EBMT Registry

Haematopoietic cell transplantation (HCT) annual/unscheduled follow-up

Guide to the completion of the EBMT data collection form:

HCT_FU_annual_v2.0

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EBMT Registry

EBMT Clinical Research & Registry Department

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Introduction

Please make sure you have already checked the **Introduction to the EBMT Registry Completion Guidelines** document latest version available under *Manuals and Reference Documents* section on EBMT website.

Haematopoietic cell transplantation (HCT) annual/unscheduled follow-up

The follow-up of HCT patients should be recorded using the HCT annual/unscheduled form. The form may be filled as a paper version before entering into the EBMT Registry, or can be entered online into the EBMT Registry database immediately. The form should be completed at the follow up date or at time of patient death, whichever occurs first.

Date of follow-up

Report the date that the annual/unscheduled follow-up occurred. If the patient died, enter the date of death. If the patient was lost to follow-up, enter the date the patient was last seen alive.

Survival status

Indicate if the patient is last known to be **Alive** or **Dead** on the date of follow-up previously noted. If the patient is lost to follow-up, tick the box for **Lost to follow-up**.

Main cause of death

Report only one main cause of death, even if it was considered to be a combination of various causes. If the cause of death is not known, select **Unknown**. Please select one of the following main causes of death:

- **Relapse or progression/persistent disease**;
- **Secondary malignancy**;
- **CT-related** - death caused by complications or infections after cellular therapy;
- **HCT-related** - death caused by complications or infections after transplant;
- **GT-related** - death caused by complications or infections after gene therapy;
- **IST-related** - death caused by complications or infections after immunosuppressive treatment (for patients treated with Bone Marrow Failure only).

If none of the suggested options fit, select **Other** and specify the cause of death in the textbox in English.

Select treatment related cause

In the case of treatment-related cause of death, select all the answer options that apply:

- **Graft versus host disease (GvHD);**
- **Non-infectious complication;**
- **Infectious complication.**

Infectious complication

In the case of an infectious complication, please specify the type of infection. In case of multiple infections with different pathogens, select all the type of infection(s) that apply:

- **Bacterial infection;**
- **Viral infection;**
- **Fungal infection;**
- **Parasitic infection;**
- **Infection with unknown pathogen.**

Please note that the category “rejection/poor graft function or failure” as contributory cause of death (previously in MedAB (auto, allo and disease-specific forms)) does not exist since the cause of death following a graft failure is generally an infection. Please note that secondary graft failure as cause of death is reportable under the list of non-infectious complications (select ‘**Fatal**’).

Was an autopsy performed

Check **No**, if no autopsy has been performed. Check **Yes** if autopsy is performed. Select **Unknown** if it is unknown an autopsy was performed.

Best Response

The best response only has to be completed for the first annual follow-up. The disease specific options for the best response can be found in Appendix 1. This section is not applicable for patients receiving HCT for Inborn errors indication diagnosis.

Best clinical/biological response after HCT

Report the patient’s best response achieved after HCT but before any subsequent treatment, even if the patient got worse again afterwards. Please refer to Appendix 1 on the form to select the best response that is appropriate for the diagnosis of the patient. This includes the response observed before any subsequent treatment. If the best response after the HCT has not been evaluated, select **Not evaluated**. If the best response after the HCT is unknown, select **Unknown.**

The best response is often achieved in the first 100 days after HCT. However, for some diseases the best response to HCT may take longer and shall be reported in the first annual follow-up form (e.g. PCM). For all indication diagnoses except for inherited disorders, report the best response achieved as per the date of follow-up. In case HCT was performed for inherited disorders, this section can be left blank.

If the patient had a relapse/progression post-HCT and received therapy for the disease relapse/progression, the response to that additional therapy should not be reported in this section. The best response prior to the relapse/progression should be reported here. The response should be captured before the start of unplanned treatment of underlying disease.

Date best response first observed

Report the date the best response was first observed. The response date is the date that the sample or image was taken for assessing the response. If the patient's best response was already achieved prior to HCT (eg. HCT in CR and best response CR) the first evaluation date after the HCT should be reported. If the date is unknown, select **Unknown**.

Graft Function

Poor graft function

Poor graft function is defined as frequent dependence on blood and/or platelet transfusions and/or growth factor support in the absence of other explanations, such as disease relapse, drugs, or infection. If poor graft function was observed - select **Yes**. If poor graft function was not observed, select **No**.

The definition for poor graft function assumes that donor chimaerism is within a desirable target level.

In contrast with graft failure, poor graft function requires some degree of allogeneic graft evidence. However, the "desirable" target level depends on the time point when it's measured, the indication for HCT (malignant versus non-malignant), intensity of the conditioning regimen, etc.

As an example, a patient with poor haematologic function but confirmation of donor source (proof of at least mixed/partial donor chimaerism), and in the absence of other explanations (disease relapse, drug toxicity, infections, GvHD, etc) represents a case of poor graft function. However, due to the dynamic nature of chimaerism, it is advisable to reassess donor chimaerism levels to confirm the results.

Note: please do not report graft failure in this section.

- If primary graft failure occurred, please report it in the Recovery section in Absolute neutrophil count (ANC) recovery
- If secondary graft failure occurred, please report this through the Non-infectious complications section.

Date of poor graft function

Report the date when the patient started requiring frequent growth factor and/or packed RBC/platelets transfusions (at least weekly transfusions and/or growth factor support for at least 4 weeks) once other

causes that could explain the poor graft function such as disease relapse, drugs, or infections have been ruled out.

Chimaerism

This section is only applicable for patients that received an allogeneic HCT.

Complete this section for every chimaerism test performed within this follow-up period (after previous follow-up) until complete donor chimaerism has been achieved (>95%). If the patient has mixed chimaerism (5%-95% for either one or both myeloid and lymphoid lineages), please, complete the section if the chimaerism results change at least 10% from the previous test.

Chimaerism test date

Report the chimaerism test date.

Source of cells tested

Indicate if **Peripheral blood** or **Bone marrow** was used as source of cells for the chimaerism test (select all that apply).

Cell types and test results

Select each cell type that was tested and indicate the percentage of donor cells. In case any other cell types were tested, please select **Other** and indicate the type of cells in the textbox in English. If the percentage of donor cells is unknown, select **Unknown**.

Preventive Therapies

This section is only applicable for patients that received an allogeneic HCT.

Immunosuppression during this follow-up period

This question is asked to know if the GvHD prevention initiated at transplant is still ongoing at this follow up.

Select **No** if the patient was not receiving preventive (immunosuppressive) therapy for GvHD post-transplant. Select **Yes** if the patient was receiving preventive therapy post-transplant. Report as **Unknown** if it is unknown if the patient was still receiving immunosuppressive GvHD preventive treatment.

Immunosuppression stopped

If immunosuppression for GvHD prevention was stopped, please report **Yes** and provide the end date of the GvHD prevention. If the therapy is ongoing, select **No**. If it is not known if the patient is still on immunosuppressive treatment, select **Unknown**.

End date

Report the date the preventive treatment for GvHD was stopped. If the patient experiences a GvHD while receiving GvHD prevention, please report the date of onset of GvHD as the end date of GvHD prevention (as this becomes GvHD treatment rather than prevention). If the stop date was not known, select **Unknown**.

Letermovir used as CMV prophylaxis during this follow-up period

Indicate whether the patient received letermovir as CMV prophylaxis during the follow-up period. Select **Unknown** if this information is unavailable.

Letermovir used as CMV prophylaxis during this follow-up period? Yes

Indicate whether the letermovir as CMV prophylaxis **Started in this follow-up period** or it was **Ongoing since the previous follow-up** assessment.

Start date

If it was **Started in this follow-up period**, provide the start date of the letermovir regimen. Select **Unknown** if the start date is not known.

Letermovir treatment stop?

In case prophylaxis was **Ongoing since previous follow-up** ,indicate whether the letermovir regimen has stopped. If **Yes**, please provide the end date of the letermovir treatment. Select **Unknown** if the end date is not known.

End date

Report the date the letermovir treatment stopped. If the stop date was not known, select **Unknown**.

Complications since the Last Follow-up - GvHD

This section should only be completed if the patient received an allogeneic HCT.

Did graft versus host disease (GvHD) occur?

If **No** GvHD occurred. If this information is **Unknown**, select the appropriate answer and proceed to the next section: 'Complications since the last report - Non-infectious complications'. Select **Yes** if GvHD occurred/were ongoing/resolved in this follow up period and proceed to the next question.

Graft-versus-host disease (GvHD) refers to a clinical syndrome caused by the response of transplanted donor allogeneic cells to histocompatibility antigens expressed on tissues of the transplantation recipient. Acute GvHD (aGvHD) refers to the appearance of an allogeneic inflammatory response in exclusively three organs: the skin (inflammatory maculopapular erythematous skin rash), the liver (hyperbilirubinemia due to cholestatic jaundice), and the gastro-intestinal (GI) tract (upper and/or lower GI tract manifestations). The diagnosis must occur in the absence of manifestations of chronic GvHD (cGvHD) and should ideally be supported by positive histological findings. cGvHD is based on either the presence of specific diagnostic signs or distinctive signs accompanied by additional confirmation (e.g. biopsy or other objective diagnostic test) in at least one target organ (skin & appendages, mouth, eyes, genitalia, oesophagus, lungs and muscles & fascia). Detailed definitions are described in the 2014 NIH Consensus (1) and 2018 EBMT—NIH—CIBMTR Task Force statement on standardised terminology (2).

Did the patient receive a systemic/immunosuppressive treatment for GvHD?

Indicate if the patient received a systemic immunosuppressive treatment for GvHD since the last follow-up. If the answer is **Yes**, specify:

Date treatment started

Report the date the systemic immunosuppressive treatment for GvHD started**.**

If immunosuppressive treatment was started before the GvHD (as prevention) and continued as GvHD treatment, please indicate the date of onset of GvHD (i.e. the date that the immunosuppression was first considered as GvHD treatment, as treatment cannot technically start until onset of GvHD).

