German Standards for Unrelated Blood Stem Cell Donations
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Preamble

These standards have been compiled by the ZKRD Standards Committee, which is composed of representatives from the ZKRD, donor centers, search units, cord blood banks and collection centers. The standards apply to the essential areas of unrelated blood stem cell donor recruitment and care, the procurement and facilitation of the respective therapeutic products and the organizations involved in these processes. The standards adhere in all essential requirements to the standards of the WMDA [16].

These standards shall guarantee a high level of quality and safety as well as a uniform procedure concerning donor recruitment, testing, search, donation and transport of hematopoietic products. This helps to protect the interests of all donors and patients, and creates a better transparency for all national and international organizations involved. The ZKRD standards are binding minimum requirements, which may be handled even stricter by individual organizations. Valid laws, guidelines and contracts in the current version will remain unaffected.

These standards are are revised and updated if needed at least once a year by the ZKRD Standards Committee. In doing so, new medical developments and legal regulations and guidelines are to be considered as well as suggestions of the organizations, which are active in the area of donor search and donor procurement.

The organizations mentioned in the following document commit themselves to comply with the standards that apply to them.

In the following text, for reasons of better legibility, the expression “blood stem cells” is used for all hematopoietic stem cells irrespective of their origin or method of collection. If only one source is concerned, this will be expressed by using the terms “bone marrow”, “peripheral blood stem cells” (hereinafter also referred to as “PBSC”) or “cord blood”.

Binding standards have been indicated by using the imperative form or the respective form of the words “must” or “must not”. Standards containing the words “recommended”, “can” or “should” are used for recommendations.

In the whole text the masculine form is used for persons of both genders.
1 Organizations Involved

1.1 Zentrales Knochenmarkspender-Register Deutschland (ZKRD)

1.1.1 Requirements

1.1.1.1 The ZKRD must have an organizational and legal form that guarantees proper financial and administrative operation.

1.1.1.2 The medical director of the ZKRD must be a licensed physician with the necessary professional skill in this field of activity. He must not be subjected to directives in his professional competence.

1.1.1.3 The ZKRD must have an appointed business administration manager, who has the necessary professional skill in this field of activity.

1.1.1.4 The ZKRD must guarantee continuous occupation of all essential functional units during regular office hours\footnote{If the term “regular office hours” is used in this document it means Monday-Friday 8.00 a.m. - 4.00 p.m. on working days.}, adequate in number and qualification. Outside office hours availability must be guaranteed for emergency cases.

1.1.1.5 It must be ensured that during regular office hours at least one person is available who has a good spoken and written command of the English language.

1.1.1.6 The ZKRD must provide an organizational chart, on which name, task and position of all employees within the organization can be seen.

1.1.1.7 There must be adequate equipment in data system technology.

1.1.1.8 Data protection and security must be guaranteed according to Chapter 10 “Data Protection, Anonymity and Record Retention”.

1.1.1.9 The ZKRD must maintain a quality management system that comprises standard operating procedures (SOPs), staff training and further education, and guarantees and documents compliance with these standards.

1.1.2 Tasks

1.1.2.1 The ZKRD is managing a central databank containing transplantation relevant data of unrelated prospective blood stem cell donors in pseudonymous form, which is updated by the German donor centers on a regular basis.
1.1.2.2 Search requests for unrelated blood stem cell donors for patients in Germany and from abroad are accepted and processed by the ZKRD exclusively.\textsuperscript{2}

1.1.2.3 The ZKRD provides lists of HLA compatible donors in pseudonymous form according to the current state of the scientific and technical knowledge to the requesting organizations (search units, foreign registries, transplant centers) without delay.

1.1.2.4 The ZKRD must ensure that all transplant centers, which use the ZKRD as an intermediary to perform searches, are accredited by the DAG-KBT or the EBMT/JACIE \textsuperscript{25} or have an equivalent accreditation by another organization.

1.1.2.5 Upon request the ZKRD activates a donor search and obtains, where required, a confirmation from the health insurances to take over the costs for the search, submitting to them auditable documents.

1.1.2.6 The ZKRD accepts requests for further typing and the shipment of blood samples, checks, if they are complete and plausible and forwards the requests to the appropriate donor centers and foreign registries.

1.1.2.7 The ZKRD reports incoming test results to the relevant institutions without delay.

1.1.2.8 The ZKRD does the billing of all services within the donor search with the relevant payers at home and abroad.

1.1.2.9 The ZKRD guarantees immediate handling and forwarding of all important processes within the donor search and donor procurement.

1.1.2.10 The ZKRD ensures documentation of all essential processes within the donor search.

1.1.2.11 The ZKRD enhances cooperation of all institutions involved in the donor search.

1.1.2.12 The ZKRD coordinates and leads the negotiations with the head organizations of the compulsory health insurances in the Project Committee (Projektkommission) \textsuperscript{24}.

1.1.2.13 The ZKRD fulfills the tasks of a national registry according to the WMDA recommendations. \textsuperscript{17}, \textsuperscript{18}, \textsuperscript{19}, \textsuperscript{20}, \textsuperscript{21}.

1.1.2.14 The ZKRD is responsible for all customs declarations for transplants from non-EU countries (third countries) imported into Germany and coordinates these with the transplant centers. The responsibility of the declaration of German transplants being exported into third countries lies with the economic owner at the time of export. The ZKRD holds a license for a simplified import process of transplants for German transplant centers. Regarding export, the ZKRD is classified as a licensed exporter and, therefore, has the right to utilize a simplified export process.

1.2 Donor Centers

1.2.1 Requirements

1.2.1.1 The donor center must have an organizational and legal form that guarantees proper financial and administrative operation.

\textsuperscript{2}Existing contracts with the NMDP concluded up to 2000-01-01 remain unaffected.

\textsuperscript{3}DRB1 typing performed free of charge by the donor centers upon request of a search unit while a donor search is active via the ZKRD is not affected thereby.
1.2.1.2 The donor center must have a medical director who is a licensed physician with the necessary professional skill in this field of activity. It must have a managing director or administrative director who is responsible for the organizational tasks in the donor center. It is possible that one person holds both the medical and the administrative position.

1.2.1.3 The donor center must appoint a person who is qualified in psychological care and counseling, who counsels the donors as a donor advocate, if required. This person shall not be affiliated with the donor center nor an institution that is caring for patients or be biased by a conflict of interests.

1.2.1.4 The personnel responsible for the education, recruitment and counseling of blood stem cell donors is subject to supervision by the medical director and must be knowledgeable of the essential processes involving donor search and blood stem cell transplantation.

1.2.1.5 The donor center must provide continuous staff coverage with qualified personnel, at least during regular office hours.

1.2.1.6 It must be ensured that during regular office hours at least one person is available, who has a good spoken and written command of the English language.

1.2.1.7 The donor center must have documentation on names, function and position of all employees within the organization.

1.2.1.8 The donor center must guarantee storage of all personal and transplantation relevant donor data as well as the transmission of donor data and test results according to the current state-of-the-art technology. For these purposes the donor center must have adequate IT support.

1.2.1.9 The donor center must have an HLA-A,-B typed file of at least 5,000 donors.

1.2.1.10 Data protection and security must be guaranteed according to Chapter 10 “Data Protection, Anonymity and Record Retention”.

1.2.1.11 The donor center must maintain a quality management system that comprises standard operating procedures (SOPs), staff training and further education, and documents compliance with these standards.

### 1.2.2 Cooperation with Other Organizations

1.2.2.1 All organizations (laboratories, collection centers, transplant centers, search units and the ZKRD) cooperating with the donor center must comply with the standards defined for them.

1.2.2.2 A cooperative agreement must be made between the ZKRD and the donor centers according to the contract with the compulsory health insurances.

1.2.2.3 A cooperative agreement must be made between the donor center and the collection centers and the donor center must ensure, that the collection center follows the applicable laws, guidelines and regulations. It is recommended that the collection center works towards a JACIE accreditation.
1.2.2.4 The donor centers cooperate in a constructive way with all organizations involved to achieve common aims.

1.2.3 **Tasks**

1.2.3.1 The donor center is responsible for the recruitment, education, registration and counseling of the donor, as well as for the organization of HLA typing and further testing.

