enter the end date. The treatment end date should be the last date the treatment was received, if known, but this is not always clear if the patient is having chemotherapy. In this case it is sufficient to use the first date of the last cycle. If unsure, try to estimate this date and put (est.) beside the date. Alternatively, add 'Unknown' if there is absolutely no information to help provide an estimate. If treatment is not finished at abstraction leave the box blank.

2.6 Treatment intent

Treatments are given for various purposes, which should be written in brackets next to the treatment itself - see below:

Priming:	pre-stem cell harvest (**Appendix V**)
Conditioning:	pre-stem cell transplant (**Appendix V**)
Prophylaxis:	to prevent disease spread
Consolidation:	to ensure remission/ prevent relapse (e.g. radiotherapy post-chemotherapy in lymphoma)
Maintenance:	to maintain/prolong remission (e.g. Rituximab in follicular lymphoma) (section 2.7)
Palliative:	(intent or approach) given to improve symptoms/ quality of life only (e.g. single fraction radiotherapy); differs from 'palliative care' treatment itself, which is the provision of comfort in the days preceding death (section 2.16)

2.7 Distinguishing treatment from maintenance and assigning response

Patients may receive induction chemotherapy, then long-term maintenance (sometimes for years). One example is FL, where 6-8 cycles of R-CHOP are followed by 2 years rituximab maintenance.

If possible, treatments/responses should be recorded separately. This distinction may be clear and easy to document (e.g. FL with PR/CR from R-CHOP, then PD on rituximab maintenance). However, it may be unclear (e.g. mantle cell lymphoma, where ibrutinib is given as treatment and continued as maintenance; similarly with myeloma and lenalidamide). Only use this approach if the distinction between intent is clear, and not for MPN or CML.

If a patient is receiving azacytidine (e.g. for AML) and HILIS reports a response to treatment (at any point), document this and separate the treatments at this point. For example, if a patient has 20 cycles of azacytidine and a BMAT post 6 cycles: document azacytadine x 6 with response (first treatment); then azacytidine x 14 (second treatment).

2.8 Clinical Trials

Use the YHHN treatment list to select the appropriate clinical trial. Add each arm/phase as a separate event, but do not record cycles. A trial flowchart can be used to facilitate documentation. These may be identified via the internet, hospital contacts or the 'YHHN New Treatment box file' in the nurses office. New protocols should be added to the box to share.

If the trial does not include randomisations, it is single entry, meaning there are no phases or arms to separate.

Treatment may be given according to trial protocol, but off-trial. In this case, separate arms/phases should be documented (e.g. AML: 17, 19, APML arms and all UKALL trials) and a comment made to explain this.

Clinical trials may be conducted for non-chemotherapy treatments (e.g. antibiotics: TOPS, TREATT, TEAMM) and should be recorded, but only where an actual treatment is given and not, for example, for a questionnaire (such as a quality of life survey).

2.9 Community Monitoring Programme

Some diseases (e.g. MBL, CLL, MGUS), are observed via HMDS's Community Monitoring Programme (CMP), during which time blood samples are sent directly from primary care to HMDS for analysis. The decision to use CMP may be made at the first hospital visit, with individuals being recalled to haematology at a later date, if necessary.

If a patient on CMP dies, their form should be passed to a YHHN/HMDS administrator, so this can be recorded.

2.10 Discharged to GP

Use this category for patients discharged from hospital to GP care. This may occur for various reasons, including: the indolent nature of the condition (e.g. MBL, CLL, MPN or MGUS); treatment not being required; following treatment success; or if no further treatment is available.

2.11 Discharged from haematology

Use for patients discharged from haematology due to other comorbidities or frailty. This may be a discharge to another hospital speciality.

2.12 Lost to hospital

Lack of patient hospital/haematology attendance (12-18 months), may be considered 'lost to hospital'. This could be due to failure to attend (patient or system error); discharge/transfer to a hospital outside YHHN; or there may be no explanation in the medical records. Patients may return into the hospital system, however, at which time abstraction should re-commence.

2.13 Non-haematological for comorbidities

Patients often have coexisting comorbidities. Only comment on comorbidities if treatment takes precedence over that of the haematological malignancy, meaning treatment of the latter is delayed or not given at all (e.g. if the patient dies). Always document what the comorbidity is and how this impacted on treatment.

2.14 Observation

'Observation' is the formal process by which patients are followed-up in haematology clinic at specific intervals (monthly/annually). It is also known as 'active monitoring' or 'watch and wait'. A clinical decision is usually made in the MDT meeting to use this approach. The time before treatment (e.g. radiotherapy) or tests to facilitate decision-making should not be recorded as observation.

Observation often continues after PD is identified, as further treatment does not always start immediately, but may depend on how well the disease/symptoms are tolerated. In this case, record observation until the day preceding start of treatment (or death), and document response as PD. Comment on the date the PD was identified and the evidence confirming this (e.g. scan or sample).

Observation can run alongside treatments categorised as supportive care or bisphosphonates.

2.15 Orchidectomy

Orchidectomy **should** be entered when there is complete removal of one or both testes in stage 1a testicular lymphoma, even if followed by consolidation/prophylactic chemotherapy.

2.16 Palliative care

Palliative care terms are complex in haematology. Treatment of incurable disease (e.g. myeloma, AML in the elderly) is usually described as being given with '**palliative intent**' or with a '**palliative approach**' and aims to prolong life, control symptoms and improve quality of life. '**Palliative care**' usually refers to 'comfort' in the last days/weeks of life and the withdrawal of treatment (except transfusions, antibiotics and steroids in some cases).

If the medical records state that treatment is given with '**palliative intent/approach**' this should be documented in brackets beside the treatment (including single fraction/short courses of radiotherapy and non-intensive chemotherapy).

If the medical records state '**palliative care**', this should be recorded as a distinct treatment episode, synonymous with end-of-life (usually the last weeks/days).

2.17 Radiotherapy

Radiotherapy is given at two YHHN centres: St James's, Leeds and Castle Hill, Hull.

Radiotherapy intent/type should be specified, as stated in medical records and HILIS treatment lists. This may include:

- Total Body Irradiation (TBI): prior to stem cell transplant
- Palliative: for symptom control rather than to prolong life or cure disease. It is usually given as a single fraction or five fractions for this purpose.
- Consolidation: post-chemotherapy to promote remission and prevent relapse. It is usually given in daily fractions over several weeks. Chemotherapy and radiotherapy are combined and considered 'first-line treatment' at analysis, in those who achieve CR or PR. After failed chemotherapy (PD) radiotherapy is considered second-line rather than consolidation.
- P_{32}: radioactive phosphorous, usually given for MPDs, such as PV.

Terms may differ somewhat in Leeds and may include the following:

- Adjuvant: used to describe upfront radiotherapy instead of the term 'consolidation'.
- Radical: also used instead of the term 'consolidation'.

Radiotherapy may be given to more than one body area at the same time. In this case, it should be recorded as a single treatment episode, with a comment, noting that two sites were targeted.

2.18 Resection

Resection **should** be used:

- When there is complete removal of the lymph node or extranodal stage 1a disease, even if this is followed by consolidation/ prophylactic chemotherapy.

Resection **should not** be used:

- When it is for diagnostic purposes.
- For removal of one or both testes.

2.19 Stem cell transplant: priming, conditioning, harvest

A stem cell transplant may be an autograft (when the patient receives their own stem cells) or allograft (when donor stem cells are received) (see **Appendix V**).

- When abstracting, document the type of transplant in brackets.
- Allografts are only conducted at Leeds (St James's Hospital).
- Types of allograft include:

Matched related donor	Mismatched related donor
Cord donor	Matched unrelated donor
Haplo-identical donor	

Priming and conditioning treatment should be documented as per YHHN treatment list, with intent recorded in brackets.

For autogafts, the stem cell harvest should be recorded as a standalone treatment (section 2.5.2), even if the stem cells are not used.

If work-up towards harvest takes place, but the harvest is not carried out, document this as a comment only, and include the reason. This information may be missing from older forms and should be added.

If treatment is being given for Graft Versus Host Disease (GVHD), or other transplant issues (e.g. with cyclosporin, budesonide etc.), do not record all episodes, just the start and end date, and comment on if this is ongoing/intermittent and why it was prescribed.

2.20 CAR T-cell therapy

CAR (Chimeric Antigen Receptor) T-cell therapy is a type of immunotherapy that is developed for each individual and involves reprogramming the patient's own immune system cells (or donor cells) which are then used to treat their cancer. It is a highly complex and potentially risky treatment. Specifically, an individual's T-cells are collected (apheresis), then modified in the laboratory before being re-introduced (CAR T-cell infusion) to the patient to target the cancer cells. Prior to this infusion, the patient usually receives some conditioning chemotherapy. Currently, it can be used to treat children with ALL and adults with DLBCL or primary mediastinal B cell lymphoma. Patients tend to go from the HMRN area to the Christie, Newcastle or London hospitals for this treatment, but it will likely become more widespread over time. CAR T-cell therapy should be documented in the same way as other treatments/trials.

2.21 Response to treatment

Record response to all chemotherapy regimens using the criteria in the disease specific sections of this manual.

Also record response to radiotherapy, unless this is given with palliative intent or as TBI prior to stem cell transplant.

Information to assess response can come from multiple sources, including laboratory results, scans and HMDS samples. If response is not formally assessed or stated in the medical records, leave the box blank and write a comment.

Copies of all scan reports should be collected, from diagnosis onwards, to facilitate decision-making about response.

If a patient has chemotherapy then radiotherapy, but only one scan is done at the end of both treatments, this can be used to assign response to both chemotherapy and radiotherapy, as long as the radiotherapy is given as consolidation.

If treatment is continuous observation, do not assign response (e.g. NE or SD); simply leave the field blank.

Do not include a response if the person died mid-treatment, even if after a scan showing PR, as the patient did not have the opportunity to respond to a full course of treatment. However, if a response occurred after several cycles (as per scan), then treatment was stopped early (e.g. because it could not be tolerated), then response should be documented, but only if the patient lives longer than a few months.

If there is an initial response to treatment, but then disease progression whilst still on treatment, use PD and write a comment explaining this.