Treatment stopped

Indicate whether systemic immunosuppressive treatment for GvHD is still ongoing from a previous follow up.

Stop date of treatment

If treatment concluded during this follow-up, report the stop date of this treatment. Mark as **Unknown** if this is not known.

Did acute GvHD occur?

Indicate if acute graft versus host disease (aGvHD) occurred within this follow-up period (including ongoing aGvHD first reported in a previous FU).

aGvHD is a consequence of donor T-cells recognizing the patient's antigens as foreign. It usually consists of dermatitis, hepatitis, and gastroenteritis. Although it usually develops within the first 100 days, it can also appear later on.

Date of onset

If aGvHD occurred, report the date of onset.

If aGvHD was reported in the previous FU event but was not resolved at that time, please register the date of onset as **Ongoing** and report the resolution in the 'aGvHD resolved?' question. Mark as **Unknown** if this is not known.

Note: The date of onset only needs to be reported on the first follow-up form where the aGvHD episode first occurred.

Maximum observed organ severity score

Select for each organ listed in the table the observed severity score. If another site was also affected, answer **Yes** in **Other site affected** and specify this site in the text field in English.

The maximum grade for acute graft versus host disease (aGvHD) is defined according to the stages presented by the skin, liver, lower and upper GI tracts and can be found in table 1.

Organ	Stage	Description
Skin	0	No rash attributable to acute GVHD
	1	Skin rash < 25% body surface
	2	Skin rash 25-50% body surface
	3	Skin rash >50% body surface
	4	Generalised erythroderma (> 50% BSA) plus bullous formation and desquamation >5% of BSA

Organ	Stage	Description
Liver	0	Total serum bilirubin < 34 µmole/L (< 2 mg/dL)
	1	Total serum bilirubin 34–50 µmole/L (2 to 3 mg/dL)
	2	Total serum bilirubin 51–102µmole/L (3.1 to 6 mg/dL)
	3	Total serum bilirubin 103–255 µmole/L (6.1 to 15 mg/dL)
	4	Total serum bilirubin >255 µmole/L (> 15 mg/dL)
Lower gut	0	Diarrhoea < 500 mL/day or<3 episodes/day for adults or diarrhoea <10 mL/kg/day or <4 episodes/day for children
	1	Diarrhoea 500–999 mL/day or 3–4 episodes/day for adults or diarrhoea 10–19.9 mL/kg/day or 4–6 episodes/day for children
	2	Diarrhoea 1000–1500mL/day or 5–7 episodes/day for adults diarrhoea 20–30 mL/kg/day or 7–10 episodes/day for children
	3	Diarrhoea >1500 mL/day or >7 episodes/day for adults or diarrhoea > 30 mL/kg/day or >10 episodes/day for children
	4	Severe abdominal pain with or without ileus or grossly bloody stools (regardless of stool volume)
Upper gut	0	No or intermittent anorexia or nausea or vomiting
	1	Persistent anorexia or nausea or vomiting

Table 1. aGvHD grading system per organ (2)

Overall maximum grade observed

Select the overall maximum grade that was observed during this follow-up. If it is not known which overall maximum grade was observed, select **Unknown**. Mark it as **Not evaluated** if overall maximum grade was not carried out.

The overall grade (or the stage of skin, liver and gut) should be mentioned in the patients' file. If not clearly stated, ask the treating physician. You should report the maximum grade seen during this follow-up period as calculated from table 2.

Grade							
1	Skin stage 1 or 2	AND	Liver stage 0	AND	Upper gut stage 0	AND	Lower gut stage 0
2	Skin stage 3	AND/ OR	Liver stage 1	AND/ OR	Upper Gut stage 1	AND/ OR	Lower gut stage 1
3	Any skin	AND	Liver stage 2 or 3	AND/ OR			Lower gut stage 2 or 3
4	Skin stage 4	OR	Liver stage 4	OR			Lower gut stage 4

Table 2. Overall maximum grade for aGvHD (2)

Steroid-refractory acute GvHD

Indicate if the patient experienced steroid-refractory acute GvHD or not. Steroid refractory aGvHD is defined as “failure to respond to standard steroid doses (defined as progression within 3–5 days of starting treatment or an incomplete response by 7–14 days) or recurrence after initial dose reduction (steroid dependence)” as stated in the EBMT handbook (3). Mark as **Unknown** if the steroid-refractory aGvHD was unknown.

Date of onset

Report the date that the aGvHD was first considered steroid-refractory. Please note that by definition, this cannot be the same date as the onset of aGvHD. If the aGvHD was already reported as steroid-refractory in the previous follow-up form but was not resolved at that follow-up, please register the date of onset as **Ongoing.** This also applies if the complication was resolved early in this follow-up period. Mark as **Unknown** if the date of onset was unknown.

Note: The date of onset only needs to be reported on the first follow-up form where the steroid-refractory aGvHD first occurred.

aGvHD resolved?

Please indicate whether the aGvHD was resolved or not by answering **Yes** or **No**. Mark as **Unknown** if the resolved status was unknown.

Date of aGvHD resolution

If the acute GvHD resolved, please report the date on which it was thought to have resolved completely. If the date is unknown, select **unknown**.

Did chronic GvHD occur?

Indicate if chronic GvHD (cGvHD) occurred or not within this follow-up period (including ongoing cGvHD first reported in a previous FU).

Date of onset

If cGvHD occurred, report the date of onset.

If the cGvHD was already reported as steroid-refractory in the previous follow-up form but was not resolved at that follow-up, please register the date of onset as **Ongoing** and, if applicable, report the resolution in the 'cGvHD resolved?' question.

Note: The date of onset only needs to be reported on the first follow-up form where the cGvHD episode first occurred.

Maximum NIH score during this period

Indicate if the maximum NIH score during this period was **Mild**, **Moderate** or **Severe**. If the score is unknown, select **Unknown**. If the NIH score was not evaluated during this period, select **Not evaluated**.

The NIH scoring system was first published in 2005 and was updated in 2014 and 2022. As described in the 2014 Diagnosis and Staging Working Group report (1), eight classical organs or sites (skin, mouth, eyes, lungs, musculoskeletal system, gastrointestinal tract, genitourinary tract, and liver) are considered for calculating global score.

Elements included in the proposed global scoring include both the number of organs or sites involved and the severity score within each affected organ. Indicate the maximum NIH score during this period, as per the results of these measurements. Instructions for physicians on assessing the NIH score can be found in the EBMT handbook (1,4) or table 3.

Mild cGvHD	1 or 2 organs involved with no more than score 1 AND Lung score 0
Moderate cGvHD	3 or more organs involved with no more than score 1 OR At least 1 organ (not lung) with a score of 2 OR Lung score 1
Severe cGvHD	At least 1 organ with a score of 3 OR Lung score of 2 or 3

Table 3. Assessing the maximum NIH score (1)

In 2022, the NIH consensus (5) recognized atypical manifestations of chronic GvHD, which should be reported in the section '**Other site affected**' below the list of organs involved. Atypical manifestations do not contribute to the global severity score.

Date maximum NIH score

Report the date the maximum NIH score was observed.

Maximum observed organ severity score

Select for each organ in the table the observed severity score. If another site was affected, answer **Yes** in **Other site affected** and specify this site in the text field.

Use the NIH scoring system as described in 'Maximum NIH score during this period'

Steroid-refractory chronic GvHD

Indicate if the patient experienced steroid-refractory chronic GvHD. Steroid refractory cGvHD is defined as "progression of cGvHD while on prednisone at ≥1 mg/kg/day for 1 to 2 weeks or stable GvHD on ≥0.5 mg/kg/day (or 1 mg/kg every other day) of prednisone for 1 to 2 months" (2).

Date of onset: steroid-refractory chronic GvHD

Report the date that the cGvHD was first considered steroid-refractory. Please note that by definition, this cannot be the same date as the onset of cGvHD. If the cGvHD was already reported as steroid-refractory in the previous follow-up form but was not resolved at that time, please register the date of onset as **Ongoing**.

Note: The date of onset only needs to be reported on the first follow-up form where the steroid-refractory cGvHD first occurred.

cGvHD resolved?

Please indicate whether the cGvHD was resolved or not. If the cGvHD resolution is unknown, select **Unknown**.

Date of cGvHD resolution

If the chronic GvHD was resolved, please report the date on which this occurred. Please, select **Unknown** if the date of cGvHD resolution is unknown.

Was overlap syndrome observed (features of both chronic and acute GvHD)

Overlap syndrome is defined as the occurrence of concomitant symptoms of chronic and acute GvHD. If overlap syndrome was observed, select **Yes**. If overlap syndrome was not observed, select **No**. If the observation is unknown, select **Unknown**.

Complications since the last report - Non-infectious complications

Did non-infectious complications occur during the follow-up period?

If no non-infectious complication other than GvHD occurred during the follow-up period or if the complication was grade 1 or 2, select **No** and proceed to the next section. If non-infectious complications with a CTCAE grade of at least 3 occurred or graft failure, pure red cell aplasia, posterior reversible encephalopathy syndrome or VOD of any grade occurred, select **Yes** and report in the table below.

For adverse events not listed in the table, specify them in the **Other** text field. Consult with Appendix 3 in the paper form which non-infectious complications should not be reported even for grades 3 and 4.

Non-infectious complication observed

Specify for each adverse event listed whether it was observed or not during the follow-up being recorded. The CTCAE gradings (v5) can be found on the website of the NIH (6). Please note that if an event can be reported in more than one type of adverse event, it should be reported only once in the most precise category (eg. a cerebral thrombosis should be reported only as a cerebral thrombosis and not also as a vascular event).

If a grading is dependent on hospitalisation but the patient was an inpatient at the time of onset, the centre will make the interpretation. If the patient had been an out-patient and the severity was such that the patient would have been hospitalised, grading will be selected accordingly.

Event newly developed or ongoing since previous follow-up

Indicate if the adverse event **newly developed** in the follow-up period (i.e. started since the last follow-up event was reported and was not present at previous follow-up) or if it was **ongoing since the previous follow-up** (i.e. the adverse event was reported at a previous follow-up and is still present at this follow-up).

