Guidance for establishing a hematopoietic progenitor cells donor follow-up registry

ARTHIQS – Deliverable 8
Work Package 5

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These Guidelines have been developed by the participants of the ARTHIQS Joint Action funded by the European Commission, Health and Consumer Protection Directorate General, Public Health and Risk Assessment Directorate, DG Sanco under Public Health Program (2014-2020), Grant Agreement 201321 01. ARTHIQS is aimed at developing guidelines for key aspects of service provision and regulation in Assisted Reproductive Technologies (ART) and Hematopoietic Progenitor Cells (HPC), in particular WP5 has been focused on the development of tools for improving safety and quality in HPC-related fields, namely donor follow-up and cord blood banks. Italian National Transplant Center (CNT-ISS) led this task related to issuing guidance for the establishment of HPC donor follow-up registries.

These Guidelines have drawn extensively on guidelines and documents commonly used in this field, as well as on existing European legislation. References to these guidelines and documents are given by footnotes.

The Guidelines are based on the requirements set out in the relevant legislation of the European Commission.

Further information on the Guidelines is available from the Joint Action website:

www.arthiqs.eu

Disclaimer:

The contents of these Guidelines are part of the Joint action ARTHIQS which has received funding from the European Union’s Health Programme (2014-2020). These contents represent the views of the authors only and are their sole responsibility; it cannot be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

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1. Institutions and Partners

ARTHIQS WP5 is co-lead by the Health Ministry of Croatia (MIZ) and by the CNT - ISS, in strict collaboration with the Italian National Blood Center (CNS- ISS). The task related to donor follow-up was assigned to ISS-CNT-CNS.

Other partners: ABM, IVO, SUKL, IPST, HTO, AFMPS-BE, BEAT, MOH-NL, KBCTIK, NTO Collaborating partners: WMDA, EBMT, FACT-NETCORD, Hospital Clínico Universitario Virgen de la Arrixaca (Murcia-Spain), Vilnius University Hospital, MOH-CY, OVSZ

2. Acronyms and definitions

2.1. Acronyms

ART: Assisted Reproduction Technologies
BM: Bone Marrow
BMDW: Bone Marrow Donor Worldwide
CBB: Cord Blood Bank
CBU: Cord Blood Unit
CA: Competent Authority
DLI: Donor Lymphocyte Infusion
EBMT: European Society for Blood and Marrow Transplantation
EC: European Commission
EDQM: European Directorate for the Quality of Medicines
EU: European Union
EUTCD: European Union Tissues and Cells Directive
FACT: Foundation for the Accreditation of Cellular Therapy
FU: Follow-up
G-CSF: Granulocyte Colony-Stimulating Factor
GF: Growth Factor
JA: Joint Action
JACIE: Joint Accreditation Committee ISCT and EBMT
HPC: Hematopoietic Progenitor Cells
HRQoL: Health-related quality of life
LY: Lymphocytes
MS: Member State
MUD: Matched Unrelated Donor
NGO: Non-Governmental Organization

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PBSC: Peripheral Blood Stem Cells
SAR: Serious Adverse Reaction
SAE: Serious Adverse Event
UCB: Umbilical Cord Blood
WP: Work Packages
WHO: World Health Organization
WMDA: World Marrow Donor Association
WBMT: Worldwide Network for Blood and Marrow Transplantation

2.2. Definitions

The definitions are reported in the Annex I.

3. Overview of the ARTHIQS JA

ARTHIQS - Assisted Reproductive Technologies and Hematopoietic stem cells Improvements for Quality and Safety throughout Europe – is a 3-year European Joint Action (JA) funded by the European Commission (EC) under the 2008-2013 Health Programme, dealing with Assisted Reproductive Technologies (ART) and Hematopoietic Progenitor Cells (HPC) for Transplantations. ARTHIQS consortium is gathering 15 partners and 9 collaborators from 18 different Member States (MS). The Agence de la Biomédecine of France is the coordinator of the ARTHIQS JA.

The two fields of action, although deeply different in practices and needs, participate together in the JA because they involve living cell donors, and fall under the 2004/23 EUTCD (European Union Tissues and Cells Directive) regulations.

Two ARTHIQS medical and scientific work packages (WPs) cover respectively ART and HPC.

The WP concerning HPC covers two different issues: HPC donor follow-up (FU) and cord blood banks.

It is widely recognized that MSs do not uniformly implement HPC donor FU procedures and practices, mainly in the related donor setting.

ARTHIQS as regards HPC has the objective to set up of shared specifications regarding the main characteristics for HPC donor (related and un-related) FU registries to be implemented locally and/or nationally.

4. Aim and scope of the guidelines

Because of the efforts of professional organizations and scientific societies, procedures are in place for HPC donor FU management. The procedures, mainly those applied to related donors, are quite different between MS, and the information reported to the Competent Authorities (CAs) are limited to the serious adverse reactions (SAR) and events (SAE) occurred during or right after the unrelated HPC donation. Specific guidelines providing indications on how to perform systematically FU of all HPC donors (unrelated and related) should be improved and harmonized among MS.
In the framework of the ARTHIQS JA, the WP5 actions focused on HPC donor FU with the aim to develop guidelines for the harmonization of the procedures applied by donor FU outcome registries for systematical donor FU.

The guidelines have the scope to set up the minimum data set and the basic organizational framework for conducting donor FU of both unrelated and related donors to be implemented by donor registries at local and national level.

The proposed donor FU model should be disseminated by the CAs to their own organizations in charge of management of HPC donors inside the country, in order to establish a common donor FU registry across Europe.

Considering that, HPC adult donor follow up is not comparable with cord blood donor (mother and newborn) follow-up the latter is out of the scope of this guideline.

5. Regulatory framework and international Standards

5.1. Regulatory framework

The World Health Organization (WHO)\(^1\) in the Guiding Principle 10 established that “High-quality, safe and efficacious procedures are essential for donors and recipients alike. The long-term outcomes of cell, tissue and organ donation and transplantation should be assessed for the living donor as well as the recipient in order to document benefit and harm. The level of safety, efficacy and quality of human cells, tissues and organs for transplantation, as health products of an exceptional nature, must be maintained and optimized on an on-going basis. This requires implementation of quality systems including traceability and vigilance, with adverse events and reactions reported, both nationally and for exported human products”.

Optimizing the outcome of HPC transplantation and the safety of HPC donors entails that under the oversight of national health authorities, donor registries and transplant programs should monitor donors and recipients in order to ensure that they both receive appropriate care. The HPC donation and transplantation procedures shall include a continuous balancing of the risks and interests of the donors as well as of the recipient.

Donor registries and transplant programs are strongly recommended to participate in national and international donor and transplant outcome registries that should be in charge of the regular reporting of any untoward consequences of HPC donation or transplantation to the responsible health authority.

Safety of living donors is critical for the future of HPC transplantation. Structured and robust vigilance and surveillance systems shall exist as part of national entities.

The EU Directive 2004/23/EC\(^2\) establishes high standards of quality and safety for procurement, testing, processing, preservation, storage and distribution of human tissues and cells intended for human applications in order to ensure a high level of health protection in the European Union (EU). HPCs fall under the mentioned Directive. Considering that in this field an intensive worldwide exchange is taking place, it is desirable to have worldwide recommendations.

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\(^1\) WHO GUIDING PRINCIPLES ON HUMAN CELL, TISSUE AND ORGAN TRANSPLANTATION as endorsed by the sixty-third World Health Assembly in May 2010, in Resolution WHA63.22

HPC used for allogeneic therapeutic purposes are procured from living donors and in order to ensure that the health status of a living donor is not affected by the HPC donation, a prior in-depth medical examination shall be performed and a medical assessment of the donor after HPC donation should be recommended.

In the section A of the Annex of the 2004/23/EC Directive, concerning “Information to be provided on the donation of cells and / or tissues” to living donors, the importance to provide complete and exhaustive information to the HPC donor is underlined.

The information must cover: the purpose and nature of the procurement, its consequences and risks; analytical tests, where they are performed; recording and protection of donor data, medical confidentiality; therapeutic purpose and potential benefits and information on the applicable safeguards intended to protect the donor. Information must be given on the necessity for requiring the applicable mandatory consent, certification and authorization in order that the tissue and/or cell procurement can be carried out.

MSs, following the provisions of the article 11 of the 2004/23/EC Directive, shall ensure that there is a system in place to report, investigate, register and transmit information about SAR and SAE potentially affecting the quality and safety of tissues and cells, and which may be attributed to the procurement, testing, processing, storage and distribution of tissues and cells, as well as any SAR observed during or after clinical application which may be linked to the quality and safety of tissues and cells.