After stem cell transplant, response should be assessed at the 100 day bone marrow biopsy and/or scan (e.g. PET/CT).

If a patient requires a second allograft (due to failure of the first), response to the initial allograft should be recorded as follows: if CR is reported on/before the 100 day bone marrow, 'NE' should be documented; if graft failure occurs after CR on the 100 day bone marrow, 'PD' should be documented and the relevant HMDS BMAT report number noted. Any other relevant comments should also be documented.

2.22 Comments

The aims of providing additional comments are as follows:

1. **Treatment:** to clarify episodes and ensure anyone using the data understands deviations from normal or expected patterns, or issues impacting on start dates (e.g. antecedent or concurrent events: see below).

2. **Missing/unusual data fields:** to explain these, so they are not perceived as errors.

3. **Antecedent/concurrent events:** to provide information on conditions of interest (i.e. autoimmune disorder, cancer, Down syndrome, HIV or solid organ transplant). These should be brief and relevant, rather than entire accounts of comorbidities or family histories.

2.23 Eastern Cooperative Oncology Group (ECOG) scale

Score	Definition
0	Able to carry out all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work.
2	Ambulatory and capable of all selfcare, but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair.
Unknown	No information available to determine score.

Complete the ECOG based on performance status at diagnosis. If the score is not documented in the medical records (which is often the case), it should be derived from information that is available (e.g. letters). Only use 'unknown' if there is nothing to determine the score from, as may be the case in indolent disease, such as CLL.

2.24 COVID-19 issues

COVID-19 Interruption: Enter this as a 'treatment' if a treatment break is introduced due to Covid-19 (e.g. to prevent hospital attendance / avoid risk of infection). Use for chemotherapy and other treatments (e.g. bisphosphonates). Use even if the same treatment is re-started (e.g. azacytidine with a break, followed by azacytidine again).

COVID-19 Modification: Use this to indicated a change in treatment type (e.g. a change in intensity to reduce the likelihood of admission); or route (e.g. IV to oral to prevent the need to come into hospital).

If there has been a change in the type of follow-up due to COVID-19 (e.g. telephone instead of face-to-face in clinic), write a comment about this.

Forms including these changes can be processed as normal.

However: If a patient is diagnosed with COVID-19, write a comment about this, including the date of diagnosis, and put the form in the box labeled 'COVID-19 Positive', situated in the cabinet in the nurse's office.

The following sections describe the data collection requirements for each specific disease type. Fields should be completed using only the categories given on these pages.

Further information is available to help you complete data collection forms in **Appendix VI** (Required attachments for data collection forms by diagnosis); **Appendix VII** (Staging and prognostic scores) and **Appendix VIII** (Specimen abbreviations).

3.0 Acute leukaemias

These include acute myeloid leukaemia (AML), acute promyelocytic leukaemia (APML), precursor T-lymphoblastic leukaemia (T-ALL) and precursor B-lymphoblastic leukaemia (B-ALL).

Cytogenetics

Do not record this, but routinely image the cytogenetic report at diagnosis.

ECOG at diagnosis

Record appropriate score: 0 to 4 or unknown (see section 2.23).

Hb

g/dL

Not stated
Not done

WBC

$x10^9/L$

Not stated
Not done

Platelets

$x10^9/L$

Not stated
Not done

Haematocrit/packed cell volume

These are measures of the same thing and should be reported as a percentage. If the value is between 0 and 1, multiply by 100.

Not stated
Not done

Neutrophils/absolute neutrophil count

$x10^9/L$

Not stated
Not done

Lymphocytes

$x10^9/L$

Not stated
Not done

Monocytes

$x10^9/L$

Not stated
Not done

Record response to each chemotherapy treatment as follows

To determine response, check HILIS for samples commonly used to assess this, including bone marrow (BMATs), peripheral blood (PB) or other (e.g. CSF). Write the HILIS number of any samples as a comment by the appropriate treatment.

If the HMDS report states 'remission bone marrow', 'no evidence of disease' or 'MRD -ve (negative)' etc., then response should be recorded as 'CR'.

If the HMDS report documents less than 5% blasts but HMDS still report a positive diagnosis then the most appropriate response to record is 'MRD'. Likewise, if the sample is reported as 'minimal residual disease detected' by HMDS.

If the HMDS report documents over 5% then this is PD.

PR can be used in children and adults if disease is outside the bone marrow (extra-osseous) and response is assessed by imaging the affected area. However, also refer to the notes/letters as the haematologists' decisions on response take precedence. If this decision is at odds with the HILIS report, try to determine the reason for this, and add a comment.

CR (complete remission)	MRD (minimal residual disease)
PD (progressive disease)	NE (non-evaluable)
SD (stable disease)	PR (partial response)

In some instances it may be difficult to assign response, even after considering the HMDS reports and the haematologist's comments. In this situation, response may be left blank, and re-assessed during future abstraction, when it may be clearer. In such cases, write a comment to explain this.

AML response in clinical trials

Bone marrow samples may be sent to trial centres, and report findings that may differ from those reported by HMDS. In this case, use the trial result and comment on reports from HMDS.

4.0 Myeloproliferative disorders

These include chronic myeloid leukaemia (CML) and myeloproliferative disorders such as polycythaemia vera, essential thrombocythaemia, primary myelofibrosis, mastocytosis, chronic eosinophilic leukaemia and hypereosinophilic syndrome. For the purposes of data collection, chronic myelomonocytic leukaemia (CMML) and other myeloproliferative/myelodysplastic neoplasms are also included in this group.

Splenomegaly & Hepatomegaly (*record each separately*)

Yes
No
Not known

Scan results override palpation in the identification of these abnormalities.

Detection method (*attach any scan reports*)

Palpation
Scan (Ultrasound/CT/MRI)
Both (Palpation & Ultrasound/CT/MRI)
Unknown
N/A

ECOG at diagnosis

Record appropriate score: 0 to 4 or unknown (see section 2.23).

Hb

g/dL
Not stated
Not done

WBC

$x10^9/L$
Not stated
Not done

Platelets

$x10^9/L$
Not stated
Not done

Haematocrit/packed cell volume

These are measures of the same thing and should be reported as a percentage. If the value is between 0 and 1, multiply by 100.

Not stated
Not done

Neutrophils/absolute neutrophil count

$x10^9/L$
Not stated
Not done

Lymphocytes

$x10^9/L$
Not stated
Not done

Monocytes

$x10^9/L$
Not stated
Not done

Erythropoietin level (*pre-treatment, normal range: 3-18*)

Low/Normal/Raised
Not stated
Not done

see overleaf for Response >>

Response

PD (progressive disease) NE (non-evaluable)

Use PD if the patient changes from observation to treatment or supportive care, or becomes refractory to treatment.

If there is definite progression to another disease (e.g. MPN to MF or AML) resulting in one treatment stopping and another starting, record this as PD. If subsequent treatment is not given, document the PD as a comment, with the HMDS number of the progression sample. Extra presentation data should be collected for the new disease on the appropriate form.

5.0 Myelodysplastic disorders

These include refractory anaemia with excess blasts (RAEB), refractory anaemia with ringed sideroblasts (RARS) and refractory cytopenia with multilineage dysplasia (RCMD).

Splenomegaly & Hepatomegaly (*record each separately*)

Yes
No
Not known

Scan results override palpation in the identification of these abnormalities.

Detection method (*attach any scan reports*)

Palpation
Scan (Ultrasound/CT/MRI)
Both (Palpation & Ultrasound/CT/MRI)
Unknown
N/A

ECOG at diagnosis

Record appropriate score: 0 to 4 or unknown (see Section 2.23).

Hb

g/dL
Not stated
Not done

WBC

$x10^9/L$
Not stated
Not done

Platelets

$x10^9/L$
Not stated
Not done

Haematocrit/packed cell volume

These are measures of the same thing and should be reported as a percentage. If the value is between 0 and 1, multiply by 100.

Not stated
Not done

Neutrophils/absolute neutrophil count

$x10^9/L$
Not stated
Not done

Lymphocytes

$x10^9/L$
Not stated
Not done

Monocytes

$x10^9/L$
Not stated
Not done

Karyotype (cytogenetics)

Interpret karyotype by referring to the cytogenetics report. If a report is not found in the notes, enter 'Unknown'. Routinely image the cytogenetics report if found in the notes.

Good:	Normal, -Y alone, del(5q) alone or del(20q) alone
Intermediate	+8 (i.e. trisomy 8), single miscellaneous, double abnormalities e.g. del (5q) and del(20q) together
Poor	Complex (i.e. ≥ 3 abnormalities) or chromosome 7 abnormalities
Unknown	

Red blood cell dependent

Yes
No
Not known

Defined as unable to maintain Hb > 10g/dL and/or receiving a transfusion at least every 8 weeks.

Cytopenias (*count one each for:*)

Haemoglobin below 10g/dL
Absolute neutrophil count below $1.8x10^9$/L
Platelet count below $100x10^9$/L

Response

PD (progressive disease)
NE (non-evaluable)

Use PD if the patient changes from observation to treatment or supportive care, or becomes refractory to treatment.

If considered high-risk MDS, or transformation to acute leukaemia occurs and chemotherapy is given, use response criteria defined in section 3.0. Also collect presentation data for the AML.

6.0 Plasma cell disorders

These mainly include myeloma, plasmacytoma and monoclonal gammopathy of undetermined significance (MGUS). If the patient has more than one type of plasma cell disorder e.g. plasmacytoma and plasma cell myeloma, record this with the HILIS report number as a comment. See **Appendix IX** for additional information about plasma cell disorders.

Paraprotein type

Immunoglobulins have heavy chain components (G, A, D, E and M) and light-chain components (kappa and lambda). Paraproteins can therefore be classified as: IgG, IgA, AgD, IgE or IgM, with further kappa or lambda sub-classification. Paraproteins are detected by serum protein electrophoresis (measuring immunoglobulin level in the blood) and immunofixation electrophoresis (identifying the type of abnormal antibody). Testing may reveal multiple paraprotein types which should be documented separately. Until the data collection forms are amended, document the paraprotein with the highest level on the form, and write a comment about other paraproteins and levels. Serum free light chain assays are used to classify and monitor light chain, non-secretory and oligosecretory myeloma. Check the blood test results and complete the fields, selecting from:

IgA	None: tested and paraprotein not found
IgD	Not done/ not appropriate (N/A)
IgE	Unknown
IgG	Light chain only
IgM	Oligosecretory
Non-secretory	

Document 'light-chain only' MGUS or myeloma if this is stated in the notes. Otherwise, record the paraprotein type.