Maximum CTCAE grade observed

Select for each adverse event the maximum CTCAE grade that was observed. If the grade is unknown, select **Unknown**.

Note, for the following complications there are different grading systems to be used:

- Graft failure (fatal/non-fatal)
- Pure red cell aplasia (fatal/non-fatal)
- Posterior reversible encephalopathy syndrome (considered severe if a patient was re-hospitalised,transferred to the ICU, experiences severe mental impairment or severe cerebral edema)
- Veno-occlusive disease (VOD)/ Sinusoidal obstruction syndrome (SOS) is diagnosed based on clinical criteria. The most recently proposed EBMT criteria can be found in table 4.

Adults	Children
Classical SOS/VOD *In the first 21 days after HSCT:* Bilirubin ≥2 mg/dL and two of the following criteria must be present: Painful hepatomegaly Weight gain >5% Ascites Late onset SOS/VOD *>21 Days after HSCT:* Classical VOD/SOS beyond day 21 Or Histologically proven SOS/VOD OR Two or more of the following criteria must be present: Bilirubin ≥2 mg/dL (or 34 µmole/L) Painful hepatomegaly Weight gain >5% Ascites AND Hemodynamical or/and ultrasound evidence of SOS/VOD	No limitation for time of onset of SOS/VOD The presence of two or more of the following: • Unexplained consumptive and transfusion-refractory thrombocytopenia • Otherwise unexplained weight gain on three consecutive days despite the use of diuretics or a weight gain >5% above baseline value • Hepatomegaly (best if confirmed by imaging) above baseline value • Ascites (best if confirmed by imaging) above baseline value • Rising bilirubin from a baseline value on 3 consecutive days or bilirubin ≥2 mg/dL within 72 h

Severity definition				
	Mild	Moderate	Severe	Very severe
Time since first clinical symptoms of SOS/VOD	>7 Days	5–7 Days	≤4 Days	Any time
Bilirubin (µmole/L)	≥34 and <51	≥51 and <85	≥85 and <136	≥136
Bilirubin kinetics			Doubling within 48 h	
Transaminases	≥2 × normal	> 2 and ≤5 × normal	>5 and ≤8 × normal	>8 × Normal
Weight increase	< 5%	≥5% and <10%	≥5% and <10%	≥10%
Renal function	<1.2 × baseline at transplant	≥1.2 and<1.5 × baseline at transplant	≥1.5 and <2 × baseline at transplant	≥2 × baseline at transplant or others signs of MOD/MOF

Table 4. Diagnostic criteria for SOS and VOD (8)

Onset date

Report the onset date when the adverse event was first observed during this follow-up period.

Resolved

If the complication was resolved in the observed period, mark as **Yes** and report the resolution date. If the complication is ongoing at time of the follow-up, select **No**. If there is no information whether the complication was resolved or not mark as **Unknown**.

Stop date

Report the date the complication was resolved.

Infectious complications

Did infectious complications occur during the follow-up period?

Answer **Yes** if any infectious complications occurred during this follow-up period.

Infections already reported on the previous follow-up need to be reported again if they were ongoing at the previous follow-up and thus continued into this follow-up. In this case, please update the information (e.g. clinical implications/localization/resolution) if any changes have occurred.

Infections already resolved at the previous follow-up do not need to be reported, unless a reactivation occurred.

Please note that the following infections do NOT need to be reported:

- Minor ophthalmologic bacterial infections (e.g. conjunctivitis treated topically; blepharitis treated topically; stye treated topically)
- External otitis treated topically
- Otitis media treated with oral antibiotics
- Isolated lip herpes simplex
- Bacterial tonsillitis or pharyngitis treated orally
- Laryngitis without viral identification managed at home by inhalations or without any intervention
- Upper respiratory tract infection (URTI) without viral/bacterial identification managed at home
- Bilateral cervical lymph node enlargement concurrent with URTI that resolved without specific treatment, together with the resolution of URTI
- Local superficial wound infection resolved under topical antibiotics (including impetigo)
- Minor skin bacterial infections (e.g. folliculitis; acne)
- Minor fungal skin infection (e.g. candidal intertrigo treated topically)
- Diaper rash treated with local antifungals

- Candidal balanitis treated topically
- Vaginal candidiasis treated topically or with a single oral dose
- Asymptomatic bacteriuria due to a pathogen not multi-resistant
- Single low urinary tract infection treated orally without need for hospitalisation
- Phlebitis following peripheral intravascular infusion that resolved after intravascular removal without treatment with antibiotics
- Any isolate that is considered part of the normal flora of the place (oral cavity, vagina, skin, stools) except if it carries an antimicrobial resistance that has clinical implications (induce isolation precautions or a pathogen-directed therapy)
- Positive culture without clinical implications (i.e. symptoms/signs of disease; administration of pathogen-directed therapy; isolation precautions or surveillance.

Bacterial infection

Indicate if the patient had a bacterial infection in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place. Report here only bacterial infections with microbiological documentation, otherwise they shall be reported as infection with unknown pathogen.

New or ongoing

Indicate if the patient had a **Newly developed** bacterial infection or if it was **Ongoing since previous assessment**.

Start date

Report the date a first positive blood or other relevant culture or diagnostic sample was obtained. In case a diagnostic sample was obtained with a delay since the symptoms of infection started – report the date when symptoms attributable to this infection started (e.g. patient with pneumonia, urine test for legionella was sent after a few days and the test result was positive).

In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

If the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again.

Type of bacteria

Select the type of bacteria by marking if it is ‘Gram-positive’, ‘Gram-negative’ or ‘Other’ (see the list in Appendix 2 of the form or available in the database).

Pathogen

Select the bacterium that caused the infection from the list in Appendix 2 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the ‘Gram-positive

bacteria other spp', 'Gram-negative bacteria other spp' or 'Bacteria other' option and enter its name in a textbox. Always report the full name of the bacterium.

Please note that some bacteria appear several times but with the emphasis on their resistance pattern. If relevant susceptibility data is unavailable, 'Gram-positive bacteria other spp' or 'Gram-negative bacteria other spp' can be selected (e.g. in case of *Pseudomonas* without information on carbapenem susceptibility (meropenem, imipenem or doripenem) choose 'Gram-negative bacteria other spp'). For *Staphylococcus aureus*: if vancomycin susceptibility is unavailable, but it is methicillin-susceptible (can appear as "oxacillin"), it should be reported as '*Staphylococcus aureus* MSSA (methicillin-susceptible)'. For '*Staphylococcus aureus* MRSA (methicillin-resistant)', indicate whether the vancomycin susceptibility was not tested, or whether it was VISA (vancomycin-intermediate) or VRSA (vancomycin-resistant) based on the minimum inhibitory concentration (MIC) for vancomycin falling within the range noted in the Appendix.

Common commensals (most commonly coagulase-negative Staphylococci, *Micrococcus* spp., *Bacillus* spp., *Propionibacterium* spp.) should be reported only if there are at least two positive blood cultures.

Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark **Unknown** if it is not possible to identify. Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, infection that requires pathogen-directed therapy, or infection that requires isolation precautions or surveillance.

Infection with clinical implications, yes:

Select all clinical implications of the infection during this follow-up period that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions or surveillance.

Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 2 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location involved during this follow-up period must be reported.

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

If the clinical information available doesn't specify the localisation of the infection, probably the infection was asymptomatic and will not have to be reported. Otherwise, the symptoms should guide the choice.

Intravascular catheter-related infection

Indicate if the infection was related to a central venous catheter (CVC). Please note that bacteraemia can be CVC-related or not CVC-related. The definition for the CVC-related bactaeremia requires one of the following:

- The same organism (genus, species, and susceptibility pattern) growing from at least 1 percutaneous blood sample culture and from the catheter tip (e.g. two coagulase- negative Staphylococci, but different species, such as *Staphylococcus capitis* and *Staphylococcus epidermidis*, or two *Staphylococcus epidermidis* with completely different susceptibilities are not the same).
- 2 blood samples for culture are obtained (1 from a catheter hub and 1 from a peripheral vein) that meet CVC-related bacteraemia criteria for differential time to positivity (DTP): growth of microbes from blood obtained through the catheter hub being detected at least 2 hours before microbial growth is detected in blood samples obtained from a peripheral vein (9).

Specify

If the infection was related to an intravascular catheter, select the type of CVC infection from the list in Appendix 4 or available in the database.

Infection resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control, and negative diagnostic tests were obtained in case the investigation was repeated, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one bacterial infectious complication during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in the table as many times as necessary.

Viral infection

Indicate if the patient had a viral infection in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place. Report here only infections with microbiological documentation, otherwise they shall be reported as infection with unknown pathogen.

New or ongoing

Indicate if the patient had a **Newly developed** viral infection or if it was **Ongoing since previous assessment**.

Start date

Report the date a first positive viral test (usually PCR or antigen) was obtained. In case a diagnostic sample was obtained with a delay since the symptoms of infection started – report here the date when symptoms attributable to this infection started (e.g. patient with encephalitis, with a positive PCR in cerebrospinal fluid done 10 days after symptoms started).

In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

In case the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again.

Pathogen

Select the virus that caused the infection from the list in Appendix 1 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the 'Viruses other' option and enter its name in a textbox. Always report the full name of the virus.

If the pathogen was CMV/EBV: was this infection a reactivation?

Answer yes, if the patient's serology tests (CMV IgG, EBNA, EBV IgG) were positive before the treatment (start of lymphodepleting/conditioning regimen) took place, or if the patient has been reported to have previously had an active CMV/EBV infection.

Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark **Unknown** if it is not possible to identify. Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, infection that requires pathogen-directed therapy, or infection that requires isolation precautions or surveillance.

Infection with clinical implications, yes

Select all clinical implications of the infection during this follow-up period that apply:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions or surveillance.

Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 3 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location during this follow-up period must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

If the clinical information available doesn't specify the localisation of the infection, probably the infection was asymptomatic and will not have to be reported. Otherwise, the symptoms should guide the choice.

