

ALLOGENEIC HAEMATOPOIETIC CELL TRANSPLANTATION (HCT) Day 0

**A Guide to the completion of the EBMT Diagnosis form:
DRAFT_AlloHCT_Day0_v0.14**

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EBMT Registry
Helpdesk Unit

EBMT Science Department



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Introduction

The EBMT has adopted the following definition for haematopoietic stem cell transplant (HCT):

TRANSFER OF STEM CELLS, DEFINED AS PROGENITOR CELLS WITH REPOPULATING CAPACITY AND THE POTENTIAL TO SUSTAIN LONG-TERM HEMATOPOIESIS, WITHIN ONE PERSON OR FROM ONE PERSON TO ANOTHER, IN A DOSE THAT IS SUFFICIENT TO RESTITUTE HEMATOPOIESIS IN ALL LINEAGES.

For an HCT to be defined as such, the aim must be to repopulate the bone marrow with the infused stem cells. There is no requirement for myeloablative therapy to be given for an HCT to be defined as such.

Allogeneic HCT (Allo-HCT) uses hematopoietic stem cells collected from another related or unrelated individual. Allo-HCT is increasingly used to treat a variety of hematologic neoplasms and nonmalignant marrow disorders (acquired and inherited), including inborn errors of metabolism.

Day 0 is considered the day of the first haematopoietic stem cell infusion if there are multiple infusions of one or several graft products over several days after the same conditioning regimen. The transplant procedure is considered to start when the conditioning regimen is initiated.

This form must be completed for all patients who received Allo-HCT. No data items should be left blank unless specifically stated in the instruction.

Allo-HCT

1. Date of this HCT:

Report the date the transplantation took place. If the patient died before the treatment took place, report the planned treatment date.

2. Centre where treatment took place:

Enter the 3-4 digits CIC of the centre responsible for this allogeneic HCT (usually, this is the centre that gives the conditioning, infuses the cells, and does the early follow-up).

NOTE: while submitting data online in the EBMT Registry application, this field will be populated automatically based on the selected CIC because it is the responsibility of the centre where the treatment took place to report data.

3. Survival status at HCT:

Indicate the survival status of the recipient at the (planned) date of the treatment. Select **Alive** if the recipient was still alive at the time of the treatment. If the treatment was initiated by starting the conditioning regimen but the patient died before infusion took place, select **Died after conditioning but before HCT**.

4. Indication diagnosis for this HCT:

Select the disease for which the reported treatment is being given. In addition, make sure that the diagnosis has been registered first, using the relevant diagnosis form. While submitting data in the EBMT Registry web application, the user will be provided with a list of diagnoses available for the patient, from which only one option can be selected.

5. Chronological number of this treatment:

Indicate the chronological number of the current treatment among other treatments (HCT, CT, IST) received by the patient throughout his/her lifetime, regardless of whether the previous treatments have been performed in your centre or other centres. It is NOT the serial number of the current treatment within all the treatments performed in your centre, and it is NOT the number of the treatments that this patient has received in your centre only.

The information about the chronological number can be obtained from the patient's medical history record.

6. Chronological number of this HCT:

Indicate the chronological number of the current HCT among other HCTs, both allogeneic and autologous, that this patient has received throughout his/her lifetime, regardless of whether the previous HCTs have been performed in your centre or other centres. It is NOT the serial number of this HCT within all the HCTs performed in your centre, and it is NOT the number of the HCT that this patient has received in your centre only.

The information about the chronological number can be obtained from the patient's medical history record.

7. Chronological number of this allogeneic HCT:

Indicate the chronological number of the current allogeneic HCT among other allogeneic HCTs that this patient has received throughout his/her lifetime, regardless of whether the previous allogeneic HCT has been performed in your centre or in other centres. It is NOT the serial number of this allogeneic HCT within all the allogeneic HCTs performed in your centre, and it is NOT the number of the allogeneic HCT that this patient has received in your centre only.

The information about the chronological number can be obtained from the patient's medical history record.

8. Chronological number of the treatment is >1:

The following section should only be filled out if the number indicated in **question 5 of the current form** is more than 1.

Submit the relevant follow-up form for the previous HCT/CT using the follow-up assessment date before reporting this Allo-HCT. It is required to capture relapse data and other events between transplants/cellular therapies.