Some myelomas/MGUSs are referred to as 'light chain only' but have an identifiable very low level paraprotein. In this case, record the paraprotein type, even if this was noted months before the diagnosis and had actually resolved at the time of diagnosis, and make a comment. See **Appendix IX** for more information on light chain only, non-secretory and oligosecretory myeloma.

Paraprotein level

Document the paraprotein level in the box. Options include:

(level) g/l	Not stated	N/A
Unquantifiable	Not done	

If paraprotein level is <1, 1-2, <2 or <3, write this in the box. It will be input as 'Not Stated', however, as this result is unlikely to be accurate.

Only use 'Unquantifiable' if this is what is recorded in the results (see **Appendix IX**).

If more than one paraprotein has been identified, record the level of each.

If paraprotein is 'none' or 'light-chain only', use N/A for level.

Urine FLC type (*often referred to as Bence Jones/urine immunofixation*)

None	IgG	Not done
Kappa	IgA/lambda	Not known
Lambda	IgG/kappa	
IgA	Both	

Serum FLC type

None	Both
Lambda	Not done
Kappa	Not known

The paraprotein is generally documented with the light chain type - e.g. for 'IgG (kappa)', in which case 'kappa' should be recorded in the box.

If a patient has a 'light-chain only' or 'non-secretory' myeloma (i.e. no heavy chain immunoglobulin component), a serum immunofixation test may have been used to identify light-chain type. If so, record this in the box. Otherwise, record the light chain that is above its normal range (usually found in brackets after the result).

If both kappa and lambda are above normal range, and neither the laboratory results nor medical records indicate both light chains are involved, use the kappa:lambda or serum FLC ratio as a guide (kappa first). If the kappa:lambda ratio is over 1.65 then the serum FLC is kappa; if less than 0.26 it is lambda.

Serum kappa

mg/l	Not known
	Not done

Serum lambda

mg/l	Not known
	Not done

Kappa:Lambda ratio

number : number or N/A (to be used if the test was not done)

Bone disease

Yes	Equivocal
No	Unknown
	Not assessed/ fully assessed

The following diseases constitute bone disease and should be categorised 'Yes':

Lytic	Fracture(s)
Plasmacytoma	

The bone disease box should be used as follows:

Yes - for any bone disease, noted on any scan. This does not have to be a full body scan.
No - when the full body is examined and no disease is found.
Equivocal - when it is unclear from the scans if disease is present or not.
Unknown - when it is not known if any scans were done to check for bone disease.
Not assessed/ fully assessed - when it is clear that no scans or full body scans were done.

People with MGUS may present with fractures, caused by osteoporosis, and be observed. This should not be categorised as 'bone disease', but should be recorded as a comment.

Scan conducted (*PET, MRI, CT and/or skeletal survey*)

This refers to PET, MRI, CT and/or skeletal survey. Options include:

Yes	Unknown
No	

If a scan has been done, enter 'Yes' and write the type of scan(s) beside the box as a comment. The specific scans will be ticked at data entry. Also attach dated copies of each report.

Skeletal survey conducted

Record the skeletal survey in the 'Scan conducted' section, as above.

Immunoglobulins (*if one is raised or suppressed, enter this)*

To complete this box you need a blood result showing the level of each immunoglobulin, i.e. an immunoglobulin profile. Ignore the immunoglobulin associated with the abnormal paraprotein and assign the appropriate category (normal, raised, suppressed) from the remaining immunoglobulins.

The full list of options include:

Normal	Suppressed	Not stated
Raised	Unknown	Not done

Importantly, some hospitals do not conduct an immunoglobulin profile, but may perform immunofixation electrophoresis, which reports 'the polyclonal background is normal' or 'normal pattern'. This does not mean the immunoglobulin level is normal, however, as this test does not examine each individual type.

If the immunoglobulin levels are both raised and suppressed, record this as suppressed, as this has more clinical significance.

ECOG at diagnosis

Record appropriate score: 0 to 4 or unknown (see section 2.23).

β2m

Sometimes this is not tested at the same time as other presentation data. The result can still be recorded, however, and the date noted in comments, but the test must have been conducted before the start of any treatment.

mg/L (units vary by hospital)	Not stated
	Not done

Creatinine

µmol/L	Not stated
	Not done

Albumin

g/L	Not stated
	Not done

Calcium (corrected/adjusted)

mmol/L	Not stated
	Not done

Hb

g/dL

Not stated
Not done

WBC

$x10^9/L$

Not stated
Not done

Platelets

$x10^9/L$

Not stated
Not done

Haematocrit/packed cell volume

These are measures of the same thing and should be reported as a percentage. If the value is between 0 and 1, multiply by 100.

Not stated
Not done

Neutrophils/absolute neutrophil count

$x10^9/L$

Not stated
Not done

Lymphocytes

$x10^9/L$

Not stated
Not done

Monocytes

$x10^9/L$

Not stated
Not done

Response

CR	(complete response)
VGPR	(very good partial response)
PR	(partial response)
SD	(stable disease)
Plateau	
PD	(progressive disease)
NE	(non evaluable)
MRD	(minimal residual disease)

Response should be completed for each chemotherapy. This is often based on a combination of tests, including paraprotein and serum free light chain level, and bone marrow biopsy. BMAT response, date of sample and HILIS ID should be recorded. For plasmacytoma, response may also be based on CT scan results, which should be routinely copied/printed.

The haematologist's interpretation of response (as noted in medical records) takes precedence and should be documented. Also record (as a comment) the results the haematologist's decision is based on (e.g. paraprotein or serum free light chain level), explaining any contradictions.

Plateau represents a post-treatment phase, when there has been a response that has subsequently levelled-off, but without signs of progressive disease.

During data analysis anything above PR (including plateau) is included as a response to treatment.

Stable disease is used when the malignancy is refractory to treatment (i.e. no response or progression), and is not categorised or analysed as a positive response.

7.0 Lymphoproliferative disorders

These include all lymphomas (B- and T-cell), chronic lymphocytic leukaemia (CLL) and lymphoproliferative disorders not otherwise specified (LPD NOS).

Bone marrow biopsy

A bone marrow biopsy is required for staging. Check for a report at diagnosis on HILIS. Sometimes the test is not done (e.g. if localised disease and normal blood results; the patient cannot tolerate the process; or the result is unlikely to influence clinical management). If no report is found, write a comment to explain why.

HMDS bone marrow and tissue samples may identify different disease subtypes. Section 7.1.4 describes how to document this.

Yes
No
Unknown

B symptoms

Use 'Yes' if positively stated. Use 'No' if the records state 'No evidence of B symptoms' or if B symptoms are mentioned but one is omitted as this indicates that these symptoms have been discussed with the patient, but not found. If nothing is documented about B symptoms use 'Unknown'.

Night sweats	*Drenching*	Yes No	Unknown
Fever	*Persistent or recurring with temperatures above 38°C during previous month*	Yes No	Unknown
Weight loss	*Exceeds 10% body weight in previous 6 months, not otherwise explicable*	Yes No	Unknown

Scan conducted

This refers to the formal staging CT or PET scan, but may include MRI if used to assess disease extent. Options include:

Yes
No
Unknown

If a scan has been done, enter 'Yes' and write the type of scan(s) beside the box as a comment. The specific scans will be ticked at data entry. Avoid using an USS, unless this is the only option, then make a comment about this.

Record the date the staging CT/PET scan was conducted on the nodal/extra-nodal sheet.

Copies of scans at staging and relapse (and any others relevant to the treatment pathway), should be collected, dated, anonymised and attached to the data collection form, in date order.

Ann Arbor stage (not CLL)

Document if recorded in notes, or on PET/CT scan. Options include:

I	III	IV
I_E	IIIE	Not documented
II	III_S	Unknown
II_E	III_{SE}	

Binet stage (CLL only)

Document if recorded in notes, or on PET/CT scan. Options include:

A	Not documented
B	Unknown
C	Not applicable

ECOG at diagnosis

Record appropriate score: 0 to 4 or unknown (see section 2.23).

Hb

g/dL

Not stated
Not done

WBC

$x10^9/L$

Not stated
Not done

Platelets

$x10^9/L$

Not stated
Not done

Haematocrit/packed cell volume

This are measures of the same thing and should be a percentage. If the value is between 0 and 1, multiply by 100.

Not stated
Not done

Neutrophils/absolute neutrophil count

$x10^9/L$

Not stated
Not done

Lymphocytes

$x10^9/L$

Not stated
Not done

Monocytes

$x10^9/L$

Not stated
Not done

Albumin

g/L

Not stated
Not done

β2m

Sometimes β2m is not tested with other blood parameters around the time of diagnosis. The result can still be recorded, as long as the test was done before the start of treatment, but the date should be noted.

mg/L (units vary by hospital)

Not stated
Not done

LDH

(Normal range varies by hospital - please determine this before completing.)

Low	Not stated
Normal	Not done
Raised	

If the patient has a diagnosis of mantle cell lymphoma please add the exact numerical LDH result and the normal LDH range for that hospital.

Paraprotein type

Immunoglobulins have heavy chain components (G, A, D, E and M) and light-chain components (kappa and lambda). Paraproteins can therefore be classified as: IgG, IgA, AgD, IgE or IgM, with further kappa or lambda sub-classification. Paraproteins are detected by serum protein electrophoresis (measuring immunoglobulin level in the blood) and immunofixation electrophoresis (identifying the type of abnormal antibody). Testing may reveal multiple paraprotein types which should be documented separately. Serum free light chain assays are used to classify and monitor light chain, non-secretory and oligosecretory myeloma. Check the blood test results and complete the fields, selecting from:

IgA	None: tested and paraprotein not found
IgD	Not done/ not appropriate (N/A)
IgE	Unknown
IgG	Light chain only
IgM	Oligosecretory
Non-secretory	

If paraprotein is ‘none’ or ‘light chain only’, use N/A for level.

