Disclaimer:
"The content of this Deliverable D3.2 represents the views of the author only and is his/her 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."

D3.2 Publication about the first year of the new software application and the importance of serious adverse events reporting

Grant Agreement number: 881553
Project acronym: SAVDON
Work Package number: WP1

Periodic report: 1st □ 2nd □ 3rd X 4th □

Period covered: from 01st January to 31st December 2020

Organisation: **World Marrow Donor Association (WMDA)**
LEAR: Eefke van Eerden
Project coordinator: Lydia Foeken
Tel: 0031 88 505 7900
E-mail: lydia.foeken@wmda.info
Organisation website address: www.wmda.info

Co-funded by
the Health Programme
of the European Union

"This Deliverable D3.2 of an activity received funding under an operating grant from the European Union's Health Programme (2014-2020)."

Content

Abbreviations

- DLI – donor lymphocyte infusion
- HPC-apheresis – haematopoietic progenitor cell - apheresis
- HPC-cord – haematopoietic progenitor cell - cord
- HPC-marrow – haematopoietic progenitor cell - marrow

Introduction

Every year, more than 21,000 volunteer donors are asked to donate blood stem cells to a patient they do not know. To ensure the continued viability of the global system using volunteer donors, donor health and safety are of critical importance.

A new central online reporting tool, introduced by the WMDA in July 2019, facilitates the reporting of Serious (Product) Events and Adverse Reactions - S(P)EARs. By using this tool, the WMDA can systematically collect and analyze information on S(P)EARs that affect donors and/or products from all WMDA stem cell donor registries and cord blood banks. Thereby, it allows the WMDA and the global community to gain insight in the occurrence of serious events and adverse effects in relation to blood stem cell donation and blood stem cell collection/processing. The data received via the online reporting tool is used in an anonymized manner to publish the S(P)EAR Annual Report.

The S(P)EAR online reporting tool allows for rapid reporting on severe incidents that require the immediate attention of all professionals in the field. When such a 'rapid alert' is identified, the rapid alert system can be used for dissemination of information to members of the international community regarding critical cases within 48 hours of submitting the report. In 2019, two rapid alerts were sent out. In April the first rapid alert was sent regarding a fatal event in an unrelated bone marrow donor. The rapid alert outlined a summary of published data on the incidence of serious adverse events associated with bone marrow donation as to help registries in addressing questions. The second rapid alert was sent in December following a report of a bone marrow product loss due to incorrect use of transfer collection system bags. The rapid alert listed recommendations for use of those type of bags. In 2020 a rapid alert was submitted on cryopreservation of stem cell products during the COVID-19 pandemic and on patient verification and extended typing. The rapid alerts of 2020 were also submitted to the Dutch Competent Authorities in order to ensure dissemination amongst EU Member States through the rapid alert platform.

This Deliverable D3.2 publication about the first year of the new software application and the importance of serious adverse events reporting is part of the 2020 work programme of the World Marrow Donor Association for the EU Third Health Programme (2014-2020). It is based on the data of the S(P)EAR Annual Report 2019 and focusses mainly on the adverse event and incident reports submitted to the WMDA by member organizations. The two rapid alert cases are also discussed. This report will be used to gain insight in the occurrence of serious events and adverse effects in relation to blood stem cell donation, collection and processing, and to provide a resource to support member registries to implement good and best reporting practices that serve to improve donor care.

The complete WMDA S(P)EAR Annual Report 2019 is freely accessible for WMDA members and available on request for people interested in the data. The rapid alerts are accessible to all interested parties, including non-members, via the WMDA website.

1. Overview of submitted S(P)EAR reports in 2019

A total of 210 S(P)EAR reports were submitted in 2019, while 206 S(P)EAR reports were submitted in 2018. Table 1 outlines the details of the received reports. In 2019, 27 different registries submitted reports, compared to 18 in the year prior. These reports can be categorized into three different categories: harm to recipient, harm to donor and risk of harm.

Harm to donor reports accounted for 73,8% of total reports (n=155), of which 56,8% (n=88) occurred within 6 months within donation (short term harm) and 43,2% (n=67) in more than 6 months after donation. More information on harm to donor reports can be found in chapter 2. Harm to recipient reports were submitted 23 times, amounting to 11% of the total reports received. More information on harm to recipient reports can be found in chapter 3. Risk of harm reports accounted for 15,2% of the total, with 32 reports that were classified as such. More information on the risk of harm reports can be found in chapter 4.