1.2.3.2 The donor center must update the donor data reported to the central registry on a continuous basis, as well as take suitable measures to keep the donors motivated.

1.2.3.3 The donor center must take suitable measures to safeguard the interests of the donor and to protect him from unjustified demands.

1.2.3.4 The donor center reports to the ZKRD on a continuous basis the performed or cancelled blood stem cell collections, indicating donor and patient numbers, the product type and the collection date, as well as further information according to the specifications of the WMDA, which the donor center will be notified of in time. This data is used by the ZKRD for statistical purposes, summary reporting within existing contracts and cooperations, as well as for the generation of match lists only.

1.2.3.5 Further tasks of the donor center are listed under Chapter 2 to 10.

1.3 **Search Units**

1.3.1 **Requirements**

1.3.1.1 As a general rule the search unit is affiliated to a transplant center, university clinic or an institution specialized in transfusion medicine. It must provide sufficient room and staff and be delimited from the other activities.

1.3.1.2 The search unit must have a medical director, who is a licensed physician with the necessary professional skill in this field of activity.

1.3.1.3 The search unit must ensure continuous staff coverage with qualified personnel.

1.3.1.4 During regular office hours at least one person must be available, who has a good spoken and written command of the English language.

1.3.1.5 The search unit must be adequately technically equipped for national and international data exchange.

1.3.1.6 It must coordinate unrelated donor searches for at least 20 patients per annum.

1.3.1.7 Data protection and data security must be guaranteed according to Chapter 10 “Data Protection, Anonymity and Record Retention”.

1.3.1.8 The search units must maintain a quality management system that comprises standard operating procedures (SOPs), staff training and further education, and documents compliance with these standards.
1.3.2 Cooperation with Other Organizations

1.3.2.1 The search unit must maintain regular information exchange with the ZKRD.

1.3.2.2 All organizations cooperating with the search unit must comply with the standards defined for them.

1.3.2.3 A cooperative agreement must be made between the ZKRD and the search unit.

1.3.3 Tasks

1.3.3.1 The search unit initiates the search for an unrelated donor for patients with an indication for blood stem cell transplantation according to the search request form (attending physician, transplant center) with the aim to identify a suitable donor.

1.3.3.2 It must guarantee a continuous exchange of information in adequate time intervals with the attending physician of the responsible transplant center about the status of the donor search and the continuity of the indication.

1.3.3.3 It must, in consultation with the transplant center and the immunogenetics laboratory, guarantee the storing of cell/DNA samples of donors selected for transplantation and of patients for quality control and scientific analysis for at least five years. In the case of scientific analyses from blood samples, the respective informed consents must be in place.

1.3.3.4 Further detailed tasks of the search unit are listed under Chapter 4.

1.4 Cord Blood Banks

1.4.1 Requirements

1.4.1.1 The cord blood bank must have an organizational and legal form that guarantees proper financial and administrative operation.

1.4.1.2 The cord blood bank must meet all requirements of the German Drug Law (AMG) [6] and the German Good Manufacturing Regulation (AMWHV) [13].

1.4.1.3 The cord blood bank must have a manufacturing license according to the German Drug Law (AMG) [6] and a medicine product authorization of the Paul-Ehrlich-Institute (PEI).

1.4.1.4 The spatial, technical and hygienic requirements for the drawing, manufacturing and quality controlling of cord blood units must follow the current state-of-the-art technology. The external collection centres (maternity clinics) must also meet the spatial, technical and hygienic requirements.

1.4.1.5 The cord blood bank must have a medical director, who is a licensed physician with the necessary professional skill in this field. It must have a managing or administrative director, who is responsible for the organizational tasks in cord blood bank. It is possible that one person holds both the medical and the administrative position.

1.4.1.6 The cord blood bank must provide continuous staff coverage with qualified personnel, at least during regular office hours. It must be ensured that during regular office hours
at least one person is available, who has a good spoken and written command of the English language.

1.4.1.7 The personnel assigned with the education, recruitment and counselling of cord blood stem cell donors is subject to supervision by the medical director and must be conversant with the essential processes within the cord blood search and blood stem cell transplantation. Job training and further education must be documented.

1.4.1.8 The cord blood bank must have an organisational chart on which all cooperating organizations (maternity clinics, laboratories) and all staff members with name and function are shown. Detailed job descriptions must be available.

1.4.1.9 The cord blood bank must guarantee storage of all personal and transplantation relevant donor data as well as the transmission of donor data and test results according to the current state-of-the-art technology. For these purposes the cord blood bank must have adequate IT support.

1.4.1.10 Data protection and security must be guaranteed according to Chapter 10 “Data Protection, Anonymity and Record Retention”. Cord blood units must be identified in a way that an assignment to donor and patient is possible within 30 years post transplantation.

1.4.1.11 The cord blood bank must maintain a quality management system that comprises standard operating procedures (SOPs), staff training and further education, and documents compliance with these standards.

1.4.2 Cooperation with Other Organizations

1.4.2.1 All organizations (laboratories, collection centres, transplant centres, search units and the ZKRD) cooperating with the cord blood bank must comply with the standards defined for them.

1.4.2.2 The cord blood bank must have cooperative agreements with all cooperating organizations.

1.4.3 Tasks

1.4.3.1 The cord blood bank must update the data of the cord blood units reported to the central registry on a continuous basis.

1.4.3.2 Before the donation the mother must be informed in writing about the whole process, especially benefits, risks, data-protective aspects and alternatives to cord blood donation. The kind of laboratory tests of the mother and the baby must be discussed. The mother must be informed explicitly about the right to receive the test results and the right to withdraw at any time. The cord blood bank must obtain a written informed consent of the adult mother.

1.4.3.3 A medical examination of the pregnant woman must be performed and documented. The following items must be considered: Process of pregnancy, risk of transmissible diseases of the mother, genetically determined diseases of the hematopoietic system in the family. Abnormalities during birth and diseases or deformities of the child must
be documented. A hemoglobinopathy testing must be performed on a CBU sample before releasing the cord blood unit.

1.4.3.4 All laboratory tests on maternal blood must be performed on samples collected within 48 hours of delivery according to the directives of the Paul-Ehrlich-Institute. From fresh blood of the baby the following tests must be performed: blood group testing ABO group and rhesus type), CMV by molecular biology testing, and HLA-A, -B, -DRB1 by molecular biology testing in an EFI- or ASHI-accredited laboratory.

1.4.3.5 If relevant positive infectious disease marker testing results or other extraordinary results occur, the mother has to be informed and counselled.

1.4.3.6 The identity of the cord blood unit must be checked using a validated process before shipment.

1.5 Collection Centers

1.5.1 The cord blood banks and collection centers must have a manufacturing license according to the German Drug Law (AMG) for all manufactured and distributed products. Furthermore they must observe the applicable laws, guidelines and regulations in their current versions. [1], [3], [5], [6], [7], [8], [9], [10], [11], [13], [22].

1.5.2 Data protection and data security must be guaranteed according to Chapter 10 “Data Protection, Anonymity and Record Retention”.

1.6 Transplant Centers

1.6.1 Blood stem cell transplantations of unrelated donors may only be performed in centers that possess the required expertise [1] and report their transplantation data to the DRST. The ZKRD verifies the criteria before starting a cooperation. From January 1st 2013, JACIE accreditation is recommended at the latest after two years of operation.

1.6.2 A transplant coordinator who is considered as contact person must be appointed and is responsible for contact with the cooperation partners.

1.6.3 The transplant center must annually report to the ZKRD the number of unrelated blood stem cell transplants according to the specifications of the WDMA.

1.6.4 The transplant center must be in possession of all licenses required by law and must observe all applicable regulations, laws and guidelines [1], [4], [7].

1.6.5 Data protection and data security must be guaranteed according to Chapter 10 “Data Protection, Anonymity and Record Retention”.

1.7 Laboratories

1.7.1 Immunogenetics Laboratory

1.7.1.1 A laboratory performing histocompatibility tests in the area of blood stem cell donation (immunogenetics laboratory)
must be accredited by EFI or ASHI in the category bone marrow and blood stem cell transplant respectively,

must as a matter of principle be in a position to meet the listed requirements of the current consensus of the DGI and the DAG-KBT [14], [15].