The EU Directive 2006/86/EC\(^3\) establishes that procurement organizations shall have procedures in place for the notification of SAR occurring to the recipient and SAE impacting on the procured tissues and cells. Furthermore, the procurement organizations shall notify to the tissue and cells establishment without delay any SAR occurring in the living donor, which may influence the quality and safety of tissues and cells (Article 5, comma 1.a).

In Article 7 of the same Directive “Member States shall submit to the Commission an annual report, by 30 June of the following year, on the notification of SARs and events received by the competent authority. The Commission shall submit to the competent authorities of Member States a summary of the reports received. The competent authority shall make this report available to tissue establishments”.

The EDQM\(^4\) Tissue and Cell guide (chapter 3.2.2) indicates the same principle.

As regards the follow-up of living donors, definitely it is recognized as an essential tool for ensuring not only the safety of HPC donors but also the safety and the quality of the donated products and indirectly the safety of the recipients.

5.2. International Standards

FACT-JACIE\(^5\) deals with issues of the donor FU in different sections (B6.3, CM6.3 and C6.3), simply underlining that transplantation programs shall have a policy for following up the HPC donors that includes routine management and collection of associated adverse events.

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6. Overview of institutions active in HPC donor management

6.1. Bone Marrow Donor Worldwide (BMDW)

Bone Marrow Donors Worldwide (BMDW) is the global database that has the task to collect data on volunteer HPC donors and cord blood units including HLA phenotypes. The database is operated by World Marrow Donor Association from January 1, 2017.

The HLA phenotypes in BMDW make it possible that transplant centers can identify a potential match for their patients. Seventy-eight adult donor registries from 53 countries and 55 cord blood unit (CBU) registries/cord blood banks from 36 countries list their donors and cord blood units in the database. The number of donors and cord blood units in the BMDW database was: 29,135 donors and 715,580 CBU's on January 1, 2017.

6.2. World Marrow Donor Association (WMDA)

In 1988 the World Marrow Donor Association (WMDA) was established by three pioneers in the field of transplantation, John Goldman (UK), E. Donnell Thomas (United States), and Jon J. van Rood (NL). WMDA is an international organization that works towards a world where high-quality, safe hematopoietic stem cell products are available for all patients in need, and to protect the rights and welfare of the stem cell donors.

The WMDA promotes international collaboration, information exchange and best practice in stem cell provision on behalf of patients and donors.

WMDA requires that donor registries operate in compliance with standardized requirements for donor selection and clinical follow up (FU) (see chapter 9 of WMDA Standards). Concerning donor clinical FU, specific rules are defined for conducting it at short and long-term and resulting data are collected by donor registries who are in charge HSC donors through dedicated forms.

Furthermore, according to WMDA Standards, adverse reactions affecting donors during and after HPC collection shall be identified, evaluated, notified, investigated through root cause analysis and documented. For these purposes WMDA has defined standard forms to be completed by donor registries for reporting SAR/SAE. The WMDA has developed donor eligibility criteria which are publicly available. WMDA has established a global biovigilance system for unrelated donors.

WMDA took over the activities of NetCord Foundation and Bone Marrow Donors Worldwide on January 1, 2017.

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6 BMDW annual report 2016
7 Standard WMDA (https://www.wmda.info/)
6.3. **EBMT Donor Outcomes Committee**

In 2015 the EBMT (European Society for Blood and Marrow Transplantation) has implemented a platform for collecting short- and long-term donor follow-up data in the EBMT ProMISe database\(^{12}\) based upon the Minimal Data set approved and recommended by the Worldwide Network for Blood & Marrow Transplantation (WBMT) in 2011. The objective was to build up a database on donor follow-up information collected by the organization responsible for collection and/or donor registries through the transplant centers, in order to be able to provide robust data on short and long-term donor safety. EMBT has also developed recommendations for donor eligibility, selection and FU.

6.4. **Worldwide Network for Blood and Marrow Transplantation (WBMT)**

The WBMT is a non-profit scientific organization with the mission to promote excellence in stem cell transplantation, stem cell donation and cellular therapy. Membership is composed of international societies in the field such as EBMT, WMDA and JACIE. It is also in official relations with WHO as a NGO. The purpose of this cooperation is to engage exclusively in scientific and educational activities and endeavors.

WBMT has organized several workshops to standardize the collection of donor follow-up data for related and unrelated donors\(^{13}\).

7. **Overview of organizations active in HPC donor management**

As regards HPC unrelated donor management different operational entities are involved, each one playing a specific role and assuming a defined responsibility in the unrelated setting.

According to the workflow of the HPC unrelated donor management, the following operational entities are involved:

**Donor center.** It is an organisation responsible for adult volunteer donor recruitment, consenting, testing, management and collection of donor personal, genetic and medical data. Donor center is in charge of the assessment of the donor health status at the time of recruitment. Donor recruitment and selection shall be performed in compliance with any relevant national laws and international regulations.

**Testing laboratories.** The testing laboratories perform histocompatibility, blood group, infectious disease, and other testing of the prospective donors and patients. They may be under the direction of a registry, a donor center or a transplant center or may be separate from these entities.

**Registry.** An organisation responsible for coordination of the search for hematopoietic stem cells from donors (including cord blood) unrelated to the potential recipient. The registry must operate within the laws of the country in which the registry resides and the personnel employed by the registry shall be qualified and trained on assisting medical decisions regarding donor selection and donations.


**Collection center.** It is a medical facility where HPC collection from volunteer adult donors takes place. The collection might include marrow aspiration, apheresis or cord blood procurement. The collection center performs the medical work-up of the donor and provides the final approval for collection. The collection center packages the donated HPC collection for transport to the Tissue Establishment.

**Tissue Establishment.** It is a tissue bank or a unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissues and cells are undertaken. It may also be responsible for procurement or testing of tissues and cells.

**Transplant center.** It is a medical facility where a patient (recipient) receives a HPC transplant. The transplant center oversees the immediate medical treatment and provides long-term follow-up of the recipient.

**Competent Authority.** It is the body which has been delegated the responsibility for ensuring that tissue and cell donation, banking and human application are appropriately promoted, regulated and monitored in the interest of donor and patient safety and public transparency on a national or regional basis by their government.

**Donor outcome follow-up registry.** It is a function that may be carried out by donor registries for the unrelated donors and by collection centers or transplant centers for related donors, according to the organizational structure of the MS. All the facilities involved should operate according to common procedures following the recommendations provided with these guidelines. The donor FU outcome registry should provide on an annual basis to the CA an activity report as described in the guideline.

The WMDA Standards cover all aspects from recruitment to stem cell collection and follow-up of unrelated HPC donors and the registries must demonstrate their commitment to comply with these standards throughout the registry accreditation process. The existence of minimum guidelines, internationally recognized and applied by donor registries, supports worldwide the uniformity in the performance of HPC unrelated donor management.

However the lack of a common standard of care for related donors may cause heterogeneous management practices across Europe.

Considering that in almost half of allogeneic HPC transplants, a related donor HPC is used, it is strongly recommended to standardize the related donor assessment, including follow-up procedures, in order to be in line with the standards applied for unrelated donors.\(^\text{14}\)

For this scope it is recommended that the CAs in the framework of the HPC donor management identify a “new” entity empowered to the function of the donor outcome follow-up registry.

It is also recommended that MSs support the donor outcome follow-up registry function, independently either if it is allocated in a local or national registry or in the CA organization, with adequate human, technical (information technology, IT) and financial resources.

In the light of sustainability it seems more appropriate to centralize the donor outcome follow-up registry function at national level (for example: donor registry) through a network able to collect data and provide regularly reports to the CA. Donor registries have already set up the infrastructure for unrelated donors and have knowledge and infrastructure to establish a donor outcome follow up registry.

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8. State of the art of HPC donor FU procedures in Europe

8.1. Survey results

As foreseen in the ARTHIQS grant, a survey on existing HPC donor FU practices has been submitted to the CAs. The questionnaire covered information about related and unrelated donors (see attached questionnaire in Annex II). Participants were also invited to send, if available, the forms used to gather medical information of the donor after HPC donation. Only five countries sent the requested forms.

Out of the total 30 EU countries involved, 20 respondents returned the questionnaire (66,6%). Of those respondents 30% declared to have a donor registry qualified or accredited by WMDA, 70% declared they did not have one. In 2013 most of the respondent MSs declared an HPCT activity rate of 201-300 allogeneic HPC transplants per 10 million population (EBMT data) confirming a good coverage of the survey. Although HPC donor FU is performed in the most countries, the procedures applied appear quite different and a standardization of these activities is missing mainly in case of related HPC donors whose follow-up is often interrupted if the outcome of the recipients is negative. Concerning unrelated HPC donors in both short-term and long-term FU procedures a donor follow-up questionnaire is applied by more than 80% of respondent countries. Blood testing is carried out by 96% of the countries in the short-term FU, the percentage goes down (50%) in case of long-term follow-up. Physical examination is performed by 56% and 31% of the countries respectively for short-term and long-term FU.