Infection resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control, and negative diagnostic tests were obtained in case the investigation was repeated, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one viral infectious complication during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in the table as many times as necessary.

Fungal infection

Indicate if the patient had a fungal infection in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place. Report here only infections with microbiological documentation, otherwise they shall be reported as infection with unknown pathogen.

New or ongoing

Indicate if the patient had a **Newly developed** bacterial infection or if it was **Ongoing since previous assessment**.

Start date

Report the date a first positive culture, PCR test or galactomannan test was obtained, or the pathogen was first identified by its typical appearance in the tissue/specimen material. In case a diagnostic sample was obtained with a delay since the symptoms of infection started – report here the date when symptoms attributable to this infection started, or when this is not known, the date of the first imaging (e.g. CNS, lungs, or liver/spleen imaging for instance in hepatosplenic candidiasis in a patient with persistent fever and negative blood cultures).

In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

In case the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again.

Type of fungi

Select the type of fungal infection by marking if it is 'Yeasts' or 'Moulds'.

Pathogen

Select the fungus that caused the infection from the list in Appendix 2 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the 'Yeasts other' or 'Moulds other' option and enter its name in a textbox. Always report the full name of the fungus. Please note that there is an option for mould infection diagnosed based on positive galactomannan only without additional microbiological confirmation.

Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, infection that requires pathogen-directed therapy, or infection that requires isolation precautions or surveillance.

Infection with clinical implications, yes:

Select all clinical implications of the infection during this follow-up period that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions or surveillance.

Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 3 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location during this follow-up period must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

Intravascular catheter-related infection

Indicate if the infection was related to a central venous catheter (CVC). Please note that fungemia can be CVC-related or not CVC-related. The definition for the CVC-related fungemia requires one of the following:

- The same organism (genus, species and susceptibility pattern) growing from at least 1 percutaneous blood sample culture and from the catheter tip
- 2 blood samples for culture are obtained (1 from a catheter hub and 1 from a peripheral vein) that meet CVC-related fungemia criteria for differential time to positivity (DTP): growth of fungi from blood obtained through the catheter hub being detected at least 2 hours before fungal growth is detected in blood samples obtained from a peripheral vein (9).

Specify

If the infection was related to an intravascular catheter, select the type of CVC infection from the list in Appendix 4 or available in the database.

Infection resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control, and negative diagnostic tests were obtained in case the investigation was repeated, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one fungal infectious complication during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in this table as many times as necessary.

Parasitic infection

Indicate if the patient had a parasitic infection in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place. Report here only infections with microbiological documentation, otherwise they shall be reported as infection with unknown pathogen.

New or ongoing

Indicate if the patient had a Newly developed parasitic infection or if it was **Ongoing since previous assessment**.

Start date

Report the date a first positive antigen or DNA test was obtained or the first positive microscopic examination was performed. In case a diagnostic sample was obtained with a delay since the symptoms of infection started – report here the date when symptoms attributable to this infection started, or when this is not known, the date of the first imaging (e.g. CNS imaging for instance in Toxoplasmosis).

In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

In case the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again.

Type of parasite

Select the type of parasitic infection by marking if it is 'Protozoa' or 'Helminths'.

Pathogen

Select the parasite that caused the infection from the list in Appendix 2 of the form or available in the database. Choose the most specific option. If the pathogen cannot be found, choose the 'Protozoa other spp' or 'Other helminths' option and enter its name in a textbox. Always report the full name of the parasite.

Infection with clinical implications

Indicate if the infection had clinical implications or not, or mark unknown if it is not possible to identify. Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, infection that requires pathogen-directed therapy, or infection that requires isolation precautions or surveillance.

Infection with clinical implications, yes

Select all clinical implications of the infection during this follow-up period that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions or surveillance.

Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 3 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location during this follow-up period must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

Infection resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control, and negative diagnostic tests were obtained in case the investigation was repeated, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one parasitic infectious complication during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in this table as many times as necessary.

Infection with unknown pathogen

Indicate if the patient had an infection with unknown pathogen in the follow-up period after the treatment (after lymphodepleting/conditioning regimen) took place.

Use this section to report clinical infections without microbiological documentation, like pneumonia, cellulitis, typhlitis etc.

New or ongoing

Indicate if the patient had a **Newly developed** infection with unknown pathogen or if it was **Ongoing since previous assessment**.

Start date

Report the date the first signs or complaints were recorded or the first positive radiology was obtained. In case an infection was found for the first time at autopsy, use the date of death, unless you can identify the date when the symptoms attributable to this infection were reported for the first time.

In case the start date was already reported on the previous follow-up form (with the **Ongoing since previous assessment** option selected), the start date does not need to be reported again.

Infection with clinical implications

Infection with clinical implications is at least one of the following: symptomatic infection in the relevant organ/system, infection that requires pathogen-directed therapy, or infection that requires isolation precautions or surveillance. Since an infection with an unknown pathogen always has clinical implications to be reported, the 'Infection with clinical implications, yes' field always has to be filled in.

Infection with clinical implications, yes

Select all clinical implications of the infection during this follow-up period that apply from suggested answer options:

- Symptoms/signs of disease;
- Administration of pathogen-directed therapy;
- Isolation precautions or surveillance.

Localisation (CTCAE term)

Select the CTCAE term for the infection from the list in Appendix 3 of the form or available in the database.

Please note that the impact of an infection can differ greatly depending on its localisation, and therefore, localisation is essential and at least 1 location during this follow-up period must be reported!

The CTCAE version that was used for the current form is version 5.0. Additional information on the CTCAE scoring can be found on the NIH website (6).

If an infectious complication with an unknown pathogen occurred and the localisation cannot be identified or is uncertain, diagnosis may be febrile neutropenia or fever (there is such a CTCAE term) since sepsis or bacteremia cannot be diagnosed without an organism.

If the clinical information available doesn't specify the localisation of the infection, probably the infection was asymptomatic and will not have to be reported. Otherwise, the symptoms should guide the choice.

Intravascular catheter-related infection

Indicate if the infection was related to a central venous catheter (CVC). For example, a purulent infection of the exit site or tunnel, without isolation of pathogen.

Specify

If the infection was related to an intravascular catheter, select the type of CVC infection from the list in Appendix 4 or available in the database.

Infection resolved

Indicate if the infection was resolved during the follow-up period. By resolved it is understood that the patient is free of symptoms/signs of this infection or symptoms/signs of this infection are under control, and the relevant imaging is compatible with expected improvement.

Contributory cause of death

In case the patient is deceased, indicate if the infection contributed to death.

If there was more than one infectious complication with an unknown pathogen during the follow-up period, repeat these questions for the subsequent infection. Copy and fill-in this table as many times as necessary.

Secondary Malignancies and Autoimmune Disorders

Did a secondary malignancy or autoimmune disorder occur?

Answer **No** if neither a secondary malignancy nor an autoimmune disorder has been observed after this HCT. Answer **Yes** if a secondary malignancy or an autoimmune disorder occurred and specify:

Was this disease an indication for a subsequent HCT/CT/IST?

If the answer is **No**, complete the non-indication diagnosis form.

If the answer is **Yes**, complete the relevant indication diagnosis form.

Additional treatment including cell therapy

Did the patient receive any additional disease treatment since the last follow-up?

Please indicate whether the patient received additional disease treatment (Relapse treatment, maintenance/preventive treatment, consolidation and/or other disease treatment) since the last follow-up. If yes, please complete the "Treatment - non-HCT/CT/GT/IST" form.

Additional cell infusions

Did the patient receive additional cell infusions?

If the patient received additional cell infusions (i.e. MSC infusion, Donor Lymphocyte Infusion (DLI), boost etc.), excluding a new HCT and/or CT treatment, select **Yes**. If the patient did not receive additional cell infusions, select **No**.

For this question, it does not matter if it was a boost or DLI. This can be clarified in the next questions.

If answered Yes, the following should be taken into account:

If the cells were infused with the aim of improving chimaerism, or preventing or treating relapses, it most likely was a DLI. The treating physician knows the aim of the infusion. In rare cases, the aim can be as for a boost and a DLI. In this case boost should be selected and the cell infusion sheet for DLI should be completed.

Is this cell infusion an allogeneic boost?

Indicate whether the cell infusion was an allogeneic boost or not.

An allogeneic boost is an infusion of cells from the same donor without conditioning, with no evidence of graft rejection. A boost is infused with the aim of providing enough hematopoietic cells to have an effect on engraftment.

If cells are not from the same donor OR there is conditioning (chemotherapy and/or TBI), then it is considered to be an HCT and not a boost.

Date of the allogeneic boost

If applicable, report the date the boost took place.

Is this cell infusion an autologous boost?

If the cell infusion was an autologous boost answer **Yes**. If it was not an autologous boost, select **No**.

An autologous boost is an infusion of pre-collected and stored autologous stem cells without conditioning.

Date of the autologous boost

If applicable, report the date the boost took place.

Note: If this cell infusion is not a boost, attach the Cell Infusion (CI) sheet available in Appendix 6, completing as many sheets as episodes of cell infusion that took place during this follow-up period; then continue with questions below.

Did the patient receive subsequent HCT/CT?

Report whether or not the patient received a subsequent HCT/CT, either at your or another centre. Please make sure that this subsequent treatment is registered using either the HCT or CT day 0 form and the disease status HCT/CT/GT/IST day 0 form.

Relapse, Progression, Recurrence of disease or Significant Worsening

Was there a relapse, progression, recurrence of disease or significant worsening of organ function related to the primary disease since last follow-up?

Indicate if there was a relapse,progression, recurrence or significant worsening of organ function related to the primary disease since the last follow-up detected by any method. If multiple instances of relapse, progression, recurrence of disease or significant worsening took place in this follow-up period, report all instances. When filling this question in the EBMT registry, click the **add** button as many times as necessary for reporting all instances. ('+ Add' on the EBMT Registry.) If the answer is **No,** proceed to the next section.