1.7.1.2 An immunogenetics laboratory that performs primary testing of patients as well as confirmatory and compatibility tests of donors and patients must in addition to [1.7.1.1] also meet the methodology requirements to identify newly defined and for allogeneic blood stem cell transplant relevant alleles according to the state of the scientific knowledge.

1.7.1.3 An immunogenetics laboratory performing the tests at recruitment must have an EFI or ASHI accreditation in the category “Donor Registry”. If there are additional tests of the donor to be done in this laboratory (HLA-A, -B, -DR, high resolution, etc.), the laboratory must have an EFI or ASHI accreditation for this technical category as well.

1.7.1.4 Data protection and data security must be guaranteed according to Chapter 10 “Data Protection, Anonymity and Record Retention”.

1.7.2 Laboratory for Blood Group and Infectious Disease Marker Testing

A laboratory that performs ABO/Rh typing and/or infectious disease marker testing

- must meet all criteria of the current guidelines given by the German Medical Association. Applicable are the “Guidelines for the Preparation of Blood and Blood Components and for the Use of Blood Components (Hemotherapy)” [5], as well as the “Guidelines of the German Medical Board for Quality Assurance of Quantitative Medical Laboratory Tests” [2] in the version valid at the time.

- must provide evidence of having regularly and successfully participated (as a rule four times a year) in appropriate external interlaboratory testing for all parameters tested.

- must guarantee data protection and data security according to Chapter 10 “Data Protection, Anonymity and Record Retention”

Infectious disease marker testing required for donor and product release must be performed in a laboratory licensed or accredited for these diagnostics.
2 Donor Registration

2.1 Information

Comprehensive information must be provided to the donor prior to registration. Information may be given through literature or in person by donor center staff. This also applies to the biological mothers prior to cord blood donation.

The information must contain the following items:

2.1.1 Reasons for the search for voluntary blood stem cell donors.

2.1.2 Methods of sample collection, i.e. blood sample collections or buccal swabs for HLA testing; the donor must be advised that further sample collections and testing may be necessary in future.

2.1.3 Information about possible storage of donor samples.

2.1.4 Information that a medical examination will be performed prior to blood stem cell donation.

2.1.5 Methods of blood stem cell donation, their risks and possible side effects.

2.1.6 Anonymity of donation (see Chapter 8.2 and 10.2).

2.1.7 Non-remuneration of donation, but refunding of expenses incurred by the donation and loss of earnings including coverage by an accident, life and disability insurance. The donor is not remunerated for the donation.

2.1.8 Voluntary nature of the donation and right of withdrawal at any time.

2.1.9 Registration with the intention of a directed blood stem cell donation is not permissible.

2.1.10 Transmission of HLA typing results and other data important for donor selection in anonymous form to national and international registries and search units.

2.1.11 Avoiding registration with multiple donor centers at the same time.

2.2 Requirements

2.2.1 The donor must be at least 18 years old.

2.2.2 The donor is deleted from the national registry at his 61st birthday.

2.2.3 The donor must assure to be healthy to the best of his knowledge and does not suffer from any of the following diseases:
• severe cardiovascular diseases
• severe pulmonary diseases
• severe kidney diseases
• severe neurological diseases
• severe metabolic diseases
• severe tropical infectious diseases, especially Malaria (active or past)
• infections with HIV, hepatitis B or C, HTLV, Syphilis (also of a sexual partner)
• systemic autoimmune diseases or other severe chronic diseases
• cancer
• genetic diseases of the blood or immune system

2.2.4 Further conditions for cord blood donations are:

• The biological mother must be able to understand the medical history questionnaire and the information in regards to language and content.

• A written medical history by means of a standardized questionnaire must be obtained and carefully evaluated.

2.3 Donor Consent

2.3.1 The consent form signed by the donor must contain the following items:

• Consent to store his personal data in the data bank of the donor center.

• Confirmation of receipt of information on the donation (including items 2.1.1 – 2.1.10 see above) and confirmation that this information has been understood.

• Consent to forward all data relevant to the search via the ZKRD to national and international registries and search units.

• Confirmation that the exclusion criteria are known.

• Consent to store and possibly test samples at a later date.

• Consent for inquiries at the registration of address office by the donor center.

• Additionally to the first five sub points the following apply to cord blood: The biological mother confirms in writing that she transfers the ownership rights of the collected cord blood to the cord blood bank and that she does not claim it for herself.

2.3.2 A written confirmation of the registration must be given to the donor. It is recommended to give the donor a copy of his signed consent form.
2.4 Further Procedures

2.4.1 The blood collection required for registration and subsequent HLA typing must be carried out by a physician or under the supervision of a physician. In case of a cord blood donation, the blood samples may also be drawn by an authorized person of the maternity room (e.g. midwife).

2.4.2 The donor center ensures that the samples drawn from the registered donor are normally HLA-A,-B typed within three months and the donor’s data are forwarded to the ZKRD without delay. In addition, HLA-DRB1 typing shall be performed. All typings must be performed by methods of molecular biology. Within the documentation, serologic data must not be derived from molecular biologic tests or vice versa. When registering cord blood units, the size of the preparation (total nucleated cell count, TNC) must be specified.

2.4.3 It is recommended that the donor is contacted annually, and the return information is documented. This must be carried out at least every three years. The donors’ data must be updated correspondingly.

Regular contact with the biological mothers who have agreed to the donation and storage of cord blood units is not required.

2.4.4 The regulations of data protection according to the Federal Data Protection Law must be observed (see Chapter 10 “Data Protection, Anonymity and Record Retention”).
3 Donor Testing

3.1 General

In case of adequate compatibility of the patient and potential donor HLA types the donor center is assigned with the organization of further donor testing via the ZKRD. The reservation concept generally only allows for testing requested with regard to the same patient. The ZKRD system supports this concept through extensive plausibility checks, but currently double registrations of donors cannot be excluded because of the donor data pseudonymisation. As soon as one suspects that a donor might be registered more than once, the ZKRD must be informed immediately. Testing twice for the same patient or parallel CT testing for different patients should be avoided for donor safety reasons.

3.2 Extent and Method of Donor Testing

3.2.1 The donor center must be able to have at least the following tests performed: HLA-class I, HLA-class II, DNA-based testing by molecular biology, at a low- to high resolution level.

3.2.2 If a stored sample is used for testing, the donor must be informed. The donor need not be informed when testing is performed on stored samples during the manufacturing process of cord blood products.

3.2.3 Testing of blood and rhesus types (AB0, RhD) and infectious disease markers (Lues, HBsAg, anti-HBc, antibodies to HIV1, HIV2, HCV and CMV) is performed at CT stage.

3.2.4 Manufacturing and examination of cord blood products is subject to the requirements of the German Medical Association and the Paul-Ehrlich-Institut. They also apply to the diagnostic methods used when examining the infectious disease markers of the pregnant woman and the fetus (cord blood) as well as to haemoglobinopathy testing.

3.3 Confirmatory Typing (CT)

The donor center organizes donor blood sample collection for confirmatory typing (CT) and the accompanying tests as well as the transport of the blood samples to the respective laboratories.

3.3.1 At the time of a CT sample request, a donor information session must be performed. Furthermore, the following must be obtained:
3.3.2 A physician should evaluate the donor health history questionnaire. In addition to the CT questionnaire evaluation form from the ZKRD, the WMDA homepage \[26\] gives detailed information. Any abnormal findings that do not lead to donor deferral must be reported to the search unit via the ZKRD.

3.3.3 ABO/Rh typing and infectious disease marker testing (see 3.2.3) must be arranged by the donor center at the time of CT blood sample shipment. Testing of infectious disease markers must always be performed on fresh blood samples and should be evaluated by a physician. In case of cord blood units, the testing of a cryopreserved sample is allowed.

3.3.4 The maximum blood sample volume that is shipped to the search unit for confirmatory testing is 50 ml. Additionally, up to 10 ml blood is sent to the donor center laboratory for ABO/Rh typing and infectious disease marker testing.

3.3.5 CT blood samples must not be used for research. According to a WMDA recommendation \[27\], a donor is regarded as a study object if additional data or samples are collected only for research purposes. If a donor shall become a study object, the study number, the title of the study, the synopsis and the approval of the ethics committee as well as the respective informed consent form in German must be provided to the donor centre and the ZKRD. After education, the donor may give his or her written informed consent.