These results highlight the need of implementing a common approach for HPC-donor FU care among MSs in order to harmonize data collection at European level and improve nationwide the HPC donor-related follow-up procedures.

The following considerations can be drawn from the analysis of the received questionnaires:

a) HPC donor FU is performed in most of respondent countries, and the procedures applied are different, also in those countries where a national WMDA qualified/accredited donor registry is present;

b) most of the countries declare to be able to link donor SARs observed during donor FU with prior comorbidities found during donor assessment

c) SARs occurring during the short and long-term FU may give significant information for improving donor selection criteria;

d) most of the countries allow multiple HPC donations from one donor for one or more patients and the time interval between two HPC donations varies among countries;

e) in the case of related donors the possibility to lose the donor during FU is high and it mainly depends on the survival of the recipient.

However, the picture obtained from the survey demonstrates that a minimum set of data is available and this data set can be the basis for developing a uniform model of donor FU in addition to the diverse information provided by published reports on follow-up and retrospective donor FU studies available in the international literature.

Nevertheless it is necessary to establish an appropriate communication flow between all the involved organizations including CAs.

Other relevant aspects to be considered are:
the need to introduce recommendations for the management of HPC related donors FU. It has been shown that related donors have a higher risk of SARs that could relate to higher ages and more comorbidities in this group\textsuperscript{15};

the need to introduce recommendations for the management of HPC pediatric donor FU\textsuperscript{16}. According to the results of the survey no specific procedures are available for pediatric donors;

developing recommendations for the management of FU after multiple donations of HPC or LY;

developing minimum recommendations for managing donor FU after LY donations.

9. Guidelines for HPC donor outcome follow-up management

9.1. Introduction

HPC transplantation is the treatment of choice for a growing number of hematologic and non-hematologic diseases.

Until twenty years ago, the HPC transplantation depended on the availability of a family donor perfectly compatible, available only in 30-40% of the patients, and bone marrow (BM) was the principle source used.

The continuous refinement of transplant procedures has gradually expanded the clinical indications and has enlarged the type of eligible patients (age, health status, comorbidities). In order to cover an increased request of HPC donors international donor registries have been created with the aim to recruit potential volunteer donors. Worldwide the number of registered donors is now over 30 million.

Today, the choice of HPC donors and the sources of HPCs have changed and transplant physicians can choose among different HPC sources - BM, granulocyte colony-stimulating factor (G-CSF)–mobilized peripheral blood stem cells (PBSC), or umbilical cord blood (UCB). The donor can be a HLA identical sibling, a matched unrelated donor (MUD), a haploidentical family PBSC or BM donor or a HLA matched or mismatched unrelated cord blood unit.

Another aspect to be considered is that about 50% of HPC products used in the world are exchanged between countries (70% in Europe), so that it is important to define harmonized and comparable practices respecting the national regulations and institutional policies in order to ensure continued efficient international collaboration\textsuperscript{17}.

This aim cannot be achieved only through the mandatory reporting of SARs, but also by applying an appropriate assessment of donor medical suitability at each stage of the HPC donation pathway.

\textsuperscript{15} Halter J et al. “Severe events in donors after allogeneic hematopoietic stem cell donation”. Haematologica. 2009;94(1)
\textsuperscript{17} WMDA annual report 2016
9.2. Responsibility

Allogeneic donor suitability must be evaluated by a licensed health care professional who is not the primary health care professional overseeing care of the recipient.

Otherwise, traditionally, the health-care professionals in charge for the treatment of the recipient are often also responsible for the evaluation of the related donor. Although there is no substantiating evidence, from time to time this situation may generate conflicts of interest with more often disadvantages for the donor than the recipient. To avoid these potential problems and to assure maximum donor protection, it is important that the donor is assessed by a physician who is not directly involved in the recipient’s care. It is important also that the physician has knowledge of donor rights and that he/she can advocate for the donor. In some transplant centers, this may be achieved by dedicated specialist personnel for donor care management, while in others, members of the transplant or related medical teams may be identified and empowered to fulfill the donor advocate role.

Clinical decisions are taken according to good clinical practice usually outside the direct monitoring of MS CAs. In line with general principles and according to national binding legal requirements, the CAs should safeguard HPC donors and collect relevant information about SAR/SAE with the aim to continuously improve donor and recipient safety. Therefore MS should establish the responsibilities at different stages of the related and unrelated donor processes and an efficient flow of information from the local level (e.g. donor center, donor registry, collection center, transplant center) to the central one (regional and national donor FU outcome registries and CAs).

The following table shows an example of matrix of responsibilities in the performance of donor FU management.

<table>
<thead>
<tr>
<th>Activities Responsibility</th>
<th>Policies definition</th>
<th>FU SOPs definition</th>
<th>Follow-up management</th>
<th>Notification of SAR</th>
<th>FU data collection</th>
<th>Monitoring processes</th>
<th>Management of notified SAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Competent Authority</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Donor FU outcome registry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Transplant Center</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Donor Center</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collection Center</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissue establishment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X (SAE)</td>
</tr>
</tbody>
</table>

In the matrix the role of Tissue Establishments consists of registering and notifying to the CAs any serious adverse event (SAEs) associated with the procurement, testing, processing, storage and distribution of HPC possibly related to the donor and having a potential impact on donor FU.

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This document is aimed at harmonizing the HPC donor FU procedures in place among MSs in order to protect the health and well-being of both related and unrelated (volunteer) HPC donors. The guidelines also describe donor management in case of DLI and multiple HPC donations. These guidelines should be disseminated by the Competent Authorities (CAs) to the donor FU outcome registries.

9.3. **Types of donor to be followed-up**

HPC collections are well established and consolidated procedures. BM collection is in general associated with mild common side effects including fatigue and pain in the site of punctures. PBSC collection requires 4-6 days of G-CSF administration and one or two HPC apheresis procedures. Side effects are commonly caused by the administration of the growth factor and include bone pain, fatigue, and headache. The availability of new mobilizing agents, used alone or in combination with G-CSF (e.g. Plerixafor used in case of poor mobilizer donors) and the development of new regimens applied also for BM collection, make it necessary to pay attention to the potential new SAR in healthy donors. The side effects of HPC collections are mostly transient and well tolerated. SARs are uncommon in healthy donors; nevertheless, all donors shall be fully informed and carefully assessed before and after HPC donation.

For this reason specific and appropriate policies and procedures for following up HPC donors are necessary. Donor FU procedures shall be applied to the following types of donors, and for any HPC source.

<table>
<thead>
<tr>
<th></th>
<th>BM</th>
<th>PBSC</th>
<th>LY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrelated Adult Donor</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Related Adult Donor</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Related Pediatric Donor</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

Related and unrelated HPC donors should be followed up according to the same procedures and the same timeframe as well.

9.4. **Counselling, timing and content of information material about FU procedures and consent**

Over the past two decades several professional organisations have worked to ensure that the process of HPC donation was performed safely and ethically.

The donor shall be informed and counselled at the time of recruitment and an initial informed consent must be obtained at that time. When the donor is selected for a specific patient, he/she shall be counselled again and a specific consent must be obtained for the requirement of blood samples for further tests, including infectious diseases markers.
At the time of work-up the donor must be extensively informed on the potential risks and consequences related to BM and PBSC collection and on the need to comply with a medical follow-up at defined time after donation. The donor should be made aware of the FU procedures (timing, type of medical assessment) and any helpful donor contact information should be registered in the donor documentation, including where applicable the contact information of the general practitioner.

The same information regarding FU procedures shall be followed in case of pediatric donors with the parents or whoever assumes parental responsibility or with the pediatric donor if he/she is able to fully understand.

9.5. **HPC donor follow-up with regard to psychosocial assessment**

The psychological condition of the donor should be assessed before donation. In particular, the motivations should be considered mainly with the aim to distinguish between the donor desire to help and the expectation of a personal gain. In case of related donors, they may have different motivations from unrelated and in general the emotional involvement is greater than in unrelated donors. After donation and during the donor FU the psychosocial impact of the HPC donation should be taken into consideration with regard to the potential influence on the quality of donor life.

In the literature there are few studies concerning the quality of life assessment in adult HSC donors. According to the literature it seems that the impact of donation on the psychosocial status of living donor is limited. However, some negative outcomes have been reported. Mild depression and family problems are the most extensively documented outcomes related to the donation.

Therefore, a donor psychosocial assessment before and after HPC donation should be included in the donor management protocol.