Paraprotein level

Document the paraprotein level in the box. Options include:

(level) g/l	Not stated	N/A
Unquantifiable	Not done	

If paraprotein level is <1, 1-2, <2 or <3, write this in the box. It will be input as ‘Not Stated’, however, as this result is unlikely to be accurate.

Only use ‘Unquantifiable’ if this is what is recorded in the results (see **Appendix IX**).

If more than one paraprotein has been identified, record the level of each.

If paraprotein is ‘none’ or ‘light-chain only’, use N/A for level.

Immunoglobulins (*see section 6.0 for more information)*

Normal	Suppressed	Not stated
Raised	Unknown	Not done

Response

CR (complete response)	PD (progressive disease)
PR (partial response)	NE (non evaluable)
SD (stable disease)	MRD (minimal residual disease: CLL only)

Information required to assign response
Response is assessed via follow-up CT/PET scan reports (which may include the radiologist's opinion), and BMAT/other biopsy results. Copies of all scans should be obtained and tissue samples checked on HILIS, with sample number and date recorded.

Medical records should be checked for comments on response, including palpable lymphadenopathy/hepatosplenomegaly. Consider all the the information available to assess response, but it is important to remember that the haematologist's decision, as written in the notes/letters, takes precedence. If there is a contradiction, try to find out why and comment on this.

Response in CLL
For CLL, blood counts (lymphocytes) and clinical symptoms are often used to assess response, rather than scans. To justify the option selected, write the information used to determine response beside the box.

MRD is an option in CLL, but should only be used if stated on a HMDS bone marrow report. If a CT scan shows CR, but the bone marrow reports MRD, use MRD. If the bone marrow shows MRD, but the CT shows anything but CR (i.e. PR, SD or PD), then document the CT response.

Stable Disease (SD)
SD should be used if the disease has not responded to chemotherapy, but has not progressed. SD is not categorised as a positive response at data analysis, so should not be used if there has been any initial response to treatment. For example, if PR is achieved after 3 x CHOP-R, but there is no further response after 6 x cycles, this should be documented as PR, not SD. PR after 3 x CHOP-R, with PD after 6 x cycles should be documented as PD.

Complete response (CR) after resection
CR can be assigned without follow-up CT/PET scan for some diseases. One example is stage 1 testicular lymphoma (DLBCL), where all the disease is resected, thus CR. In such cases, further CT/PET would have no clinical significance.

Differing response on PET/CT scans
A mid-treatment PET may report CR, but the follow-up CT shows lymph nodes >1cm, that were inactive on the PET. The decision to assign CR or PR should be made based on the individual's long-term clinical picture, and whether this suggests remission or progression.

7.1 Determining and recording disease involvement

Disease site(s) should be determined and recorded after examining pathology (HILIS), radiology (CT/PET, MRI and possibly ultrasound) and clinical evidence (palpation, blood results). Staging CT and PET charts (one of each) should be completed at diagnosis (pre-treatment), with the appropriate boxes ticked to reflect the sites involved.

Record PET scan findings only on the PET form. Use the CT form to document disease identified via CT, MRI and possibly USS, as well as positive HMDS results (marrow/peripheral blood, biopsy) and palpable lymph nodes (>1cm). Disease noted by HMDS, or that is palpable, should be recorded on the CT form, even if no scan was conducted. In this case, write a comment explaining the source of the findings you have documented.

Complete the charts carefully as the ticked boxes are used within HILIS to calculate stage. Ensure all information 'fits' - i.e. scan findings correspond with Ann Arbour staging (as per medical records) and treatment. Identify/explain any contradictions, and if lymph node/extra-nodal involvement is unclear, write 'Check CT' or 'Check PET' on the sheet, and a comment explaining what is required.

If lymphadenopathy or other apparent abnormality is palpable to the clinician but not considered significant on the scan report, then it should not be ticked, as this could incorrectly upstage the disease. However, a comment should be made about this.

If palpable lymph nodes are noted, but a scan is not conducted to verify this, the box should be ticked and marked with a 'P'.

The tissue biopsy site should be ticked (if positive), and marked with a 'B'.

7.1.1 Criteria for identifying involvement: CT (and MRI/USS)

Use this form to document CT findings, but also MRI and USS.

Involvement is defined as lymph nodes greater than 1cm (10mm) in size. Occasionally, nodes may be smaller, but considered significant by the radiographer due to their appearance (e.g. large numbers, matted etc.). In such cases write 'Check CT' on the form and a comment. Do not tick the box if you are in doubt about involvement.

7.1.2 Criteria for identifying involvement: PET scan

Use this form to document PET findings only.

Raised Standardised Uptake Volume (SUV: considered significant by the radiographer or above background/liver levels) indicates disease involvement, regardless of lymph node size (smaller or greater than 1cm).

SUV maximum (SUVmax) is the highest documented value given in the PET report, and should be recorded on the form. If not stated, this should be recorded as 'Not Documented'. Deauville score does not need to be documented, unless completing a follow-up scan form.

7.1.3 Multiple HMDS sample testing

Sometimes the HMDS report will relate to more than one sample, for example, peripheral blood (PB) and a bone marrow biopsy. This does not necessarily mean the disease has been identified in both areas. Indeed, if disease has been found in the bone marrow, the PB may not even be examined. The sites involved can be identified from the tests performed and by reading the HMDS report comments in full; if you are in doubt, however, queries should be placed in the 'Involvement checks' box in the ECSG nurses room, where the decision will be made by the ECSG data analyst/biochemist.

7.1.4 Multiple disease subtypes

HMDS may identify different disease subtypes in the same person from different samples. For example, CLL may be found in a lymph node sample, and LPD NOS in the BMAT. In this case, the marrow should not be ticked as it is not infiltrated by CLL. Instead, add a comment about the subsequent diagnosis, and the HMDS report number and date. If the disease in the additional sample is more advanced than the original, or is of a higher grade, ask the study coordinator how to proceed.

7.1.5 Bulky disease

- A node or nodal mass must be 10cm or greater to meet the criteria for bulky disease.
- This is usually documented in the staging scan report (CT/PET), but could also be documented on the MDT report or by the clinician in the medical records.
- Comment on the source of information used to identify the disease as bulky (i.e. radiology, MDT, medical records).
- 'Bulky' refers to lymphadenopathy and should not be ticked for enlarged spleen.

7.1.6 Extensive disease

This is often noted on the scan report, but not always. It applies when disease is widespread and involves most of the nodal groups. This should be determined on a patient-by-patient basis.

7.2 Nodal and extranodal involvement

HILIS uses an algorithm to independently calculate stage despite what is written in the presentation data box. To do this, it uses the findings from the CT and PET scans, as documented on the disease involvement forms at data collection.

Each disease involvement chart (CT and PET) is divided into 2 sections: the left to record nodal involvement; the right for extra-nodal as shown below. The lymph node diagram (section 7.2.1) provides a guide for locating involved areas.

If the CT scan findings differ significantly from the PET or MDT decision regarding disease stage (e.g. upstaging or downstaging), still use the CT scan to complete the CT disease involvement chart. However, a comment should be added to explain the difference, which will help the data analyst.

Nodal involvement:

Site	L | R
Waldeyer's ring:	☐
Neck:	☐ ☐
Infraclavicular:	☐ ☐
Axillary/Pectoral:	☐ ☐
Arm:	☐ ☐
Thymus:	☐
Hilar:	☐ ☐
Mediastinal:	☐
Para-aortic:	☐
Spleen (palpable):	☐
Mesenteric:	☐
Iliac:	☐ ☐
Inguinal/Femoral:	☐ ☐
Popliteal:	☐ ☐
Bulky disease:	☐

Extranodal involvement:

Site	L | R
Blood:	☐
Bone:	☐
CNS:	☐
GIT:	☐
GU:	☐
Liver:	☐
Marrow:	☐
Muscle:	☐
Orbit:	☐ ☐
Pericardium:	☐
Pulmonary:	☐ ☐
Salivary gland:	☐ ☐
Skin:	☐
Thyroid:	☐
Other:	
Extensive:	☐

7.2.1 Anatomical distribution of lymph nodes

Axillary / Pectoral

Apical axillary
Lateral (surface) axillary
Central axillary
Brachial axillary
Interpectoral
Subpectoral
Paramammary
Parasternal (internal mammary)

Infraclavicular

Hilar

Mediastinal

A. Paratracheal
B. Mediastinal
C. Retrocrural

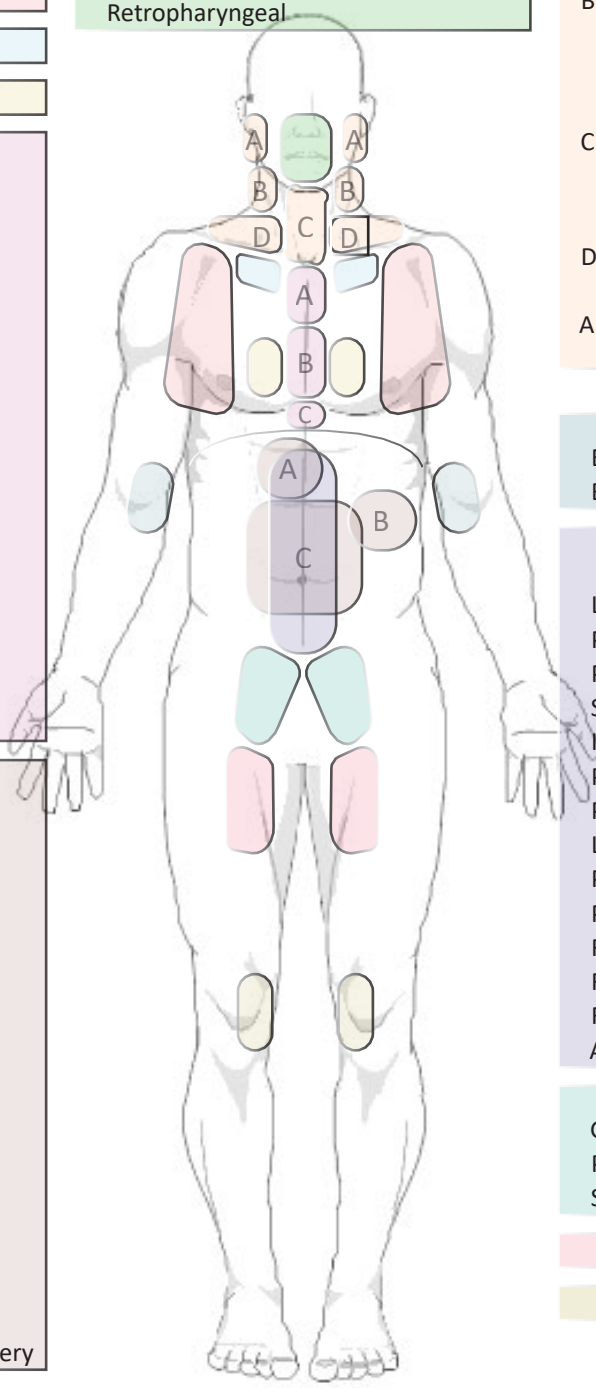
Additional:
Aortopulmonary
Cardiophrenic
Chest wall
Internal thoracic
Paracardiac
Paraoesophageal
Pericardiac
Pericarinal
Precardiac
Prevascular
Subcarinal