If a blood sample is to be used for research purposes, these must be specified and the donor center must be informed via the ZKRD. The donor’s written informed consent must be obtained prior to using blood samples for research. The principal investigator must provide the study number, the title of the study, a synopsis and the approval of the ethics committee.

3.3.6 The blood tubes must be labeled with the donor and patient number and the collection date. The packaging must nationally meet the packing and shipping instructions of PI 650 IATA-DGR and internationally the packing instructions 650 of IATA (International Air Transport Association).

3.3.7 The potential donor is reserved by the ZKRD for 60 days after the date of blood sample collection.

3.3.8 The temporary or permanent unavailability of a donor or a cord blood unit must be immediately reported via the ZKRD to the requesting search unit.

3.3.9 The medical director of the donor center or his/her authorized representative must inform the donor of abnormal infectious disease marker results and possible follow-up testing.

3.4 Confirmatory Typing Results

3.4.1 In case of discrepancies between the HLA typing results, a definite resolution of the discrepancy must be obtained. In case of a continuing discrepancy, repeat testing on
a fresh donor sample (e.g. blood sample or buccal swab) and a stored cord blood sample, respectively must be performed. The donor and the cord blood unit, respectively are temporarily deferred during this time. All organizations involved must be informed about the result of the repeat testing.

3.4.2 In case the search unit provides concordant HLA typing results of a higher resolution level, the donor center must upgrade the donor typing accordingly.
4 Donor Search

4.1 General

4.1.1 The search request is made by a transplant center or the patient’s attending physician in agreement with a transplant center.

4.1.2 The search unit has to assure itself of the necessity of extending the search to unrelated donors by obtaining documentation of the unsuccessful family search.

4.1.3 Before initiating an unrelated search, two HLA typing results of separately drawn patient blood samples must be available. One of these HLA typings must be performed by an immunogenetics laboratory on behalf of the search unit. These tests must be performed at a level of resolution as defined in the current contracts and agreements.

4.1.4 The following must be available to the search unit and the ZKRD:

- Medical report on the indication for transplantation
- Patient consent including information on patient’s health insurance
- Guarantee of payment form signed by health insurance or patient (submission to the ZKRD only).

4.1.5 The medical director of the ZKRD or a person authorized by him verifies the indication for the unrelated donor search. In case the blood stem cell transplantation is considered a developmental therapy whose efficacy is being assessed in clinical studies, the ZKRD must be provided with the clinical protocol and its approval by the ethical committee. In urgent cases, the latter can be submitted later.

By activating the search for a German patient the ZKRD confirms search cost coverage. This implicates no claim for refunding by the German compulsory health insurances.

4.2 Search Procedure

4.2.1 The exchange of data on the national and international level must take place via the ZKRD.

\[^{4}\]At least one HLA-A,-B,-C,-DRB1 and DQB1 testing must have been performed by molecular biology at high resolution level.

\[^{5}\]This does not apply for contracts with the NMDP concluded before January 1, 2000.
4.2.2 The search strategy must be agreed upon and documented by the search unit and the responsible physician of the transplant center. It should be known if also cord blood units are to be included in the search.

4.2.3 The responsible physician of the transplant center has to instruct the search unit in writing about search strategy changes.

4.2.4 Confirmatory testing of potential donors must be performed according to the HLA typing requirements and resolution levels as defined in the current consensus of the DGI and the DAG-KBT \[14, 15\].

When releasing a donor, part of the typings is sufficient. However, one locus must basically be completely typed.

If confirmatory testing of cord blood is done, a complete typing result (HLA-A, -B, -C,-DRB1 and -DQB1, molecular biology, high resolution) is always to be delivered (independent from release or reservation request).

4.2.5 The CT typing result must be forwarded immediately via the ZKRD to the donor center and it must be indicated if the donor is to be reserved for the patient concerned.

4.2.6 The director of the accredited HLA laboratory evaluates the HLA compatibility of donor and patient and provides a written report to the attending physician and the transplant center, respectively.

The transplanting physician is responsible for the final selection of the donor.

### 4.3 Search Cancellation

The search must be cancelled immediately for the following reasons:

- Patient’s death
- Discontinuation of indication.

\[6\] HLA-A,-B,-C,-DRB1 and -DQB1, HLA-typed by molecular biology at high resolution level.
5 Requesting and Preparing Blood Stem Cell Donations (Donor Work-up)

5.1 Work-up Request

5.1.1 After the availability of the results of donor confirmatory and infectious disease testing and other transplant-relevant data, the transplant center decides if the donor is acceptable. The transplant center requests this donor for blood stem cell donation either at the ZKRD or at the donor center. In case of cord blood transplant, the selected cord blood unit is requested and its transport is organized. For the request the ZKRD form CB_003 (see Appendix B) or an equivalent is used for medical prescription.

5.1.2 The ZKRD forms WU_003, WU_004, WU_005, (see Appendix B) or an equivalent are used for medical prescription in order to request donor work-up and to communicate important data during the work-up process. If transplant centers or donor centers use their own forms they must match the ZKRD forms in form and content.

5.1.3 It is recommended to send work-up requests to the donor centers via the ZKRD, including all relevant correspondence.

5.1.4 The requested cell dose should at least correspond the minimum cell counts mentioned in the current guidelines [1]. The transplant center must justify requests of much higher cell counts.

5.1.5 For non-standard diagnosis a copy of the clinical study protocol and its approval by the responsible ethical committee must be provided for review by the medical director of the donor center or cord blood bank or their authorized representative.

5.1.6 Parallel work-up requests of different donors for the same recipient are generally not allowed. If parallel work-up requests should become necessary in justified exceptional cases the ZKRD, the donor centers and the donors involved must be informed and must agree.

5.1.7 A blood stem cell request without prior CT testing of the respective patient/donor pair should only be considered if particular urgency is documented or if several concordant CT results are on record for the donor. In individual cases, a parallel request is possible if the following conditions are fulfilled:
- The patient’s search must be “active”.
- The patient must be registered with high resolution HLA at all 5 loci, which also applies to foreign patients.
- The donor’s HLA must have been confirmed at high resolution from at least one fresh blood sample (e.g. as CT for a different patient).
- For an especially urgent parallel request, the donor’s HLA at the loci A, B and DR must have been tested using molecular biology testing and the probability for a 9/10 match must be at least 90% in addition to the conditions previously listed. Additionally, further acceptance criteria (e.g. CMV, accepted HLA differences) must be taken into account.

The parallel request of a CT and a blood stem cell donation must be submitted via the ZKRD.

The following reasons may justify a parallel request of a CT and a blood stem cell donation with special urgency:

- donor deferral during a work-up
- primary or secondary graft failure
- urgent need of transplantation due to failure of induction therapy or known high-risk leukaemia
- relapse

In the case of a parallel request of CT and blood stem cell donation, the donor has only a short time to decide about the donation. This fact must especially be taken into consideration during counseling (see chapter 5.3).

5.1.8 In exceptional cases, cryopreservation of a blood stem cell product at the transplant center prior to the beginning of the recipient conditioning therapy may be requested. The medical director of the donor center or his authorized representative must review and document these requests.

5.2 Donor Insurance

5.2.1 The donor center must arrange a procurement of an accident, life and disability insurance contract for the donor.

5.2.2 The donor should obtain a copy of the insurance policy.

5.3 Donor Information

5.3.1 The donor must be informed of at least the items in Appendix C.1.

5.3.2 Before the physical examination at the collection center, the donor must have been given information on the procedures of work-up and collection by an appropriately
trained donor center coordinator. In cases of a parallel request of CT and blood stem cell donation, special attention must be paid to the circumstance that the donor must be able to make a free and well-considered decision in spite of urgency.

5.3.3 The donor information session about the blood stem cell donation and its risks and side effects must be performed and documented by the collection center physician.

5.3.4 The donor information session about the risks and side effects of anesthesia for bone marrow collections must be performed and documented by an anesthesiologist or a physician of the department of anesthesia.

5.4 Donor Medical Evaluation

5.4.1 The donor medical evaluation must cover at least the items in Appendix C.2.

5.4.2 The donor medical evaluation must be performed at a collection center designated by the donor center.

5.4.3 A physician who must not be member of the transplant team or the team directly in care of the recipient determines the donor eligibility for blood stem cell donation.