8.1. Reason for this HCT:

Select the main reason for this subsequent HCT from the list.

Relapse/progression after previous treatment (HCT/CT) - If the patient required this subsequent HCT as a result of a return of signs and symptoms of a disease after a period of improvement observed post the previous treatment.

Complication after previous treatment (HCT/CT) - If the patient required this subsequent HCT as a result of a complication that developed after the previous treatment.

Primary graft failure - If the patient required this subsequent HCT as a result of a failure of initial engraftment of donor hematopoietic cells.

Secondary graft failure - If the patient required this subsequent HCT as a result of a loss of donor hematopoietic cells following initial engraftment.

Secondary malignancy - If the patient required this subsequent HCT as a result of a secondary malignancy.

If the reason the patient required this subsequent HCT is not available in the list, check the **Other** box and report the reason in the textbox in English.

8.2. Date of the last treatment before this one:

Report the date of the previous treatment before this allogeneic HCT.

8.3. Type of the last treatment before this one:

Select the type of the previous treatment before this allogeneic HCT from the list.

8.4. Was the last treatment performed at another institution?

Indicate if the previous treatment was performed in another institution than the one performing this allogeneic HCT. If the answer is **Yes** also report:

8.4.1. CIC (if known):

Report the CIC of the centre where the previous treatment took place (if known).

8.4.2. Name of institution:

Report the name of the centre where the previous treatment took place.

8.4.3. City:

Report the city in which the institution where the last treatment took place is located.

Donor & Graft Information

9. Is this HCT part of a multiple (sequential) graft program/protocol?

Sometimes patients are entered into protocols that include more than one transplant. A typical example might be the use of an autologous transplant to prepare the patients for a non-myeloablative (reduced intensity) allograft. In this case, the allograft would be number 2 out of 2 pre-programmed transplants. In this example, the 'AUTOLOGOUS HAEMATOPOIETIC CELL TRANSPLANTATION (HCT) - Day 0' form and 'DISEASE STATUS AT HCT/CT/IST - Day 0' form should have been completed for the first transplant.

Some patients may have received a transplant (autologous or allogeneic) prior to this procedure as part of earlier disease management. In this case, the current transplant is not part of a multiple-graft program.

A subsequent transplant that has been programmed to happen only if an intermediate event takes place (ie: relapse) should not be considered a part of a multiple transplant program.

Select **Yes** if the patient received the current allogeneic HCT as a part of a multiple (sequential) graft program/protocol. Otherwise, select **No**.

9.1. Chronological number of this HCT as part of multiple (sequential) graft program/protocol for this patient:

If you answered **Yes** to the previous question, also indicate the chronological number of the current allogeneic HCT in the program.

If this is the first allogeneic HCT for this patient, complete the patient HLA section in the database.

IMPORTANT NOTE

LABORATORY RESULTS WITH HLA TYPING must be added to the database for all the patients.

When submitting a paper form, please always enclose a copy of the histocompatibility laboratory results.

When you enter data directly into the database please ensure the HLA typing is complete. Some national registries will enter this data on your behalf, for example, BSBMT Registry in the UK.

Check the manual on HLA data entry for more details.

10. Multiple donors (CB units):

Indicate whether products used in this transplant belonged to more than one donor by selecting **No** or **Yes**. If you answered **Yes**, also report the **Number of donors**. The number should never be equal to 1.

This can be the case when the transplant involves cord blood (CB): multiple CB units (CBU) being used in one HCT is not rare.

IMPORTANT NOTE:

The form provides space to fill in up to 1 donor. If the patient had more than 1 donor, copy the next section as many times as necessary and fill in the information for each individual donor separately, indicating the sequential number assigned to each donor.

11. Did the donor consent to having their data in the EBMT registry?

Centres should download and fill in the Donor Consent Form in the appropriate language for each of their donors, as the law requires that the donor consents to the data being transferred to the EBMT.

EBMT shall provide the Informed Consent Form to the participating sites for data reporting to EBMT. The reporting centre shall be responsible for ensuring that the Informed Consent Form is in compliance with applicable laws and meets the minimum requirements as indicated by the Informed Consent templates on this web page. No centre is exempt from obtaining donor consent before submitting data to the EBMT.

Indicate if the donor consented to share the data with the EBMT registry by selecting **Yes** or **No**. If the donor did not consent, only data items marked with an asterisk (*) can be filled out.