Mesenteric

A. Celiac/coeliac
Portocaval
B. Pancreatosplenic
Splenic (hepatic) hilar
Gastro hepatic
C. Mesenteric
Superior mesenteric
Inferior mesenteric
Paracolic
Ileocolic
Left colic
Prececal
Retrocecal
Superior rectal
Portal
Peri-coeliac
Porto-hepatic
Peri-pancreatic
Peri-portal
Nodal small bowel mesentery

Waldeyers Ring

Pharyngeal tonsil (adenoids)
Tubal tonsil
Palatine tonsils
Lingual tonsils (base/back of tongue)
Tongue (base/back)
Oropharynx
Naso-pharynx
Soft/hard palate
Retropharyngeal



Neck

A. Preauricular
Infrauricular
Occipital } Retroauricular
Mastoid }
Parotid node
Superficial parotid node
Deep parotid node
Intraglandular parotid node
Mastoid
B. Submental
Submandibular/Submaxillary
Upper Cervical
Anterior jugular
Superficial jugular
C. Medium and Lower Cervical
Prelaryngeal
External jugular
Lateral jugular
D. Supraclavicular (scalene)

Also: Triangle lymph nodes
Jugulodigastric

Arm

Epitrochlear
Brachial

Paraaortic
(Periaortic)

Lateral aortic
Preaortic
Postaortic (Retroaortic)
Subaortic
Intermediate lumbar
Paracaval
Pericaval
Lateral caval
Precaval
Postcaval
Retroperitoneal
Renal
Retrocaval
Aortocaval

Iliac

Gluteal
Pelvic/sidewall
Sacral

Inguinal/Femoral

Popliteal

Extra-nodal

Site	Area to tick
Brain	CNS
Spinal cord/nerves	CNS
Adnexal	GU
Cervix	GU
Kidney	GU
Testicle(s)	GU
Uterus	GU
Renal hilar	GU
Obturator	Muscle
Sternocleidomastoid	Muscle
Adrenal	Other
Breast tissue	Other
Diaphragm	Other
Omentum (lining of abdomen)/omental fat	Other (or mediastinal if nodal)
Pancreas	Other
Tip of tongue	Other
Small bowel mesentery (lining of abdomen)	Other
Lingular lobe	Pulmonary
Parotid gland	Salivary gland
Sub-mandibular gland	Salivary gland
Sub-lingual gland	Salivary gland
Sub-cutaneous tissue	Skin

Directional terminology

Site	Area to tick
Peri, para	Near, beside, around, alongside
Posterior, retro	Behind
Anterior, pre	In front of
Sub, infra	Below
Cranial	Towards the head
Caudal	Towards the tail/hind part
Proximal	Towards the beginning
Distal	Furthest from beginning
Inferior	Below (opposed to superior)
Intra	Within
Lateral	To left or right (opposed to medial)
Medial	In the middle (opposed to left or right)
Posterior	Back, behind
Superior	Above (opposed to inferior)

Other terminology

Invading	Spread into
Abutting	Adjoin, border, adjacent to
Encasing	Enclose, surround
Impinge	Trapping of soft tissue

7.2.2 Spleen involvement

The spleen is considered part of the nodal lymphatic system. A palpable spleen (splenomegaly) usually signifies disease and should be recorded as such. Radiology (CT/PET/MRI/USS) can be used to assess equivocal splenomegaly and evidence of disease may be described as focal defects or splenomegaly.

7.2.3 Peripheral blood

On the CT form, tick the peripheral blood involvement box if confirmed on HILIS. Otherwise leave the box blank. If a PB and other test sample is reported, check to see which the diagnosis refers to (see section 7.1.3 and 7.1.4).

7.2.4 CNS disease

CNS disease is rare but can occur. It may be detected either in the CSF by HMDS or on imaging of the brain and spine. If you are uncertain about CNS involvement, specify the investigation results (e.g. from lumbar puncture or brain CT scan) as a comment.

7.2.5 Liver involvement

A palpable liver usually signifies disease and should be recorded as such. Radiological (CT/PET/MRI/USS) evidence of disease is often described as multiple focal defects or hepatomegaly.

7.2.6 Marrow involvement

On the CT form, tick the 'marrow' box if BMAT involvement is confirmed by HMDS, and write the HILIS report number next to the box, and the report authorisation date. Write 'Clear' if the report is negative and the report number/date, or 'Not Done' if not tested. PET confirmed marrow involvement should be recorded on the PET chart, if it is clearly involved and not equivocal.

7.2.7 Lung involvement

This can be demonstrated radiologically (in the absence of infection) or through histology. Pleural effusion should only be documented as disease involvement where pleural fluid has been tested and disease involvement confirmed by HMDS.

7.2.8 'Other'

On both the CT and PET form, tick 'Other' for extra-nodal disease that does not fit into existing categories on the scan sheet. There may be more than one 'Other' site – list all that are included in this category.

7.3 Differentiating nodal from extra-nodal disease

Differentiating nodal from extra-nodal disease involvement can be difficult. Complicating factors include:

- Disease may occur in an extra-nodal site (small bowel mesentery), but in the lymph nodes of that site, therefore reflecting nodal disease.
- Terms describing nodal disease sites (e.g. 'mediastinal' lymph nodes) are also used for extra-nodal sites ('soft tissue mass in mediastinum').
- The same terms may be used to describe lymph nodes or extra-nodal abnormalities (e.g. 'soft tissue').
- Extra-nodal and nodal sites are numerous, and described in different ways, so not all sites can be shown or named in section 2.7.1.
- The affected site could involve several nodal/extra-nodal components (e.g. chest wall nodes, including soft tissue, muscle, bone and/or skin), and it may be difficult to differentiate these.
- 'Hilar' is an area where structures (e.g. blood vessels) enter an organ (e.g. 'renal hilum'), so disease in this area may be nodal or extra-nodal.
- Reporting does not always clearly differentiate between nodal/extra-nodal disease.
- Reporting is not standardised, and techniques vary by radiographer, so there may be a lack of consistency.

Strategies to help:

- Use medical records and the clinician's interpretation as a guide to disease involvement.
- Refer to follow-up scan reports, as these can help determine disease involvement and nodal/extra-nodal sites at staging.
- Check biopsy site and results on HILIS.
- Check the Ann Arbour stage (**Appendix VII**) recorded by the haematologist (if documented) in the medical records and compare this to scan results.
- Check treatment as an indication of disease involvement (e.g. radiotherapy only, or high-dose chemotherapy + CNS prophylaxis).
- Search the internet for information on nodal groups.

Appendix I - Inclusion/exclusion criteria: examples

Scenario 1: A patient living in the YHHN area is diagnosed with a haematological malignancy whilst outside the area. They are initially treated/stabilised in the non-YHHN hospital, then return home, and are treated at a YHHN hospital.

Example: A patient is diagnosed and has staging tests for myeloma whilst in Spain on holiday, then returns home (Hull) and is treated at Castle Hill hospital.

Example: A patient with a home address in Wakefield first presents to a hospital in Sheffield (where they are a student), and is diagnosed with AML and given initial treatment. They then return home and receive further care at Pinderfields Hospital.

Decision: INCLUDE

Action: Record presentation data and any initial treatment from the transfer letters/ information. Ask for the treating hospital to be added if necessary (see **Appendix IV**).

Scenario 2: A patient is diagnosed with a haematological malignancy whilst living in the YHHN area, then moves out of the area.

Example: A student (e.g. from the University of York) is diagnosed with Hodgkin lymphoma via York Hospital. The student has a home address in Manchester and returns home for treatment.

Example: A person is diagnosed and treated for CML in Bradford, then decides to relocate and moves to London to live permanently.

Decision: INCLUDE

Action: Abstract all available information, then use 'Lost to Hospital'.

Scenario 3: A haematological malignancy specimen is processed by HMDS, but the person was diagnosed and/or is being and treated elsewhere. This may occur because HMDS is a specialist centre, or is processing all specimens within a clinical trial.

Example: A patient lives in Newcastle and was diagnosed with CLL and treated there. After multiple relapses the patient is referred to St James's hospital (Leeds) for trial treatment, then returns to Newcastle for observation.

Example: A patient lives in Australia and was diagnosed with DLBCL and treated there. Relapse occurs during a UK holiday and one cycle of chemotherapy in given at York hospital, before the flight home to continue treatment.

Decision: EXCLUDE

Action: Make a note of the reason for the exclusion on the data collection form before passing it on to the data manager.