5.4.4 The donor eligibility for anesthesia for bone marrow collections must be determined by an anesthesiologist or a physician of the department of anesthesia.

5.4.5 The donor clearance for blood stem cell donation must be performed by a qualified physician from the collection/apheresis center and documented by his or her signature [5]. Verification of the corresponding data by a second person is recommended.

5.5 Donor Informed Consent

5.5.1 By signing the consent form the donor confirms to be informed of the preparations for and the procedures of collection and the associated risks including the consequences for the recipient if he withdraws his consent to donate after the beginning of the recipient conditioning therapy. The donor confirms in writing that he has understood the information provided and that all his questions have been fully answered.

5.5.2 If the medical evaluation reveals that a central venous line cannot be excluded, a sonographic evaluation is recommended. If a central venous line still cannot be excluded, the donor should only be cleared for bone marrow donation or a different donor should be searched for. In documented exceptions, an apheresis with a central venous line may be planned at the time of medical evaluation if the donor gives his written consent and also consents to cryopreservation of the preparation if the transplant center wishes.

If an insufficient venous situation for a peripheral donation becomes apparent only just at the day of apheresis, a central venous line may be placed under clinical conditions as a documented, justified exception. A central venous line should only be placed for one-day aphereses. As site of insertion, the femoral vein should be preferred. The donor’s written informed consent is necessary.
5.5.3 Already on the day of the medical evaluation for peripheral blood stem cell apheresis the donor’s written consent for a bone marrow collection in the event of an unsuccessful mobilization and collection of peripheral blood stem cells must have been obtained.

5.5.4 If the donor declines a bone marrow collection in the emergency mentioned above, the donor’s written consent for cryopreservation of the peripheral blood stem cell product prior to the beginning of the recipient conditioning therapy must be obtained. In addition, the transplant centre must be informed about this circumstance and must agree with the proceeding.

5.5.5 If it is planned to cryopreserve the blood stem cell product, the donor must be informed of the possibility that the product may not be used and may be discarded. Without the donor’s written consent, the product must not be cryopreserved.

5.5.6 The donor’s written consent indicates that aliquots of the preparation may be cryopreserved at the transplant center for a subsequent infusion at a later date if more blood stem cells were collected than needed for the recipient. The donor must consent to the disposal of the aliquots if they are no longer needed for the recipient.

5.5.7 If a transplant center wishes to use blood samples, product parts or data collected as a part of the donation for scientific purposes in an anonymous way, the specifications in chapter 3.3.5 apply. After being informed accordingly, the donor can give his or her written informed consent.

5.6 Procedures

5.6.1 The transplant center must be informed as early as possible if the requested cell dose is not feasible based on the experience at the collection center. At the time of donor clearance at the latest, the donor center must initiate the verification of the prescription (ZKRD Forms WU_007, WU_008 or WU_021, respectively – Appendix B).

5.6.2 The donor center must inform the transplant center if they are unable to collect the requested volume of the pre-collection donor blood samples (maximum 50 ml) or the donor peripheral blood samples on the day of collection.

5.6.3 After the receipt of the donor clearance for blood stem cell donation (ZKRD Form WU_009 – Appendix B) including the collection date as confirmed by the donor center, the transplant center must confirm in writing the collection date, the start date of the recipient conditioning therapy and the transplant date.

5.6.4 The recipient conditioning therapy must not be initiated until donor clearance for blood stem cell donation including the results of the donor infectious disease testing have been reported in writing to the transplant center (ZKRD Form WU_009 – Appendix B).

5.6.5 Donor G-CSF injections must not begin until the transplant center has confirmed the collection date.

5.6.6 If the collection or transplant is cancelled, the transplant center and the donor center respectively must ensure that the cancellation request has arrived at the appropriate center.
5.6.7 At the latest at the time of donor clearance for blood stem cell donation, the donor center must inform the donor of an emergency telephone number.

5.6.8 The organizations involved in the coordination of work-up, blood stem cell collection and transplant must exchange emergency telephone numbers.

5.6.9 The ZKRD should be copied with the data and communication of work-up and blood stem cell collection if the work-up is not coordinated by the ZKRD.

5.6.10 The decision regarding the number of aphereses is the responsibility of the collection physician. If the recommended minimum dose\(^7\) is reached or, if a higher dose is requested and the cell dose collected is less than 10\% below the requested dose, the transplant centre should not be consulted and the collection should be concluded.\(^8\)

5.6.11 Parts of the preparation can be cryopreserved for later therapeutic use for the same patient. One donor’s cell product is solely destined for the therapy of a specific patient. A whole or partly cryopreservation of the cell product can only be performed with the donor’s written consent. It may only be used as a whole or in parts for research purposes in ethically approved studies with the donor’s written consent. In case the research purpose is no longer given, the preparation has to be discarded. This applies to cord blood preparations analogously pursuant to the FACT standards. The donor centre must be informed in detail of the processing of the product.

5.6.12 On the day of collection, in addition to the guideline-conform infectious markers\(^5\), the following laboratory parameters are to be performed by the collection unit at a minimum:

- before every PBSC apheresis after G-CSF stimulation: blood count (automated), sodium, potassium, calcium
- before every bone marrow collection or non-stimulated apheresis: blood count

For estimation of the apheresis time, before every first PBSC apheresis after G-CSF stimulation, it is recommended to evaluate the amount of CD34 positive cells in the peripheral blood. Additional blood examinations fall to the physician’s responsibility and the individual donor situation.

Information pertaining to post-donation donor testing is included in chapter 8.3.

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\(^7\) status 2014-12-18: 4 x 10\(^6\) CD34 positive cells/kg recipient weight

\(^8\) The reverse is NOT applicable - of course the collection physician must always decide about continuing or concluding the collection in terms of the donor, independent from the requested cell number.
6  Multiple Donations/Multiple Transplantations

6.1 Multiple Donations

6.1.1 These standards do not apply to cord blood donations. These standards apply to second and subsequent blood stem cell donations (marrow, peripheral blood stem cells) or other blood product donations (donor lymphocytes, whole blood) of a specific donor for a recipient.

6.1.2 After the first donation the donor is reserved for two years for the initial recipient in order to be available for a subsequent donation. During this time the donor is not available for another patient.

6.1.3 After the first donation the donor is asked whether he is available for a subsequent donation for the same recipient if needed. The answer is documented.

6.1.4 Because of the clinical situation, minimum time intervals between donations cannot be defined.

6.1.5 The results of the medical evaluation (section 5.4) in the normal range are a basic requirement for a subsequent donation. The donor has to be reserved for the patient he donated to for at least two years. In the case of the patient’s death the donor is to be barred for a year after donation.

6.1.6 A donor who has already donated must not be asked to donate for a second recipient unless no equally compatible donor is available. In such a case, a review by the ZKRD is mandatory.

6.1.7 After a donor has donated twice, it is recommended not to make them available for further donations except lymphocyte donations. A donor should not donate for more than two different patients, and should only donate two times at maximum via each method of donation (PBSC or bone marrow).

6.2 Multiple Transplantations

6.2.1 The transplant center must outline in writing the clinical justification for a further blood stem cell donation for a patient who already received an allogeneic transplant. The medical director of the donor center or the authorized representative must review the request. This regulation is valid regardless of whether the previous transplantation
was carried out with blood stem cells from the same (WU_017, see Appendix B) or a different donor (informal justification).

6.2.2 The written request must include:

- Proposed time frame for transplantation
- Recipient’s preparative therapy plan if applicable
- Data from previous transplant and the current clinical condition of the recipient
- Request forms for bone marrow or peripheral blood stem cells: ZKRD forms WU_003 or WU_004, WU_017 (Appendix B)
- Request forms for donor lymphocytes: ZKRD forms WU_001 and WU_005 (Appendix B)

6.2.3 For non-standard indications or therapies whose efficacy is being assessed in clinical studies, the transplant center must provide a copy of the clinical study protocol and its approval by the responsible ethical committee.

6.3 Procedures for Peripheral Blood Stem Cell and Bone Marrow Requests

The procedures (donor information, medical evaluation, collection) are as for a first donation (section 5.2 – 5.6).