12. Date of birth:

Indicate the donor's date of birth.

The year of birth is a compulsory field (*), while month and date fields are strongly recommended ones.

NOTE:

The date of birth is important information used to avoid patient duplication and accurately calculate the donor's age at the time of donation. Failure to provide the full date of birth (due to legal, ethical, or any other reason) will result in increasing the chances of donor duplication in the system.

13. *Age at time of donation:

If it is not possible to indicate the donor's date of birth, indicate the age of the donor (in years) at the time of the donation procedure. This data item is optional.

14. *Age in months:

If it is not possible to indicate the donor's date of birth and the donor was younger than 1 year, indicate his/her age at the time of the donation procedure in months. This data item is optional.

15. *Sex (at birth):

Indicate the donor's biological sex as **Male** or **Female**.

The sex of the donor, which you may find in the histocompatibility forms, is important in relation to Graft versus Host Disease (GvHD).

16. Donor Identification:

It has become increasingly important from the clinical and the legal point of view, to be able to use joint information for the patient and donor(s) pair for each transplant. For this reason, it is very important that, while keeping anonymity, the donor data can be traced. This can only be done if the unique identification codes for the donors are stored.

It is for this reason that the EBMT is requesting the information below. Although this may look unnecessary, it cannot be stressed enough how important it is to be able to identify the correct set of data and, given the current situation, where there are no agreements on how to identify donors uniquely, it is best practice to collect all possible unique identifications.

16.1. Donor ID given by the treating centre (mandatory):

If the donor comes from an unrelated donor registry, please enter the code/number given to the donor by the donor registry. If the donor is related, please enter the code/number by which the donor is identified in your centre. This data item is very important and hence marked as mandatory.

16.2. Global registration identifier for donors (GRID):

Indicate the GRID of the donor. Global Registration Identifier for Donors (GRID) was developed by WMDA¹ to ensure the secure, reliable, and unambiguous assignment of donors.

The GRID standard is a 19-character donor identifier composed of three elements: Issuing Organization Number (ION), Registration Donor Identifier, and Checksum (shown below).



16.3. ION code of the Donor Registry or Cord Blood Bank (mandatory):

The ION identifies organisations that issue GRIDs and is assigned by ICCBBA² in its role as an issuing agency under ISO 15459. A unique random ION is assigned to each issuing organisation. The ION is a 4-digit number between 1000 and 9999. It shall be encoded and interpreted by reference to the ICCBBA GRID Issuing Organization Database published and maintained by ICCBBA on the ICCBBA Website. The ION shall be used as the first 4 characters within a GRID to create global uniqueness and may also be used for other purposes (e.g., databases) to identify organisations that assign GRIDs.

WMDA list is available at: <https://share.wmda.info/display/WMDAREG/Database>.

This list also contains some, but not all, Cord Blood banks.

Enter the ION code in the form. For reference, you can find a [conversion table](#) of the ION codes and former BMDW codes in our Document Center. This data item is very important and hence marked as mandatory.

16.4. EuroCord code for the Cord Blood Bank (if applicable):

EuroCord also keeps a list of Cord Blood Banks. If you know the code given by EuroCord, indicate it here.

¹ <https://wmda.info/professionals/optimising-search-match-connect/why-global-identifier/>

² <https://www.iccbba.org/about-iccbba>

16.5. Name of Donor Registry or Cord Blood Bank:

Enter the name of the donor registry, or, in the case of cord blood, the name of the cord blood bank in full.

PLEASE NOTE that most countries are now centralised under one ION code (e.g.: the UK are under Antony Nolan, but donations can take place under any UK donor registry), so if you know the Name of the Donor Registry, please write it in this field, after you provide the ION code.

16.6. Donor ID given by the Donor Registry or Cord Blood Bank:

It is an identification given by the Donor Registry or the Cord Blood Bank to the donor.

NOTE:

The CIBMTR and NMDP have requested that the donor ID given by the registry be entered as a number only with retaining the leading zero (if applicable).

Therefore, do not enter dashes between numbers, do not add “NMDP” or other characters to the beginning of the donor id, and do not drop leading zeroes.