Type

Report if a **relapse or recurrence of disease** is reported, or a **(continuous) progression or significant worsening** . Relapse or Recurrence of Disease is defined as active disease after complete remission for malignant diseases, or after absence of symptoms for non-malignant diseases. (Continuous) progression or worsening is defined as active disease without complete remission since diagnosis or since last main treatment for malignant diseases, or continuous active disease without absence of symptom since last main treatment for non-malignant diseases

Date of relapse/progression/recurrence/significant worsening

Report the date of the relapse/progression/recurrence/significant worsening since HCT. If the date is not known, select **unknown**.

Medullary involvement

Indicate if the marrow or blood were affected by the disease. Please be aware that although the vast majority of acute leukaemias involve the invasion of the bone marrow by blasts, there are cases where blast invasion is only found in organs other than the bone marrow (e.g. choromas).

Medullary relapse is when malignant cells are only found in the bone marrow. In case of extramedullary relapse, malignant cells are found in sites other than the bone marrow, such as soft tissues or organs.

Extramedullary involvement

Extramedullary involvement (EMI) refers to disease cells found in organs or tissue outside the blood or bone marrow. The most common sites of extramedullary disease are the central nervous system (CNS), skin and ovaries/testes.

Involvement at time of relapse (If the relapse was extramedullary or both medullary and extramedullary)

Report if **Skin**, **CNS** (central nervous system) or **Testes/Ovaries** were involved at time of relapse. Also indicate if any other site was involved. If yes, please specify this in the textfield in English.

Disease status (Only for malignancies)

Disease detected?

Select **No** if disease was not detected (patient in CR). In order to answer No to this question, all performed tests need to be negative. Select **Yes** if disease was detected by at least one method and proceed to the next questions.

The list of performed tests depends on the patient's diagnosis. It must be the treating physician, who decides if criteria for that particular patient is met and that all relevant tests are performed. If this criteria are not met: not all relevant tests are performed or results of the tests are inconclusive select **Unknown**.

Date last assessed

Report here the date disease was last assessed.

Method, specify

Select all the options that apply if the method used was **Haematological** (including Flow cytometry, Serum Protein Electrophoresis and Immunofixation), **Radiological**, **Molecular, Cytogenetic** or if it was an **Other** method not listed above. In case another method was used, specify it in the textbox in English.

Disease Status (Disease specific)

Disease status at his follow-up or at time of death

Indicate the disease status at this follow-up or at time of death corresponding to indication diagnosis by selecting from the list provided in Appendix 1.

The disease status is split into disease specific sections:

- Acute leukemias
- Chronic leukemias
- Plasma cell neoplasms
- MPN, MDS, MDS/MPN overlap syndromes
- Lymphomas
- Solid tumours
- Bone marrow failure syndromes (BMF) including aplastic anaemia (AA)
- Autoimmune disorders
- Haemoglobinopathies
- Other diagnoses

The instructions for completing appendix 1 can be found in appendix 1 of this document.

Pregnancy after HCT

Has patient become pregnant or impregnated another person since the last follow-up?

If the patient has not become pregnant or has not impregnated another person since the last follow-up, select **No** and proceed to the next section. If the patient has become pregnant or has impregnated another person since the last follow-up select **Yes** and provide details. Select Unknown if it is not known.

Did the pregnancy result in a live birth?

If the patient has become pregnant or has impregnated another person since the last follow-up, answer **Yes**. If the pregnancy resulted in a live birth, indicate the **Year of birth** and **Month of birth** of the child, or mark the date **Unknown** if the date is not available.

Answer **No** if pregnancy did not result in a live birth and indicate the **Date of spontaneous or induced termination** (YYYY/MM/DD) or mark the date as **Unknown**. In case of multiple spontaneous or induced terminations, report the date of the first such event.

Select **Still pregnant at time of follow-up** if the patient/the person they impregnated was still pregnant at the time of the follow-up.

If there is no detailed information about the pregnancy and whether or not it resulted in a live birth, select **Unknown**.

If multiple pregnancies occurred in the follow-up period, the live birth should be prioritised in reporting, in the absence of the live birth, ongoing pregnancy should be prioritised: if one pregnancy resulted in live birth and another not, report the live birth only; if there occurred any terminated pregnancy and the other pregnancy is ongoing as of this follow-up date, select *Still pregnant at time of follow-up* answer option.

Appendix 1 - Disease specific best response and disease status

The disease status and best response are split into disease specific sections which can be found in appendix 1 of the follow-up form. This section is separated into disease status for:

- Acute leukaemias;
- Chronic leukemias;
- Plasma cell neoplasms;
- MPN, MDS, MDS/MPN overlap syndromes;
- Lymphomas;
- Solid tumours;
- Bone marrow failure syndromes (BMF) including aplastic anaemia (AA);
- Autoimmune disorders;
- Haemoglobinopathies;
- Other diagnoses.

Acute leukaemias

This section is applicable to acute myeloid leukaemias (AML), precursor lymphoid neoplasms (PLN) and other acute leukaemias.

Acute leukaemias disease status or best response

Select the disease status or best response from the following list, consult with criteria described in table5:

- Complete remission (CR)
- Not in complete remission

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively. If reporting the disease status, also indicate the minimal residual disease (MRD) status.

Disease status or best response	
Complete remission (CR) is defined as meeting all of the following response criteria for at least four weeks: ● <5% leukemic blasts in the bone marrow ● No blasts with Auer rods (applies to AML only) ● No extramedullary disease (e.g., CNS, soft tissue disease)	**Not in complete remission:** In accordance with the defined criteria for complete remission (CR), a patient would not attain complete remission if they do not fulfil at least one of the complete remission criteria.

Table 5. Acute leukaemias disease status or best response.

Minimal residual disease (MRD)

Only for the disease status section, report the MRD status of acute leukaemia according to the guidelines provided below.

Chronic leukaemias

The chronic leukaemias section is split into chronic myeloid leukaemia (CML) and chronic lymphocytic leukaemia (CLL), prolymphocytic leukaemia (PLL) and other chronic leukaemias.

Chronic myeloid leukaemia disease status or best response

Select the disease status or best response from the list:

- Chronic phase (CP) and type of remission (haematological, cytogenetic, molecular)
- Accelerated phase
- Blast crisis

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status or best response		
Chronic phase (CP)	**Accelerated phase (AP)**	**Blast crisis (BC)**
• None of the features of accelerated phase or blast crisis	• Bone marrow or peripheral blood blasts 10%-19% • Peripheral blood basophils ≥ 20% • Presence of additional clonal cytogenetic abnormality in Ph+ cells (ACA)[a]	• Bone marrow or peripheral blood blasts ≥ 20% • Extramedullary blast proliferation (myeloid sarcoma) • Presence of morphologically apparent lymphoblasts (>5%) warrants consideration of lymphoblastic crisis

Table 6. International Consensus Classification (ICC) criteria for Chronic Myeloid Leukaemias.

[a]Second Ph, trisomy 8, isochromosome 17q, trisomy 19, complex karyotype, or abnormalities of 3q26.2.

Number

If the disease status or best response was chronic phase (CP), accelerated phase or blast crisis, select the number of this status.

If the disease status or best response was chronic phase (CP) also indicate:

Haematological remission

If the patient was in Chronic phase (CP), report if haematological remission was achieved (answer Yes), or not achieved (answer No) according to the criteria provided in table 7. Answer Not evaluated if it was not evaluated or Unknown if it cannot be verified if it was evaluated or not.

Cytogenetic remission

If the patient was in Chronic phase (CP), report if cytogenetic remission was achieved (answer Yes), or not achieved (answer No) according to the criteria provided in table 7. Answer Not evaluated if it was not evaluated or Unknown if it cannot be verified if it was evaluated or not.

Note: A patient in cytogenetic remission must be in haematological remission but could still present a molecular relapse. This is because the cytogenetic technique has a higher resolution than haematological measurements but lower resolution than molecular methods.

Molecular remission

If the patient was in Chronic phase (CP), report if molecular remission was achieved (answer Yes), or not achieved (answer No) according to the criteria provided in table 7. Answer Not evaluated if it was not evaluated or Unknown if it cannot be verified if it was evaluated or not.

Note: A patient in molecular remission must also be in cytogenetic and haematological remission. This is because molecular techniques have a higher resolution than both haematological and cytogenetic measurements.

Disease status or best response (only CP)		
Haematological remission	**Cytogenetic remission**	**Molecular remission**
Haematological remission is defined by a patient meeting all of the following: ● WBC < 10 x 10^9 /L ● Haemoglobin > 11.0 g/dL ● Platelet Count < 450 x 10^9 /L ● Normal Differential (<1% precursor cells) ● No palpable splenomegaly ● No extramedullary disease	Cytogenetic remission is defined by: ● 0% t(9;22) positive metaphases together with haematological remission ● A minimum of 20 analysable metaphases must be assessed for appropriate evaluation of a cytogenetic remission. Remission should be confirmed with repeated cytogenetic analysis within 4 to 12 weeks	Molecular remission is defined by: ● Cells with the BCR::ABL1 fusion protein are not detectable, in the peripheral blood and /or the bone marrow, by an assay with a sensitivity to allow detection of one t(9;22) positive cell in 10^5 to 10^6 RT-PCR cells. The result should be confirmed by two consecutive tests done at least 4 weeks apart.

Table 7. Definitions of haematological, cytogenetic and molecular remission for patients in chronic phase.

Minimal residual disease (MRD)

Only for disease status section report the MRD status of chronic myeloid leukaemia according to the guidelines provided below.