6.4 Procedures for Donor Lymphocytes and Whole Blood Requests

6.4.1 Leukapheresis
All blood tests as listed in Appendix C.2.2 must be performed/repeated. At that time the donor’s general health and suitability for donation should be appropriately evaluated. On the day of the leukapheresis the donor is physically examined to assess his eligibility for donation.

6.4.2 Whole Blood
The following criteria are applicable: Item 2.1.4 of the “Guidelines for the Preparation of Blood and Blood Components and the Use of Blood Components (Hemotherapy)” [7].
7 Transport

7.1 General

7.1.1 The transplant center is responsible for the transport. It authorizes a courier to transport the product. The courier must be informed about the product and the transportation conditions.

7.1.2 The product must be transported in a shatterproof and temperature insulating container that is labelled with the warning as described under 7.2. The courier must supply the transport container.
Bone marrow and peripheral blood stem cells must be hand carried during the whole transport by an authorized courier whose name is known by the donor center, collection center and transplant center.
It is recommended to hand carry donor lymphocytes as well. Unaccompanied shipment may be organized if requested by the transplant center and allowed by the donor center.
On request by the transplant center cord blood and whole blood can be shipped by a commercial courier.
The transport temperature must be monitored and documented.
Cryopreserved cord blood units must be transported in a liquid nitrogen shipper (“dry shipper”) that is normally provided by the cord blood bank. The cord blood bank coordinator is responsible for packaging the cryopreserved product in the dry shipper for transport.
Unappropriate transport conditions and deviations must be documented.

7.1.3 In general, the temperature specified by the transplant center needs to be maintained. The product temperature needs to be monitored and logged electronically [1].

7.1.4 The product must be transported without delay ensuring an expedient and safe delivery.
When a car is used for transportation, two couriers should be provided.

7.1.5 In the event of courier travel by air flight, the product must be transported as carry-on luggage.

7.1.6 The collection center must check the identity of the courier and the product.

7.1.7 If there are justified doubts about a proper transport, the head of the donor center/collection center must take measures to guarantee a proper transport.
Locked dry shippers may be transported in the cargo hold of aircraft. The courier should monitor the loading of the dry shipper.
7.1.8 The courier details are to be determined and notified to all parties concerned in time before the onset of the transport: within Germany 3 working days, internationally 5 working days prior to collection.

7.1.9 In cooperation with the transplant center, when importing products from (non-EU) third countries, the ZKRD declares the product at customs and provides the necessary customs documentation based on the courier details. The responsibility for the declaration of German products being exported into third countries lies with the economic owner at the time of export. For exports into third countries, the donor center is responsible for handing over the customs documentation to the courier; for imports from third countries, the transplant center or the commercial courier company is responsible.

7.2 **Product Labeling**

The product must be labeled according to current laws, guidelines and regulations [1], [5], [6], [28]. Due to the small size of cryopreserved cord blood product bags there might not be enough space to list all data on the product label. Data, which does not have to be listed on the product label, will be provided on a separate document.

The label of the container must contain the following warnings:

- MEDIZINISCHER TRANSPORT: Vorsichtig behandeln
- NICHT BESTRAHLEN!
- Menschliche Zellen zur Transplantation
- Von Hitzequellen fernhalten, nicht einfrieren
- Unverzüglich weitergeben!
- MEDICAL SPECIMEN: Handle with care
- DO NOT X-RAY!
- Living human cells for transplantation
- Do not place near heat, do not freeze
- Immediate delivery required!

7.3 **Accompanying Documentation**

7.3.1 Accompanying Document

The document accompanying the product must contain the following [1], [6]:

- All data of the product label
- Name and address of donor center, collection center and the name of the responsible physician including telephone and fax number
• Product specification
• Donor infectious disease markers including date
• Recipient name and number
• Name and address of transplant center including contact person’s name, telephone and fax number
• For cryopreserved cord blood units: Information about the preparation of the transplantation (product thawing, washing etc.) and a recipient follow-up form for documentation of clinical outcome to be returned to the cord blood bank
• Name and signature of the person at the collection center handing over the product to the courier
• Date and time of product handover to the courier
• Name and signature of courier.

Additionally, the current laws, guidelines and regulations must be followed.

7.3.2 Documents for Airport Security
For courier travel by air flight, the courier must carry documentation for security that comprise the following:

• Name of courier
• Identity card number/passport number
• Flight itinerary, especially departure/arrival airports, departure and arrival dates and times and flight number
• Product specification
• Warning that the transplant may not be X-rayed and that every transport delay should be avoided.

7.3.3 For courier travel by air flight, the airport security authorities, the airlines and if international transport is involved the Federal Border Guard of the respective airports must be informed of the product transport.

7.4 Courier

7.4.1 Courier Requirements
The institution which provides the courier must ensure proper product transport and compliance with the following requirements:

• He must know and understand the significance of the product.
• He must have been approved by the donor center, collection center or transplant center, and they must have trained him.

• He must not be related to the donor or recipient.

• He must be an experienced traveler and know how to deal with typical incidents during transport of stem cells or travel disruptions.

• He must not have other commitments or interests until he has delivered the product.

• For international transport, he must have an internationally valid credit card with an adequate available credit limit.

• For international transport, he must have adequate command of English.

• A back-up flight should be booked.

Furthermore the applicable laws, guidelines and regulations of the country must be followed as well as the standards and recommendations of the WMDA.

7.4.2 Courier Responsibilities

• When accepting the product, he must check the number and type of requested product bags and samples. He must check the labeling and the accompanying documents for information as detailed in section 7.2 and 7.3.1.

• He must place the product bags properly in the transport container (this does not apply to dry shippers).

• He must inform the aircraft staff about the medical transport at flight booking, at check-in, at the gate and in the aircraft.

• During export into third countries or import from third countries, the courier must generally show the respective documentation at the customs. Hence the transport may not be significantly delayed.

• He must never leave the product unattended (this does not apply to dry shippers).

• In addition to the documents as listed in section 7.3.1 and 7.3.2 he must carry the following documents during product transport:
  – Product Prescription Form
  – Emergency contact numbers of transplant center and donor center

• He must promptly inform the transplant center of possible delays.

• He must hand over the product to a staff member of the transplant center.

• He must record the delivery and report it to the donor center.

• He must always maintain recipient and donor confidentiality.
8 Post Donation Donor Follow-up

8.1 General

8.1.1 Directly following the donation, the responsible collection center physician is responsible for the evaluation of the donor’s well-being.

8.1.2 The collection center physician is responsible to assess if and for how long the donor is unable to work and issues a medical certificate of disability if necessary. The donor center must pay for any loss of earnings this incurs.

8.1.3 The donor center is responsible for the donor follow-up after the donor’s discharge from the collection center by the collection center physician in charge.

8.1.4 The donor center and collection center, respectively must keep records of all corresponding donor contacts, his statements relating to the donation and all initiated examinations and therapies.

8.1.5 Serious events and adverse effects during and after a donation as well as during mobilisation must be reported to the ZKRD according to the WMDA SEAR program. Annual reporting is required even if there were no events.

8.1.6 Serious events and adverse effects at collection, processing, transport or at/post transfusion of the cells which affect the safety and quality of the cells and therefore the safety of the recipient must be reported to the ZKRD according to the WMDA SPEAR program. Annual reporting is required even if there were no events.

8.1.7 There are no risks for the donor (newborn baby) associated with a properly performed donation of cord blood. Therefore, cord blood banks are not required to perform donor follow-up.

8.2 Donor Contacts

8.2.1 The donor center must contact the donor by telephone or in person within one week of the donation to evaluate his physical and emotional well-being. Content-related recommendations can be found in WMDA forms\(^9\). It must be documented if the donor center is unable to reach the donor.

8.2.2 If the donor has any unusual complaints, a medical evaluation must be performed. The responsible collection center physician must be informed about it.

\(^9\)status 2014-12-18: www.worldmarrow.org forms DF1 and DF2
8.2.3  6 months, 1, 2, 5 and 10 years after donation, the donor must be contacted by sending a questionnaire (see appendix B).

8.3  Post Donation Donor Testing

8.3.1  As a minimum, a blood count is to be performed after every apheresis or bone marrow collection. Additional blood examinations fall into the physician’s responsibility and depend on the individual donor situation depending on the blood volume processed or the volume of the collection, respectively.