Appendix II - Additional presentation data for subsequent disease

EGU Number:		Date of additional presentation data:	

All diagnoses

ECOG	[0-4]
Hb	[g/dL]
WCC	[x10^9/L]
Platelets	[x10^9/L]

HCT/PCV	[%]
Neutrophils	[x10^9/L]
Lymphocytes	[x10^9/L]
Monocytes	[x10^9/L]

Acute leukaemias

Cytogenetics report	[not recorded but image and attach]

Myeloproliferative disorders

Splenomegaly	[yes/no/not known]
Hepatomegaly	[yes/no/not known]

Detection method	[pal/scan/both/unknown/NA]
Erythropoeitin level	[low/normal/raised/not stated/not done]

Myelodysplastic disorders

Splenomegaly	[yes/no/not known]
Hepatomegaly	[yes/no/not known]
Cytopenias	[0-3]

Detection method	[pal/scan/both/unknown/NA]
Karyotype	[good/intermediate/poor/unknown]
Red cell dependent	[yes/no/not known]

Plasma cell disorders

Paraprotein type	[IgA/IgD/IgE/IgG/IgM/IgG+IgM/ IgG+IgA/Light-chain only/Non-secretory/none/unknown]
Paraprotein level	[g/L /unquantifiable/ not stated/not done]
Urine FLC type	[x10^9/L]
Serum FLC type	[x10^9/L]
Serum kappa	[mg/L /not known/not done]
Serum lambda	[mg/L /not known/not done]
Kappa:lambda ratio	[number:number/NA]
Bone disease	[yes/no]

Scan conducted	[yes/no/unknown]
Skeletal survey	[yes/no/unknown]
Immunoglobulins	normal/raised/suppressed/ unknown/not stated/not done
β_2M	[mg/L /not stated/not done]
Creatinine	[µmol/L /not stated/not done]
Albumin	[g/L /not stated/not done]
Calcium (corrected/adjusted)	[mmol/L /not stated/not done]

Lymphoproliferative disorders

Bone marrow biopsy	[yes/no/unknown]
Sweats	[yes/no/unknown]
Fever	[yes/no/unknown]
Weight loss	[yes/no/unknown]
Scan conducted	[CT/PET/both/none]
Ann-Arbour	[I-IV/not documented/ unknown]
Binet staging (CLL only)	[A/B/C/not documented/ unknown]

Albumin	[g/L /not stated/not done]
β_2M	[mg/L /not stated/not done]
LDH	[low/normal/raised/not stated/not done]
Paraprotein type	[IgA/IgD/IgE/IgG/IgM/IgG+IgM/IgG+IgA/ Light-chain only/Non-secretory/none/ unknown]
Paraprotein level	[g/L /unquantifiable/not stated/not done]
Immunoglobulins	[normal/raised/suppressed/unknown/ not stated/not done]

Appendix III - Follow-up data abstractions

1. Check existing information on the form and make any amendments required so the abstraction meets the current quality standards and contains the correct information.

2. Enter details of treatment response if this was not available at prior abstraction (e.g. if a scan to assess response had not been conducted before the last abstraction).

3. Check the quality of photographs/printed information (e.g. scans) and replace if necessary.

4. Continue adding new information to the abstraction form, following on from the last entry date.

5. Redact any identifiable information (e.g. patient details on scans), using a marker pen or other specialist equipment.

6. Return the form to the ECSG nurses office.

7. Enter the date the follow-up was returned to the office on the HMRN Registration log, in the Follow Up Form section.

8. Place the form in the specific follow-up box if the work has been done for a stand-alone audit, or the general follow-up box if not (usually for deceased patients), to be input by one of the study nurses.

9. After input, forms are re-scanned by the study administrator, and re-filed with any existing data collection for that patient.

Appendix IV - List of treating hospitals

The following is a list of YHHN treating centres, showing how these should be recorded on the data collection form:

Airedale Hospital, Steeton, Keighley:	Airedale
Bradford Royal Infirmary, Bradford:	Bradford
Calderdale Hospital, Halifax:	Calderdale
Castle Hill Hospital, Cottingham, Hull:	Hull
Dewsbury District Hospital, Dewsbury:	Mid Yorks
Diana Princess of Wales Hospital, Grimsby:	Grimsby
Harrogate District Hospital, Harrogate:	Harrogate
Huddersfield Royal Infirmary, Huddersfield:	Calderdale
Leeds General Infirmary, Leeds:	Leeds
Pinderfields General Hospital, Wakefield:	Mid Yorks
Pontefract Hospital, Pontefract:	Mid Yorks
St James's University Hospital, Leeds:	Leeds
Scarborough Hospital, Scarborough:	Scarborough
Scunthorpe General Hospital, Scunthorpe:	Scunthorpe
Wharfedale Hospital, Otley, Leeds:	Leeds
York Hospital, York:	York

A number of treating centres outside YHHN can also be input. These may be needed if, for example, a a patient is initially diagnosed, treated or has a transplant outside the area.

Centres that can be input include:

The Christie (Manchester)
Lincoln County
Middlesborough
Newcastle
Nottingham
Sheffield

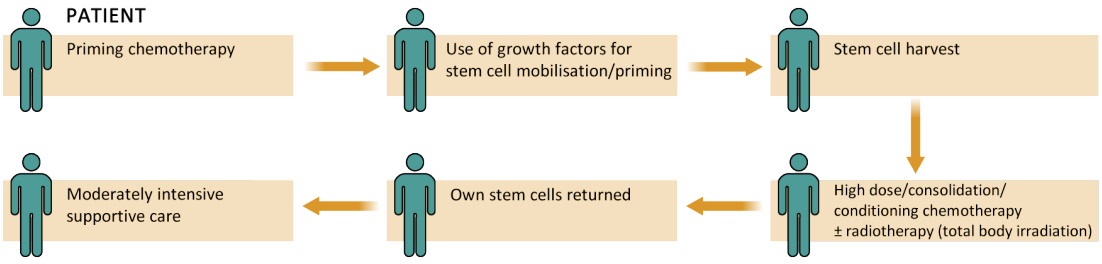
Appendix V - Stem cell transplant pathways

Stem cell transplantation (SCT)

SCT is used to treat lymphoma, myeloma and leukaemia, as well as some MPNs and MDSs. There are two main types of transplant: autologous and allogeneic. Autologous involves extraction of the patient's own stem cells, which are returned to them at a later date; allogeneic transplant is from donor cells. Stem cells are generally collected from the peripheral blood of the patient/donor, but may be collected from other sites (e.g. bone marrow, umbilical cord). All transplant patients are assessed for response at 100 days with either a bone marrow biopsy and/or CT scan, depending on the disease.

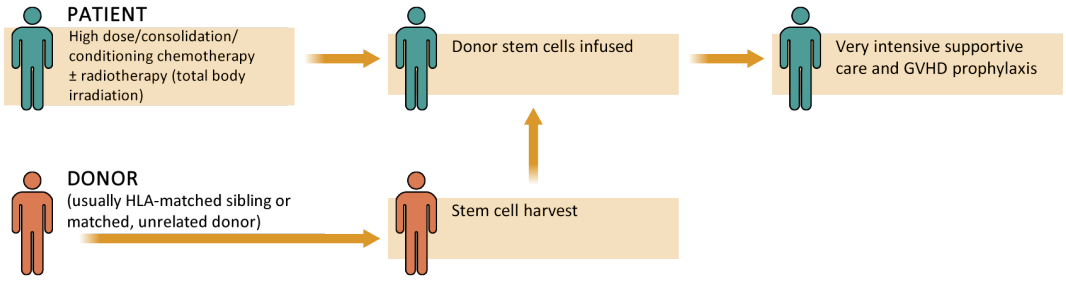
Autologous/autogenic stem cell transplant, high dose treatment with stem cell support, BMT

This process typically begins with delivery of standard induction chemotherapy, priming chemotherapy, use of growth factors to stimulate stem cells, then stem cells harvest. This is followed by high dose conditioning chemotherapy and sometimes radiotherapy (total body irradiation: TBI), prior to return of the patient's own stem cells (see diagram below). Harvests are only carried out at St. James's Hospital, but transplantation is done at St James's, Castle Hill and Mid-Yorkshire hospitals, with the process being amended to suit individual patient characteristics.



Allogeneic stem cell transplant, allograft, donor stem cell transplant, BMT

Patients have high-dose or reduced intensity conditioning chemotherapy and often radiotherapy (TBI), before receiving donor stem cells from a relative, unrelated donor, or umbilical cord extraction. This process is more intense than autologous transplant, and may involve sustained hospitalisation, and intensive care and treatment, sometimes for graft versus host disease and virus reactivation. Such transplants are only performed at St James's Hospital (see diagram below).



More information

You can find more information in standard haematology texts, or online, for example at Macmillan or Myeloma UK websites.

Appendix VI - Required attachments for data collection forms

Acute leukaemias

- Cytogenetics report at presentation

Myeloproliferative neoplasms

- Radiology reports from liver and spleen assessment at presentation (ultrasound/CT/MRI) - not necessary if results are NAD

Myeloproliferative/myelodysplastic neoplasms

- Radiology reports from liver and spleen assessment at presentation (ultrasound/CT/MRI) - not necessary if results are NAD

Myelodysplastic syndromes

- Radiology reports from liver and spleen assessment at presentation (ultrasound/CT/MRI) - not necessary if results are NAD
- Cytogenetics report at presentation

Plasma cell disorders

- MRI/CT/USS (or any other scan) report at presentation
- Report from skeletal survey at presentation

Lymphoproliferative neoplasms

- All radiology reports (e.g. CT, PET) at presentation and all subsequent progressions/relapses

Appendix VII - Staging and prognostic indices

Ann Arbor staging system

Stage	Definition
I	Involvement of a single lymph node region or lymphoid structure (e.g. spleen, thymus, Waldeyer's ring).
I_E	Involvement of a single extralymphatic organ or site.
II	Involvement of two or more lymph node regions on the same side of the diaphragm. The number of regions involved can be indicated by a subscript (e.g. II_3).
II_E	Involvement of a single extralymphatic site **contiguous or proximal** to a known nodal site plus involvement of one or more lymphoid region(s) or structure(s) the same side of the diaphragm.
III	Involvement of lymphoid regions or structures on both sides of the diaphragm.
III_E	**Localised** involvement of a single extralymphatic site **contiguous or proximal** to known nodal site plus involvement of lymphoid regions or structures on both sides of the diaphragm.
III_S	Localised splenic involvement plus involvement of lymphoid regions or structures on both sides of the diaphragm.
III_{SE}	Fulfilling the definitions of both III_E and III_S.
IV	Diffuse or disseminated involvement of one or more extralymphatic organs or tissues with or without associated lymph node involvement. Liver involvement is always considered diffuse and therefore stage IV. Marrow involvement also indicates elevation to stage IV.