1.1 Type of product

In all report types (harm to donor, harm to recipient and risk of harm) the majority of reported incidents occurred with HPC-apheresis (71%) and HPC-marrow (21%) products (Figure 1). This is to be expected, as HPC-apheresis and HPC-marrow products make up the majority of used products in blood stem cell donation.

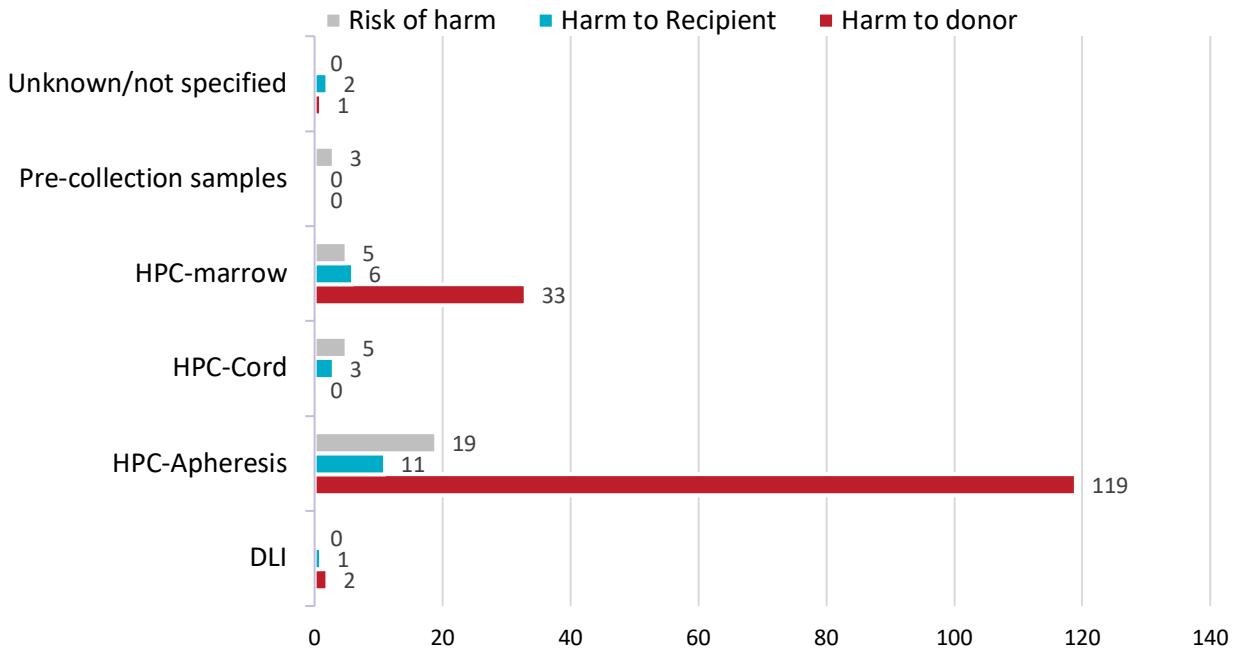

Figure 1: Type of (intended) cell product

1.2 Severity of reaction

The severity of a reaction has to be specified for short term harm to donor reports and in harm to recipient reports and is optional in other reports (Figure 2). Different gradations for the severity of a reaction exist varying from mild (grade 1) to death (grade 5). In the majority of reports that registered a reaction severity, it was classified as grade 1 (mild reaction) to grade 3 (severe reaction). In 16% the severity was considered to be life-threatening (n=21) or even death (n=4). The cases were death was reported all occurred with donors. In 1 case an unexpected donor death was the reason to send out a rapid alert to all healthcare professionals involved in stem cell donation. One donor died after suicide and another died of a pre-existing condition unrelated to the donation process. In the last case, death of the donor was reported 11 years after donation due to pancreatic cancer (which technically is not considered a S(P)EAR because it occurred more than 10 years after donation), but due to the outcome the report was submitted, nevertheless.

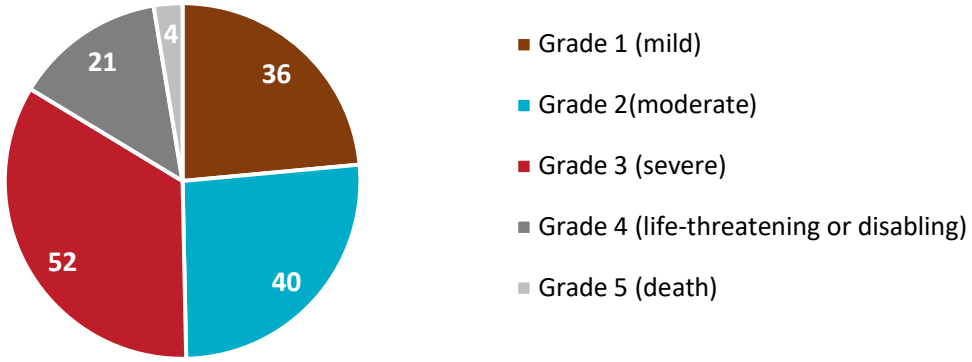

Figure 2: Severity of reaction[*]