Chronic lymphocytic leukaemia (CLL), prolymphocytic leukaemia (PLL) and other chronic leukaemias disease status or best response

Select the disease status or best response from the list according to the criteria provided in tables 8-11:

- Complete Remission (CR)
- Partial Remission (PR)
- Progression
- Stable Disease (SD)

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Group	Parameter	Complete Remission (CR)	Partial Remission (PR)	Stable Disease (SD)	Progressive Disease (PD)
A	Lymph nodes	None ≥1.5 cm	Decrease ≥50% (from baseline)*	Change of −49% to +49%	Increase ≥50% from baseline or from response
	Liver and/or spleen size†	Spleen size <13 cm; liver size normal	Decrease ≥50% (from baseline)	Change of −49% to +49%	Increase ≥50% from baseline or from response
	Constitutional symptoms	None	Any	Any	Any
	Circulating lymphocyte count	Normal	Decrease ≥50% from baseline	Change of −49% to +49%	Increase ≥50% over baseline
B	Platelet count	≥100 × 10^9/L	≥100 × 10^9/L or increase ≥50% over baseline	Change of −49 to +49%	Decrease of ≥50% from baseline secondary to CLL
	Haemoglobin	≥11.0 g/dL (untransfused and without erythropoietin)	≥11 g/dL or increase ≥50% over baseline	Increase <11.0 g/dL or <50% over baseline, or decrease <2 g/dL	Decrease of ≥2 g/dL from baseline secondary to CLL
	Marrow	Normocellular, no CLL cells, no B-lymphoid nodules	Presence of CLL cells, or of B-lymphoid nodules, or not done	No change in marrow infiltrate	Increase of CLL cells by ≥50% on successive biopsies

Table 8. Response evaluation according to 2018 iwCLL criteria.

*Sum of the products of 6 or fewer lymph nodes (as evaluated by CT scans and physical examination in clinical trials or by physical examination in general practice).

†Spleen size is considered normal if <13 cm. There is not a firmly established international consensus of the size of a normal liver; therefore, liver size should be evaluated by imaging and manual palpation. For

the EBMT Registry, clinical (palpation) evaluation only without CT-scan (or alternate imaging), according to routine practice, is accepted.

Disease status or best response CLL	
Complete Remission (CR)	See table 8 for detailed criteria. All of the criteria have to be met. But: ● If a patient has all CR criteria but has persistent cytopenia, the patient can be considered as a CR as an adaptation of these guidelines. ● If a patient has all criteria of a CR but bone marrow evaluation has not been performed (even with persistent cytopenia), the patient can be considered as a CR as an adaptation of these guidelines.
Partial Remission (PR)	See table 8 for detailed criteria. At least 2 of the parameters of group A and 1 parameter of group B need to improve if previously abnormal; if only 1 parameter of both groups A and B is abnormal before therapy, only 1 needs to improve. Clinical (palpation) evaluation only without CT-scan (or alternate imaging), according to routine practice, is accepted.
Stable Disease (SD)	See table 8 for detailed criteria. All of the criteria have to be met. Constitutional symptoms alone do not define PD.
Progression	At least 1 of the criteria of group A or group B has to be met. Sequential imaging is not warranted in CLL outside clinical trials and is not required for the EBMT Registry.

Table 9. Additional clarifications for Chronic lymphocytic leukaemias disease status classification.

Group	Parameter	CR (all met)	PR (≥2 in A and ≥1 in B)	SD (all met)	PD (≥1 in A or B met)
A	Lymph nodes	long-axis diameters to <1.0 cm	Decrease ≥30% in SLD	Change of − <30% to + ≤20%	Increase >20% in SLD
	Spleen†	Spleen size <13 cm	Decrease ≥50% in vertical length beyond normal from baseline	Change of −49% to +49% beyond normal from baseline	Increase ≥50% in vertical length beyond normal from baseline
	Constitutional symptoms	None	Any	Any	Any
	Circulating lymphocyte count	$<4 \times 10^9$/L	$\leq 30 \times 10^9$/L and decrease ≥50% from baseline	$>30 \times 10^9$/L or change of −49% to +49%	Increase ≥50% from baseline
	Marrow	T-PLL cells <5% of mononuclear cells	Any	Any	Any
	Any other specific site involvement*	None	Any	Any	Any
B	Platelet count	$\geq 100 \times 10^9$/L	$\geq 100 \times 10^9$/L or increase ≥50% from baseline	Change of −49% to +49%	Decrease of ≥50% from baseline
	Haemoglobin	≥11.0 g/dL (untransfused)	≥11 g/dL or increase ≥50% from baseline	<11.0 g/dL or <50% from baseline, or change <2 g/dL	Decrease of ≥2 g/dL from baseline
	Neutrophils	$\geq 1.5 \times 10^9$/L	$\geq 1.5 \times 10^9$/L or increase ≥50% from baseline	Change of −49% to +49%	Decrease of ≥50% from baseline

Table 10. T-PLL response evaluation according to the T-PLL consensus criteria.

SLD: sum of long-axis diameters of up to 3 target lesions

*Pleural or peritoneal effusion, skin infiltration, central nervous system involvement.

† For the EBMT Registry, clinical (palpation) evaluation only without CT-scan or alternate imaging, according to routine practice, is accepted.

Disease status: additional clarifications T-PLL	
Complete Remission (CR)	See table 10 for detailed criteria. All of the criteria have to be met, however a few exceptions are possible: ● If a patient has all CR criteria but has persistent cytopenia, the patient can be considered as being in CR as an adaptation of these guidelines. ● If a patient has all criteria of CR but bone marrow evaluation has not been performed (even with persistent cytopenia), the patient can be considered as being in CR as an adaptation of these guidelines.
Partial Remission (PR)	See table 10 for detailed criteria. At least 2 of the parameters of group A and 1 parameter of group B need to improve if previously abnormal; if only 1 parameter of both groups A and B is abnormal before therapy, only 1 needs to improve. Clinical (palpation) evaluation only without CT-scan (or alternate imaging), according to routine practice, is accepted.
Stable Disease (no change, no response/loss of response)	See table 10 for detailed criteria. All of the criteria have to be met.
Relapse (untreated)	Evidence of PD in a patient who has previously achieved the criteria of a CR or PR for 6 months or more after the last dose of CLL therapy.
Progressive Disease (PD)	At least 1 of the criteria of group A or group B has to be met. Sequential imaging is not warranted in CLL outside clinical trials and is not required for the EBMT Registry. Constitutional symptoms alone do not define PD.

Table 11. Additional clarifications for T-PLL disease status classification.

Progression sensitivity

If the disease status or best response was progression, indicate if the progression was **resistant** to the last chemotherapy regimen the patient received, or if it was **sensitive**. If this is not known, select **unknown**.

Minimal residual disease (MRD)

Only for disease status section report the MRD status of chronic lymphocytic leukaemia according to the guidelines provided below.

Plasma cell neoplasms

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in table 12:

- Complete remission (CR)
- Stringent complete remission (sCR)
- Very good partial remission (VGPR)
- Partial remission (PR)
- Stable disease (no change, no response/loss of response)
- Progression
- Relapse

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status	
Complete remission (CR)	Absence of detectable monoclonal immunoglobulin in serum and monoclonal light chains in the urine by immunofixation. The detection of monoclonal immunoglobulin, even at low levels which are too weak to quantitate, is not a CR. • <5% of plasma cells in bone marrow aspirate • Disappearance of any soft tissue plasmacytomas. • No increase in size or number of lytic lesions if assessed (radiographic studies are not mandatory) If any of the above investigations have not been done, even if the others are indicative of a CR, the status should be registered as VGPR. Where CR has already been attained (bone marrow evaluation included) it may not be necessary to do a bone marrow evaluation again to confirm that the patient is still in CR (all other criteria confirming CR). Therefore, the patient is still in CR.

Stringent complete remission (sCR)	All of the following: • CR as defined above • normal free light (FLC) chain ratio • Absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence
Very good partial remission (VGPR)	One or more of the following: • Serum and urine M-protein detectable by immunofixation but not on electrophoresis • >=90% reduction in serum M-protein plus urine M-protein level <0.1g/ per 24h In addition, there must be no increase in size or number of lytic lesions if assessed (radiographic studies are not mandatory) If any of the above investigations have not been done, even if the others are indicative of a VGPR, the status should be registered as PR.
Partial remission (PR)	All of the following: • >50% reduction in serum M-protein plus reduction in 24h urinary M-protein by >=90% or to <0.2g/ per 24h. • A reduction of more than 50% in the size of soft tissue plasmacytomas if present at pre-treatment • No increase in size or number of lytic lesions if assessed (radiographic studies are not mandatory) In the absence of measurable serum and urine M-protein, the following criteria applies: • A decrease in the difference between involved and uninvolved free light chain (FLC) of more than 50% If the FLC assay cannot be measured, the following criteria apply: • >=50% reduction in plasma cells provided baseline bone marrow plasma cell percentage was >=30% • A reduction of more than 50% in the size of soft tissue plasmacytomas if present at pre-treatment
Stable disease(no change, no response/loss of response)	Does not meet the criteria for CR, VGPR, PR or progressive disease (includes the old Minimal response (MR) criteria)

Progression	One or more of the following: • Increase of 25% or more in measurable monoclonal immunoglobulin in serum and urine (absolute increase must be >=0.5g/dL). This is not applicable to light chain myelomas • Increase of 25% or more in urinary light chains (absolute increase must be >=0.2g/ per 24h) • An increase of 25% or more in bone marrow plasma cells (absolute % must be >=10%) • Increase of old/appearance of new osteolytic bone lesions on x-ray • Appearance of soft tissue plasmacytoma • Development of hypercalcemia (corrected serum calcium >11.5 mg/dL or 2.65 mmol/L) that can be attributed solely to the plasma cell disorder In the absence of measurable serum and urine M-protein, the following criterium applies: • An increase of 25% or more in the difference between involved and uninvolved free light chain (absolute increase must be >0.01g/dL from nadir)
Relapse	Clinical relapse requires one or more of the following criteria: • Direct indicators of increasing disease and/or end organ dysfunction (CRAB features) related to the underlying clonal plasma-cell proliferative disorder. • Development of new soft tissue plasmacytomas or bone lesions • Increase of 50% (and at least 1 cm) in the size of existing plasmacytomas or bone lesions. • Hypercalcemia (> 11.5 mg/dL) • Decrease in haemoglobin of > 2 g/dL • Rise in serum creatinine by 2 mg/dL or more

Table 12. Plasma cell neoplasms disease status or best response.

Number

Select the number of the status.

Was the patient on dialysis during this follow-up period?

Report whether the patient was on dialysis during this follow-up period. Select **Unknown** if this information is unavailable.

