ZKRD Zentrales
Knochenmarkspender-
Register Deutschland

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German Standards for Unrelated Blood Stem Cell Donations

This translation is intended to aid in reading the original document and is not legally binding. The text was translated to the best of our knowledge, and no responsibility is taken for translational errors or outdated content.

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Contents

Preamble

These standards have been compiled by a Standards Committee, which is composed of representatives from the ZKRD, donor centers, search units, cord blood banks, collection centers and transplant 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 [1].

These standards shall guarantee a high level of quality and safety as well as harmonized procedures with regards to processes and documentation as well as data protection. This helps to protect the interests of all donors and patients, and creates better transparency for all national and international organizations involved. The German standards are binding minimum requirements, which may be handled more strictly by individual organizations. Valid laws, guidelines and contracts in the current version will remain unaffected.

These standards are reviewed and updated if needed at least every two years by the Standards Committee. In doing so, new medical developments, regulations and guidelines are to be considered as well as suggestions of organizations, which are active in the area of donor search and donor procurement.

The organizations mentioned in this document commit themselves to comply with the standards that apply to their organization.

In the following text, for reasons of better readability, 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”, “cord blood” or “undirected stem cell products from aphereses”.

Binding standards have been indicated by using the imperative form or the respective form of the words “must” or “not permitted”. Standards which are suggested contain wording such as “recommended”, “can” or “should”.

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

When forms are referred to, generally the name of the respective ZKRD form is used. Forms may be replaced by documents with an equivalent content.

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 operation and adequately qualified staffing of all essential functional units during regular office hours. Where the term ”regular office hours” is used in this document, the following applies:
Monday-Friday 8.00 a.m. - 4.00 p.m. on working days.
Outside of office hours availability must be guaranteed for emergency cases.

1.1.1.5 It must be ensured that at least one person is always 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 The ZKRD must maintain a quality management system at least corresponding to the definition of the WMDA standards. It must ensure and document compliance with these Standards comprising especially document management, records, staff training and further education, complaint management and traceability.

1.1.2 Duties

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 are accepted and processed by the ZKRD exclusively. Generally this also applies to search requests from abroad.[1,2]

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 without delay.

1.1.2.4 Upon request the ZKRD activates a donor search and obtains, where required, a confirmation from health insurers to cover the costs for the search, by submitting to them auditable documents.

1.1.2.5 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.

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

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

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

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

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

1.1.2.11 The ZKRD coordinates and leads the negotiations with the head organizations of the compulsory health insurances in the Project Committee (Projektkommission) [15].

1.1.2.12 The ZKRD fulfills the duties of a national registry according to the corresponding WMDA Standards and recommendations [1][23].

1.1.2.13 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 utliize a simplified export process.

1.2 Donor Center

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.

[1] Existing contracts with the NMDP concluded up to 2000-01-01 remain unaffected.

[2] 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. The medical director or a designated representative must have the necessary professional qualification for 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 1.1.1.4. It is permitted to deviate from the regular office hours (e.g. 9:00 - 15:00) if reachability in the case of an emergency is assured.

1.2.1.6 It must be ensured that during regular office hours 1.1.1.4 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 The donor center must maintain a quality management system that corresponds to the minimum requirements regarding a quality management system for the respective institution according to the definition of the WMDA standards. It shall particularly comprise standard operating procedures (SOPs) and records, staff training and further education, complaint management and traceability, and it shall document compliance with these Standards.

1.2.2 Cooperation with Other Organizations

1.2.2.1 All organizations cooperating with the donor center must comply with the standards defined for them.

1.2.2.2 A cooperative agreement between the ZKRD and the donor center must be in place.

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.

1.2.3 Duties

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. Further information may be necessary according to the current specifications of the WMDA, which the donor center will be notified of in due 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 duties of the donor center are listed under Chapter 2 to 10.

1.3 Search Unit

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. Staff qualification should include training in a medical, medical technical or scientific profession. Additional experience in the areas of histocompatibility/immunogenetics is recommended; alternatively completion of the WMDA Search Coordinator Certification Programme is a suitable qualification.

1.3.1.4 During regular office hours 1.1.1.4 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 The search unit must maintain a quality management system that corresponds to the minimum requirements regarding a quality management system for the respective institution according to the definition of the WMDA standards. It shall particularly comprise standard operating procedures (SOPs) and records, staff training and further education, complaint management and traceability, and it shall document 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 between the ZKRD and the search unit must be in place.

1.3.3 Duties

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 immunogenetics laboratory, guarantee the storage of cell/DNA samples from donors selected for transplantation and from patients for quality control and scientific analysis for at least five years. In the case of scientific analyses from blood samples, an approval of the ethics committee and the respective informed consents must be in place.

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

1.4 Cord Blood Bank

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) [7] and the German Good Manufacturing Regulation (AMWHV) [14]

1.4.1.3 The cord blood bank must have a manufacturing license according to the German Drug Law (AMG) [7] and a medicine product authorization of the Paul-Ehrlich-Institut (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 1.1.1.4. It must be ensured that 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 Cord blood units must be identified in a way that an assignment to donor and patient is possible for 30 years after transplantation.

1.4.1.11 The cord blood bank must maintain a quality management system that corresponds to the minimum requirements regarding a quality management system for the respective institution according to the definition of the WMDA standards. It shall particularly comprise standard operating procedures (SOPs) and records, staff training and further education, complaint management and traceability, and it shall document compliance with these Standards.

1.4.2 Cooperation with Other Organizations

1.4.2.1 All organizations 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.

1.4.2.3 A cooperative agreement between the ZKRD and the cord blood bank must be in place. It may be integrated in an agreement between the ZKRD and the respective donor center.

1.4.3 Duties

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

1.4.3.2 Before the donation the mother must be informed in writing about the whole process, especially benefits, risks, data protection 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: Developments during the pregnancy, risk of transmissible diseases of the mother, genetically determined familial diseases of the hematopoietic system (including the biological father and all 4 grandparents). Abnomalies during birth and diseases or deformities of the child must be documented. 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 +/- 7 days of delivery according to the guidelines of the German Medical Board [2] as well as directives of the Paul-Ehrlich-Institut.

1.4.3.5 If relevant positive infectious disease marker testing results or other extraordinary results are determined, the mother must be informed and counselled by a physician.

1.4.3.6 The cord blood bank ensures that samples collected are normally tested within three months and that data is promptly transmitted to the ZKRD, utilizing a distinct identifier. At a minimum, the following data is necessary for registration of a product: AB0 blood group and rhesus type, product size (total nucleated cell count, TNC) as well as HLA-A, -B, -C and -DRB1 (low or high resolution by molecular techniques). HLA must be determined in an EFI- or ASHI-accredited laboratory.
All typing must be performed using molecular techniques. In the documentation, serologic data is not to be derived from molecular data or vice versa.

1.4.3.7 Before the product is shipped the identity of the cord blood unit must be checked using a validated process.

1.5 Collection Centers

1.5.1 Centers collecting, manufacturing or distributing hematopoietic stem cell products from peripheral blood or bone marrow must possess the respective manufacturing license according to the German Drug Law (AMG) corresponding to §13 or §20b/c, respectively, as well as a permit from the federal authority according to §21a AMG for direct application in a known individual. It is recommended that collection centers work towards obtaining a JACIE accreditation. Furthermore, they must observe the applicable laws, guidelines and regulations in their current versions. [2], [18], [3], [7], [8], [9], [10], [14], [19].