Example:

Incorrect	Correct	Explanation
0257-8376-2	025783762	No dashes between numbers
NMDP0323-4119-0	032341190	No additional characters, no dashes between numbers
81706343	081706343	Keep leading 0's
US033941345	033941345	No additional characters
0699-30685	069930685	No dashes between numbers

The reason for this is to ensure data integrity and facilitate the identification of the donor when EBMT shares the data to the CIBMTR for those centres that have requested it.

16.7. Patient ID given by the Donor Registry or Cord Blood Bank:

It is an identification given by the Donor Registry or the Cord Blood Bank to the recipient. Although this is currently an optional field, it is extremely important information, which helps in identifying the correct set of data. It is always the best practice to collect all possible unique identifications.

17. *Donor EBV status:

Epstein-Barr virus (EBV) is a widespread human herpesvirus (HHV4), infecting the majority of children, that establishes lifelong latent infection in the host memory B cells. This virus accounts for post-transplantation lymphoproliferative disorder (PTLD), one of the most serious allogeneic hematopoietic cell transplantation complications.

Report the laboratory result of the EBV antibody testing as **Negative** or **Positive** (positive EBV VCA IgG or EBNA assay results). If the testing was not performed, select **Not evaluated**. If the results of the testing are not known, report **Unknown**.

18. *Donor CMV status:

Human cytomegalovirus (CMV) is a betaherpesvirus in the same family as human herpesvirus-6 and -7. As the other herpesviruses, CMV remains in the human body after primary infection for life. In allogeneic HCT recipients, the most important risk factors for CMV disease are the serologic status of the donor and recipient. Approximately 30% of seronegative recipients transplanted from a seropositive donor (D+/R-) develop a primary CMV infection.

Report the laboratory result of the CMV antibody testing as **Negative** or **Positive** (positive CMV IgG assay result). If the testing was not performed, select **Not evaluated**. If the results of the testing are not known, report **Unknown**.

19. Is the donor an HbS trait carrier?

Report if the donor is an HbS trait carrier based on the blood test results by selecting either **No** or **Yes**. This question should be answered only if the patient was diagnosed with Sickle Cell Disease.

20. Did this donor provide more than one stem cell product:

For each donor indicate whether the donor provided more than one stem cell product.

One stem cell product - cells were obtained using the same mobilisation cycle and collection method regardless of the number of collection days.

Multiple stem cell products - cells were obtained using more than one mobilization technique/cycle, and/or collection method.

If the donor provided one product only (e.g. PB), answer **No** and fill in details on "Donor 1" - "Product Number 1".

If more than one product was obtained from the same donor (e.g. BM and PB), answer **Yes** and fill out details on "Donor 1" - "Product 1" and "Donor 1" - "Product 2". In addition, specify the **Number of different stem cell products from this donor**.

IMPORTANT NOTE:

The form provides space to fill in up to 2 products per donor. If there were more than 2 products per donor, copy the relevant section as many times as necessary and fill in the information for each product separately.

21. *Source of stem cells:

Indicate the stem cells' source by selecting only one option from the list. If the source of the stem cells is not available in the list, check the **Other** box and specify the source in the textbox in English.

22. *Graft manipulation ex-vivo including T-cell depletion:

An ex-vivo (same as *in vitro*) manipulation is a "treatment of the graft in the laboratory". Graft manipulation is performed to define and optimise the volume and cellular composition of stem cell sources like apheresis products, bone marrow, or umbilical cord blood.

Indicate if the graft was manipulated ex-vivo by selecting either **No** or **Yes**. If answered **Yes**, select the manipulation type from the list of options.

T-cell (CD3+) depletion - Removal of T-cells (CD3+) from the donor graft. Depletion of T-cells (CD3+) provides almost untouched grafts with potential antileukemic effectors (e.g., NK cells) enabling fast engraftment and reliable prevention of GvHD.

T-cell receptor $\alpha\beta$ depletion - Selective depletion of T cells expressing the $\alpha\beta$ T cell receptor. This allows for the removal of cells responsible for GvHD and PTLD but maintains hematopoietic progenitor and stem cells for engraftment (CD34+ cells), as well as cells to elicit graft-versus-tumor effect and provide anti-infective activity (such as gamma-delta T cells and natural killer cells).

B-cell depletion (CD19+) by MoAB - B-cells are depleted from the graft by using monoclonal antibodies. Please, do not record anti-CD20 antibody treatment of the patient here.

NK cell depletion by MoAB - NK cells are depleted from the graft by using monoclonal antibodies.