Several psychometric aspects may be considered for the donor psychosocial FU. A partial list is suggested by ELIPSY that may be applied also to the HPC donor, it includes:

- donor quality of life before and after donation;
- mental health / psychological well-being assessed before and after donation;
- socioeconomic status;
- donor social support;
- employment status;
- expectations and motivations of the donor;
- information received about the donation procedure;
- information received about possible outcomes for the recipient;
- customer satisfaction of the donor during the donation procedure.

9.6. **Types of donor follow-up to be performed**

The best practice for conducting the HPC donor FU should include the following:

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*Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry*
- a specific questionnaire for the collection of information on the physical and psychological status of the HPC donor;
- a medical interview conducted by health professional if a deeper investigation needs to be performed in case of pathological conditions occurring after HPC donation and possibly related to it;
- a physical examination in any case it needs;
- blood testing including at least blood cell count where necessary;
- diagnostic exams in case of further clinical information are necessary.

Each of the mentioned tools could be used alone or in combination at different time after HPC donation.

Although it is recognised that HPC donation can determine a small but unavoidable risk of harm for the donor, it is the ethical and legal responsibility of the collection center/donor registry to minimize any ‘avoidable’ risk. To achieve this aim any pre-existing clinical condition potentially increasing the risk of harm before, during and after HPC collection shall be investigated in depth. If there is any doubt about the eligibility of the donor in the presence of a particular medical condition, it is recommended to carefully assess the donor to prevent any potential harm.

The FU process shall include two different phases: the short-term FU, from the date of collection until one year after, and the long-term FU, from the second until the tenth year after collection.

### 9.6.1 Short-term FU

In the timeframe of the short-term FU the donor health status should be evaluated at regular intervals during the first year after the last HPC donation. In the first month after HPC donation (very short-term follow-up) it is proposed that the donor should be evaluated at the day 1, 7 and 30, including blood testing. It is very important to interview the HPC donor taking note of any described symptoms or issues possibly caused by the HPC donation. Interview and physical examination are strongly recommended in cases of HPC donors with comorbidities that did not affect itself their eligibility but that can place the donor at higher risk of developing side effects. The FU time schedule can be changed according to the donor situation or needs. This condition can occur more often in the case of related HPC donors.

After the first month a donor health assessment should be carried out at 12 months if the donor has not reported any problems.

### 9.6.2 Long-term donor FU

HPC collection is not without risks. Immediate risks can be related to the anesthesia and physical trauma in case of BM donation, growth factor administration and apheresis procedures in case of PBSC donation. Furthermore, long-term clinical hypothetical risks can be linked to the HPC depletion and the immune system stimulation, potentially able to cause the development of malignancies.

Performing clinical assessments at least once a year would result in a close follow-up. However this time schedule needs a substantial amount of resources. Therefore it would be helpful that MSs address a more stringent FU procedure at least in case of potentially more vulnerable groups of donors (elderly donors, multiple donations, donors mobilized with new agents).

Long-term donor FU refers to the period following the first year after the last HPC donation and should be extended for at least ten years after (WMDA definition).
During the long-term donor FU donor health assessment should be performed at least at 1, 5 and 10 years after HPC donation. Annual and biannual FU should be encouraged.

Considering that full donor compliance with the long-term FU procedures is a difficult goal to achieve, it is recommended to construct and maintain a solid contact system. A donor follow-up questionnaire should be submitted to the donor for the collection of information about his/her health status. The questionnaire should explore if pathological conditions or diseases occurred after HPC donation. If the donor indicates any conditions that could possibly be related to the donation process, a deeper medical evaluation of the donor should be carried out in order to assess the relationship – if any - with the HPC donation.

At the moment a greater amount of information is collected at short-term rather than at long-term donor FU. Many HPC donors are lost at the long-term FU, mainly related donors whose family recipient has had a poor clinical outcome after transplantation or the donor has moved without updating his or her contact information.

The donor FU data would be greatly improved if all the donors (related and unrelated) were included and reported to the donor FU outcome registry.

### 9.6.3 Minimum data set to be recorded after HPC donation procedure

Information on short- and long-term donor outcomes is important to ensure maximum donor safety. In recent years the HPC transplant scenario is significantly changed mainly in regard to donor characteristics (increasing the median age of related donors leading to potentially more donors with occult or manifest comorbidities at the time of donation) and collection procedures (introduction of reduced-intensity conditioning regimens resorting to the need of multiple donations of therapeutic cells). In the described scenario FU procedures become extremely important to collect any relevant information for assessing the donor safety at short- and long-term after donation.

Current available data concerns mainly unrelated donors and comes from the numerous donor outcome registries existing in different countries. Other different scientific institutions participate in the collection of FU data and outcomes of related donors, demonstrating that the experience of side effects occurs frequently and with the same patterns in related donors too. A small but real risk of SAE exists for both unrelated and related donors and in the latter group, current experience suggests that the risk seems to be higher, even though some reporting bias and the lack of adequate amount of prospective follow-up data have to be considered (see footnote 14).

Because of the rarity of serious side effects, the goal to obtain useful information in terms of quality and quantity of data may only be achieved by large international participation including unrelated and related donors. In the light of the need to collect comparable data from MS, it is important to establish standardized FU procedures for both related and unrelated donors with the scope to collect information on short- and long-term outcomes of HPC donation and to form a solid basis for future donor selection and counselling that use WBMT recommendations.

Long-term FU data should be taken into consideration for addressing the best donor risk assessment and for discussing how to maintain HPC collection procedures safe. The proposed minimum data set has the main aim to obtain information on potential long-term complications such as the incidence and type of malignancies and autoimmune disorders, occurring in all types of HPC donors.

Taking into account the WMDA forms in use for the unrelated donors (see footnote 9) and the donor outcome data collection forms proposed by EBMT on the basis of WBMT recommendations (see footnote 13), the following minimum data set is recommended for the application in both unrelated and related donors.

---

9.6.4 Minimum data set at the time of HPC donation

Donor data
- Donor identification code (Donor ID)
- Date of birth or age at donation
- Sex
- Relationship to the recipient (twin, sibling, other family member, unrelated donor)
- Acceptable comorbidities or familiarity conditions at the time of the HPC donation
- Concurrent therapies if applicable

Collection data
- Start date (the day of first administration of GF in case of HPC mobilization, the day of anesthesia in case of BM)
- Donation completed: YES or NO
- Type of donation (PBSC, BM, LY)
- Number of collections (in case of PBSC or LY)
- Subsequent donations (Type)
- Interval between subsequent donations
- Growth factors or biosimilars
- Days of administration
- Other drugs used for mobilization (biosimilar or biological agents).

9.6.5 Minimum data set to be recorded during short-term FU procedures

Donor and collection data (Identification Donor Code - IDC, age, date of collection, type of donation, 1° or 2° donation)
Time of data reporting (day 1, 7, 30)
Questionnaire. In the form at least the following items should be explored:
- donor physical and emotional status,
- any relevant problem occurring after start of the donation procedure,
- donor’s assessment of the quality of information received before and during collection
- donor’s assessment of the quality of care provided by the staff,
- donor’s general judgment on the donation experience.
Donor should be followed from the first injection of a mobilizing agent, the start of anaesthesia or the start of apheresis (in case of non-stimulated leucapheresis, e.g. for DLI) until the day after collection through physical examination and at least blood testing (complete blood cells count including platelets).
Further examination should be applied in case the donor notifies any clinical problems in the short term after donation.
Where this occurs, the clinical problems should be investigated in depth and the FU procedures tailored for the specific situation in short and long-term FU.
In case of LY donation the same questionnaire may be applied at least 1 month after donation. If the donor performs several LY donations, it should be taken into consideration to assess any change in the donor immunophenotype.22

9.6.6 Minimum data set to be recorded during long-term FU procedures

Donor and collection data (Identification Donor Code - IDC, age, date of collection, type of donation, 1° or 2° donation)

Follow-up at year(s) post donation: 1, 5, 10 (other time schedules may be applied)

Questionnaire. In the form used at least the following items should be explored:

- donor physical and emotional status,
- any relevant problem occurring after donation,
- feedback on the most recent medical examination carried out by the donor’s general practitioner,
- information on current medications if applicable,
- information on recent blood testing results if available,
- information on contacts with the health care system.

The personnel performing the donor interview should pay serious attention to the following diseases if alerted by the donor:

**Malignancy**

Type: Hematologic
Non-hematologic malignancy

Status: Confirmed / Unconfirmed

**Auto-immune diseases**

Type: One organ
More than one organ / Systemic

Status: Confirmed / Unconfirmed

**Other diseases**

Donor survival status:
Alive
Death

Cause of death

9.7. Definition and reporting of complications possibly related with the HPC donation procedure

In case of diseases occurring in the donor, the International Classification of Diseases code (ICD 10)\(^{23}\) should be used for data reporting. The ICD code should be used for the reporting of the cause of death too.