1.5.2 A cooperative agreement between the ZKRD and the collection center must be in place.

1.6 Transplant Center

1.6.1 Transplantation of blood stem cell products from unrelated donors may only be performed in centers that possess the required expertise [2] and report their transplant data to the DRST. It is recommended to achieve JACIE accreditation [20] within two years after commencing with these transplant services, at the latest.

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 [2], [5], [8].

1.6.5 A cooperative agreement between the ZKRD and the transplant center must be in place.

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 [**?**], [17].

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.

1.7.2 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 ”Guideline for the Preparation of Blood and Blood Components and for the Use of Blood Components (Hemotherapy)” [3], as well as the ”Guidelines of the German Medical Board for Quality Assurance of Quantitative Medical Laboratory Tests” [4] in the current version.

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 maternal donors prior to cord blood donation.

Staff of the donor center or cord blood bank (as well as hospital staff working with the cord blood bank), which is responsible for or actively involved in informing donors or pregnant women (e.g. requirements, exclusion criteria, consent, etc.) must have been previously trained. This training shall be documented.

The information must contain the following items (items marked with * do not apply to cord blood donation):

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 9.2 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 itself.

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

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

2.1.10 Transmission of HLA typing results and other data important for donor selection in pseudonymized 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 for Registration

2.2.1 The donor must be at least 17 years old for their data to be transmitted to the ZKRD. For donors under 18 years of age, the ZKRD automatically issues the status of "not available" (TU) until they have reached the age of 18.

2.2.2 As of a donor's 61^{st} birthday, they are no longer registered with the national registry nor do they appear on match lists. At this point only data required by regulation is retained according to the applicable retention period. Donors should be informed accordingly by the donor center.

2.2.3 By signing the registration documents the donor assures to the best of their knowledge that they are healthy and are not afflicted by any of the following medical conditions:

- severe cardiovascular disease
- severe pulmonary disease
- severe kidney disease
- severe neurological disorder
- severe metabolic disease
- tropical diseases and severe chronic infectious diseases
- infections with HIV, hepatitis B or C
- systemic autoimmune diseases or othere severe chronic illnesses
- cancer
- severe illness of the blood or immune system
- severe psychological disorders

2.2.4 Further conditions for cord blood donations are:

- The biological mother must be able to understand the medical history questionnaire and the included information, in language and content, without being distracted by aspects of labor.
- A written medical history by means of a standardized questionnaire must be obtained and carefully evaluated.

2.3 Donor Consent

2.3.1 The signed donor consent form must include the following items:

- consent to store personal data in the database 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 centers
- confirmation of acknowledgement of exclusion criteria
- consent to store and possibly perform further HLA or other transplantation relevant testing, which does not fall under the Gendiagnostikgesetz (German Genetic Diagnostics Law) on the samples at a later date
- consent to the donor center requesting current contact data via the residents' registration office.
- In addition to the first five subpoints, the following applies 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 no personal claims regarding possession are made.

2.3.2 A written confirmation of the registration must be given to the donor. It is recommended to issue the donor an identification card and/or provide them with a copy of their consent.

2.4 Further Procedures

2.4.1 If a blood sample is collected for donor registration, this must be performed 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 delivery room (e.g. midwife).

2.4.2 The donor center ensures that the samples drawn from the registered donor are HLA-A, -B, -C, -DRB1, and -DQB1 typed, normally within three months. Donors are registered using the internationally recognized GRID (Global Registration Identifier for Donors) and their data is promptly forwarded to the ZKRD.
All typing must be performed using molecular techniques. In the documentation, serologic data is not to be derived from molecular data or vice versa.

2.4.3 It is recommended that the donor is contacted annually, and that the return information is documented. Every five years at the latest, the contact data must be checked and documented.

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

3 Donor Testing

3.1 General

In the case of adequate HLA-compatibility of the patient and a potential donor, requests for further donor testing are transmitted to the donor center 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 it is suspected 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 Requests for HLA testing must be able to be fulfilled using molecular techniques at high resolution.

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 testing of cord blood products is subject to the requirements of the German Medical Association as well as the Paul-Ehrlich-Institut. This also applies to the diagnostic methods used regarding infectious disease markers of the pregnant woman and the infant (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 conducted. If tests are to be performed in addition to HLA testing, specifications of the German

Genetic Diagnostics Law must be observed as applicable. Furthermore, the following must be obtained:

- donor health history questionnaire (see Appendix C)
- signed donor consent form (see Appendix C).

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 [24] 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 evaluated by a physician. In case of cord blood units, testing is performed on a stored sample, if possible, on an attached segment.

3.3.4 The maximum blood sample volume that is shipped to the search unit for confirmatory testing is 50 ml. Additionally, up to 20 ml blood is sent to the donor center laboratory for ABO/Rh typing and infectious disease marker testing.

3.3.5 CT blood samples are generally not to be used for research purposes.

According to a WMDA recommendation [25], 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 being informed accordingly, the donor may give their written consent.

3.3.6 The blood tubes must be labeled with the currently valid donor identification number (GRID), patient number and the collection date. Packaging and shipment must meet the regulations of the International Air Transport Association (IATA-DGR) relevant for the shipment of dangerous goods.

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 A physician of the donor center must inform the donor of any pathological findings.

3.4 Confirmatory Typing Results

3.4.1 In case of discrepancies between HLA typing results, the discrepancy must be clearly resolved. In case of a continuing discrepancy, repeat testing on a fresh donor sample (e.g. blood sample or buccal swab) must be performed; for cord blood a separate retained sample is to be used. The donor or the cord blood unit 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 levol of resolution, the donor center must upgrade the donor typing accordingly.

3.4.3 When reporting results of confirmative typing, the donor can generally be reserved for 3 additional months. An extension can be granted by the donor center to accommodate changes in the patient's medical status.

3.5 Health and Availability Check

3.5.1 Under certain conditions a health and availability check (HAC) can be requested during the search process, in lieu of CT sample procurement. The following criteria need to be fulfilled to request a HAC:

- DNA-based high resolution typing results for at least HLA-A, -B, -C, -DRB1 and -DQB1 must be available for the donor. If high resolution typing results at these loci are not yet available for the patient, the probability for the desired match grade (usually 10/10 or 9/10) must be at least 90%.
- The donor has already had at least one previous confirmatory typing test (high resolution), tested on a new blood sample
  or
  there must be documented urgency for the transplantation, e.g. based on the specific diagnosis and the desired time frame for transplantation. Urgency is justified if transplantation must take place within 6 weeks after the search has been initiated. Regarding the diagnosis, the DAG-KBT guidance on stem cell transplantation [6] (section "Indikationen") is to be observed.

3.5.2 To protect the interests of donors, a HAC should be the preferred option for donors who have previously been requested for CT with consistent, high resolution results. Should the donor center have records of previous CT results, the requesting institution will be contacted and requesting a HAC will be recommended.

3.5.3 A donor information session must be conducted while performing a HAC. As is the case with confirmatory typing requests, the health history questionnaire is used to determine medical eligibility, and donor consent is obtained. Additionally, donor availability is checked.