Symptom suffices

A patient's status with regards to 'B' symptoms is also taken into account using the following suffices:

Suffix	Definition
For all stages	
A	No symptoms
B	Persistent or recurrent fever (>38°C) during previous month Night sweats (should be drenching) Weight loss (10% body weight over 6 months with no other explanation)

Cotswold modifications (updated Ann Arbor)

Bulky disease is denoted by the suffix 'X'.

For most regions this is defined as enlargement of a single node or conglomerate nodal mass to 10cm or above. For mediastinal disease this has been defined by the Cotswold meeting as a thoracic ratio of maximum transverse mass diameter greater than or equal to 33% of the internal transverse thoracic diameter measured at the T5/6 intervertebral disc level on chest radiography.

Stage III may be subdivided into:

- III_1, with or without splenic, hilar, celiac, or portal nodes;
- III_2, with para-aortic, iliac, mesenteric nodes

International Prognostic Index (IPI)

Adding the scores for each individual case gives the IPI risk group as follows:

Suffix	Risk
0 - 1	LOW
2	LOW - INTERMEDIATE
3	HIGH - INTERMEDIATE
4	HIGH

Risk factor	Score +0	Score +1
Age (years)	< 60	> 60
Stage (Ann Arbor)	I or II	III or IV
Number of extranodal sites	0 or 1	> 1
Performance status (ECOG)	0 or 1	> 1
Serum LDH	Normal	Elevated

Age-adjusted IPI

There is an age-adjusted IPI for patients aged 60 years and under:

Score	Risk
0	LOW
1	LOW - INTERMEDIATE
2	HIGH - INTERMEDIATE
3	HIGH

Risk factor	Score +0	Score +1
Stage (Ann Arbor)	I or II	III or IV
Performance status (ECOG)	0 or 1	> 1
Serum LDH	Normal	Elevated

Follicular lymphoma IPI (FLIPI)

Score calculated as with IPI but

IPI	Risk
0 - 1	LOW
2	INTERMEDIATE
≥ 3	HIGH

Risk factor	Score +0	Score +1
Age (years)	< 60	> 60
Stage (Ann Arbor)	I or II	III or IV
Number of nodal sites	≤ 4	> 4
Performance status (ECOG)	0 or 1	> 1
Serum LDH	Normal	Elevated
Serum Hb	≥ 12g/dL	< 12g/dL

Hodgkin lymphoma - Hasenclever Index

Score calculated as with IPI but

IPI	Risk
< 2	LOW
≥ 3	MODERATE TO HIGH

Risk factor	Score +0	Score +1
Serum albumin	≥ 40g/l	< 40g/l
Haemoglobin	> 10.5 x 10^9/l	< 10.5 x 10^9/l
Age	< 45	≥ 45
Ann Arbor stage	I - III	IV
WBC	< 15 x 10^9/l	> 15 x 10^9/l
Lymphocytes	≥ 0.6 x 10^9/l	< 0.6 x 10^9/l
Gender	Female	Male

Chronic lymphocytic leukaemia - Binet Staging System

Stage	Definition
A	No anaemia or thrombocytopenia Less than three lymphoid areas enlarged*
B	No anaemia or thrombocytopenia Three or more lymphoid areas enlarged*
C	Anaemia (Hb less than 10 g/dl) and/or Platelets less than $100x10^9$/l

*Lymphoid areas are cervical, axillary & inguinal lymphadenopathy (uni- or bilateral), spleen and liver.

MDS International Prognostic Scoring System

There is an age-adjusted IPSS for patients aged 60 years and under:

Score	Risk
0	LOW
0.5 - 1.0	INTERMEDIATE - 1
1.5 - 2.0	INTERMEDIATE - 2
≥ 2.5	HIGH

Risk factor	0	0.5	1.0	1.5	2.0
BM blasts %	< 5	5 - 10	-	11 - 20	21 - 30
Karyotype	Good	Intermediate	Poor	-	-
Cytopenias	0 - 1	2 - 3	-	-	-

Appendix VIII - Specimen abbreviations

BMA	Bone marrow aspirate	**LFU**	Lymph node biopsy, fixed & unfixed
BMAT	Bone marrow aspirate & trephine	**LSL**	Lymph node biopsy, slide
CF	CSF	**LU**	Lymph node biopsy, unfixed
CHIA	Chimerism, allograft	**PB**	Peripheral blood
CHIB	Chimerism, baseline	**PBS**	Peripheral blood, stem cell
CHIM	Chimerism, mini-allograft	**RBL**	Spleen, block
CMP	Community monitoring	**RF**	Spleen, fixed
DBL	Skin, block	**RFU**	Spleen, unfixed
DF	Skin, fixed	**RSL**	Spleen, slide
DFU	Skin, fixed & unfixed	**RU**	Spleen, unfixed
DSL	Skin, slide	**SE**	Serum
DU	Skin, unfixed	**TBL**	Bone marrow trephine, block
EF	Effusion	**TBP**	Bone marrow trephine, fixed
GBL	GI tract biopsy, block	**TSL**	Bone marrow trephine, slide
GF	GI tract biopsy, fixed	**URI**	Urine
GFU	GI tract biopsy, fixed & unfixed	**XA**	Miscellaneous tissue aspirate
GSL	GI tract biopsy, slide	**XBL**	Miscellaneous tissue, block
GU	GI tract biopsy, unfixed	**XF**	Miscellaneous tissue, fixed
HS	Haematological slide	**XFU**	Miscellaneous tissue, fixed & unfixed
LA	Lymph node aspirate	**XSL**	Miscellaneous tissue, slide
LBL	Lymph node biopsy, block	**XU**	Miscellaneous tissue, unfixed
LF	Lymph node biopsy, fixed		

Appendix IX - Further information on plasma cell neoplasms (MGUS, myeloma, plasmacytoma etc)

Normal plasma cells in the bone marrow produce a range of immunoglobulins (antibodies), which fight infection. Plasma cell abnormalities cause diseases such as MGUS, myeloma (including light chain myeloma, non-secretory and oligosecretory), plasmacytoma, amyloid light chain (AL) amyloidosis and Waldenstrom's macroglobulinaemia (WM). Further information can be found here: www.myeloma.org.uk/wp-content/uploads/2018/05/Myeloma-UK-Infopack-for-newly-diagnosed-myeloma-patients.pdf; and here: www.bmj.com/content/bmj/344/bmj.e3033.full.pdf.

Briefly, abnormalities due to DNA damage cause the plasma cell to divide uncontrollably in the bone marrow. These abnormal cells secrete large amounts of one type of abnormal immunoglobulin, which cannot fight infection and is called a paraprotein or M-protein (monoclonal protein). Rather than comprising up to 5% of the bone marrow (normal function), in myeloma the abnormal plasma cells proliferate to the extent that they make-up 10-90% of total bone marrow cells.

Immunoglobulins have heavy chain components (G, A, D, E and M) and light chain components (kappa and lambda). Paraproteins can therefore be classified as: IgG, IgA, AgD, IgE or IgM, with further kappa or lambda sub-classification. Paraproteins are detected by serum protein electrophoresis (measuring immunoglobulin level in the blood) and immunofixation electrophoresis (identifying the type of abnormal antibody). Serum free light chain assays are used to identify and monitor light chain, non-secretory and oligosecretory myeloma.

Specific plasma cell diseases are described below:

MGUS

Defined as the presence of a monoclonal paraprotein in the serum or urine, or an abnormal serum free light chain in light chain only MGUS, with no evidence of myeloma, AL amyloidosis, WM, and no myeloma related end organ damage. Serum paraprotein is <30 g/L and bone marrow clonal plasma cell <10%, with low level plasma cell infiltration in the trephine biopsy.

Symptomatic myeloma

Differentiated from MGUS by having ≥ plasma cells in the bone marrow or proven extramedullary plasmacytoma; in addition to end-≥organ/tissue impairment, as indicated by any one of the following: raised calcium, renal impairment, anaemia, and bone lesions. Paraprotein is also present in serum or urine (generally >30g/L IgG, or >25g/L of IgA, or 1g/24 hour of urine light chain; but can be lower if symptomatic), or it may be that the light chain ratio alone is abnormal.

Asymptomatic (smouldering) myeloma

Criteria include: Serum paraprotein IgG or IgA ≥30g/l or urine monoclonal protein ≥500mg/24hr and/or clonal bone marrow plasma cells 10-60% AND absence of myeloma defining events (end-organ damage) and/or amyloidosis.

Light chain only myeloma

Occurs when the paraprotein only has a light chain component (kappa or lambda) and not a heavy chain (IgA, G, M, D or E). An increase in either of the light chains, giving an abnormal free light chain ratio will be present in the serum (blood) or urine (Bence Jones urine test).

Non-secretory myeloma

Abnormal myeloma cells that do not produce any detectable paraprotein in the blood or urine using the standard electrophoresis test.

Oligosecretory myeloma

Abnormal myeloma cells that produce very low but detectable levels of paraprotein (serum paraprotein <1.0 g/dL, urine/Bence-Jones <200 mg/24hrs, free light chains <10 mg/dL).

Unquantifiable paraprotein level

Sometimes used when the level is too low to calculate. This term should only be used if results/notes state 'unquantifiable' or 'too low to quantify'. Blood results of <1 or 1-2g/L may also be given; rather than the paraprotein level being too low to quantify, this means the laboratory equipment could not produce an accurate measurement. In this case 'unquantifiable' cannot be used and the exact result should be written in the box.

Plasmacytoma of bone (osseous plasmacytoma)

Localised bone tumour consisting of monoclonal plasma cells and no other lesions/features of myeloma. Plasmacytoma of bone is classified as bone disease.

Extraosseous plasmacytoma (extramedullary)

Localised plasma cell disease arising in non-bone soft tissue, with no other lesions/features of myeloma. Most occur in the upper respiratory tract (oropharynx, nasopharynx, sinuses and larynx), but they also arise in the GI tract, lymph nodes, bladder, CNS and breast. Extraosseous plasmacytoma is not bone disease.

Waldenstrom's macroglobulinaemia (WM)

This is lymphoplasmacytic lymphoma with bone marrow involvement and IgM paraprotein. It is important to note that HMDS don't use WM as a diagnosis, but it is used clinically. Patients with an HMDS diagnosis of MYD88 mutated B-cell lymphoproliferative disorder or marginal zone lymphoma may be clinically diagnosed as WM.