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\(^{23}\)http://apps.who.int/classifications/icd10/browse/2016/en

Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry
9.8. **Follow-up of pediatric donor**

The scientific literature shows that in the pediatric setting BM is the most commonly used source. PBSC collection after G-CSF mobilization has also been used recently in pediatric HPC donors but its use is not recommended.

The serious side effects described in adult HPC donors after G-CSF administration (vascular events, splenic enlargement, or rupture) have been rarely reported in children. The long-term effects, potentially related to G-CSF have never been reported in case of pediatric donors. Even though many other drugs are not specifically licensed for pediatric use, in the case of pediatric donors mobilized with G-CSF, the informed consent signed by the parents shall clearly include this issue and the parents shall be made aware of the potential long-term side effects of the mobilizing agents.

The short-term FU should be carried on in the same way of adult donor FU; concerning long-term FU, the child should be followed up with a higher frequency in the first period and any serious side effect should be fully investigated. It is also recommended to prolong the duration of the long-term FU over the time limit (ten years) suggested for adult HPC donors. Special care is recommended for pediatric donors younger than four years because of higher risk of complications both at the time of BM and PBSC collection.

It is recommended that MSs develop best practices, general recommendations, and specific standard operating procedures for the FU in very small HPC donor children.

**Quality of life of pediatrics donors**

A multidisciplinary team including psychologists should perform the pediatric donor’s assessment before and after HPC donation. Children who are being evaluated as potential HPC donors deserve special attention because their fears and concerns may be complex and accompanied by significant ambivalence, as showed by one of the first large-scale, longitudinal, multicenter investigations of pediatric HSC donor Health-related quality of life (HRQoL).\(^2\) The study findings demonstrate that approximately 20% of donors at each time point had very poor HRQoL, child self-reported HRQoL was significantly lower than parent proxy-reported HRQoL, and significantly lower than that of norms at pre-donation and 4 weeks post-donation, and younger children were at particular risk of poor HRQoL.

Despite future investigations and studies need to be performed focused on the reasons for HRQoL deficits among pediatric donors, it is strongly recommended that all centers have a psychosocial clinician in their staff, who regularly assesses the child and parents HRQoL concerns and provides psychosocial support during and after HPC donation. Dedicate resources are required to follow this issue with the aim to minimize such risks of poorer HRQoL in this context, and to support interventions and policy changes to ensure positive experiences for these donors.

9.9. **FU after second/subsequent HPC or LY donations**

A second HPC or LY donation is allowed from the donor for the same patient or for a different patient. For the same patient the second HPC donation should be allowed in case of early graft failure or relapse.

Donor follow-up should be conducted according to the policy and procedures defined by the donor FU outcome registry. In case of HPC or LY donation the time schedule and the operating methods of the FU shall be the same of those applied after the first donation.

While a donor can routinely be asked to donate HPC twice for the same or a different recipient, a third or subsequent donation should be very carefully considered and it should be carried out according to specific policies including a careful assessment of the donor.

It is recommended that a donor, who donated HPC for a patient, remains available for the same patient for at least 1 or 2 years, and then he/she may donate for a different patient. Concerning LY collection, it can be requested within the first 2 years after transplantation particularly if the patient has been treated with reduced intensity conditioning regimen. In rare situation LY donation may be delayed up to 2 years from the time of HPC transplant. It is recommended that the total number of LY donations does not exceed two subsequent collections; more than two LY donations should be avoided. In order to reduce LY donation it is strongly recommended to cryopreserve LYs previously collected and not used.

Even though no scientific data are available to support a specific rule about how many donations of BM versus PBSC should be allowed, nevertheless it is recommended that the CA defines a policy to establish a maximum number of HPC donation in order to take care of the donor health status in general.

Concerning LY collection, it can be requested within the first 2 years after transplantation particularly if the patient has been treated with reduced intensity conditioning regimen. In rare situation LY donation may be delayed up to 2 years from the time of HPC transplant. It is recommended that the total number of LY donations does not exceed two subsequent collections; more than two LY donations should be avoided. In order to reduce LY donation it is strongly recommended to cryopreserve LYs previously collected and not used.

9.10. Data reporting

The proposed minimum data set for HPC/LY donor FU has the scope to standardize and harmonize the information collected by the existing institutions at local and national level across Europe. Starting from this first objective, the proposal of a basic functional entity, the donor outcome follow-up registry, performing related and unrelated FU data collection and providing a systematic reporting to the CAs, is the second goal of the JA. The proposed donor outcome follow-up registry should be acceptable for all EU MSs.

Considering that, the HPC donor centers are already in charge of the unrelated donor FU and that these facilities in most of the MSs work in compliance with WMDA international standards ensuring consistency in the unrelated donor care, it could be reasonable to recommend that the same entities take care of the related donor FU too.25

However, according to the survey results, in many MSs other different entities (e.g. collection centers and/or transplant centers) are in charge of HPC related donors including FU procedures. This scenario may be considered to be the reason for the differences between unrelated and related

donor standards of care and underlines the problem of potential conflicts of interest if the team responsible for related donors is the same who is in charge of the recipients.

The main potential advantages for tasking donor outcome follow-up registries to be the reference organization for both related and unrelated donors are that the same standardized procedures would be applied, possibly supported by dedicated IT, for the reporting of a minimum FU data set to the CAs and that the CA can entrust this function to specifically trained staff, not directly responsible for the HPC recipient.

The donor outcome follow-up registry may also need expertise in pediatric donor FU and in the management of FU of elderly donors or donors with health disorders, since suitability criteria for related donors are often less stringent than for unrelated donors. Therefore each MS should define, under the organizational point of view, how to comply with the harmonization of the HPC donor FU management, applying the minimum data set and the common format here proposed.

Independently of the national organization, the CAs should receive at least on an annual basis the following information on donor FU management:

**DONOR ASSESSMENT POST HPC DONATION**

**Annual Report**

**DONATION DATA**

Number of donors and donations of cellular products in the reporting year:

<table>
<thead>
<tr>
<th></th>
<th>BM</th>
<th>PBSC</th>
<th>LY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N.</td>
<td>N.</td>
<td>N.</td>
</tr>
<tr>
<td>N. donor</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>N. donations</td>
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</tbody>
</table>

Unrelated Adult Donor

Related Adult Donor

Related Pediatric Donor

Number of donors donating multiple cellular products:

<table>
<thead>
<tr>
<th></th>
<th>HPC - LY</th>
<th>LY - LY</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrelated Adult Donor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Related Adult Donor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Related Pediatric Donor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry*
FOLLOW – UP DATA
How many donors were lost to follow-up#?

<table>
<thead>
<tr>
<th></th>
<th>HPC/LY</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>30 d</td>
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<tr>
<td>Unrelated Adult Donor</td>
<td></td>
</tr>
<tr>
<td>Related Adult Donor</td>
<td></td>
</tr>
<tr>
<td>Related Pediatric Donor</td>
<td></td>
</tr>
</tbody>
</table>

Number and type of SAR* occurring during FU

<table>
<thead>
<tr>
<th>IDC</th>
<th>BM</th>
<th>PBSC</th>
<th>LY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Short</td>
<td>Long</td>
<td>Short</td>
</tr>
</tbody>
</table>
| ICD: ICD 10 Coding ([http://apps.who.int/classifications/icd10/browse/2016/en](http://apps.who.int/classifications/icd10/browse/2016/en))

# Lost to follow-up
In according to EBMT DONOR OUTCOME DATA MANUAL this definition applies in case of:
- any contact with the donor has been lost (follow the guidelines of your center on how many attempts to contact the donor have to be done for this status to be acceptable).
- the donor refused to be followed up.

*Type of SAR
The unexpected SAR should be reported using ICD 10 Coding ([http://apps.who.int/classifications/icd10/browse/2016/en](http://apps.who.int/classifications/icd10/browse/2016/en)).

It is recommended to use the classification suggested in the Appendix I of the EBMT DONOR OUTCOME DATA MANUAL (see footnote 12), that summarizes the most frequent clinical diseases possibly related to HPC donation. In the Appendix three different sections are present:

A1: Selection of SAE during donation procedure
A2: Selection of malignancies to be recorded during long-term follow-up
A3: Selection of autoimmune disorders to be recorded during long-term follow-up
They classify the events during donation procedure or during long-term FU.