3.5.4 Atypical donor information listed in the health history questionnaire must be evaluated by a physician.

3.5.5 The donor center reports the expected eligibility and availability of the donor to the ZKRD upon completion of the information session. Finally, further results and applicable transplant relevant information are reported to the ZKRD.

3.5.6 After the results are transmitted, the donor remains reserved for 90 days. In justified cases the reservation may be extended at the request of the transplant center. If no

response is received from the transplant center, the donor is released after these 90 days.

3.5.7 If the donor is subsequently requested to donate, the required confirmatory typing must be performed during the workup by means of pre-collection blood samples (see 5.1.7).
The procedure for national donors, who have not previously been requested for a HAC, but are requested for a parallel CT and workup due to urgent medical reasons of the patient, is described in 5.1.7.

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 cooperation with a transplant center.

4.1.2 If the physician verifies in the medical report that a search for an unrelated donor is necessary, the search can be initiated.

4.1.3 For data protection purposes, before retrieving preliminary results ("PRE-Search"), the patient or their legal representative needs to provide consent (e.g. ZKRD form SU_006).

4.1.4 Before initiating an unrelated search, two HLA typing results of separately drawn patient blood samples must be available. At the latest, correct entry of patient HLA must be checked by the search unit at the time of activation of the search by the search unit (status "NEW").

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.[3]

4.1.5 When initiating the search, the following documentation must be available to the search unit and the ZKRD:

- Medical report on the indication for transplantation
- Patient informed consent including information on patient's health insurance [15]
- Guarantee of payment form signed by health insurance or patient (submission to the ZKRD only).

The medical report and the patient informed consent are not to be older than three months. If the search continues for an extended period of time or is resumed, the medical report and patient informed consent must be reissued after twelve months.

4.1.6 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,

[3] At least one HLA-A,-B,-C,-DRB1 and DQB1 testing must have been performed using molecular technique at high resolution level.

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 compulsary 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]

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 typing 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-HSZT [17]. [5]
Under certain conditions a CT test can be performed after a health and availability check 3.5 or parallel to a workup request 5.1.7.

If eliminating a donor, partial typing is sufficient. However, generally one locus must be completely typed.

If confirmatory testing of cord blood is done, a complete typing result (HLA-A, -B, -C, -DRB1 and -DQB1, molecular technique, high resolution) is always to be provided (independent of if the unit is to be released or reserved).

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 results of HLA compatibility tests of the patient and donor are compiled by an appropriately accredited HLA laboratory. The laboratory provides the written report to the search unit and the attending physician or transplant center.

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 death
- change/discontinuation of indication.

[4] This does not apply for contracts with the NMDP concluded before January 1, 2000.
[5] HLA-A,-B,-C,-DRB1 and -DQB1, HLA-typed using molecular technique at high resolution level.

5 Requesting and Preparing Blood Stem Cell Donations (Donor Workup)

5.1 Workup 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 as described in 5.1.2.

In case of cord blood transplant, the selected cord blood unit is requested and its transport is organized.

5.1.2 It is recommended to send workup requests including all associated correspondence to the respective cooperative partner via the ZKRD. If the request is sent directly to the donor center, the ZKRD must receive a copy of the request from the transplant center.

5.1.3 The request of a donor workup including communication of important data is done with the ZKRD forms `WU_001` and `WU_002`. The ZKRD forms `WU_003`, `WU_004` and `WU_005` are used as the medical prescription (see Appendix C). Cord blood units are requested using ZKRD form `CB_003` as the medical prescription.

5.1.4 The requested cell dose should at least correspond the minimum cell counts mentioned in the current guidelines [2]. The transplant center must justify requests of much higher cell counts.

5.1.5 For non-standard diagnoses (see [6]), a copy of the clinical study protocol and its approval by the responsible ethical committee must be provided. Approval by the director or medical consultant of the donor center or cord blood bank must be documented.

5.1.6 Parallel workup requests of different donors for the same recipient are generally not permitted, rather they are only possible for justified exceptional cases (e.g. high risk that the donor is unsuitable or cannot proceed, serious medical necessity). Parallel requests submitted solely to determine the earliest collection date will be denied for donor protection reasons. If parallel workups are requested, all parties involved (the ZKRD, the donor centers involved) must be informed and have agreed. The affected (backup) donors shall also be informed accordingly.

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 a health and

availability check has already been performed (see 3.5). The following circumstances can justify such a request for reasons of particular urgency:

- donor deferral during a workup
- primary or secondary graft failure
- urgent need of transplantation, e.g. due to failure of induction therapy or known high-risk leukaemia
- relapse.

Under the following conditions, and in such exceptional cases, a parallel request for a CT and workup is possible:

- The patient's search status must be "active".
- The patient must be registered with high resolution HLA at the 5 loci HLA-A, -B, -C, -DRB1 und -DQB1 (this also applies to international patients).
- The donor's HLA at the loci A, B, C, DRB1 and DQB1 must have been tested using molecular technique at high resolution and the probability for a 9/10 match must be at least 90%. Additionally, further acceptance criteria (e.g. CMV, accepted HLA differences) must be taken into account.
- The donor's HLA should have been confirmed at high resolution on at least one new blood sample (e.g. as CT for a different patient).

The parallel request for CT and a blood stem cell donation must be submitted via the ZKRD or the respective donor registry.

The CT result must be provided before the donor begins with G-CSF application or before patient conditioning is initiated.

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

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 A.1.

5.3.2 Before the physical examination at the collection center, the donor must have been given information on the procedures of workup 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 A.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 eligibiliy 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 the responsible physician of the collection/apheresis center [2][3]. Verification of the corresponding data by a second person is recommended. After being signed by the physician, the donor clearance is transmitted to the partners involved (`WU_009`).

5.5 Donor Informed Consent

5.5.1 By signing the consent form donors confirm that they have been informed about the course of events and associated risks involved in the preparatory procedure for and execution of a stem cell collection, as well as the consequences for the recipient if they withdraw their consent to donate after recipient conditioning has already begun. The donor confirms in writing that they have understood the information provided and that all questions have been answered. They receive a copy of the consent document.

5.5.2 If the medical evaluation reveals that due to difficult peripheral venous access a central venous catheter (CVC) cannot be excluded, the donor should only be cleared for bone marrow donation or a different donor should be searched for. Because of the potential complications involved, a CVC should be avoided if possible. In documented exceptional cases, an apheresis procedure using a central venous catheter may be planned at the time of medical evaluation if the donor gives their written informed consent. The CVC can only be inserted by an appropriately qualified physician, and the positioning of the catheter is to be evaluated using an imaging procedure. According to the DGTI recommendations [27][28] specific donor counseling must be performed, and it is required that the operator (physician) has appropriate training in the utilization of these catheters. The insertion and removal of the CVC must be performed under the oversight of the qualified physician. If insufficient venous access for

a peripheral donation is not determined until the day of collection, a CVC may be used in documented and justified exceptional cases upon written consent of the donor.

5.5.3 On the day of the medical evaluation for peripheral blood stem cell apheresis, it must be documented if the donor generally consents to a bone marrow collection if mobilization or the collection does not proceed as planned. If the donor declines a bone marrow collection in the emergency mentioned above, or if a bone marrow collection is not possible for medical reasons, the donor's written consent for cryopreservation of the peripheral blood stem cell product must be obtained prior to commencing with patient conditioning. Additionally, the transplant center must be informed of these circumstances immediately and agree to proceeding (WU_038).