CD34+ enrichment - Positive selection of CD34 cells. The manipulation provides a graft with a very low number of T cells and therefore allows to avoid GvHD very effectively.

Genetic manipulation - This is a procedure by which techniques of gene transfer/transduction are used to alter the structure and characteristics of genes in the graft before the cell infusion.

If the manipulation type is not available in the list, check the **Other** box and specify the manipulation procedure in the textbox in English.

Also, select **No** if the manipulation consisted of plasma and/or red cells and volume reduction.

Report only manipulations performed at the transplant centre. If the cells, particularly, cord blood cells have been manipulated before reaching the transplant centre, these manipulations should not be reported here.

NOTE:

Alemtuzumab (Campath) is sometimes added to the bag containing the cells, and gets infused into the patient together with these same cells during the transplantation. This treatment is known as "Campath in the bag". In this case, the difference between ex vivo and in vivo treatment is blurred. To avoid double reporting of the same treatment, we advise that, until further notice, "Campath in the bag" is not reported here. Hence, do not select **T-cell (CD3+) depletion**, if "Campath in the bag" was used.

23. *HLA match type and patient/donor relation:

The outcome of HCT depends in part on the matching between the donor and the recipient for the human leukocyte antigens (HLA), encoded by a group of genes on chromosome 6; genes and products are labelled as major histocompatibility complex (MHC). The HLA system is the most polymorphic genetic region in the human genome.

A set of HLA gene alleles, called a haplotype, is inherited from each parent; therefore, the probability that a child inherits and shares both parental haplotypes with a full sibling is 25%. Such an HLA-identical sibling is still considered an optimal donor for young patients.

Indicate the type of donor by selecting one of the options:

Related donor, type - a donor who is blood-related to the patient. This includes monozygotic twins, siblings, parents, aunts, uncles, children, cousins, half-siblings, etc.

Unrelated donor, type - a donor who has no known blood relation to the patient.

23.1. *Related donor, type:

Report whether the HLA matched or not between the related donor and the patient. If both haplotypes matched, select **Match (*)**. Otherwise, select **Mismatch (*)**.

23.1.1. *Degree of matching:

If you answered **Mismatch** to the previous question, specify the degree of matching by selecting one of the options:

One haplotype mismatch - the donor is mismatched in exactly one haplotype with the recipient.

***Partial haplotype mismatch** - the donor is partially mismatched with the recipient.

For the latter option also specify the **number of mismatched HLA alleles** ranging from 1 to 6 by selecting only one option.

23.1.2. *Mismatch at locus:

Indicate the locus at which the mismatch was observed by checking all the options from the list that apply to your particular case.

23.1.3. *Both haplotypes confirmed by family studies?

Genotypic HLA identity should be confirmed by family studies for all six HLA loci (to exclude recombination) wherever possible. For both matched and mismatched related donors, select **No**, if no

confirmation was done, otherwise select **Yes**. If it is unknown whether both haplotypes were confirmed by family studies, select **Unknown**.

23.1.4. Relationship to patient:

For both matched and mismatched related donors, indicate the biological relationship of the donor to the recipient by selecting one of the options from the list:

Syngeneic (monozygotic twin) - the donor is a twin who developed from the same zygote as the patient and thus shares the same histocompatibility genes. This option can only be selected for matched, related donors.

Sibling - a brother or a sister of the patient including a non-monozygotic twin.

For other relatives, select **Other related** and specify the relationship type by checking one of the options from the list. If the relationship type is not available in the list, check the **Other** box and specify the type in the textbox in English.

23.2. *Unrelated donor, type:

If the donor has no blood relation with the patient, provide the data below.

23.2.1. *Degree of HLA matching:

Indicate the degree of HLA matching for the unrelated donor by selecting one of the options:

Full match (10/10) - a donor is matching for the HLA-A, -B, -C, -DRB1 and -DQB1 loci.

Single HLA mismatch (9/10) - a donor with one mismatch (antigen or allele) in any of the HLA-A, -B, -C, -DRB1, and -DQB1 loci.

>=2 HLA mismatches (<9/10) - a donor with more than one (antigen or allele) mismatch in any of the HLA-A, -B, -C, -DRB1, and -DQB1 loci.