8.3.2  30 days post donation, the donor center has to arrange for at least the following tests: blood count, protein, creatinine, uric acid, and in the case of bone marrow donation, additionally ferritin.

8.3.3  The medical assessment of relevant pathological findings must be initiated by the donor center.

8.3.4  Findings that may affect the recipient must be reported to the transplant center.
9 Post Transplant Recipient Follow-up

9.1 Information About the Recipient’s Condition Post Transplant

9.1.1 If the preparation is not infused, the collection center, the donor center and the cord blood bank, respectively, as well as the ZKRD must be informed about the disposition of the preparation. Alternatively only the ZKRD may be informed for forwarding to the respective partners.

9.1.2 The recipient must be informed and his consent must be obtained prior to submitting and using any medical follow-up data. According to the drug licensing procedures of the Paul-Ehrlich-Institut, the cord blood banks must collect recipient follow-up data.

9.1.3 Upon request, the transplant center must inform the ZKRD or the donor center of the recipient’s condition at 3 months, 1 year, 2 years and 5 years post transplant (e.g. ZKRD forms F0_002 and F0_003 – Appendix B).

9.2 Donor Recipient Contact

9.2.1 Donor and recipient may share anonymous correspondence post transplant. Any correspondence must be screened by the ZKRD and the donor center respectively to ensure all personally-identifying information is removed before it is forwarded.

9.2.2 Direct contact between donor and recipient is not allowed until after two years after the first transplant date at the earliest. Before any direct contact is allowed the donor center and the transplant center must inform both the donor and the recipient or his legal guardian of the benefits and risks of direct contact, and they must obtain their signed consent authorizing the release of personal information. (ZKRD Form EV_001 and EV_002 – Appendix B). After a subsequent donation of the same donor on behalf of the same recipient, direct contact is allowed one year after retransplant at the earliest. It is recommended to organize at least one written contact between donor and recipient before anonymity is cleared. The date of retransplantation does not shorten the initial period of two years.

9.2.3 Direct contact between the core family of a deceased recipient/donor and the donor/recipient is allowed without a waiting period if both parties have signed an informed consent form. If third parties want to reveal the anonymity after the death of a patient/donor, the core family of the patient/donor have to agree.
10 Data Protection, Anonymity and Record Retention

10.1 Data Protection

10.1.1 All institutions involved must have a data protection officer.

10.1.2 The personnel must be informed about the regulations of data protection and must commit themselves in writing to observe the data protection regulations. This also includes medical information with respect to legal requirements involving physician’s confidentiality. Only a physician may inform a donor about abnormal findings.

10.1.3 Data security must be ensured. The spacious condition in particular must ensure that only authorized staff has access to donor and patients records.

10.1.4 The protection of an individual against unlimited data collection, recording, use and transfer of his personal data must be guaranteed according to the Federal Data Protection Law [12] and the German Social Security Code X (protection of social data) [23]. Furthermore, the corresponding federal state data protection laws, state archive laws and health care laws are also applicable.

10.2 Anonymity

In the course of all processing steps and manufacturing processes the anonymity of donors and patients must be strictly maintained and protected. For the protection of anonymity the following applies:

- Access to personal data of donor and patient must be limited to authorized institutions (e.g. donor center, collection center).
- All donor related information that is communicated externally must not contain names but only pseudonymous codes.
- Neither the donor’s name or patient’s name nor any other information providing indication of their identity must be circulated.
- After a collection or transplantation, upon request, the donor and patient may be informed about gender, origin and age of their partner in a general way that the anonymity will be sustained.

For donor and recipient contact, see also section 9.2.
10.3 Record Retention

10.3.1 Records

The following records must be retained:

- Donor records: Consent forms, documentation of information sessions and medical measures, health history questionnaires, all records documenting HLA typing and examination results.

- Patient records: Search requests, diagnostic findings, medical reports, consent forms and documents pertaining to search initiation, search results and requests and results of further testing.

10.3.2 Description of Record Retention

Records and all electronic data are to be kept secured from unauthorized access. Details are regulated by the Federal Data Protection Law.

10.3.3 Retention Periods

The requirements of record retention must be in compliance with the regulations for record retention of medical services according to the respective Medical Association’s professional code of conduct or other legal instructions.

Due to possible controversial cases/questions of liability, patient records should be retained until the end of the civil law limitation period of 30 years after the conclusion of treatment. In case of uncertainty the longer period is valid. This period starts with the end of the year in which the last entry is made. This is also valid for records of donors who have donated blood stem cells or have been pretreated for this purpose.

10.3.4 Disposal of Records

After expiration of the retention period, records must be discarded either by the center itself or by a qualified external disposal company in a way to render record reconstruction impossible.
References


Members of the Standards Committee

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## Appendix: Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>ALAT</td>
<td>Alanine Aminotransferase</td>
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<tr>
<td>AMG</td>
<td>Arzneimittelgesetz (German Drug Law)</td>
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<td>AMWHV</td>
<td>Arzneimittel- und Wirkstoffherstellungsverordnung</td>
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<tr>
<td>Anti-HBc</td>
<td>Hepatitis B Core Antibody</td>
</tr>
<tr>
<td>AP</td>
<td>Alkalische Posphatase (alcaline phosphatase)</td>
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<tr>
<td>ASAT</td>
<td>Aspartate Aminotransferase</td>
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<tr>
<td>ASHI</td>
<td>American Society for Histocompatibility and Immunogenetics</td>
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<tr>
<td>BÄK</td>
<td>Bundesärztekammer (German Medical Association)</td>
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<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
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<tr>
<td>CRP</td>
<td>C-Reactive Protein</td>
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<tr>
<td>CT</td>
<td>Confirmatory Typing</td>
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<tr>
<td>DAG-KBT</td>
<td>Deutsche Arbeitsgemeinschaft für Knochenmark- und Blutstammzelltransplantation (German Working Party for Marrow and Blood Stem Cell Transplantation)</td>
</tr>
<tr>
<td>DGI</td>
<td>Deutsche Gesellschaft für Immungenetik (German Society for Immunogenetics)</td>
</tr>
<tr>
<td>DNA</td>
<td>Desoxyribonucleic Acid</td>
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<tr>
<td>EBMT</td>
<td>European Group of Blood and Marrow Transplantation</td>
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<tr>
<td>EBV</td>
<td>Epstein-Barr Virus</td>
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<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
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<tr>
<td>EFI</td>
<td>European Federation of Immunogenetics</td>
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<tr>
<td>Gamma GT</td>
<td>Gamma-Glutamyl-Transferase</td>
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<tr>
<td>G-CSF</td>
<td>Granulocyte Colony Stimulating Factor</td>
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<tr>
<td>HBsAg</td>
<td>Hepatitis B Surface Antigen</td>
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<tr>
<td>HCG</td>
<td>Human Chorionic Gonadotrophin</td>
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<tr>
<td>HCV</td>
<td>Hepatitis C Virus</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>HLA</td>
<td>Human Leukocyte Antigen</td>
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<tr>
<td>HTLV</td>
<td>Human T-Lymphotropic Virus</td>
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<td>IATA-DGR</td>
<td>International Air Transport Association - Dangerous Goods Regulations</td>
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<td>LDH</td>
<td>Lactate Dehydrogenase</td>
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<td>NMDP</td>
<td>National Marrow Donor Program</td>
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<td>PBSC</td>
<td>Peripheral Blood Stem Cells</td>
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<td>PCR</td>
<td>Polymerase Chain Reaction</td>
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<td>Abbreviation</td>
<td>Description</td>
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<td>--------------</td>
<td>-------------</td>
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<tr>
<td>PTT</td>
<td>Partial Thromboplastin Time</td>
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<tr>
<td>SEAR</td>
<td>Serious Events and Adverse Effects Registry</td>
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<tr>
<td>SGB</td>
<td>Sozialgesetzbuch (Social Security Code)</td>
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<tr>
<td>SOP</td>
<td>Standard Operating Procedure (Working Instruction)</td>
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<tr>
<td>SPEAR</td>
<td>Serious Product Events and Adverse Effect Registry</td>
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<tr>
<td>TNC</td>
<td>Total nucleated cell count</td>
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<td>WMDA</td>
<td>World Marrow Donor Association</td>
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<tr>
<td>ZKRD</td>
<td>Zentrales Knochenmarkspender-Register Deutschland</td>
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Appendix: ZKRD Forms and Questionnaires