*only mandatory for harm to honor (<6 months) and harm to recipient reports

1.3 Imputability

The imputability of an adverse reaction (see Figure 3) can be categorized as: definite (conclusive evidence beyond reasonable doubt for attribution to donation or infusion of the cell product), probably (evidence in favour of attribution to donation or infusion of the cell product), possible (evidence is indeterminate), unlikely (evidence is clearly in favour of attribution to alternative causes), excluded (conclusive evidence beyond reasonable doubt for attributing adverse reaction to alternative causes), or not assessable (insufficient data for imputability assessment).

In harm to donor adverse reactions that occurred within 6 months after donation, the majority (62,5%) reported a probable (n=13) or definite (n=37) imputability score. Harm to recipient reports also most often (60,9%) received an imputability score of probable (n=4) or definite (n=10).

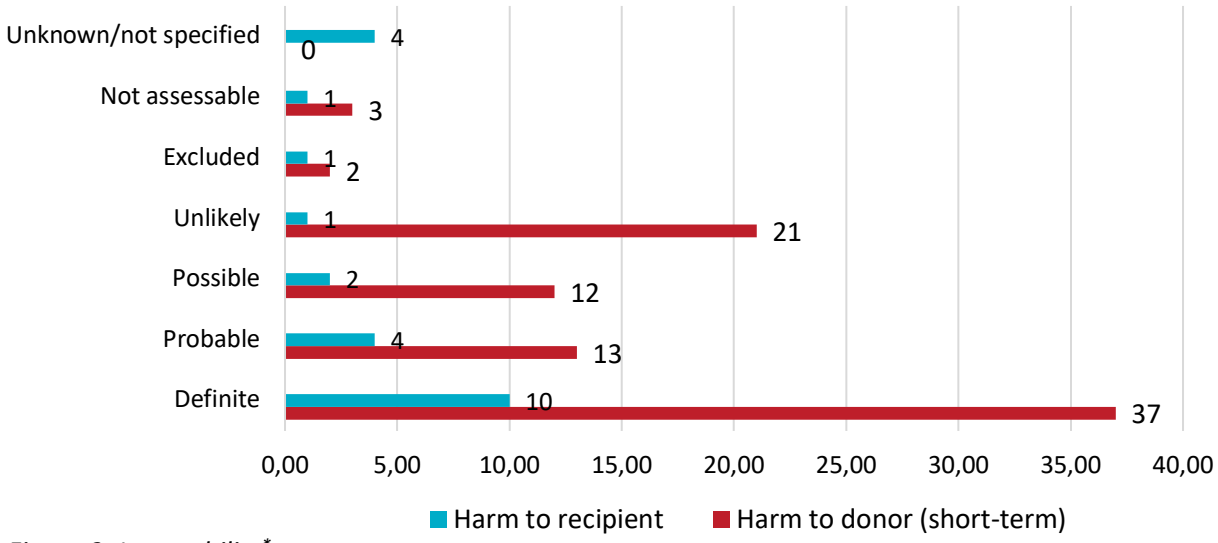

*Figure 3: Imputability**

**only mandatory for harm donor (<6 months) and harm to recipient reports*

1.4 Transplant performed as planned

When a report is submitted as a harm to recipient (n=23) or a risk of harm (n=32) type of report, the reporter is asked to specify if the transplant was performed as planned (Figure 4). In the majority of cases (60%), the transplant did take place as planned. In 12,7% of reports, the transplant could still go ahead but either on a later date (n=5) or by using a different product (n=4).