23.2.2. HLA-DPB1 matching:

Indicate the matching type for HLA-DPB1 locus for the unrelated donor. Select **Match** if the donor and the recipient matched at HLA-DPB1 locus. If there was one mismatch, select **At least 1 mismatch**. If no genotyping was performed, report it as **Not typed**.

23.2.3. *Mismatch at locus:

Indicate the locus at which the mismatch was observed for the unrelated donor by checking all the options from the list that apply to your particular case.

IMPORTANT NOTE:

LABORATORY RESULTS WITH HLA TYPING must be added to the database for all the donors.

If submitting a paper form, please always enclose a copy of the histocompatibility laboratory results.

When you enter data directly into the database please ensure the HLA typing is complete. Some national registries will enter this data on your behalf, for example, BSBMT Registry in the UK.

Check the manual on HLA data entry for more details.

Additional Assessments

24. Are there Donor-Specific Antibodies (DSA) against HLA?

The presence of donor-specific anti-HLA antibodies (DSA) is associated with a higher risk of Graft Failure in the context of haploidentical cord blood and unrelated donor transplants, and it may in fact translate into a reduced overall survival.

Indicate if clinically significant donor-specific anti-HLA antibodies were detected by selecting **No** or **Yes**.

Select **Unknown**, if it is not known whether the antibodies were detected. Select **Not evaluated** if testing for clinically significant donor-specific antibodies was not performed.

24.1. HLA loci the DSA are directed against:

If you answered **Yes** to the previous question, also specify the HLA locus against which the antibodies are directed.

24.2. Did the patient have desensibilisation therapy?

If you answered **Yes** to question 24 and the patient's diagnosis was registered using the 'Haemoglobinopathies' form, also indicate if the patient had desensibilisation therapy by selecting **No** or **Yes**. If answered **Yes**, also specify the type of therapy.

24.3. Are the DSA red cell antibodies?

If you answered **Yes** to question 24 and the patient's diagnosis was registered using the 'Haemoglobinopathies' form, also indicate whether the antibodies are directed against red blood cells by selecting **No** or **Yes**.

24.3.1. Are they cross-reacting with the red cells of the donor?

If you answered **Yes** to the previous question, indicate whether the antibodies cross-react with the red cells of the donor by selecting **No** or **Yes**.

Patient Serological Status

25. Patient EBV status:

See question 17 for instructions.

26. Patient CMV status:

See question 18 for instructions.

Preparative Regimen

27. Preparative (conditioning) regimen given?

Conditioning is the preparative regimen that is administered to patients undergoing HCT before the infusion of stem cell grafts. The pretransplant conditioning may consist of TBI and/or chemotherapy. However, there are instances when a preparative regimen may not be given: for example, for Primary Immunodeficiency Disorders.

In some cases, especially in patients with MDS and blasts in the bone marrow, or in patients with refractory or non-complete remission prior to an allograft, it is becoming increasingly common to use AML-like therapy followed immediately (usually after 3 days) by mainly reduced conditioning regimen

(e.g. FLAMSA regimen). In such cases, the AML-like therapy should be reported as part of the preparative regimen (conditioning).

If a preparative regimen was given select **Yes**, otherwise select **No**.

NOTE:

Fill in this section if the patient is still alive but has not received HCT due to health reasons, regardless of whether the conditioning was complete or not.

Please contact the Registry Helpdesk (registryhelpdesk@ebmt.org) for more information and guidance.

28. Drugs given?

Indicate if the preparative regimen consisted of drug treatment (any active agent, including chemotherapy, monoclonal antibody, polyclonal antibody, serotherapy, etc.) by selecting **Yes** or **No**. If answered **Yes**, specify the treatment in question 30.

29. What type of conditioning regimen was used?

Indicate the type of the conditioning regimen by selecting one of the following:

Myeloablative conditioning (MAC) - the conventional preparative regimen that consists in ablation of the marrow with pancytopenia which can last for over a month, require CT for marrow recovery, and results in complete donor chimaerism.

Examples of standard intensity conditioning regimens for adults and older children. (Dosages have to be adapted for young children)

- Busulfan 16 mg/kg po / 3.2 mg/kg iv + cyclophosphamide 120-200 mg/kg
- Cyclophosphamide 120 mg/kg fractionated, TBI 12 Gy (fractionated) ± Anti-Thymocyte Globulin
- TBI 10-14 Gy; Busulfan 16 mg/kg po/ 3.2 mg/kg iv; ± other agent
- 200 mg/m² Melphalan

Example of a sequential conditioning regimen:³

³ The following sequence is a borderline case, but considered by the Definitions Committee to be Standard (myeloablative) conditioning.