All current versions of forms and questionnaires are provided at the ZKRD homepage [http://www.zkrd.de]. → "'Partner-Login’’ → “’zu den Formularen”’ bzw. "’zu den Fragebögen’’"
C Appendix: Preparing Blood Stem Cell Donations: Donor Information and Medical Evaluation

C.1 Donor Information

The donor information session must be conducted by an adequately trained person using terms that are easily understood by the donor. Information must be given to the donor at the time of the donor medical evaluation at the latest and must include at least the following:

C.1.1 Information about the Request and Procedures

- Donor exclusion criteria for blood stem cell donations
- Therapeutical value of blood stem cell donations and possible benefit for the recipient
- Information if the planned transplantation is developmental and if its efficacy is assessed in clinical studies
- Donation methods: bone marrow and peripheral blood stem cell collection
- Product preference of transplant center
- Examinations before and after donation and the donor’s right to have the results explained as well as the physician’s general duty to inform the donor in case of suspicious findings
- Preparatory pre-collection procedures and the procedure of the blood stem cell collection
- Required blood sample collections (pre-collection samples and blood samples on the collection day)
- Time commitment
- Anonymity
- Non-remuneration of donation
• Extent to which donor expenses will be compensated by the donor center
• Type and extent of insurance coverage
• Information on safeguards to protect the donor
• Possibility of consulting a donor advocate
• Instructions for the time of G-CSF mobilization and availability of contact information of the physician on duty
• Requirement of bone marrow donation if the G-CSF mobilization is unsuccessful or must be interrupted
• Possibility of second or subsequent blood stem cell or blood product requests for the same recipient (e.g. in the event of relapse or non-engraftment)
• Protocol requirement of second or subsequent blood products
• Requirement of signed donor consents (section 5.5)
• Right to withdraw at any time, however the donor must be informed of and understand the risk up to death risk for the recipient should the donor withdraw after the beginning of the recipient conditioning therapy.

C.1.2 Information about Risks

• Risks and side effects of pre-donation examinations, anesthesia, marrow donation, administration of G-CSF and peripheral blood stem cell donation by apheresis and other blood product donations
• Marrow donation: Possible need for allogeneic blood transfusion in emergencies
• Peripheral blood stem cell donation: Possible need for allogeneic blood transfusion (e.g. thrombocyte transfusion) in emergencies; explicit reference to G-CSF’s side effect profile
• Possible use of a central venous line for apheresis and associated risks if blood stem cells cannot be collected using peripheral veins
• Information regarding the risk of infectious disease transmission to the recipient by blood stem cell transplantation

C.2 Donor Medical Evaluation

C.2.1 Medical Examination

• Health history
• Physical examination
• Resting ECG
- Abdomen sonography, in particular a spleen sonography if peripheral blood stem cell donation is performed
- Chest X-Ray (recommendation)
- Pulmonary function testing (recommendation)
- For peripheral blood stem cell donations: Assessment of peripheral venous access

C.2.2 Blood Tests

During donor medical examination, the testing below must be performed. The infectious disease testing must be performed on a blood sample that has been drawn within 30 days before donation. It may need to be repeated (see chapter C.2.4).

- Complete blood count with differential, CRP
- Coagulation testing (Quick’s test, partial thromboplastin time)
- Sodium, potassium, calcium, ferritin, creatinine, uric acid, urea, ALAT, ASAT, lactic dehydrogenase (LDH), alkaline phosphatase, gamma-glutamyl transferase, total bilirubin, recommended before bone marrow collection: choline esterase
- Total protein, protein electrophoresis
- TSH
- Blood sugar
- Infectious disease testing (additional testing must be performed if mandated by the most current guidelines [1]): Syphilis test, HbsAg, anti-HBe, anti-HCV, anti-HIV 1 and 2, CMV IgG and IgM, anti-HTLV 1 and 2, HIV-PCR, HCV-PCR, EBV IgG and IgM, recommendation: toxoplasmosis IgG and IgM
- Blood group testing (ABO group and rhesus type)
- Irregular antibodies
- For female donors: Pregnancy testing (Beta-HCG testing to exclude pregnancy)

C.2.3 Procedures

- In case of statements in the medical history or findings that may increase the risk for the donor but do not necessarily exclude him from donation: The donor must be counseled regarding the statements and findings and the associated additional risks. The counseling must be documented in writing. The donor has the right to decline donation.
In case of statements in the medical history or findings that may increase the risk for the recipient: The transplant center must be informed of the statements and findings and must determine whether the statements or findings increase the risk to the recipient. Statements or findings that increase the recipient risk must be reported to the recipient and he must be counseled regarding the increased risk. The counseling must be documented in writing. The transplant center must communicate in writing if the donor is acceptable.

The examining collection center physician must notify the donor center in writing of the results of the medical evaluation and donor eligibility for collection.

The donor center must report the donor clearance for collection and the results of the donor infectious disease testing on the appropriate form (ZKRD Form WU_009 – Appendix B) to the ZKRD, the transplant center or the international registry if the examining collection center physician determines that the donor is eligible for donation and the donor has signed the consent to donate form.

The donor must be informed about abnormal findings and examinations resulting from them.

Counseling of female donors of childbearing age regarding safe methods of contraception must be documented in writing. Repeated exclusion of pregnancy is recommended two days before the first G-CSF injection or bone marrow collection, respectively.

### C.2.4 Repeat Examinations

Infectious disease testing must be repeated if results were from testing more than 30 days prior to the scheduled collection.

If more than eight weeks have elapsed since the donor medical evaluation, the following examinations must be repeated (this applies also in the event of a subsequent donation for the initial recipient):

- Between 8 and 12 weeks since the most recent complete donor medical evaluation: Interview with the donor to determine if there are any changes to the donor’s condition or health history. Repeat infectious disease testing. Female donors: Repeat pregnancy testing.

- Between 12 weeks and 6 months since the most recent complete donor medical evaluation: In addition to the above-listed items: Repeat all blood testing according to section C.2.2.

- The donor medical evaluation must be repeated in its entirety if more than 6 months have elapsed since the most recent complete evaluation.
## D Appendix: List of Differences between Versions 9 and 10

<table>
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<td>&quot;severe infectious diseases&quot;, &quot;Furthermore he must assure...&quot;</td>
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| 2.4.2         | deleted| "(valid for first-time reporting of donors from January 1st 2012)"
<pre><code>           | added  | &quot;When registering...&quot;                                                   |
</code></pre>
<p>| 3.1           | added  | new from &quot;The reservation concept...&quot;                                  |
| 3.3.2         | modified| &quot;must&quot; to &quot;should&quot;                                                      |
|               | added  | &quot;In addition...detailed information&quot;                                   |
| 3.3.3         | added  | &quot;and should be evaluated by a physician&quot;                                |
| 3.3.5         | added  | &quot;According to a WMDA... written informed consent.&quot;                     |
| 5.1.7         | added  | new paragraph                                                           |
| 5.3.2         | added  | &quot;In cases of a parallel...&quot;                                            |
| 5.4.5         | added  | &quot;and documented by his or her signature&quot;                                |
| 5.5.2         | added  | &quot;a sonographic evaluation...cannot be excluded anyway,&quot;                |
| 5.5.4         | added  | &quot;In addition,...&quot;                                                      |
| 5.5.7         | modified| newly phrased including link to chapter 3.3.5                         |
| 5.6.10        | added  | new paragraph                                                           |
| 5.6.12        | modified| newly phrased, link to [5]                                              |
| 6.1.1         | deleted| &quot;buffy coat&quot;                                                            |
| 6.1.6         | added  | &quot;In such a case,...&quot;                                                   |
| 6.1.7         | modified| newly phrased and extended                                              |
| 6.4           | deleted| &quot;Buffy Coat&quot;                                                            |
| 6.4.2         | deleted| &quot;Buffy Coat and&quot;                                                       |
| 7.1.3         | modified| newly phrased                                                           |
| 7.1.9         | added  | new paragraph                                                           |
| 7.2           | added  | &quot;The label of the container...&quot;                                        |</p>
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