5.5.4 The donor's written consent indicates that a portion of the product may be cryopreserved at the transplant center for subsequent treatment of the patient, if more blood stem cells were collected than needed for the recipient (5.7.1). If the donor does not agree, the transplant center must be informed. The donor consents to the disposal of the product if it is no longer needed for the recipient.

Additionally, at this point the donor must be asked if an alternative use for purposes in accordance with section 5.7.4 is to be excluded.

5.5.5 If a transplant center wishes to use blood samples, product samples 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 is informed in writing in a timely manner of the receipt of the donor request as well as the planned schedule (see data in WU_041). Additionally, international registries/transplant centers must be informed concerning which infectious disease markers are routinely tested for donor clearance, and that further testing, if needed, must be clarified.

5.6.2 If stem cells or cell products are requested from an unrelated donor of a foreign registry, the transplant center can ask the ZKRD to request licensure documents and GMP certification of the respective foreign institutions.

5.6.3 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 C).

5.6.4 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.

5.6.5 After the receipt of the donor clearance for blood stem cell donation (ZKRD Form WU_009) 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.

5.6.6 Health issues arising during the medical examination which prohibit donor clearance or permit donor clearance by exception only must be communicated in written form to the transplant center (WU_043 or WU_038 as applicable).

5.6.7 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 (WU_009).

5.6.8 Donor G-CSF injections are not to be initiated until the transplant center has confirmed the collection date.

5.6.9 If the collection or transplantation is postponed or cancelled, the respective donor center or transplant center must ensure in writing that the corresponding cooperative partner has received the cancellation or postponement, even if it has previously been communicated by phone.

If a postponement is initiated by a transplant center, the current condition of the patient as well as the planned timeframe should be communicated. For postponements of more than 3 months, this information must be communicated.

5.6.10 The donor center must inform the donor of an emergency telephone number, at the time of donor clearance for blood stem cell donation at the latest.

5.6.11 The organizations involved in the coordination of workup, blood stem cell collection and transplant must exchange emergency telephone numbers. The emergency number must be accessible 24 hours a day, 7 days a week.

5.6.12 The ZKRD should receive a copy of the data and communication concerning workup and blood stem cell collection if the workup is not coordinated by the ZKRD.

5.6.13 The decision regarding the number of aphereses is the responsibility of the collection physician. If the recommended minimum dose[6] [2] is reached or, if a higher dose is requested and the cell dose collected is less than 10% below the requested dose, the transplant center should not be consulted and the collection should be concluded.[7]

5.6.14 The stem cell product as a whole or portions thereof may only be used for research purposes in ethically approved studies if the donor has provided written consent. If the product can no longer be used for the original purpose, the preparation is to be discarded or can, if additional consent has been obtained, be utilized as described in section 5.7.4. This applies to cord blood preparations analogously, pursuant to the ”NetCord-FACT International Standards for Cord Blood´´ [21]. The donor center must be informed in detail of the processing of the product.

5.6.15 On the day of collection, in addition to the guideline-conform infectious markers [2][3], 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

[6] status 2019-02-19: 4 x 10^6 CD34 positive cells/kg recipient weight

[7] 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.

- before every bone marrow collection or non-stimulated apheresis: blood count

For estimation of the apheresis time after G-CSF stimulation, when beginning with the first PBSC apheresis the amount of CD34+ cells in the peripheral blood is determined. Additional blood tests are determined by the responsible physician, and are dependent upon the individual donor situation.

5.6.16 At the time of donation, the donor's blood is tested for infectious disease markers according to the applicable guidelines [2][3]. The transplant center must be provided with the results of infectious disease marker testing from the day of collection. Positive test results of product sterility testing must also be provided to the transplant center, together with pathogen differentiation and an antibiogram.

5.6.17 Upon completion of the donation, until the donor is discharged, the respective collection center physician is responsible for the follow-up care of the donor. The donor center must be informed about the course of the donation.
After each apheresis (stem cell as well as lymphocyte apheresis) or bone marrow collection at least one blood count must be performed. Additional blood tests are determined by the responsible physician, and are dependent upon the individual donor situation.

5.6.18 It is the responsibility of the collection center physician to assess if and for how long the donor is unable to work and to issue the corresponding medical certificate if necessary. The donor center must be informed of the duration of the medical leave. The donor center must cover any loss of earnings incurred as a result.

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

5.6.20 After transplantation the transplantation date is to be reported to the ZKRD or donor center in a timely manner.

5.7 Cryopreservation

Stem cell products collected from unrelated donors are normally intended for direct distribution and the immediate transplantation in a specific patient. If the product as a whole or portions thereof are to be cryopreserved, further aspects regarding donor safety and information must be observed.

Part of the collected stem cell product may also be separated off for manufacturing of an undirected stem cell product, which may subsequently be cryopreserved, if mandated by a donor center and if specific conditions are met. This is coordinated with the donor, collection center and, if applicable, the requesting transplant center. Additional regulatory requirements must be adhered to with respect to undirected donations. This process is described in more detail in section 11.

5.7.1 The blood stem cell product should be completely used, if possible. Parts of the preparation can be cryopreserved for later therapeutic use for the same patient. It must be taken into account that a donor´s cell product is only intended for the therapy of a specific patient. The cryopreservation of the complete cell product or a portion therof can only be performed if the donor has provided written consent. If the donor does not consent, the transplant center must be informed. The donor center is to be informed in detail of the use and/or cryopreservation of the product (see also 5.5.4).

5.7.2 Lymphocytes are treated like stem cell products with the exception that portioning and cryopreservation of part of the product generally can be performed. This requires the consent of the donor. If the first portion is not infused within 14 days after collection, the donor center must be informed in a timely manner.

5.7.3 In exceptional cases, cryopreservation of a blood stem cell product at the transplant center prior to the initiation of recipient conditioning may be requested. The medical director of the donor center or his authorized representative must review and document justification for such requests.
If it is planned to cryopreserve the stem cell product, the donor must be informed of the possibility that the product may not be used and possibly may need to be discarded. Without the donor's written consent, the product may not be cryopreserved by the transplant center.
After collection of a product, and upon request of the donor center, the transplant center is to provide information as to if and when a cryopreserved product was infused. The transplant center is to provide the reasons, should infusion be delayed. The donor is to be informed about the current status.

5.7.4 Procedure for non-infused cryopreserved products

Directed products, which have been cryopreserved by the transplant center or collection center and were not infused, can be handled as described in the following subsections.

5.7.4.1 The transplant center informs the donor center, and justifies in detail why utilization of the product for the patient is not possible. If a different use of the product is possible, the donor is informed in detail and separate consent is obtained. If the donor does not consent to an alternative use of the product, the stem cell preparation must be professionally disposed of.

5.7.4.2 The transplant center can provide the donor center with a request for utilization under the scope of a scientific project. This requires details on the specific use of the product. If donor data is also to be used for the project, further requirements of the GDPR (General Data Protection Regulation) must be adhered to. Additionally, documents such as the template for donor consent, approval of an ethics committee and the study protocol need to be provided. The donor center evaluates the request, also with regards to the project's alignment with their corporate purpose. If a positive decision is reached, the donor center obtains donor consent.