Started in this follow-up period

Select this option if dialysis started during this follow-up period.

Start date

If the answer to the previous question was **Yes**, report the start date of dialysis. If the start date is not known, select **Unknown.**

Ongoing since previous follow-up

Select this option if dialysis started during a previous follow-up period and was still ongoing during this follow-up.

Did dialysis stop?

Report whether dialysis was stopped during this follow-up. Select **Unknown** if this information is unavailable.

End date

Report the dialysis end date. If the dialysis stopped but the end date is not known, select **Unknown**.

Minimal residual disease

Complete this section only if the patient disease status is reported for patients with an AL, CLL leukaemia or a plasma cell neoplasm diagnosis.

If the patient is in haematologic CR, but has evidence of disease by more sensitive assessments including molecular, flow cytometry or cytogenetic methods, mark it as **Positive**. If the MRD assay cannot detect malignant cells mark it as **Negative**. Mark it as **Not evaluated** if MRD status evaluation was not carried out during the follow-up period.

Positive minimal residual disease

If there was positive minimal residual disease, indicate if this was **increasing**, **stable** or **decreasing**. If the level is not known, select **unknown**. A change in MRD should be confirmed within 4 weeks, in a second consecutive sample, preferably with a BM sample. The definitions are as follows:

- **Increasing** (>1 $\log_{10}$ increase between any 2 positive samples measured in the same tissue (PB or BM));
- **Stable** (<1$\log_{10}$ between any 2 positive samples measured in the same tissue (PB or BM));
- **Decreasing** (>1 $\log_{10}$ decrease between any 2 positive samples measured in the same tissue (PB or BM)).

Date MRD status evaluated

Report the date the MRD status was evaluated. If the date is not known, select **unknown**.

Sensitivity of MRD assay

Select the appropriate sensitivity of the MRD assay from the list.

Method used

Select the most sensitive method that was used to assess the MRD status.

Myeloproliferative neoplasms (MPN), Myelodysplastic neoplasms (MDS), MDS/MPN overlap syndromes

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in the corresponding tables 13-15:

- Complete remission (CR);
- Improvement but no CR;
- Primary refractory phase (no change);
- Relapse;
- Progression/worsening.

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

MPN Disease status or best response	
Complete remission (CR)	The 4 following criteria must be true: 1. Resolution of disease-related symptoms and signs including palpable hepatosplenomegaly 2. Haemoglobin (Hb) ≥ 10g/dL, platelet ≥ 100 $\times 10^9$/L and neutrophils ≥ 1 $\times 10^9$/L 3. <2% immature myeloid cells (<5% in splenectomized patients) 4. Normal bone marrow histology and fibrosis grade no higher than 1
Improvement but no CR	Requires one criterion in absence of progression: 1. Hb increase of 2g/dL or transfusion independence 2. Spleen reduction of 50% 3. 100% increase in platelet count and absolute platelet count of at least 50 $\times 10^9$/L 4. 100% increase in absolute neutrophil count (ANC) and an ANC of at least 0.5 $\times 10^9$/L
Primary refractory phase (no change)	Treatment with intent to achieve remission was given, but no remission was achieved.
Relapse	Loss of complete remission.
Progression/Worsening	Requires one of the following: 1. Progressive splenomegaly 2. Leukaemic transformation (increase of peripheral blood blast percentage of at least 20%)

Table 13. MPN disease status or best response.

MDS Disease status or best response	
Complete remission (CR)	For patients with MDS with increased blasts: Complete remission was achieved if marrow blast count was below 5% and normalisation of peripheral blood counts was observed for at least 4 weeks. For patients with other types of MDS: normalisation of PB counts.
Improvement but no CR	**1) Haematological response (in patients with cytopenia)** ● If haemoglobin < 11g/dl, erythroid response (>11 g/dl); ● If platelets <100g/l, platelet response (>100 g/l); ● If neutrophils < 1g/l, neutrophil response (>1g/l); ● If >0% peripheral blasts, response when 0% peripheral blood blasts; ● If transfusion dependant (red blood cells), independence of transfusion achieved (8 weeks without transfusions); ● If transfusion dependant (platelets), independence of transfusion achieved (8 weeks without transfusions) **2) Marrow blast response (in patients with increased marrow blasts):** A decrease of 50% in marrow blasts, but still >5% marrow blasts.
Primary refractory phase (no change)	Treatment with the intent to achieve remission was given, but no remission was achieved.
Relapse	Loss of complete remission.
Progression/ Worsening	More blasts in BM than before treatment.

Table 14. MDS disease status or best response.

MDS/MPN Disease status or best response	
Complete remission (CR)	Marrow blast count < 5% and a normalisation of peripheral blood counts was observed for at least 4 weeks.
Improvement but no CR	Bone marrow blasts decreased by ≥ 50% after pre-treatment but still > 5%. All CR criteria were abnormal before treatment.
Primary refractory phase (no change)	Treatment with intent to achieve remission was given, but no remission was achieved.
Relapse	Loss of complete remission.
Progression/Worsening	Higher blast count in the BM and/or PB than before treatment. Worsening of cytopenias (anaemia and/or thrombocytopenia). Progression from the MD- to the MP-variant of CMML.

Table 15. MDS/MPN disease status or best response.

Number

If the disease status or best response was complete remission (CR) or relapse, select the number of this status.

Lymphomas

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in table 16:

- Chemorefractory relapse or pression, including primary refractory disease
- Complete remission (CR)
- Partial remission
- Stable disease (no change, no response/loss of response)
- Untreated relapse (from a previous CR) or progression (from a previous PR)

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status or best response		
Complete remission (CR)	Complete absence of disease, no signs or symptoms of the original disease. Only applicable if the Complete Remission was evaluated by CT-scan or MRI methods.	Confirmed (
		Unconfirmed (Only applicable if the Complete Remission was evaluated by CT-scan or MRI methods.)
Partial response (PR) with or without prior CR	Reduction in the disease of 50% or more	
Stable disease (no change, no response/loss of response)	Less than 50% reduction in the disease burden.	
Untreated relapse from previous CR/untreated progression from previous PR	Worsening of the disease status in patients in PR or re-appearance of the lymphoma in patients in CR, such as: recurrence of disease or systemic symptoms (B-symptoms), patient remains untreated after the relapse or progression.	
Chemorefractory relapse or progression, including primary refractory disease	Does not present any of the features of any type of remission after treatment.	

Table 16. Lymphomas disease status or best response.

Complete remission: confirmed

Indicate if the complete remission was **confirmed** or **unconfirmed**. Unconfirmed means a complete response with persistent scan abnormalities of unknown significance. If it is not known if the complete remission was confirmed, select **unknown**.

Solid tumours

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in table 17:

- Complete remission (CR)
- First partial remission
- Partial remission (PR)
- Progressive disease
- Relapse
- Stable disease (no change, no response/loss of response)

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status or best response		
Complete remission (CR)	Disappearance of all target lesions and all non-target lesions and normalisation of tumour marker level.	**Unconfirmed** complete response with persistent scan abnormalities of unknown significance
		Confirmed CR with No abnormalities detected in scan
		Unknown if it is not known if the complete remission was confirmed, select unknown
First partial remission	The patient achieved a reduction in disease of > 30% or more for the first time ever, but did not achieve complete remission[a]	
Partial remission (PR)	The patient achieved partial remission not for the first time.	
Progressive disease (PD)	At least 20% increase in the sum of diameters of target lesions, in addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progression).	
Relapse	Reappearance of disease in patients whose last disease status was complete remission.	**Sensitive:** patient achieves a reduction of >30% in the disease burden after treatment for this relapse.

Disease status or best response		
		Resistant: patient has not achieved a reduction of more than 30% in the disease burden after treatment for this relapse.
		Unknown: if it is not known if the relapse was resistant or sensitive, select unknown.
Stable disease (no change, no response/loss of response)	Target Lesions: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum length diameters since the treatment started. Non-Target Lesions: Persistence of one or more non-target lesion(s) or/and maintenance of tumour marker level above the normal limits	

Table 17. Solid tumours disease status or best response.

a. As per RECIST 1.1 guidelines https://pubmed.ncbi.nlm.nih.gov/19097774/

Bone marrow failures (incl. AA)

Disease status or best response

Select the disease status or best response from the list according to the criteria provided in table 18:

- Complete remission (CR)
- Partial remission (PR)
- Haematological improvement (HI); NIH partial response
- Stable disease (no change, no response/loss of response)
- Relapse/Progression

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Disease status or best response	Severe aplastic anaemia	Moderate aplastic anaemia	Genetic BMF

Complete Remission (CR)	All of the following: ● No evidence of clonal evolution, by marrow cytogenetic and flow cytometry ● Peripheral blood counts: haemoglobin >10 gr/dL, absolute neutrophils >1.0 x 10^9/L, platelets >100 x 10^9/L	All of the following: ● No evidence of clonal evolution, by marrow cytogenetic and flow cytometry ● Peripheral blood counts: haemoglobin normal for age, absolute neutrophils >1.5 x 10^9/L, platelets >150 x 10^9/L	All of the following: ● Haemoglobin higher than the inferior limit according to age, transfusion independence. For age-related reference values ● Absolute neutrophils ≥1.5 × 10^9/L up to age 18 years, ≥1.8 × 10^9/L, in adults from 18 years ● Platelets >150 x 10^9/L, transfusion independence
Partial Remission (PR)	All of the following: ● No evidence of clonal evolution, by marrow cytogenetic and flow cytometry ● No longer meeting criteria for diagnosis of SAA ● Transfusion independence (defined as no need of any PRBC or platelet transfusion) ● Peripheral blood counts: haemoglobin >8 gr/dL, absolute neutrophils >0.5 x 10^9/L, platelets >20 x 10^9/	At least one of the following: ● No evidence of clonal evolution, by marrow cytogenetic and flow cytometry ● Transfusion independence (if previously required) doubling or normalisation of at least one cell line ● Peripheral blood counts: haemoglobin >10 gr/dL, absolute neutrophils >1.0 x 10^9/L, platelets >100 x 10^9/L	All of the following: ● Haemoglobin ≥8 < 10 gr/dL, transfusion independence ● Absolute neutrophils ≥0.5 <1.0 × 10^9/L ● Platelets ≥20 <50 × 10^9/L, transfusion independence

Haematological improvement (HI); NIH partial response	No longer meeting criteria for diagnosis of SAA, in absence of CR or PR	No longer meeting criteria for diagnosis of MAA or genetic BMF, in absence of CR or PR	One or two of the following: ● Haemoglobin ≥8 < 10 gr/dL, transfusion independence; or ● Absolute neutrophils ≥0.5 < 1.0 × 10^9/L; or ● Platelets ≥20 <50 × 10^9/L, transfusion independence
Stable disease (no change, no response/loss of response)	Patients who have not achieved a CR, PR, HI, relapse or progression will be considered to have a stable disease.		