10. Annexes

10.1. Annex I: Table of definitions

<table>
<thead>
<tr>
<th>Terms</th>
<th>Definition</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allogeneic (use)</td>
<td>Cells or tissues removed from one person and applied to another.</td>
<td>Directive 2004/23/EC</td>
</tr>
<tr>
<td>Apheresis</td>
<td>A medical technology in which the blood of a donor is separated into its component parts, the desired component is removed, and the remaining components are returned to the donor.</td>
<td>FACT-JACIE Standard 6° Edition</td>
</tr>
<tr>
<td>Cellular therapy product</td>
<td>PBSC collected in peripheral blood by apheresis; BM: bone marrow source of HPC or mesenchymal stem cells; Unstimulated leukapheresis: donor lymphocytes (DLI) collected by apheresis or blood donation.</td>
<td>Donor Manual Outcome EBMT</td>
</tr>
<tr>
<td>Collection/Procurement facility (center)</td>
<td>A medical facility where HPC collection from volunteer donors actually takes place.</td>
<td>WMDA 20140101-STD- Standards, effective January 1, 2014</td>
</tr>
<tr>
<td>Competent Authority</td>
<td>The body which has been delegated the responsibility for ensuring that tissue and cell donation, banking and human application are appropriately promoted, regulated and monitored in the interest of donor and patient safety and public transparency on a national or regional basis by their government.</td>
<td>EDQM 3rd Edition 2017</td>
</tr>
<tr>
<td>Donor</td>
<td>Every human source, whether living or deceased, of human cells or tissues.</td>
<td>Directive 2004/23/EC</td>
</tr>
<tr>
<td>Donor center</td>
<td>An organisation responsible for</td>
<td>WMDA 20170101-BCST-</td>
</tr>
<tr>
<td>Terms</td>
<td>Definition</td>
<td>Reference</td>
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</tr>
<tr>
<td>donor recruitment, consenting, testing, management and the collection of donor personal, genetic, medical data</td>
<td>Standards, effective January 1, 2017</td>
<td></td>
</tr>
<tr>
<td>Granulocyte colony-stimulating factor (G-CSF)</td>
<td>A cytokine that stimulates the bone marrow to produce granulocytes (white cells) and HPC and cause these cells to mobilize (move) to the peripheral blood where they can be collected from the veins for transplantation</td>
<td>WMDA 20170101-BCST-Standards, effective January 1, 2017</td>
</tr>
<tr>
<td>Hematopoietic progenitor cells (HPC)</td>
<td>The progenitor cells, which give rise to blood and immune system cells. These cells are found in bone marrow, growth factor stimulated peripheral blood, and umbilical cord blood.</td>
<td>WMDA 20170101-BCST-Standards, effective January 1, 2017</td>
</tr>
<tr>
<td>Informed consent</td>
<td>A procedure whereby information concerning the donation process is presented to the donor or to the donor’s next of kin, without coercion, with an opportunity for them to ask questions, after which specific approval is documented.</td>
<td>EDQM 3rd Edition 2017 Directive 2006/17/EC</td>
</tr>
<tr>
<td>Long-term FU</td>
<td>It is defined as the time period following the first year after donation and extending for at least ten years.</td>
<td>WMDA 20170101-BCST-Standards, effective January 1, 2017</td>
</tr>
<tr>
<td>Procurement</td>
<td>A process by which tissue or cells are made available</td>
<td>Directive 2004/23/EC</td>
</tr>
<tr>
<td>Procurement organisation</td>
<td>A health care establishment or a unit of a hospital or another body that undertakes the procurement of human tissues and cells and that may not be accredited, designated, authorised or licensed as a tissue establishment.</td>
<td>Directive 2006/17/EC</td>
</tr>
<tr>
<td>Recipient</td>
<td>A person into whom an organ, tissue or cells is/are grafted/implanted.</td>
<td>EDQM 3rd Edition 2017</td>
</tr>
<tr>
<td>Registry</td>
<td>An organisation responsible for coordination of the search for hematopoietic stem cells from</td>
<td>WMDA 20170101-BCST-Standards, effective January 1, 2017</td>
</tr>
<tr>
<td>Terms</td>
<td>Definition</td>
<td>Reference</td>
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<tr>
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<td>--------------------------</td>
</tr>
<tr>
<td>donors (including cord blood) unrelated to the potential recipient.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAR</td>
<td>An unintended response, including a communicable disease, in the donor or in the recipient associated with the procurement or human application of tissues and cells that is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs, hospitalization or morbidity;</td>
<td>Directive 2004/23/EC</td>
</tr>
<tr>
<td>Serious adverse event</td>
<td>Any untoward occurrence associated with the procurement, testing, processing, storage and distribution of tissues and cells that might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions for patients or which might result in, or prolong, hospitalization or morbidity;</td>
<td>Directive 2004/23/EC</td>
</tr>
<tr>
<td>Short-term FU</td>
<td>From the end of the donation procedure up to 30 days after donation</td>
<td>Donor Manual Outcome EBMT</td>
</tr>
<tr>
<td>Start date of donation procedure</td>
<td>The donation procedure starts with the first injection of a mobilizing agent, the start of anesthesia or the start of apheresis (in case of non-stimulated leukapheresis, e.g. for DLI). Even if the preparative actions (i.e. start of injections, apheresis or anesthesia) are stopped prematurely (due to donor or recipient reasons) the activity fulfills the definition of a donation procedure and the donor should be registered and followed.</td>
<td>Donor Manual Outcome EBMT</td>
</tr>
<tr>
<td>Testing laboratories</td>
<td>These laboratories perform the histocompatibility, blood group, infectious disease, and other testing of the prospective donors and patients.</td>
<td>WMDA 20170101-BCST-Standards, effective January 1, 2017</td>
</tr>
<tr>
<td>Terms</td>
<td>Definition</td>
<td>Reference</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Time of collection</td>
<td>The time of day at the end of the cellular therapy product collection procedure.</td>
<td>FACT-JACIE Standard 6th Edition</td>
</tr>
<tr>
<td>Tissue Establishment</td>
<td>It is a tissue bank or a unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissues and cells are undertaken. It may also be responsible for procurement or testing of tissues and cells.</td>
<td>Directive 2004/23/EC</td>
</tr>
<tr>
<td>Transplantation center</td>
<td>A healthcare establishment, a team or a unit of a hospital or any other body which undertakes the transplantation of organs and is authorised to do so by the Health Authority under the regulatory framework in the member state concerned.</td>
<td>EDQM 3rd Edition 2017</td>
</tr>
<tr>
<td>Work-up</td>
<td>At this stage, a volunteer donor has been identified as an acceptable match for a patient, agrees to donate HPC after a full donor information and counselling session, and is medically evaluated for their fitness to donate HPC.</td>
<td>WMDA 20170101-BCST- Standards, effective January 1, 2017</td>
</tr>
</tbody>
</table>
10.2. Annex II: Questionnaire on HPC donor follow-up registries

WORKPACKAGE

QUESTIONNAIRE on HSC DONOR FOLLOW-UP REGISTRIES

<table>
<thead>
<tr>
<th>COMPETENT AUTHORITY</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>COUNTRY</td>
<td></td>
</tr>
</tbody>
</table>

SECTION A: Unrelated donors

1. Does your country collect HSC donor follow-up information?

- [ ] YES
- [ ] NO

2. If yes, who does collect information in your country?

- [ ] National Registry
- [ ] Regional/local Registry
- [ ] Competent Authority
- [ ] Competent Authority (blood)
- [ ] Competent Authority (tissue&cells)
- [ ] Other (specify) __________________________________________________________________

3. If data are collected at regional/local level are they reported to a national body?

- [ ] YES
- [ ] NO

If yes:

- [ ] At the National Registry
- [ ] At the National Competent Authority
- [ ] Other (specify) __________________________________________________________________

4. For which kind of donation are data collected?

- [ ] Bone marrow (BM)
- [ ] Peripheral blood HSC (PBSC)
- [ ] Both

5. Did your country define standard procedures for donor follow-up?

- [ ] YES
- [ ] NO
8. If yes, do the procedures define standard criteria for:

<table>
<thead>
<tr>
<th>□ Short term follow-up (within 1 month*)</th>
<th>□ Long term follow-up (within 10 years*)</th>
<th>□ Both</th>
</tr>
</thead>
</table>

(*as WMDA standards)

7. Concerning the short term follow-up does it include:

- Questionnaire (if Yes, when(*)
- Blood testing (if Yes, when(*)
- Physical examination (if Yes, when(*)
- Other diagnostic tests (specify type and timing(*))

8. Concerning long-term follow-up does it include?

- Questionnaire (if Yes, when(*)
- Blood testing (if Yes, when(*)
- Physical examination (if Yes, when(*)
- Other diagnostic tests (specify type and timing(*))

9. Does your Country collect SARE during donor follow-up?

- □ YES
- □ NO

Are you able to correlate SARE events to originally reported donor comorbidities?