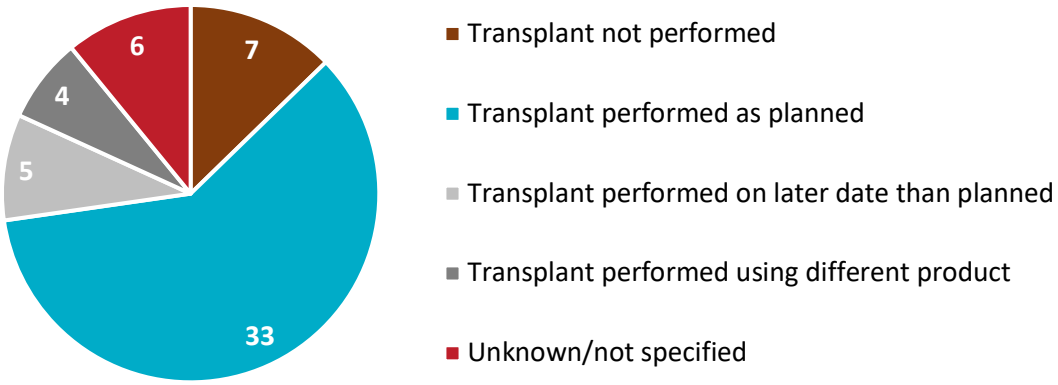

*Figure 4: Was the transplant performed as planned?**

*only displayed for risk of harm and harm to recipient reports

	HARM TO DONOR	HARM TO RECIPIENT	RISK OF HARM	TOTAL
TOTAL REPORTED	155	23	32	210
- Short term harm (<30 days)	88			88
- Long term harm (>= 30 days)	67			67
PHASE INCIDENT OCCURRED IN				
- Collection	5	3	5	13
- Distribution	-	1	2	3
- Donor aftercare	20	-	-	20
- Donor assessment	4	1	4	9
- Donor search and selection	1	-	1	2
- Mobilisation	3	-	4	7
- Processing	1	3	1	5
- Transplant	-	9	7	16
- Transport	-	1	5	6
- Other/unsure	1	-	1	2
- Unknown/not specified	121	5	2	128
TYPE OF (INTENDED) PRODUCT				
- DLI	2	1	-	3
- HPC-apheresis	119	11	19	149
- HPC-cord	-	3	5	8
- HPC-marrow	33	6	5	44
- Pre-collection samples	-	-	3	3
- Unknown/not specified	1	2	-	3
CRYOPRESERVATION				
- Yes	1	1	3	5
- No	-	2	7	9
DONOR DETAILS				
- Sex: male	88	1	17	106
- Sex: female	67	-	14	82
- Sex: not specified	-	22	1	23
- Average age [median(range)]	33,5 [32 (18-58)]	-	32,1 [31 (19-51)][1]	32,7 [32 (18-79)]

1. Excluding HPC-cord donations

Table 1: overview of all submitted S(P)EAR reports in 2019

2. Harm to donor reports

In a harm to donor report an adverse reaction in a donor during or after donation procedure is reported. The same category can be used to report other negative consequences for a donor, such as unnecessary procedures. In harm to donor, there is a specification made between long term harm and short-term harm: short term harm refers to harm that occurs within 6 months after donation and long-term harm would occur after that period of time.

A total of 155 harm to donor incidents were reported. Short term harm (less than or equal to six months after donation) was reported in 56,8% of the cases (n=88) and in 43,2% (n=67) of the reports harm to donor occurred more than six months after donation, which we classify as long-term harm. In 119 harm to donor reports, the type of (intended) product was HPC-Apheresis (76,8%), 33 were HPC-marrow (21,3%), 2 reports of DLI (intended) products (1,3%), and in 1 case (0,6%) it was not specified or the product type was unknown.

2.1 Type of harm to donor

	N	TIME AFTER DONATION IN DAYS [MEDIAN(RANGE)]
Acute systemic toxicity during mobilization or collection	12	0(-1-1)
Allergic reaction	11	0(-4-21)
Autoimmune disease	19	731 (2-2769)
- Long term	11	1096 (373 – 2769)
- Short term	8	43.5 (2-415)
Haematological malignancy / neoplasia	10	1078 (92-4687)
- Long term	8	1344 (547-4687)
- Short term	2	109 (92-126)
Infection	11	6 (0-364)
Mechanical damage	4	1 (0-5)
Non-haematological malignancy / neoplasia	43	1642 (16-4017)
- Long term	39	1461 (37-4017)
- Short term	4	54 (16-92)
Thrombotic / embolic	3	34 (34-62)
None of these categories are applicable	42	9 (-4 – 2542)
- Cardiovascular and cerebrovascular disease	2	-
- Psychiatric / psychogenic disorder	2	-
- Musculoskeletal / joint affection	2	-
- Neurological disease	4	-
- Unnecessary donor burden	2	-

- Other	30	-
TOTAL	155	

2.1.1 Malignancies

	N	TIME AFTER DONATION IN MONTHS/YEARS [MEDIAN(RANGE)]
Breast cancer	18	4.25 years (3 months – 7 years)
Colorectal cancer	3	5.3 years (5.3 – 10 years)
Haematological malignancy / neoplasia	10	3 years (3 months – 13 years)
Intracranial neoplasia	4	4.5 years (1.8 – 7 years)
Melanoma	3	3 months (3 months)
Nasopharynx cancer	4	3.3 years (1 month – 9.7 years)
Testicular cancer	4	5.5 years (1 month – 9.3 years)
Other	7	5.4 years (1 – 10 years)
TOTAL	53	