Relapse / Progression	Any of the following events after a haematological response (CR or PR): • Meeting again the criteria for SAA • Requirement of transfusion support (if not due to independent medical conditions) • Decrease in any of the peripheral blood counts as follows: Decrease to less than 50% of the medium sustained count during remission if: absolute neutrophils <1.0 x 10^9/L, platelets <50 x 10^9/L; or Or in any case if: absolute neutrophils <0.5 x 10^9/L , platelets <20 x 10^9/L The peripheral blood count decrease must be: • Not due to any independent concomitant medical condition • Demonstrated in at least 3 tests over a period of 2 weeks • Not responding to re-introduction of low dose cyclosporin A	After a haematological response (CR or PR), once again meeting the criteria for MAA	All of the following: • Haemoglobin <8 gr/dL or transfusion dependence • Absolute neutrophils <0.5 × 10^9/L • Platelets <20 × 10^9/L or transfusion dependence

Table 18. BMF (incl. AA) disease status or best response.

Did transfusions stop during the follow-up period?

If the disease status is reported for bone marrow failures, indicate if transfusions stopped since the last follow-up. If the patient was never transfusion dependent, select **patient was never transfusion dependent**.

If the transfusions are ongoing, select **no**. If the transfusions did stop, select **Yes** and complete the next questions. If the patient is transfusion independent and was transfusion dependent at a previous follow-up, select **ongoing transfusion independence since last follow-up**. If the transfusion status is not known, select **unknown**.

Did the patient return to transfusion dependency afterwards?

If the patient became transfusion independent since the last follow-up, but is back to needing transfusions within this follow-up period, select **yes**. If they continue to be independent of transfusions after stopping in this follow-up period, select **no**. If it is not known if the patient went back to needing transfusions, select **unknown**.

First transfusion date

If the patient stopped transfusions during the follow-up period but went back to being transfusion dependent, report the first transfusion date after the transfusion free period. If the date is not known, select **unknown**.

Autoimmune disorders

Disease status or best response

Select the disease status or best response from the list:

- **No evidence of disease**- the patient has achieved complete absence of disease, there are no signs or symptoms of the original disease described.
- **Improved**
- **Unchanged** - Patients who have not demonstrated complete absence of disease, improvement in symptoms, or deterioration of symptoms will be classified as **Unchanged**.
- **Worse**

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Haemoglobinopathies

The haemoglobinopathies section is split into thalassemia and sickle cell disease.

Thalassemia best response

Select the best response that was achieved since the main treatment:

- Transfusion independent
- Transfusions required

For clarification, transfusion independence is typically defined as going 8-12 weeks without needing transfusions, without a specific haemoglobin threshold.

If the best response is not known or was not evaluated, select **Unknown** or **Not evaluated**, respectively.

Date of last transfusion

If a patient reached transfusion independence, report the date of the last transfusion after main treatment the patient received. If the date is not known, select **Unknown**.

Date of first transfusion

If a patient still requires transfusions, report the date of the first transfusion the patient received after main treatment due to haemoglobin deficiency (recurrence of disease). If the date is not known, select **Unknown**.

Thalassemia disease status

Patient requires transfusions during follow-up period

Indicate if the patient requires transfusions during follow-up period after haematopoietic recovery by selecting **No** or **Yes**.

Patient requires transfusions, Yes

If a patient is transfusion dependent indicate whether at this follow-up period the **Return to transfusion dependence after HCT or transfusion free period** occurred or patient **Ongoing transfusion dependence since previous assessment.**

Date of first transfusion

If a patient has returned to transfusion dependence after main treatment or transfusion free period during this follow-up period, report the date of the first transfusion after main treatment or transfusion free period. If the date is not known, select **Unknown**. If a patient has ongoing transfusion dependence

since the previous assessment and the date was reported at the previous follow-up form, do not report the date here, the question will be disabled.

Number of units

Report the number of transfusion units patient received during this follow-up period. If the exact number is not known, select **Unknown**.

Did transfusions stop?

Indicate if the patient stopped receiving the transfusions. If the patient stopped transfusions and did not require more during this follow-up period, select **Yes.**

Date of last transfusion

If the patient stopped transfusions during the reporting period, provide the date when the last transfusion was administered. If it is not known, select **Unknown**.

Sickle cell disease best response

Select the best response that was achieved since the main treatment:

- No return of sickling episodes. Patients are considered to have no return of sickling episodes when they have shown an absence of sickle cell crises.
- Return of sickling episodes. When sickle cell crises reoccur.

If the best response is not known or was not evaluated, select **Unknown** or **Not evaluated**, respectively.

Date of first episode

If a patient has returned to sickling episodes, report the date of the first episode after main treatment. If the date is not known, select **unknown**.

Sickling episodes occur during follow-up period

This should only be completed when reporting the disease status. Indicate if there were no more recurrent sickle cell episodes after HCT by selecting **No**. If recurrent sickling episodes were present after HCT, select **Yes**. If it is not known if the sickling episodes returned, select **Unknown**.

Sickling episodes occur during follow-up period, Yes

Indicate whether the sickling episodes first return after gene therapy or there was an ongoing presence of sickling episodes since last follow-up assessment.

Date of first episode

If the sickling episodes reoccurred for the first time since the main treatment, report the date of the first sickling episode. If the date is not known, select **Unknown**.

Number of SCD episodes (during follow-up)

If the sickling episodes first returned after main treatment, report the number of sickling episodes which occurred during this follow-up period. If the number is not known, select **Unknown**.

Other diagnosis

Disease status or best response

Select the disease status or best response from the list:

- **No evidence of disease -** the patient has achieved complete absence of disease, there are no signs or symptoms of the original disease described.
- **Improved**
- **Unchanged -** Patients who have not demonstrated complete absence of disease, improvement in symptoms, or deterioration of symptoms will be classified as **Unchanged**.
- **Worse**

If the disease status or best response is not known or was not evaluated, select **unknown** or **not evaluated**, respectively.

Cell Infusion Sheet

The following completion guidelines refer to the completion of appendix 4 of the annual/unscheduled follow-up form, the cell infusion sheet.

Please report each cell infusion episode performed during the follow-up period in a separate cell infusion sheet, completing as many sheets as episodes of cell infusion that took place. Cell infusion treatment is often given as sequential cell infusions through a series of days or even weeks. In order to make the data comparable, one episode of cell infusion treatment (one “CI)” is defined as any number of cell infusions that take place for the same indication within 10 weeks from first to last infusion. If the indication for the treatment changes within the 10 weeks, that would be considered as 2 separate episodes of cell infusion (2 “CI”), with the 2nd episode starting on the 1st day infusions were given after the change in indication.

Do not use this cell infusion sheet for any boost. All boosts shall be registered inside the HCT follow-up form.

Chronological number of CI episode for this patient

Report the chronological number of this cell infusion episode for this patient.

Date of the first infusion

Report the date of the first infusion within this episode.

Number of infusions within 10 weeks

Report the number of infusions within 10 weeks. Count only infusions that are part of the same regimen and given for the same indication.

Source of cells

Indicate if the source of cells are **allogeneic** and/or **autologous**, check all that apply.

Type of cells

Select the type of cells, check all that apply:

- **Lymphocytes (DLI);**
- **Mesenchymal;**
- **Fibroblasts;**
- **Dendritic cells;**
- **NK cells;**
- **Regulatory T-cells;**
- **Gamma/delta cells;**
- **Virus-specific T-cells.**

If the type of cells is **virus specific T-cells,** also specify the virus the T-cells were directed against.

If the type of cells is not listed, select **Other** and specify the type of cells in the text field in English.

Disease status at time of this cell infusion

Indicate the disease status at time of this cell infusion corresponding to indication diagnosis by selecting from the list provided in Appendix 1.

The disease status is split into disease specific sections:

- Acute leukemias;
- Chronic leukemias;
- Plasma cell neoplasms;

- MPN, MDS, MDS/MPN overlap syndromes;
- Lymphomas;
- Solid tumours;
- Bone marrow failure syndromes (BMF) including aplastic anaemia (AA);
- Autoimmune disorders;
- Haemoglobinopathies;
- Other diagnoses.

The instructions for completing appendix 1 can be found in appendix 1 of this document.

If the disease status has not been evaluated, select **Not evaluated**. Select **Unknown** if the disease status at the time of this cell infusion is not known.

Indication

Select all the indications for this cell infusion episode that apply:

- **Planned/protocol;**
- **Prophylactic;**
- **Treatment of acute GvHD;**
- **Treatment of chronic GvHD;**
- **Treatment PTLD, EBV lymphoma;**
- **Treatment for primary disease;**
- **Mixed chimaerism;**
- **Loss/decreased chimaerism;**
- **Treatment of viral infection other than EBV;**
- **Poor graft function;**
- **Infection prophylaxis.**

If the indication is not listed, select **Other** and specify it in the text field in English.

Acute GvHD - maximum grade *(after this infusion episode but before any subsequent cell infusion/HCT/CT)*

Indicate the maximum grade (Grade scale 0 - 4) of acute GvHD. If the grade is unknown but aGvHD is present, select **Present but grade unknown**.

Date Acute GvHD onset after cell infusion

Report the aGvHD onset date after the cell infusion. If the date is not known, select **unknown**.

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