5.7.4.3 The transplant center can provide the donor center with a request for utilization for validation purposes. This requires details on the specific use of the product as well as on the management of donor data (e.g. anonymization). The donor center evaluates the request, and if a positive decision is reached, obtains donor consent.

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 donation the donor is reserved for two years for the recipient in order to be available for a subsequent donation if necessary. The donor is flagged in match lists as being reserved for a specific patient. During this time the donor is not available for another patient. Alternatively the donor can be temporarily deferred for two years (TU, reason: TX). Due to this temporary unavailability the donor is not listed on match lists, and they will not be listed until three months before expiration of the temporary deferral.
In case of the patient's death, the donor is deferred for at least one year after donation.

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

6.1.4 Because of varying clinical situations, a minimum time interval between donations cannot be defined.

6.1.5 If a further donation is possible depends on the results of the medical evaluation and if these permit another 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. Such cases mandate a review by the registry (normally the ZKRD).

6.1.7 A donor may generally donate twice, for a maximum of two different patients. After a donor has donated twice, it is recommended not to make them available for further donations (except lymphocyte donations). A further stem cell donation shall only be permitted in cases of urgent medical need, and even then more than two of the same type of donation (bone marrow or PBSC) are not permitted. The ZKRD (for German patients) or the registry responsible for an international patient must review the donor situation (see 6.1.6).

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) 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
- Request forms for donor lymphocytes: ZKRD forms WU_001 and WU_005

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 further Requests

6.3.1 Peripheral Blood Stem Cells or Bone Marrow

Procedures (donor information, insurance, informed consent, medical evaluation and collection) are the same as for a first donation (5.2 – 5.6).

6.3.2 Lymphocytes

General procedures (donor information, insurance, informed consent, medical evaluation and collection) are the same as for a stem cell donation (5.2 – 5.6). Those standards only relevant for the collection of peripheral blood stem cells or bone marrow do not apply.

All blood tests listed in Appendix A.2.2 must be performed/repeated. The donor's general health and suitability for donation should be appropriately evaluated up front.

For donors who have previously donated peripheral blood stem cells within the last 24 months, the donor center arranges the examination according to A.2.2 as well as donor insurance 5.2, and also arranges that the donor receives the informed consent form for the lymphocyte donation. When the test results are available, donor eligibility can be evaluated after an interview of the donor by the collection center physician (health history since last donation, remarks on the collection, etc.). Unusual findings can necessitate further diagnostic procedures. The physical examination is performed at the latest on the day of the leukapheresis.

The donor information session and medical evaluation is to be moved up and cannot be postponed until the day of leukapheresis, for reasons of donor or patient safety:

- if the previous donation is longer than 24 months ago (procedure analogous to stem cell collections (5.2 – 5.6), although instumental diagnostics may be waived if no abnormal findings are detected)
- if the donor wishes an earlier appointment
- if abnormalities have arisen since the previous donation (also during donor follow-up) or if deemed necessary by the physician.

6.3.3 **Whole Blood**

For whole blood, the following criteria are applicable: Item 2.4.1 of the ”Guideline for the Preparation of Blood and Blood Components and the Use of Blood Components (Hemotherapy)” [3]).

7 Transport

7.1 General

7.1.1 Responsibilities

Either the transplant center (clinical institution) or the collection center (manufacturer) is responsible for product transport. If not otherwise documented in writing, the transplant center is generally responsible for the transport. Couriers must be commissioned in writing.

The contracting institution must ensure that the transport is carried out according to these standards. Transports must additionally be performed according to the WMDA guidelines [26].

Documentation on the performance of transports, as well as documents on the instruction of couriers, must be provided by the contracting institution upon request of the ZKRD.

7.1.2 Transport Conditions

The product must be transported in a rigid, shatterproof thermally insulated container whose labelling includes 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!

Additionally the emergency contact data and 24-hour phone number of the ZKRD and/or of the institution responsible for the transport must be clearly visible on the outside of the transport container.

Bone marrow, peripheral blood stem cells and donor lymphocytes must be hand-carried during the whole transport by an authorized courier whose details have been conveyed to the donor center, collection center and transplant center. Upon request by the transplant center, whole blood can be shipped unaccompanied.

Inadequate transport conditions and serious adverse incidents must be documented and immediately reported to the ZKRD. Deviations (e.g. opening of the transport container by airport security staff) must also be documented (see also 8.1.5).

The institution responsible for the transport specifies the transport conditions. The product temperature must be electronically logged during the complete transport procedure. The transport temperature must be documented.

7.1.3 Transport Arrangements

Transport to the transplant center must be carried out using efficient and safe means of travel.

In the event of courier flight travel, a direct flight should be booked, if available. A backup flight should be arranged or a flexible ticket should be booked to allow for rebooking on short notice. At the time of booking, the flight must be declared as a medical flight. The transport box must be transported as carry-on luggage. The courier must be able to see to container at all times, and it must be stored to prevent falling, getting bumped or exposure to other impact. The box is to be placed on the adjacent seat or on the floor in the foot area.

When a motor vehicle is used for transportation, it is recommended that the person driving the vehicle is not at the same time the courier accompanying the product. Travel times are to be taken into consideration when planning the transport. Dependant upon the distance and the travel conditions, the donor center may require an additional person to accompany the transport or that the courier arrives earlier. If a courier arrives alone to pick up the product, and there are justified doubts regarding its proper transport, the donor center or collection can initiate further measures, as described in 7.1.7.

The courier must be aware of alternative modes of transport (e.g. due to bad weather, flight cancellation, etc.) and have appropriate contingencies in place.

If deviations from the original travel route occur, e.g. due to rebooking or a change in courier, the organizations involved must be informed either directly by the courier or via the registry.

7.1.4 Courier Details

The courier details are to be communicated to all parties concerned by 5 working days prior to collection at the latest. The details must contain the following information at a minimum:

- courier information (name, identity card number/passport number, mobile number, citizenship)

- date and time of arrival at the collection site/city of the collection center
- travel itinerary with backup option
- name and phone number of their hotel at the collection site

On arrival at the city where the collection center is located, the courier must contact the collection center to clarify details regarding pick-up of the product. If travel to the collection center involves a long trip, the courier should arrive the day before collection takes place.

7.1.5 Notification of Airport Security

Based on the information received from the commercial courier or from the transplant center, the ZKRD notifies airport security of all products for German patients transported by air travel.

Additionally, products collected for German donor centers, which are to be transported by air travel, are also reported to airport security by the ZKRD, upon request of the donor center.

Security staff of the departure, arrival and transit airports, as well as the airlines involved, are informed of courier flights based on the documents listed in 7.2.2.

7.1.6 Customs Notification

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.

For exports to third countries the ZKRD, which is registered as a licensed exporter, notifies customs of the product to be exported and compiles the customs documents, in cooperation with the respective donor center.

For exports to third countries, the donor center (in cooperation with the collection center, as applicable) is responsible for handing over the customs documents to the courier at the time of product pick-up. For imports from third countries, the transplant center or the commercial courier company is responsible for providing the courier with the documents before they depart.

7.1.7 Product Transfer

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

If there are justified doubts regarding proper transport when the product is being picked up, the responsible staff member of the collection center must immediately inform the institution which contracted the courier, and other institutions involved in the coordination of the transport as applicable, in order to take any necessary measures to guarantee appropriate transport of the product.