- □ YES
- □ NO

10. If your Country collect SARE during donor follow-up, please specify to whom they are reported

- □ National Competent Authority
- □ Regional Authority
- □ WMDA
- □ Other (specify) _______________________

11. Please attach herewith a copy of the form utilized in your country to collect HSC donor follow up, either in doc or pdf and if possible together with a translation in English

**Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry**
12. Do you apply multiple donation rules?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>

Multiple HSC donations are possible towards only one patient?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>

If yes, which is the maximum number of donations?
BM .......................  PBSC ...........................
Lymphocytes ............................... 

Multiple HSC donations are possible towards several patients?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>

If yes, which is the maximum number of donations?
BM .......................  PBSC ...........................
Lymphocytes ............................... 

Which is the minimum interval between 2 donations:

<table>
<thead>
<tr>
<th>BM</th>
<th>BM and PBSC</th>
<th>PBSC</th>
<th>PBSC and Lymphocytes</th>
<th>Lymphocytes</th>
</tr>
</thead>
</table>

13. In case of multiple donations, do you consequently report follow-up duration to the second/last donation day?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>
SECTION B: Related donors

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does your country collect HSC donor follow-up information?</td>
<td>[ ] YES  [ ] NO</td>
</tr>
<tr>
<td>2. If yes, who does collect information in your country?</td>
<td>[ ] National Registry  [ ] Regional/local Registry  [ ] Competent Authority tissue&amp;cells  [ ] Competent Authority blood  [ ] Other (specify)</td>
</tr>
<tr>
<td>3. If data are collected at regional/local level are they reported to a national body?</td>
<td>[ ] YES  [ ] NO</td>
</tr>
<tr>
<td>If yes:</td>
<td>[ ] At the National Registry  [ ] At the National Competent Authority  [ ] Other (specify)</td>
</tr>
<tr>
<td>4. For which kind of donors are data collected?</td>
<td>[ ] Bone marrow (BM)  [ ] Peripheral blood HSCHSC  [ ] Both</td>
</tr>
<tr>
<td>5. Did your country define standard procedures for donor follow-up?</td>
<td>[ ] YES  [ ] NO</td>
</tr>
<tr>
<td>6. If yes, do the procedures define standard criteria for:</td>
<td>[ ] Short term follow-up  [ ] Long term follow-up  [ ] Both</td>
</tr>
<tr>
<td>How long is your long term follow-up?</td>
<td></td>
</tr>
<tr>
<td>7. Concerning the short term follow-up does it include?</td>
<td>(*) For example: if you do the questionnaire in the first day and one week after donation you should indicate in the line +1 and +7</td>
</tr>
<tr>
<td>Questionnaire (if Yes, when (*))</td>
<td></td>
</tr>
<tr>
<td>Blood testing (if Yes, when (*))</td>
<td></td>
</tr>
<tr>
<td>Physical examination (if Yes, when (*))</td>
<td></td>
</tr>
<tr>
<td>Other diagnostic tests (specify type and timing(*))</td>
<td></td>
</tr>
<tr>
<td>8. Concerning long-term follow-up does it include?</td>
<td>(*) For example if you do the questionnaire in the first month and one year after donation you should indicate in the line +1 and +12</td>
</tr>
<tr>
<td>Questionnaire (if Yes, when(*))</td>
<td></td>
</tr>
<tr>
<td>Blood testing (if Yes, when (*))</td>
<td></td>
</tr>
<tr>
<td>Physical examination (if Yes, when (*))</td>
<td></td>
</tr>
</tbody>
</table>
9. Do you have a specific paediatric donor follow-up?

☐ YES  ☐ NO

10. Are there different procedures for paediatric short term and long term follow-up?

☐ YES  ☐ NO

If yes please specify:

**Short term follow-up**

("For example if you do the questionnaire in the first day and one week after donation you should indicate in the line +1 and +7")

☐ Questionnaire (if Yes, when\( ^* \)____________________)

☐ Blood testing (if Yes, when \( ^* \)____________________)

☐ Physical examination (if Yes, when \( ^* \)____________________)

☐ Other diagnostic tests (specify type and timing \( ^* \)____________________)

**Long term follow-up**

("For example if you do the questionnaire in the first month and one year after donation you should indicate in the line +1 and +12")

☐ Questionnaire (if Yes, when \( ^* \)____________________)

☐ Blood testing (if Yes, when \( ^* \)____________________)

☐ Physical examination (if Yes, when \( ^* \)____________________)

☐ Other diagnostic tests (specify type and timing \( ^* \)____________________)

11. Please attach herewith a copy of the form utilized in your country to collect HHC donor follow up, either in doc or pdf and if possible together with a translation in English

12. Do you apply multiple donations rules for related-donors?

☐ YES  ☐ NO

If yes, which is the maximum number of donations?

BM ....................  PBSC ...................... Lymphocytes

...........................................................
Which is the minimum interval between 2 donations:

<table>
<thead>
<tr>
<th>Type</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM</td>
<td></td>
</tr>
<tr>
<td>BM and PBSC</td>
<td></td>
</tr>
<tr>
<td>PBSC</td>
<td></td>
</tr>
<tr>
<td>PBSC and Lymphocytes</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes</td>
<td></td>
</tr>
</tbody>
</table>

13. In case of multiple donations, do you consequently report follow-up duration to the second/last donation day?

- [ ] Yes
- [ ] No

9. Does your Country collect SARE during donor follow-up?

- [ ] YES
- [ ] NO

Are you able to correlate SARE events to reported donor comorbidities?

- [ ] YES
- [ ] NO

10. If your Country collect SARE during donor follow-up, please specify to whom they are reported

- [ ] National Competent Authority
- [ ] Regional Authority
- [ ] WMDA
- [ ] Other (specify)

Thank you!

Please remember to send this questionnaire dully completed no later than ………………. to

CNT – letizia.lombardini@iss.it; paola.diciaccio@iss.it; CNS – simonetta.pupella@iss.it
10.3. Annex III: Results of the HPC donor follow-up survey

One of the main aims of WP5 is to increase and ensure the safety of HSC donors.

A questionnaire has been set up to carry out a detailed survey on existing HSC donor follow up registries, practices, and data collected. Once data are consolidated, we will have a clearer picture of the different situation in EU countries about HSC donor follow up (not only data collected by WMDA).

A guideline related to the mail safety issues criteria & standard data set, IT specifications, governance for a national registry, etc. will be drawn in close collaboration with WMDA and circulated among selected stakeholders. This guideline will then be disseminated to Competent Authorities (CAs) and HSC donor centres.
WP5 (HSC for Transplantation) is co-led by the Ministry of Health (MoH) of Croatia and ISS – Italian National Transplant Centre (CNT)

<table>
<thead>
<tr>
<th>WPS Associated Partners</th>
<th>WPS Collaborating Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ABM – France</td>
<td>• WMDA – The Netherlands</td>
</tr>
<tr>
<td>• Socialstyrelsen – Sweden</td>
<td>• EBMT – Spain</td>
</tr>
<tr>
<td>• Sulk – Czech Republic</td>
<td>• FACT-NETCORD – Spain</td>
</tr>
<tr>
<td>• IPST – Portugal</td>
<td>• CBE – Belgium</td>
</tr>
<tr>
<td>• HTO – Greece</td>
<td>• Vilnius University Hospital – Lithuania</td>
</tr>
<tr>
<td>• MFH – Malta</td>
<td>• MoH – Cyprus</td>
</tr>
<tr>
<td>• AFMPS – Belgium</td>
<td></td>
</tr>
<tr>
<td>• BEAT – Bulgaria</td>
<td></td>
</tr>
<tr>
<td>• MOH – The Netherlands</td>
<td></td>
</tr>
<tr>
<td>• KBCTIK – Poland</td>
<td></td>
</tr>
<tr>
<td>• NTO – Slovakia</td>
<td></td>
</tr>
</tbody>
</table>

Order of Partners as in the Technical Annex

⇒ This second version was sent on April 13rd, 2015 to all Associated and Collaborating Partners and the list of Cells Competent Authorities not involved in the Action plan in order to guarantee the widest coverage for this investigation: Austria, Cyprus, Denmark, Estonia, Finland, France, Germany, Ireland, Island, Latvia, Lithuania, Luxembourg, Malta, Norway, Poland, Romania, Slovenia, Spain, The Netherlands.

⇒ In July all questionnaires returned have been reviewed regarding their completeness and consistency and were subsequently summarized in this report.
Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry
2A and B. Who collects information in your country?

**UNRELATED**
- BG, SI, SK*
- DK, IT, UK

**RELATED**
- BE, BG, DK, FI, HU, PT, SI, SK*, PL

National Registry: BE, CZ, FI, HR, IE, LT, NL, PT
CA cell: FR

- Central (CA cell and National Registry)
- No Central: Regional / Local Registry
- No Central: Other (All TC)
- Both: National Registry / DC + Collection Centre
- Both: CA cells/TC + Harvesting Unit

* SK reports data also to a National Registry (see question 9.1A: Where are centers of collection at regional/local level and to whom are they reported to a national body?)