	D-15	D-14	D-13	D-12	D-11	D-10	D-9	D-8	D-7	D-6	D-5	D-4	D-3	D-2	D-1	D0
Cytarabine	2 x 1000 mg/m ²	2 x 1000 mg/m ²	2 x 1000 mg/m ²	2 x 1000 mg/m ²												
Fludarabine	30 mg/m ²	30 mg/m ²	30 mg/m ²	30 mg/m ²												
Amsacrine	100 mg/m ²	100 mg/m ²	100 mg/m ²	100 mg/m ²												
Anti-Thymocyte Globulin												0.5 mg/kg	2.5 mg/kg	3 mg/kg		
Busulfan								4 x 0.8 mg/kg	4 x 0.8 mg/kg	4 x 0.8 mg/kg	4 x 0.8 mg/kg					

Reduced intensity conditioning (RIC) uses lower, less toxic doses of chemotherapy and radiation than the conditioning regimen that is given before standard allogeneic Transplantations. These regimens are used for certain patients who are older, who have organ complications or who are otherwise not healthy or strong enough to undergo standard allogeneic transplantation.

There are many different reduced-intensity conditioning protocols and the intensity of the chemo-radiotherapy can vary from levels very close to conventional conditioning to regimens based only on immunosuppression. However, not all reduced-intensity protocols are non-myeloablative. The following guidelines should be followed to determine whether a regimen is truly non-myeloablative:

Any regimen with 50% or less equivalence to a standard conditioning regimen is considered non-myeloablative. This includes not only the 50% reduction of the total dose of a given drug (or TBI) but also the use of a single drug in a standard dose but without other drugs (or TBI) usually included in the standard protocol.

The standard conditioning regimens vary according to the disease, so the non-myeloablative regimens will also vary. **The addition of ATG or any mono or polyclonal antilymphocyte antibody or the addition of purine analogues does not change the intensity category.**

The above definition can be applied also to published protocols not included in the examples below.

Examples of reduced intensity conditioning regimens⁴

⁴ Only regimens with dosages equal to or below these limits should be classified as non-myeloablative.

- Cyclophosphamide 1200 mg/m² ± Anti-Thymocyte Globulin
- Cyclophosphamide ≤ 60 mg/kg ± TBI ≤ 6 Gy (fractionated) ± purine analogue ± Anti-Thymocyte Globulin
- Melphalan ≤ 100 mg/m² ± purine analogue ± Anti-Thymocyte Globulin
- Melphalan 70-140 mg/m² ± purine analogue ± Alemtuzumab
- Busulfan ≤ 8 mg/kg po / 1.6 mg/kg iv ± TBI ≤ 6 Gy (fractionated) ± purine analogue ± Anti-Thymocyte Globulin

30. Specification and dose of the preparative regimen:

Select all the agents (chemotherapy, antibodies, hormones, etc.) received by the patient as a part of the preparative regimen. They must all have been given before the actual date of cell infusion (HCT date or Day 0). If collecting data retrospectively or if drugs were stopped due to adverse events or early death, please, still register the drugs which were given. With respect to antibodies, only indicate the ones infused directly into the patient before administration of the graft and not those used ex vivo for graft manipulation. Any drugs, antibodies, etc. administered after the transplantation should not be entered here.

If the drug/agent is not available on the list, select **Other** and report the generic drug/agent name(s) in the textbox in English.

Please consult the **LIST OF CHEMOTHERAPY DRUGS/AGENTS AND REGIMENS** on the EBMT website for drug/agent names. This document provides alternative names for many drugs/agents. Once you have found the drug/agent of interest on the list, add its database name to the table.

In addition, indicate the administered cumulative dose as specified in the treatment protocol. Multiply the daily dose in mg/kg or mg/m² by the number of days (e.g. for Busulfan given 4 mg/kg daily for 4 days, the total dose to report is 16 mg/kg.) Report the dose units as either **mg/m²** or **mg/kg** for non-radioactive agents and as either **mCi** or **MBq** for radioactive ones. If the dose is reported in a unit other than those listed, convert the dose to the appropriate unit.