7.1.8 Product Labeling

The product must be labeled according to current laws, guidelines and regulations [2], [7], [14], [22], [1], [26].

7.1.9 Transport of Cryopreserved Cord Blood

Depending on the request of the transplant center, cord blood units can be shipped unaccompanied. Cryopreserved cord blood units are transported in a liquid nitrogen shipper (dry shipper), which is normally provided by the cord blood bank.

Staff of the cord blood bank packs the cryopreserved product in the dry shipper for transport. The product temperature must be logged and documented during transport. The dry shipper must be transported in an upright position, and impact to the shipper is to be avoided. The dry shipper must be qualified and validated for the shipment of cryopreserved cord blood units.

Dry shippers may be transported in the cargo hold of an aircraft. The courier shall monitor the loading of the dry shipper.

7.2 Accompanying Documentation

7.2.1 Accompanying Documentation

The documents accompanying the product must meet the requirements of the Paul-Ehrlich-Institut (`www.pei.de`: Mindestanforderungen für die Behältnisbeschriftung auf dem Primärbehältnis bzw. auf der äußeren Umhüllung von Stammzellzubereitungen) and the respective approvals according to §21a AMG [7].

The accompanying documentation and/or the label must also fulfill the following minimum requirements of the WMDA:

- product name
- cell count and, if applicable, processing
- product code
- recipient identification
- donor identification number
- donor AB0/Rh group
- date and time of collection (not for cord blood units)
- name and address of the transplant center and contact details

In addition to the regulatory requirements, the address of the donor center must also be included.

Also, the name of the person handing over the product at the collection center, as well as the date and time of product transfer, are to be documented.

7.2.2 Documents for Airport Security

When traveling by air, the courier must carry a document for airport security containing the information listed below. This document is provided to the courier by the ZKRD, in cooperation with the donor center:

- name of courier
- identity card number/passport number
- flight itinerary, especially departure and arrival airports, departure and arrival data and flight numbers
- designated use of the product
- Warning that the transplant should not be X-rayed and that the transport shall not be delayed.

7.2.3 Customs Documents

For products which are imported from third countries or are exported to third countries, the courier must carry the necessary customs documents during the transport and provide these to the respective Customs Office (see also 7.1.6). The transport should not be substantially delayed due to clearing customs. When planning the transport, sufficient time should therefore be allotted.

7.3 Courier

7.3.1 Courier Requirements

The institution which provides the courier, or the commercial courier company, must ensure that product transport is carried out according to the requirements listed in 7.1.1.

The courier is responsible for ensuring that the product is transported safely from the collection center to the transplant center in the shortest possible time and in compliance with the above mentioned specifications.

The courier must fulfill the following requirements:

- He must be of full legal age.
- He must know and understand the significance of the product.
- He must have received training on the WMDA guidelines [26] and have been deemed as suitable by the institution responsible for the transport.
- He must not be related to the donor or recipient.
- He must be an experienced traveler (and for international transports should have international travel experience) and know how to manage travel disruptions or typical incidents during the transport of stem cells. It is recommended that the

courier gain experience in transporting products nationally prior to performing international transports.

- He must not have other commitments or interests until he has delivered the product.
- For international transport, he must have adequate command of the English language. Additional knowledge of the language used in the countries to be visited is also helpful.

It is recommended to suitably insure the courier and the product.

Furthermore, the applicable regulations of the country must be adhered to, as well as the standards and recommendations of the WMDA.

Should the courier not meet the above mentioned requirements, the institutions involved can refuse to use the designated courier for the specific assignment. In such cases, it is the responsibility of the institution which is responsible for the transport to promptly organize a different courier.

7.3.2 Courier Tasks

The courier is responsible for the following tasks when performing a transport:

- On arrival at the city where the collection center is located, the courier must contact the collection center to confirm arrival and clarify details regarding the pick-up of the product.
- On the day of collection, he must arrive at the collection center at the arranged time and provide proper identification.
- When accepting the product, he must crosscheck the number and type of product bags and requested samples. He must check the labeling and the accompanying documents according to the information detailed in sections 7.1.8 and 7.2.1. Product transfer is confirmed and documented in writing by the responsible person at the collection center and the courier.
- He must place the product bags properly in the transport container.
- At check-in, at the gate and in the aircraft he must inform the staff about the medical transport, and he must make sure the product is not x-rayed during the security check. Should an incident occur, the institution responsible for the transport must be contacted to determine how to proceed.
- He must declare the product at customs according to 7.2.3 as required.
- He must never leave the product unattended (this does not apply to dry shippers).
- In addition to the documents as listed in section 7.2.1, he must carry the following documents during product transport:
  - product prescription

  - donor infectious disease marker test results
  - prescription verification

- Furthermore, during transport the courier must have the following personal documents with him:
  - identification card/passport (valid for at least another 6 months)
  - travel itinerary and tickets (for flights, train, etc.), hotel reservation
  - for international transports, a sufficient amount of foreign currency
  - for international transports, an internationally valid credit card with a reasonable limit and a mobile phone with international roaming
  - if required for international transports, dependent upon the countries visited, a valid visa. Immigration and visa specifications must be clarified by the courier in due time before departure, as necessary.
- He must be able to access the name, address and 24-hour phone number of contact persons at all institutions involved in the transport.
- He must hand over the product to the designated staff member of the receiving institution. The staff member must confirm transfer and receipt of the product in writing. When handing over the product, the courier and the staff member of the receiving institution must crosscheck the labeling of the product and sample tubes for correctness and completeness. Documentation of transfer of the product is transmitted to the donor center.
- The complete transport procedure must be documented using `TM_017` or a comparable form.
- The courier must always maintain donor and recipient confidentiality and is not permitted to pass on any correspondence or gifts between the donor and recipient.
- During the complete transport procedure, the courier may not consume nor be under the influence of alcohol, drugs or other substances with similar effects.

7.3.3 Equipment

The courier must utilize the following equipment for the transport and be trained in its proper use:

- a rigid, shatterproof thermally insulated transport box, which has been validated for the transport of bone marrow, peripheral blood stem cells and donor lymphocytes, has warning labels as specified in 7.1.2, and is equipped with appropriate coolant packs
- an electronic data logger for recording, monitoring and documentation of the transport temperature
- disposable plastic gloves, in order to remove the product from the box for a possible inspection (e.g. at airport security).

8 Post-Donation Donor Follow-up

8.1 General

8.1.1 Donor follow-up immediately after donation, as well as assessment of the donor's ability to return to work, are covered in section 5.6.

8.1.2 The donor center is responsible for donor follow-up after the responsible physician has discharged the donor from the collection center.

8.1.3 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.

8.1.4 Serious adverse reactions during and after a donation (of stem cells and lymphocytes) or during mobilisation of stem cells, as well as events which resulted in the risk of such a reaction, must be reported by the donor center to the ZKRD as part of the WMDA SEAR program. If no reactions or events occured, this is to be confirmed during routine monitoring.

8.1.5 Serious adverse events during collection, processing, transport or at/after transfusion of cells from unrelated donors, as well as situations which resulted in the risk of such an event, and which affect the safety and quality of the cells and therefore the safety of the recipient, must be reported by donor centers, collection centers, transplantation centers and cord blood banks to the ZKRD as part of the WMDA SPEAR program. Couriers are to inform their contractor, who then initiates reporting. If no reactions or events occurred, this is to be confirmed during routine monitoring.