Monoclonal immunoglobulin deposition disease (MIDD)

This includes two main categories: **primary amyloidosis** (AL amyloidosis: amyloid light chain) and, more rarely, **systemic light and heavy chain deposition disease**. These diseases are characterised by the deposition and accumulation of immunoglobulins in the soft tissue, which compromise organ function. Affected sites include kidneys, heart, liver, subcutaneous fat, GI tract, peripheral nerves and bone marrow.

Appendix X - Data collection forms

HMRN Data Collection:

Please enter data into boxes, and amend any incorrect or missing details:

Patient Name:		**HILIS ID:**	
Date of Birth:		**NHS No:**	
HMDS Number:		**Report Date:**	
Source:		**Specimen:**	

Demographics:

Gender:	M / F	**Date of diagnosis:**	
Address at diagnosis:			
GP address:			
1st appointment on:		**Palliative date:**	
Date of death:			

Antecedent / concurrent events:

Event:	
Therapies:	chemotherapy / radiotherapy / both

Treatment history:

Centre:	[name]				
Treatment:	[treatment name]				
Trial:	[trial name]				
Start date:		**End date:**		**Response:**	

Presentation data:

ECOG:	[0 - 4]	**Hb:**	[g/dL]
WBC:	[$x10^9$/L]	**Platelets:**	[$x10^9$/L]
PCV:	%	**Neutrophils:**	[$x10^9$/L]
Lymphocytes:	[$x10^9$/L]	**Monocytes:**	[$x10^9$/L]

Comments:

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Antecedent / concurrent events:

Event:	
Therapies:	chemotherapy / radiotherapy / both

Treatment history:

Centre:	[name]				
Treatment:	[treatment name]				
Trial:	[trial name]				
Start date:		**End date:**		**Response:**	

Presentation data:

Splenomegaly:	[Y/N]	**Detection:**	
Hepatomegaly:	[Y/N]	**Detection:**	
ECOG:	[0 - 4]	**Lymphocytes:**	[x10^9/L]
WBC:	[x10^9/L]	**Neutrophils:**	[x10^9/L]
Hb:	[g/dL]	**Monocytes:**	[x10^9/L]
PCV:	[%]	**Platelets:**	[x10^9/L]
Erythropoietin:	[range]		

Comments:

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1st appointment on:		**Palliative date:**	
Date of death:			

Antecedent / concurrent events:

Event:	
Therapies:	chemotherapy / radiotherapy / both

Treatment history:

Centre:	[name]				
Treatment:	[treatment name]				
Trial:	[trial name]				
Start date:		**End date:**		**Response:**	

Presentation data:

Splenomegaly:	[Y/N]	**Detection:**	
Hepatomegaly:	[Y/N]	**Detection:**	
ECOG:	[0 - 4]	**Lymphocytes:**	[x10^9/L]
WBC:	[x10^9/L]	**Neutrophils:**	[x10^9/L]
Hb:	[g/dL]	**Monocytes:**	[x10^9/L]
PCV:	[%]	**Platelets:**	[x10^9/L]
Karyotype:		**Marrow CD34:**	[%]
RBC dependent:	[Y/N]	**Cytopenias:**	[0-3]

Comments:

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Source:		**Specimen:**	

Demographics:

Gender:	M / F	**Date of diagnosis:**	
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1st appointment on:		**Palliative date:**	
Date of death:			

Antecedent / concurrent events:

Event:	
Therapies:	chemotherapy / radiotherapy / both

Treatment history:

Centre:	[name]				
Treatment:	[treatment name]				
Trial:	[trial name]				
Start date:		**End date:**		**Response:**	

Presentation data:

Paraprotein type:		**Pp level:**	[g/L]
Urine FLC type:		**Serum kappa:**	[mg/L]
Serum FLC type:		**Serum lambda:**	[mg/L]
Bone disease:		**Kappa:Lambda ratio:**	
Bone lesions:	[0-99]	**β_2m:**	[mg/L]
MRI scan:	[Y/N]	**Creatinine:**	[µmol/L]
Skeletal survey:	[Y/N]	**Hb:**	[g/dL]
Immunoglobulins:	[normal / suppressed]	**Albumin:**	[g/dL]
ECOG:	[0 - 4]	**Calcium:**	[mmol/L]
Platelets:	[x10^9/L]	**WBC:**	[x10^9/L]
Neutrophils:	[x10^9/L]	**PCV:**	%
Monocytes:	[x10^9/L]	**Lymphocytes:**	[x10^9/L]

Comments:

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Date of death:			

Antecedent / concurrent events:

Event:	
Therapies:	chemotherapy / radiotherapy / both

Treatment history:

Centre:	[name]				
Treatment:	[treatment name]				
Trial:	[trial name]				
Start date:		**End date:**		**Response:**	

Presentation data:

ECOG:	[0 - 4]	**Hb:**	[g/dL]
BM biopsy:	[Y/N]	**WBC:**	[$x10^9$/L]
Sweats:	[Y/N]	**Lymphs:**	[$x10^9$/L]
Fever:	[Y/N]	**Albumin:**	[g/L]
Wt. loss:	[Y/N]	**β_2m:**	[mg/L]
CT Scan:	[Y/N]	**LDH:**	[range]
Ann-Arbor:	[I - IV]		
Paraprotein:	[range]	**Paraprotein lvl:**	[g/L]
PCV:	%	**Neutrophils:**	[$x10^9$/L]
Monocytes:	[$x10^9$/L]	**Immunoglobulins:**	[range]

Comments:

HMRN Data Collection:

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Date of Birth:		**NHS No:**	
HMDS Number:		**Report Date:**	
Source:		**Specimen:**	

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Date of death:			

Antecedent / concurrent events:

Event:	
Therapies:	chemotherapy / radiotherapy / both

Treatment history:

Centre:	[name]				
Treatment:	[treatment name]				
Trial:	[trial name]				
Start date:		**End date:**		**Response:**	

Presentation data:

ECOG:	[0 - 4]	**Hb:**	[g/dL]
BM biopsy:	[Y/N]	**WBC:**	[x10^9/L]
Sweats:	[Y/N]	**Lymphs:**	[x10^9/L]
Fever:	[Y/N]	**Albumin:**	[g/L]
Wt. loss:	[Y/N]	**β_2m:**	[mg/L]
CT Scan:	[Y/N]	**LDH:**	[range]
Binet:	[A, B, C]	**Platelets:**	[x10^9/L]
Paraprotein:	[range]	**Paraprotein lvl:**	[g/L]
PCV:	%	**Neutrophils:**	[x10^9/L]
Monocytes:	[x10^9/L]	**Immunoglobulins:**	[range]

Comments:

PET scan imaging data

PET scan imaging data:

Date:		SUV_{max}:	
Sequence:	[Initial / Follow-up]	Deauville:	[Follow-up only]

Nodal involvement:

Site	L | R
Waldeyer's ring:	☐
Neck:	☐ ☐
Infraclavicular:	☐ ☐
Axillary/pectoral:	☐ ☐
Arm:	☐ ☐
Thymus:	☐
Hilar:	☐ ☐
Mediastinal:	☐
Para-aortic:	☐
Spleen:	☐
Mesenteric:	☐
Iliac:	☐ ☐
Inguinal/femoral:	☐ ☐
Popliteal:	☐ ☐
Bulky disease:	☐

Extranodal involvement:

Site	L | R
Blood:	☐
Bone:	☐
CNS:	☐
GIT:	☐
GU:	☐
Liver:	☐
Marrow:	☐
Muscle:	☐
Orbit:	☐ ☐
Pericardium:	☐
Pulmonary:	☐ ☐
Salivary gland:	☐ ☐
Skin:	☐
Thyroid:	☐
Other:	
Extensive disease:	☐

CT scan imaging data:

Date:	
Sequence:	[Initial / Follow-up]

Nodal involvement:

Site	L | R
Waldeyer's ring:	☐
Neck:	☐ ☐
Infraclavicular:	☐ ☐
Axillary/pectoral:	☐ ☐
Arm:	☐ ☐
Thymus:	☐
Hilar:	☐ ☐
Mediastinal:	☐
Para-aortic:	☐
Spleen:	☐
Mesenteric:	☐
Iliac:	☐ ☐
Inguinal/femoral:	☐ ☐
Popliteal:	☐ ☐
Bulky disease:	☐

Extranodal involvement:

Site	L | R
Blood:	☐
Bone:	☐
CNS:	☐
GIT:	☐
GU:	☐
Liver:	☐
Marrow:	☐
Muscle:	☐
Orbit:	☐ ☐
Pericardium:	☐
Pulmonary:	☐ ☐
Salivary gland:	☐ ☐
Skin:	☐
Thyroid:	☐
Other:	
Extensive disease:	☐

Appendix XII - Treatment specific instructions

Treatment	Instruction
ABVD/AVD	Sometimes ABVD is started, then the 'B' (bleomycin) is dropped. This may be due to a good response after initial treatment (i.e. PET negative after 2 cycles or more). Or it may be dropped at any point due to intolerance or toxicities. If dropped due to a good response, the ABVD episode should be ended and a new AVD treatment started. If stopped due to intolerance/toxicities, then ABVD should continue, with a comment explaining that the bleomycin was stopped, and the reason for this.
Aspirin in MPD	If GP initiated, use 'unknown' for the start date and add a comment
Aspirin in myeloma	No need to record as a treatment
Azacytadine	Split treatment/maintenance at first CR/MRD+ only
CEP-701	Patients on AML 15 and AML 17 are randomised to receive CEP-701 if they have a FLT3 mutation. CEP-701 (a tablet) is prescribed alongside each cycle of the trial. It is administered 2 days after the end of each chemo cycle for a maximum of 28 days and before the next cycle of chemo starts. CEP-701 should be documented separately (under the appropriate trial name) for its full duration.
PUVA	Light therapy, usually for skin lymphoma. There are many types, but just document PUVA and write a comment about the type.
Topical steroids	Only document for skin lymphoma. If already prescribed by the GP at the time of diagnosis, still record as a treatment with 'unknown' start date and a comment explaining the reason for this.