30.1. For Busulfan:

30.1.1. Route of administration:

If the patient received busulfan as part of the preparative regimen, indicate the route of administration by selecting one of the options from the list.

30.1.2. Drug monitoring performed:

If the patient received busulfan as part of the preparative regimen, indicate if AUC-based drug monitoring was performed by selecting **No** or **Yes**.

30.1.3. Total AUC:

If you answered **Yes** to the previous question, specify the total AUC value.

30.1.4. AUC unit:

Report the total AUC units as either **mg x hr/L** or **micromol x min/L** or **mg x min/mL**. If the total AUC is reported in a unit other than those listed, convert it to the appropriate unit.

30.2. For Carboplatin:

30.2.1. Drug monitoring performed:

If the patient received carboplatin as part of the preparative regimen, indicate if AUC-based drug monitoring was performed by selecting **No** or **Yes**.

30.2.2. Total AUC:

If you answered **Yes** to the previous question, specify the total AUC value.

30.2.3. AUC unit:

Report the total AUC units as either **mg x hr/L** or **micromol x min/L** or **mg x min/mL**. If the total AUC is reported in a unit other than those listed, convert it to the appropriate unit.

31. Total body irradiation (TBI):

Indicate if the patient underwent total body irradiation as part of the preparative treatment. If the answer is **Yes**, specify also:

31.1. Total prescribed radiation dose as per protocol:

If the patient received total body irradiation as part of the preparative treatment, report the total prescribed dose in Gy.

31.2. Number of fractions:

If the patient received total body irradiation as part of the preparative treatment, report the number of fractions.

31.3. Number of radiation days:

If the patient received total body irradiation as part of the preparative treatment, report the number of radiation days.

GvHD Prophylaxis

This is an immunosuppressive treatment that is given to the patient in a prophylactic manner to prevent the development of GvHD. If collecting data retrospectively, please specify the drugs which were intended to be given.

Patients receiving syngeneic transplants do not receive this treatment.

32. GvHD prophylaxis or preventive treatment:

Indicate if GVHD prophylaxis was given by selecting **No** or **Yes**. If you answered **Yes**, specify the type of treatment given by selecting one of the options:

Drugs - Select all the agents (chemotherapy, antibodies, hormones, etc.) received by the patient as a part of the immunosuppressive treatment.

Most of the time, the immunosuppressive treatment includes cyclosporine and methotrexate.

Cyclosporine may also be given alone. More recently, newer agents are being used for the prevention of GvHD: tacrolimus, mycophenolate mofetil, and monoclonal antibodies such as alemtuzumab (Campath). If the patient was given "Campath in the bag" (see question 22), report it here.

If the drug/agent is not available on the list, select **Other** and report the generic drug/agent name(s) in the textbox in English.

Please consult the **LIST OF CHEMOTHERAPY DRUGS/AGENTS AND REGIMENS** on the EBMT website for drug/agent names. This document provides alternative names for many drugs/agents. Once you have found the drug/agent of interest on the list, add its database name to the table.

32.1. For Anti-Thymocyte Globulin|Anti-Lymphocyte Globulin

32.1.1. Product name:

If the patient received anti-thymocyte globulin or anti-lymphocyte globulin as part of the GvHD prophylaxis or preventive treatment, report the product name.

32.1.2. Origin:

If the patient received anti-thymocyte globulin or anti-lymphocyte globulin as part of the GvHD prophylaxis or preventive treatment, report the origin of the globulin by selecting one of the options from the list. If the origin is other than rabbit or horse, select **Other** and report the origin in the textbox in English.

Extracorporeal photopheresis (ECP) - is a treatment currently being used to prevent GvHD which does not involve the use of drugs.

If the type of immunosuppressive treatment is not available on the list, select **Other** and specify the type in the textbox in English.

In the case of T-cell-depleted transplants, there may be no additional therapy to prevent GvHD. Do not report therapy given after the development of aGvHD. Instead, report it in the follow-up form.

Please note that for unrelated donors and mismatched related transplantations, anti-thymocyte globulin or anti-lymphocyte globulin, and/or corticosteroids (DAF) may be given some time before the start of the conditioning regimen. In this case, the immunosuppressive therapy aims to facilitate engraftment and forms part of the preparative regimen, therefore, it should not be reported here.