8.1.6 Should a serious illness of the donor occur long-term, which could affect the health of the patient, this must also be reported to the ZKRD as part of the SPEAR program. The transplant center must be informed accordingly. Likewise, cases must be reported and the donor center informed, if the transplant center diagnoses a serious illness of the patient, which may have been transmitted by the donor.

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 (for stem cell and lymphocyte donations) to evaluate his physical

and emotional well-being. Content-related recommendations can be found in WMDA forms[8]. 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 accordingly.

8.2.3 6 months, 1, 2, 5 and 10 years after stem cell donation, the donor must be contacted by sending a questionnaire (see appendix C).

8.3 Post Donation Donor Testing

8.3.1 30 days after stem cell donation, the donor center or collection center has to arrange for at least the following tests:

- after stem cell aphereses: differential blood count, ASAT, ALAT, uric acid
- after bone marrow collections: differential blood count, ferritin

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

8.3.3 Pathological findings which may affect the recipient must be reported to the transplant center.

[8] status 2025-06-01: www.wmda.info, form DF1

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, donor center and the cord blood bank, respectively, as well as the ZKRD as appropriate, must be informed about the disposition of the preparation. Alternatively only the ZKRD may be informed for forwarding to the respective partners. In the case of cryopreserved products, standard 5.7.3 is to be observed.

9.1.2 The recipient must be informed and provide his consent before the transplant center transmits or uses any medical follow-up data. Medical data is not to be communicated to the donor, rather only general information is to be provided (e.g. alive, good general condition, patient is able to work again).

Recipient follow-up by cord blood banks is performed according to stipulations of the drug licensing procedure of the Paul-Ehrlich-Institut.

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 and 2 years post transplant (e.g. ZKRD form `PTX_006`).

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 permitted until two years after the first transplant date at the earliest. Before any direct contact is permitted, both parties must be informed of the benefits and the risks of direct contact by the donor center (for the donor) and the transplant center (for the patient), and both the donor and the recipient or his legal guardian must sign the corresponding consent form (ZKRD forms `PTX_001` and `PTX_002`). Should the patient receive a further transplant from the same donor, direct contact is possible one year after the second transplantation at the earliest. It is recommended to organize at least one written contact between donor and recipient before lifting anonymity. The date of the second transplantation does not shorten the initial required period of two years.

9.2.3 Direct contact between family members of a deceased recipient/donor and the donor/recipient is allowed without a waiting period if both parties have signed an in-

formed consent form. If third parties want to lift the anonymity after the death of a patient/donor, family members of the patient/donor must consent.

10 Data Protection, Anonymity and Record Retention

10.1 Data Protection

10.1.1 All institutions involved are required to ensure data protection and data security according to this section.

10.1.2 All institutions involved must have a data protection officer.

10.1.3 Staff must be informed about data protection regulations and must commit themselves in writing to observe data protection norms. This includes special protection of medical information with respect to a physician's requirement of medical confidentiality. Only a physician may inform a donor about pathological findings.

10.1.4 Data security must be ensured. In particular, spatial conditions must ensure that only authorized staff has access to donor and patient records.

10.1.5 The protection of an individual against unlimited collection, retention, use and transfer of his personal data must be warranted according to applicable data protection laws (e.g. [11], [12]) and the German Social Security Code X (protection of social data) [16]. Furthermore, corresponding state data protection laws, state archive laws and health care laws also apply.

10.1.6 After expiration of the respective retention period, records must be disposed of and data deleted [11]. This must be performed professionally.

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. Important measures are that:

- only the necessary personal data of the donor and the patient may be given to the entitled institutions (e.g. donor center, collection center) for the purpose of undertaking the stem cell donation,
- donor-related information that is communicated externally must not contain names but only pseudonymous codes,

- after a collection or transplantation and only upon request, the donor and patient may receive data on gender and approximate origin/age of the partner in a way that the anonymity will be maintained.

The transplant center is responsible for ensuring that all necessary measures are taken to prevent donor data (e.g. donor identification number, date of birth) from becoming accessible to patients (e.g. by using a sleeve to cover product labelling).

For donor and recipient contact, see also section **??**.

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. 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.

11 Undirected Products (from an apheresis)

Undirected products (from an apheresis), which have been manufactured on behalf of a donor center in conjunction with a directed stem cell donation, in general fall under the scope of the German Standards for a directed donation. Deviations and further explanation with regards to these undirected products are described in this section.

Institutions involved in the manufacturing or requesting of undirected stem cell products from aphereses must additionally adhere to these standards. In general, collection of the directed product has priority.

Within the framework of manufacturing and testing, the guidelines of the German Medical Association as well as the requirements of the Paul-Ehrlich-Institut must be adhered to.

11.1 Requirements

11.1.1 General

11.1.1.1 If based on the overall situation of the donor and patient, an excess of cells can be expected, a portion of the product, which is not needed for the immediate treatment of the patient, may be collected on behalf of the donor center.

11.1.1.2 It is not permitted to administer a higher dose of or additional G-CSF in order to collect an additional product. Aphereses cannot be conducted on a second day of collection, if these are exclusively for the purpose of collecting an undirected product (for cryopreservation). The duration of apheresis should not exceed 5 hours, and the amount of blood processed should not exceed four times the body's blood volume[2].

11.1.1.3 The collection and manufacturing of undirected stem cell products may only be conducted in facilities with the appropriate manufacturing license and approval/permission by the authority (see [7][14]).

11.1.2 Counseling and Consent

11.1.2.1 Already at the time of medical examination, the suitability of the donor must be determined and they must be informed of the process (e.g. longer duration of apheresis, cryopreservation), as well as possible consequences (e.g. advantages and disadvantages of such a collection, especially for the donor and patient).

11.1.2.2 The donor must be informed of the ownership of the product as well as its possible utilization.

11.1.2.3 Written consent must be obtained from the donor. This consent is to be obtained independently of consenting to the collection for the directed donation.

11.1.3 Cryopreservation

If it is planned to have an undirected product cryopreserved, the donor center organizes this during the workup procedure with a facility in possession of the appropriate manufacturing license and authority approval/permission. The stem cell bank or the donor center preliminarily mandates a courier with the transport of the collected product.

11.2 Collection Process

11.2.1 On the day of collection, the CD34+ cell count is determined using a donor blood sample. Based on this cell count, the blood volume is calculated which needs to be processed in order to achieve the quantity of CD34+ cells requested by the transplant center.

If during apheresis the requested cell count for the directed product has presumably been achieved, consent for collection of an additional product must again be confirmed by the donor and documented by the apheresis physician.

11.2.2 After completion of the apheresis, the count of the collected product is determined and the product is divided up, if applicable. It must be taken into account that the directed product contains at least the requested target cell count. The requested directed product is promptly handed over to the courier, while the remaining portion is processed and cryopreserved on behalf of the donor center. Both products are labelled as to their identification and further use according to current laws, regulations and guidelines [7][14][22][2].

11.2.3 The transplant center must be informed in writing that the donor center has initiated storage of an undirected product (as an exceptional case). Upon request, the transplant center can have the product reserved for the patient for up to 3 months. The reservation may be extended upon further request of the transplant center, if justification is provided. The donor remains reserved for the patient within the scope of the directed donation (see 6.1.2 6.1.6 6.1.7).