2.1.2 Haematological malignancy / neoplasia

	N	TYPE OF PRODUCT	TIME AFTER DONATION IN MONTHS/YEARS
Essential thrombocythemia	1	PBSC	3 months
Hodgkin's lymphoma	1	PBSC	4 months
Hodgkin's lymphoma	1	PBSC	2.5 years
Diffuse large B-cell lymphoma	1	BM	2.5 years
Polycythaemia vera	1	PBSC	4 years
Diffuse large B-cell lymphoma	1	PBSC	4 years
Mantel cell lymphoma	1	PBSC	5 years
Hodgkin's lymphoma	1	BM	5 years
Acute myeloblastic leukaemia (AML)	1	PBSC	8 years
Chronic myeloid leukaemia (CML)	*1*	*PBSC*	*13 years**
TOTAL	10		

* Technically not a SEAR (>10 years)

2.1.3 Autoimmune disorders

	N	TIME AFTER DONATION IN DAYS [MEDIAN(RANGE)]
Alopecia areata	3	53 (32-415)
Ankylosing spondylitis	1	2191
Crohn's disease	1	123
Multiple sclerosis	3	1461 (814-1836)
Rheumatoid arthritis	3	373 (60-730)
Sarcoidosis	1	2769
Other[1]	7	731 (2-1827)
TOTAL	19	

Other: diabetes, colitis ulcerosa, severe thrombocytopenia, hashimoto's thyroiditis, combined asthma/lymphocytic colitis/gastritis, reactive arthropathies, raynaud syndrome

2.1.3 Other type of harm

	N	TIME AFTER DONATION IN DAYS [MEDIAN(RANGE)]
Cardiovascular and cerebrovascular disease	2	1 (1)
Musculoskeletal / joint affection	2	204 (204)
Neurological disease	4	2 (0-254)
Psychiatric / psychogenic disorder	2	5(5)
Unnecessary donor burden	2	18.5 (14-23)
Other	30	2.5 (-121-2542)
TOTAL	42	

3. Harm to recipient reports

The harm to recipient category is used to report an adverse reaction in a recipient during or after the infusion of a cell product. This category can also be used to report any harm in a recipient as a consequence of product quality issues, delay in delivery etc.

A total of 23 harm to recipient incidents were reported. The majority of incidents followed after HPC-Apheresis (47,8% (n=11)) and after HPC-Marrow transplants (26% (n=6)). Three (3) reported on incidents of HPC-Cord transplant and 1 after DLI. In two cases graft type was not specified.

Harm to the recipient occurred during transplant in 9 cases, 3 during collection, 3 during processing, 1 during distribution, 1 during donor assessment, 1 during transport. For 5 incident reports it was unknown or not specified in which phase the incident occurred. Regardless of the incident that occurred, 13 transplants could still be performed as planned, 3 were performed on a later date than planned, 2 were performed using a different product and in 3 cases the transplant could not be performed. For 2 incidents this remains unknown or it is not specified.

3.1 Type of harm to recipient

	N
Cardiovascular	1
Cytogenic abnormalities	1
Donor cell derived malignancy	2
Infusion related non-specific symptoms	1
Transmitted bacterial infection	1
Other	14
- Delayed arrival of product	2
- Loss of product	1
- No product collected	1
- No problem or incident detected	1
- Product quality issue	5
- Other[1]	5
Unknown/unspecified	3
TOTAL	23

1. Extended delay to transplant (1); delayed HPC infusion (1); significant ABO mismatch (1); possible transmitted monoclonal gammopathy (1); possible exposure to cancer cells (1)

4. Risk of harm reports

Risk of harm refers to any problems or incidents that could have had (but did not have) negative consequences for the donor or the recipient or the system as a whole. This category also includes cases in which a deviation of standard procedures occurred.

Thirty-two (32) risk of harm incidents were reported. Nineteen (19) incidents took place after HPC-Apheresis, 5 following HPC-Cord, 5 following HPC-Marrow and 3 after pre-collection. Risk of harm incidents occurred during various phases of the procedure, but mainly during transplant (n=7), transport (n=5) and transport (n=5).

The majority of transplants (n=20) were performed as planned, 4 transplants were not performed, 2 were performed on a later date than planned, 2 transplants were performed using different product and for 4 incidents it was not specified or it was unknown.