9.1A and B. Does your country collect SARE during donor follow up?

<table>
<thead>
<tr>
<th>Unrelated</th>
<th>Related</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE, CZ, DK, FI, HR, HU, IE, IT, NL, PL, PT, SE, SK, SI, UK</td>
<td>LV, MT, DG</td>
</tr>
<tr>
<td>BE, BG, CZ, DK, FI, HR, HU, IE, IT, NL, PL, SE, SK, SI</td>
<td>LV, MT, LT, PT, UK</td>
</tr>
</tbody>
</table>

Unrelated: 16 countries report SARE to CA – 12 countries report SARE to WMDA (HU: only to WMDA)
Related: 13 countries report SARE to CA – 4 countries report SARE to WMDA (HU: only to WMDA)

**Deliverable No. 8:** Guide for establishing a hematopoietic progenitor cells donor follow-up registry
9.2A and B. Are you able to correlate SARE events to originally reported donor comorbidities?

4. A and B. For which kind of donation are data collected?
5A and B. Did your country define standards procedures for donor follow up?

Question 9.B. Among related*: 5 countries have specific pediatric follow up

6A and B. Short and/or Long term follow up

unrelated

related

*Mean value of long term: 5.3 years
Median value of long term: 4.5 years (range 1 – 10 y)

Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry
7A. Concerning the short term follow-up does it include:

16 countries

- 31% Other diagnostic tests
- 50% Physical examination
- 94% Blood testing
- 81% Questionnaire

(*) for example: If you do the questionnaire in the first month and one week after donation you should indicate the line +1 and +7.
8A. Concerning the long term follow-up does it include:

**UNRELATED**

16 countries

FR, HU, PL, SI: if needed

- Other diagnostic tests: 31%
- Physical examination: 31%
- Blood testing: 50%
- Questionnaire: 87%

7B. Concerning the short term follow-up does it include:

**RELATED**

11 countries

FR, HU, PL, SI: if needed

- IT: upper abdomen echography at 1 month for PBSC donors: 100%
- Other diagnostic tests: 81%
- Physical examination: 82%
- Blood testing: 64%
- Questionnaire: 100%
7B. Concerning the short term follow-up does it include:

timing per country (in days*)

Questionnaire

Blood testing

Physical examination

(*) for example: if you do the questionnaire in the first month and one week after donation you should indicate in the line 1 and 1*.

8B. Concerning the long term follow-up does it include:

11 countries

- PL*: all depends on SOPs at level of Procurement Centre
- Other diagnostic tests
- Physical examination
- Blood testing
- Questionnaire

---

Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry
12A. Do you apply multiple donation rules?

**UNRELATED**

- BG, MT

**18 (90%)**

BE, CZ, DK, FI, FR, HR, HU, IE, IT, LV*, NL, PL, PT, SE, SI, SK, UK

**1 (5%)**

LV* no replies to the following questions

12.1A. Multiple donations are possible towards only one patient? If yes, is the maximum number of donations

**Country** | **MAX BM** | **MAX PBSC** | **MAX Lymphocytes**
---|---|---|---
BE | - | - | -
CZ | 2 | 2 | no max
FR | no max | 1 | no max
HR | 1 | 2 | no limit
HU | clinical decision | clinical decision | clinical decision
IE | 2 | 2 | no limit
IT | max 3 total donation | no limit
NL | 2 | - | -
PL | clinical decision (usually 2) | clinical decision (usually 1-2) | clinical decision (usually no limits)
SE | 2 | 2 | 2
SI | 2 | 2 | no limit
SK | 1 | 1 | -

12.2A. Multiple donations are possible towards several patients? If yes, is the maximum number of donations

**Country** | **MAX BM** | **MAX PBSC** | **MAX Lymphocytes**
---|---|---|---
BE | 2 | 2 | -
CZ | - | - | -
DK | 1 and 2 | 2 | 2 only registry
FI | 3 | 3 | -
HR | 1 | 2 | no limit
HU | clinical decision | clinical decision | clinical decision
IE | 2 | 2 | no limit
IT | 2 | 2 | no limit
NL | 2 | 0 | undefined
PL | clinical decision | clinical decision | clinical decision
PT | 2 | 2 | -
SE | 2 | 2 | 2
SK | max 4 total donations | no limit

**Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry**
12.3B. Which is the minimum interval between 2 donations:

**UNRELATED**

<table>
<thead>
<tr>
<th>Country</th>
<th>BM-BM</th>
<th>BM-PB</th>
<th>PB-PB</th>
<th>PB-Lym</th>
<th>Lym-Lym</th>
</tr>
</thead>
<tbody>
<tr>
<td>CZ</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>DK</td>
<td>NA</td>
<td>not defined</td>
<td>not defined</td>
<td>not defined</td>
<td>not defined</td>
</tr>
<tr>
<td>FI</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>FR</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
</tr>
<tr>
<td>HR</td>
<td>NA</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>-</td>
</tr>
<tr>
<td>HU</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
</tr>
<tr>
<td>IE</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
</tr>
<tr>
<td>IT</td>
<td>&gt; 20 days</td>
<td>&gt; 20 days</td>
<td>12 months</td>
<td>30 days</td>
<td>30 days</td>
</tr>
<tr>
<td>LT</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>NL</td>
<td>6 weeks</td>
<td>6 weeks</td>
<td>6 weeks</td>
<td>6 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>PL</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>clinical decision</td>
</tr>
<tr>
<td>PT</td>
<td>1 month</td>
<td>1 month</td>
<td>1 month</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SI</td>
<td>-</td>
<td>not defined</td>
<td>not defined</td>
<td>not defined</td>
<td>not defined</td>
</tr>
<tr>
<td>SK</td>
<td>-</td>
<td>6 months</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>UK</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
</tr>
</tbody>
</table>

12B. Do you apply multiple donation rules?

**RELATED**

[Diagram showing the distribution of responses regarding the application of multiple donation rules.]

---

*Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry*
### 12.1B. If you apply multiple donation rules, which is the maximum number of donations?

<table>
<thead>
<tr>
<th>Country</th>
<th>MAX BM</th>
<th>MAX PB</th>
<th>MAX Lym</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>BG</td>
<td>—</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>CZ</td>
<td>2</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>DK</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>FI</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>HR</td>
<td>1</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>IT</td>
<td>3 donation (BM + PB)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>LV</td>
<td>—</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>PL</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>PT</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>SI</td>
<td>2</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>SK</td>
<td>1</td>
<td>1</td>
<td>—</td>
</tr>
</tbody>
</table>

### 12.2B. Which is the minimum interval between 2 donations:

<table>
<thead>
<tr>
<th>Country</th>
<th>BM-BM</th>
<th>BM-PB</th>
<th>PB-PB</th>
<th>PB-Lym</th>
<th>Lym-Lym</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>BG</td>
<td>—</td>
<td>4 weeks</td>
<td>1 month</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CZ</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>DK</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>FI</td>
<td>2 - 3 weeks</td>
<td>1 week</td>
<td>3 weeks</td>
<td>2 - 3 months</td>
<td>NA</td>
</tr>
<tr>
<td>HR</td>
<td>NA</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>IT</td>
<td>&gt; 20 days</td>
<td>&gt; 20 days</td>
<td>12 months</td>
<td>30 days</td>
<td>30 days</td>
</tr>
<tr>
<td>LV</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>4 weeks</td>
<td>—</td>
</tr>
<tr>
<td>PL</td>
<td>clinical decision</td>
<td>clinical decision</td>
<td>—</td>
<td>—</td>
<td>clinical decision</td>
</tr>
<tr>
<td>PT</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>SI</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>SK</td>
<td>—</td>
<td>6 months</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>
13A and B. In case of multiple donations, do you consequently report follow-up duration to the second/last donation day?

**UNRELATED**
- BE, DK, FI, FR, HR, HU, IE, IT, LT, NL, PL, PT, SE, UK
  - 70%

**RELATED**
- HU, LT, MT, PT, UK
  - 69%
- BE, BG, DK, FI, FR, HR, IE, IT, LV, NL, PL, SE, SK
  - 18%

**Overview of the EU countries involved and the respondents**

**HSCT - rates in Europe 2013**

- N. autologous transplants per 10 million population
  - 0 or no report
  - 1 - 50
  - 51 - 100
  - 101 - 150
  - 151 - 200
  - 201 - 300

**European Society for Blood and Marrow Transplantation**

**Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry**
10.4 Annex IV: Flow chart of information in case of donor FU

Deliverable No. 8: Guide for establishing a hematopoietic progenitor cells donor follow-up registry