11.3 Requesting of a Product

11.3.1 After the product has been released by the responsible facility, the undirected product is brought onto the market and the data needed for match lists is provided accordingly. The product can be requested by transplant centers worldwide.

11.3.2 For searches for an undirected stem cell product, standards regarding donor searches in section 4 apply accordingly.

11.3.3 Before the product is infused, the identity must be confirmed by either the transplant center or the providing facility based on additional HLA testing using a reference sample.

11.3.4 The product is requested through the ZKRD or the donor center. The donor center coordinates provision of the product with the stem cell bank. Similarly to workups involving directed donations or cord blood, the product is to be requested using an appropriate form.

11.4 Patient Follow-up

Upon request of the donor center, the transplant center must disclose if and when the product was transplanted. Concerning the progress of the patient (recipient follow-up), the donor center is to be informed at the foreseen points in time (see 9.1.2 9.1.3).

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A Appendix: Preparing Blood Stem Cell Donations: Donor Information and Medical Evaluation

A.1 Donor Information and Counselling

The donor must be informed about the details of the donation by an adequately trained person using terms that are easily understood by the donor. Additionally, the counseling about the donation and related medical intervention is done by the collection center's physician. Translating may only be done by a professionally or linguistically competent person who is not related to the donor. During the medical evaluation, at the latest, the donor must be informed and counseled about the following:

A.1.1 Information About the Donor Request and Related Procedures

- Product preference of the transplant center
- Expenditure of time
- 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 donor safety measures
- Possibility of consulting a donor advocate if needed
- 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 or if the treatment protocol requires a subsequent donation)

A.1.2 Donor Medical Counseling

A.1.2.1 Request and Procedure

- Donor exclusion criteria for blood stem cell donations

- 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
- 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 pathological 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)
- Instructions for the time of G-CSF mobilization and availability of a physician on duty including contact information
- Requirement of bone marrow donation if the G-CSF mobilization is unsuccessful or must be interrupted
- Requirement of signed donor consents (section 5.5)
- Right to withdraw at any time, however the donor must understand that if he/she withdraws after the beginning of the recipient's conditioning therapy, the recipient is in danger of death.

A.1.2.2 Risks

- Risks and side effects of anesthesia, marrow donation, administration of G-CSF and collection of peripheral blood stem cells and other blood products
- Peripheral blood stem cell collection: explicit reference to G-CSF's side effect profile
- Peripheral blood stem cell collection: possible use of a central venous catheter (CVC) for apheresis and associated risks if blood stem cells cannot be collected using peripheral veins
- Information regarding the risk of transmission of infectious, genetic or malignant diseases to the recipient via blood stem cell transplantation

A.2 Donor Medical Evaluation (Work-up)

A.2.1 Medical Examination and Counseling

- Medical counseling by the physician
- Health history

- Physical examination
- Resting ECG
- Abdomen sonography, in particular a spleen sonography if peripheral blood stem cell donation is performed
- Chest X-ray as needed
- Pulmonary function test as needed
- For peripheral blood stem cell donations: assessment of peripheral venous access

A.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 A.2.4).

- differential blood count, CRP
- Coagulation test (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 current guidelines [2]): Syphilis test, HBsAg, HBc Ab, HBV (NAT), HCV Ab, HCV (NAT), HEV (NAT), HIV-1 and -2 Ab, CMV IgG and IgM, HTLV-1 and -2 Ab, EBV IgG and IgM, recommendation: toxoplasmosis IgG and IgM
- Complete blood group testing and declaration according to the current hemotherapy and stem cell guidelines [3], [2]
- For female donors: Beta-HCG testing to exclude pregnancy

A.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 in writing (WU_038) 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) 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 pathological findings and examinations which may be necessary for further clarification.
- 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.

A.2.4 Repeat Examinations

If more than 30 days have elapsed between the donor medical evaluation and blood stem cell or lymphocyte collection, individual examinations must be repeated (this also applies in the event of a subsequent donation for the initial recipient):

- Between 30 days 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 marker testing; recommended to repeat pregnancy testing of female donors.
- 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 A.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.

B Appendix: Abbreviations

ALAT	Alanine Aminotransferase
AMG	Arzneimittelgesetz (German Drug Law)
AMWHV	Arzneimittel- und Wirkstoffherstellungsverordnung
Anti-HBc	Hepatitis B Core Antibody
AP	Alkalische Posphatase (alcaline phosphatase)
ASAT	Aspartate Aminotransferase
ASHI	American Society for Histocompatibility and Immunogenetics
BÄK	Bundesärztekammer (German Medical Association)
CMV	Cytomegalovirus
CRP	C-Reactive Protein
CT	Confirmatory Typing
CVC	Central Venous Catheter
DAG-HSZT	Deutsche Arbeitsgemeinschaft für Hämatopoetische Stammzelltransplantation und Zelluläre Therapie (German Working Group for Hematopoetic Stem Cell Transplantation and Cellular Therapy)
DGI	Deutsche Gesellschaft für Immungenetik (German Society for Immunogenetics)
DNA	Desoxyribonucleic Acid
EBMT	European Group of Blood and Marrow Transplantation
EBV	Epstein-Barr Virus
ECG	Electrocardiogram
EFI	European Federation of Immunogenetics
FACT	Foundation for the Accreditation of Cellular Therapy
Gamma GT	Gamma-Glutamyl-Transferase
G-CSF	Granulocyte Colony Stimulating Factor
GRID	Global Registration Identifier for Donors
HAC	Health and Availability Check
HBsAg	Hepatitis B Surface Antigen
HCG	Human Chorionic Gonadotrophin
HCV	Hepatitis C Virus
HEV	Hepatitis E Virus
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
HTLV	Human T-Lymphotropic Virus
IATA-DGR	International Air Transport Association - Dangerous Goods Regulations

IgG	Immunoglobulin-G
IgM	Immunoglobulin-M
JACIE	Joint Accreditation Committee ISCT EBMT
LDH	Lactate Dehydrogenase
NAT	Nucleic Acid Test/Nucleic Acid Amplification Test Technology
NMDP	National Marrow Donor Program
PASZT	Pädiatrische Arbeitsgemeinschaft für Stammzelltransplantation und Zelltherapie (Pediatric Working Group for Stem Cell Transplantation and Cell Therapy)
PBSC	Peripheral Blood Stem Cells
PTT	Partial Thromboplastin Time
SEAR	Serious Events and Adverse Effects Registry
SGB	Sozialgesetzbuch (Social Security Code)
SOP	Standard Operating Procedure (Working Instruction)
SPEAR	Serious Product Events and Adverse Effect Registry
TNC	Total nucleated cell count
WMDA	World Marrow Donor Association
ZKRD	Zentrales Knochenmarkspender-Register Deutschland

C Appendix: ZKRD Forms and Questionnaires

All current versions of forms and questionnaires are provided on the ZKRD homepage. For English versions please see:

`http://www.zkrd.de/en`
→ "Partner Login"
→ "Forms"
Includes forms for search, work-up, cord blood, transport management, donor-recipient contact and follow-up (patient).

The official versions of the donor health history questionnaire, consent form at CT stage and the donor follow-up questionnaire are in German and, therefore, not provided on the website for international partners.

D Appendix: List of Changes

Please see this appendix in the (original) German version for the complete list of changes in comparison to the previous version of these standards.