4.1 Type of risk of harm

	N	TIME AFTER DONATION IN DAYS [MEDIAN(RANGE)]
Delayed arrival of product	3	1 (1-2001)
Loss of product	3	4321 (4-7001)
No problem or incident detected	2	2 (1-3)
No product collected	1	-4 (-4)
Potential product quality issue[2]	5	2 (0-1840)
Product quality issue[1]	12	1.5 (0-35)
Other	4	1.5 (-4-36)
Unknown/unspecified	2	n.a.

1. Product quality issue: e.g., bacterially contaminated, virally infected or other infection of product, incorrect labelling, incorrect samples, incorrect cell counts, low viability, wrong product supplied

2. Potential product quality issues: e.g., positive donor testing, problem with storage temperature

5. Rapid alerts

Two rapid alerts were sent out in 2019 and two rapid alerts in 2020. In April 2019 a rapid alert following a fatal event in an unrelated bone marrow donor was sent out to the community, summarizing published data on the incidence of serious adverse events associated with bone marrow donation as to help professionals in the field in addressing questions. The second rapid alert was disseminated within the community following the loss of a bone marrow product due to incorrect use of transfer collection system bags. This rapid alert listed recommendations for use of those type of bags.

In 2020, also two rapid alerts were released by WMDA. As this report is focused on the reporting year 20219. We wanted to share these two rapid alerts as well.

5.1 Rapid alert 1 (April 2019): fatal event in an unrelated bone marrow donor

WMDA			
Document type	Information	Donor Care	SEAR
Document reference	20190412-SEAR	Approved by	Chair
Version	1	Approval date	20190412
Drafting date	April 12th, 2019	Status	Public

A fatal event in an unrelated Bone Marrow donor

This statement is being issued following the preliminary notification of the death of an unrelated bone marrow (BM) donor in the US. This very sad case has raised many questions and this statement is intended as a reminder of published data on the incidence of serious adverse events associated with BM donation that may help you in addressing those questions. If there are further details or results of analysis available that need to be shared with you, we will send you those as soon as possible.

Fatal or life-threating complications among unrelated donors of hematopoietic stem cells are exceedingly rare. The World Marrow Donor Association (WMDA) is aware of one donor death in >250 000 collections which occurred between 1988 and 2018. The donor died of complications following a central venous catheter (CVC) placement for PBSC collection in 2011[1]. There are no previous reports of unrelated donor deaths during bone marrow collection.

In 2014, a paper was published indicating that bone marrow donors have a risk of developing serious adverse events of 2.38%. The study used standardized FDA definitions that include death, life-threatening events, persistent or significant disability, but also unplanned inpatient hospitalization or prolongation of existing hospitalization to characterize an event as a serious adverse event[2].

True life-threatening complications (such as pulmonary embolism, aspiration) have been reported in a frequency of approximately 1 in 200[2] to 1 in 5 000 bone marrow collections[3].

A number of fatal incidents in related donors have been described, however, the health criteria for related donors are less strict than the criteria for unrelated donors. Related donors are older (no upper age limit, substantially higher mean age even in the comparable group age 18 – 60) and comorbidities (especially cardiovascular[4]), that would lead to deferral for an unrelated donor are widely accepted.

The World Marrow Donor Association is a global association that is collecting data on serious adverse events occurring in unrelated donors and in the number of unrelated transplants[5].

[1]https://share.wmda.info/pages/viewpage.action?pageId=297107627&preview=/297107627/333718963/20110824-CLWG-SEAR%20Alert%20August%202011.pdf
[2]http://www.bloodjournal.org/content/123/23/3655
[3] https://www.bbmt.org/article/S1083-8791(17)30302-6/fulltext
[4] http://www.haematologica.org/content/94/1/94
[5] https://www.nature.com/articles/bmt2013104

5.2 Rapid alert 2 (December 2019: loss of a bone marrow product due to incorrect use of transfer collection system bags

matching donors • serving patients

World Marrow Donor Association
Schipholweg 57
2316 ZL Leiden
The Netherlands

+31 (0) 88 505 7900
mail@wmda.info
www.wmda.info

VAT: 803974917B02
IBAN: NL61ABNA0421708514
BIC: ABNANL2A
CC: 40448326

To WMDA members and affiliated transplant & collection centres, professional societies and all that this may concern

S(P)EAR alert: December 2019

Description of the serious events
The S(P)EAR Committee of WMDA has recently been notified of a serious event in which a bone marrow product was completely lost, as described in more detail below. A subsequent donation was necessary. Both donor and patient are progressing as expected.

The bone marrow product was lost because transfer bags from a bone marrow collection system were ruptured during centrifugation for plasma separation at the transplant centre.

This is the second time that an incident of this sort was reported to WMDA. In the previous case, a sufficient portion of the product could be salvaged and used for a successful transplant. In both cases, the manipulation step was consistent with standard operating procedure, and not the result of error.

Root cause analysis
These frequently-used transfer bags are generally not certified or validated for centrifugation, storage, or cryopreservation.

Recommendations of the WMDA S(P)EAR Committee

- Transplant centres should be aware that these transfer bags are generally unsuitable for centrifugation. Before any processing steps are undertaken, it is recommended that stem cell products be transferred to a bag which is validated by the manufacturer and any appropriate regulatory agency for the purpose intended. WMDA further recommends that transplant centres and processing stem cell laboratories check the specifications of all bags to ensure consistency with any intended use, including but not limited to manipulation (*e.g.*, centrifugation), storage, and infusion.
- WMDA recommends that the transplant centre be provided with any necessary documentation and/or statements regarding type and specification of transfer bags no later than at hand-over of the stem cell product.

5.3 Rapid alert 3 (June 2020): adverse events and reactions related to cryopreservation of stem cell products during the COVID-19 pandemic

WMDA	WMDA Rapid Alert May 2020			
	Document type	Rapid Alert	Pillar	Donor Care
	Document reference	20200611-SEAR Rapid Alert	Approved by	Board
	Version	2	Approval date	20200611
	Drafting date		Status	Public

To WMDA members and affiliated transplant & collection centres, professional societies and all whom this may concern.

S(P)EAR alert: May 2020 - update 11 June 2020 in red

Adverse events and reactions related to cryopreservation of stem cell products during the COVID-19 pandemic.

In order to ensure the safe arrival of hematopoietic stem cell products at the transplant centre prior to the start of patient conditioning, cryopreservation of the product on arrival is strongly recommended[12], if not locally required[3], and has been since early March, 2020. Where the anticipated prolonged travel times may be prolonged, some requesting registries/transplant centres may prefer cryopreservation at collection.

While WMDA's S(P)EAR Committee[4] has so far received no reports or notifications of serious events or reactions *directly* related to COVID-19 infection, we have been informed of several cryopreservation-related reports. Adverse events include unintended (due to miscommunication) cryopreservation at the collection site, a cryopreserved product that was misplaced and hence partly thawed during transport, and several PBSC or BM products with (anticipated) low cell count after thawing, where the product could not be used, or the same donor was requested for an urgent second donation.

While cryopreservation is certainly justified in the light of travel restrictions, transport limitations, and potential impact on donor and recipient availability, additional expert assessments, procedures, and policies for registries and donor / collection and transplant centres are absolutely required, as would be the case for any situation requiring cryopreservation (including of autologous products) in compliance with FACT-JACIE International Standards for Hematopoietic Cellular Therapy (7th edition)[5], and AABB Standards for Cellular Therapy Services (9th edition)[6].

The following are strongly recommended:

- Agree and make clear written specifications about where the cryopreservation will take place. Transplant centres and sending registries should feel free to ask for accreditation certificates from processing facilities that are responsible for cryopreserving the hematopoietic stem cells.
- Assess the feasibility of the request of the transplant centre before collecting the product. Attempts should be made to determine whether it will be possible to obtain the required cell counts taking into account the potential losses during cryopreservation.
- If the above cannot be comfortably expected and if shipping and donor availability are not deemed critical, consult with the transplant centre about continuing without cryopreservation.
- Adjust transport arrangements if the product is going to be transported after cryopreservation and make sure the transport is performed by a courier company specialized in transport of cryopreserved stem cells in dry shippers, according to accepted standards.
- Make sure that the site performing the transplant has implemented validated assays and test procedures for the evaluation of thawed cellular therapy products[5].
- If the post-thaw viable cell count tested on a representative sample is too low for successful engraftment, consider the option to check if it is feasible that the donor donates for a second time

5.4 Rapid alert 4 (July 2020): timely patient verification and extended typing

	WMDA SEAR Rapid Alert			
	Document type	Form-Rapid Alert	Approved by	ED
	Document	F-DC-001-Rapid Alert	Approval date	20200701
	Version	1	Pages	Page 1 of 2
	Pillar	Pillar 3-DC – Donor Care	Status	Public

To WMDA members and affiliated transplant & collection centres, professional societies and all whom this may concern.

S(P)EAR alert

Timely Patient Verification and Extended Typing

WMDA S(P)EAR Committee has received three (3) reports of serious incidents in which the patient's extended and/or verification HLA-typing was performed ***after*** final donor selection. The results showed a significant mismatch or even complete discrepancy with the typing on which the donor was matched.

In one case the collection of bone marrow had already been completed and in another case the donation procedure had already been started (initial dose of granulocyte colony stimulating factor (G-CSF) been injected).

Due to the pandemic, an increasing number of transplant centres have implemented the recommendation to delay the start of conditioning until the safe arrival of the hematopoietic stem cell product followed by cryopreservation and storage of the product until transplantation. This practice increases the risk that final checks on the patient side are delayed. If the results of the final checks were to be discrepant with previous test results, this might result in unnecessary donor burden.

As a preventive measure, the S(P)EAR Committee deems it necessary to add a recommendation to the existing accreditation standards[1,2,3,4], with the aim that transplant centres specifically require the patient's HLA-typing to be complete and verified ***before*** final donor selection.

In conclusion and endorsed by the WMDA Board, the S(P)EAR Committee makes the following recommendation for best practice during final donor selection stage:

"Transplant centre must confirm the final donor selection and assess and confirm the recipient's eligibility for a scheduled transplant before the donor starts the donation procedure (i.e. start of mobilization or hospital admission for bone marrow donation).

This confirmation should, at a minimum, be based on

- patient's verification and extended HLA-typing;
- HLA match grade with the donor;
- Other important conditions such as, but not limited to:
  - a recent recipient health status
  - sufficient financial resources for transplant expenses
  - sufficient capacity in the transplant centre.

Additional information or criteria may be required at the discretion of the providing donor registry. Where cryopreservation is planned, the donor centre or registry should define the necessary data before approval of a cryopreservation request. If this information is not provided in a timely manner, the donor centre, collection centre or (receiving) registry may decide not to proceed with the donation request.

References:

1. World Marrow Donor Association International Standards for Unrelated Hematopoietic Stem Cell Donor Registries, WMDA Standard 6.04.1 (find here the weblink: https://wmda.info/wp-content/uploads/2020/02/WMDA-Standards-2020-copyright-version-Final-table-of-content-.pdf)
2. FACT-JACIE International Standards for Hematopoietic Cellular Therapy, Standard B 6.4.12.2 (find here the weblink: https://www.ebmt.org/sites/default/files/2018-06/FACT-JACIE%207th%20Edition%20Standards.pdf)
3. European Federation for Immunogenetics Standards for Histocompatibility & Immunogenetics Testing, EFI Standard E 5.3.4.3.2 (find here the weblink: https://efi-web.org/committees/standards-committee)
4. American Society for Histocompatibility and Immunogenetics Standards for Accredited Laboratories, ASHI Standard D5.3.3.1.3.2 (find here the weblink: https://cdn.ymaws.com/www.ashi-hla.org/resource/resmgr/docs/standards/2019/approved/2020_0221_-_clean_2019_ashi_.pdf)

6. Future directions – lessons learnt

WMDA has developed an infrastructure to report serious adverse events and reactions in the unrelated donor setting. The system has been set up as well to accommodate related donations as well.

In 2020, WMDA focused on encouraging transplant centres to report their related donor events as well to WMDA. Therefore, several promotions were set up to create awareness for the benefit of reporting and lessons that might be learnt from reporting.

The COVID pandemic made it impossible to go to international meetings to do the promotion. Therefore, a digital approach has been set up. The online educational materials are described in deliverable 3.1 of this European Operational Grant.

The reaching out to the related donors require additional expertise. This was not covered by the current members of the SPEAR Committee. A new member was recruited who is specifically responsible for related donor reports.

A few bugs were identified in the reporting system, which caused challenges for the reporter. For example, the age of a cord blood donor needed to be recorded (which is not applicable). These bugs were solved in 2020.

The pandemic made clear the importance of reporting and sharing experience. WMDA was pro-active and leading in bringing key messages to the healthcare professionals. This was crucial because new approaches needed to be developed on ensuring that good quality products remain available for patients urgently needing a transplant. The SEAR/SPEAR reporting system was leading in alerting quickly the community and to alert on potential harm.

The biggest challenge in the nominator and how to ensure that all incidents are reported to WMDA. WMDA has a reliable reporting on the number of unrelated transplants and donations on a global scale. Based on this information, WMDA identified a few organisations that were underreporting. These organisations have been invited for a personal consultation hour to identify reasons why they are underreporting. The most common reason was that organisations were not familiar with the system. In 2021, main focus will be to get organisations more familiar with the system and to provide benefits by publishing educational reports.