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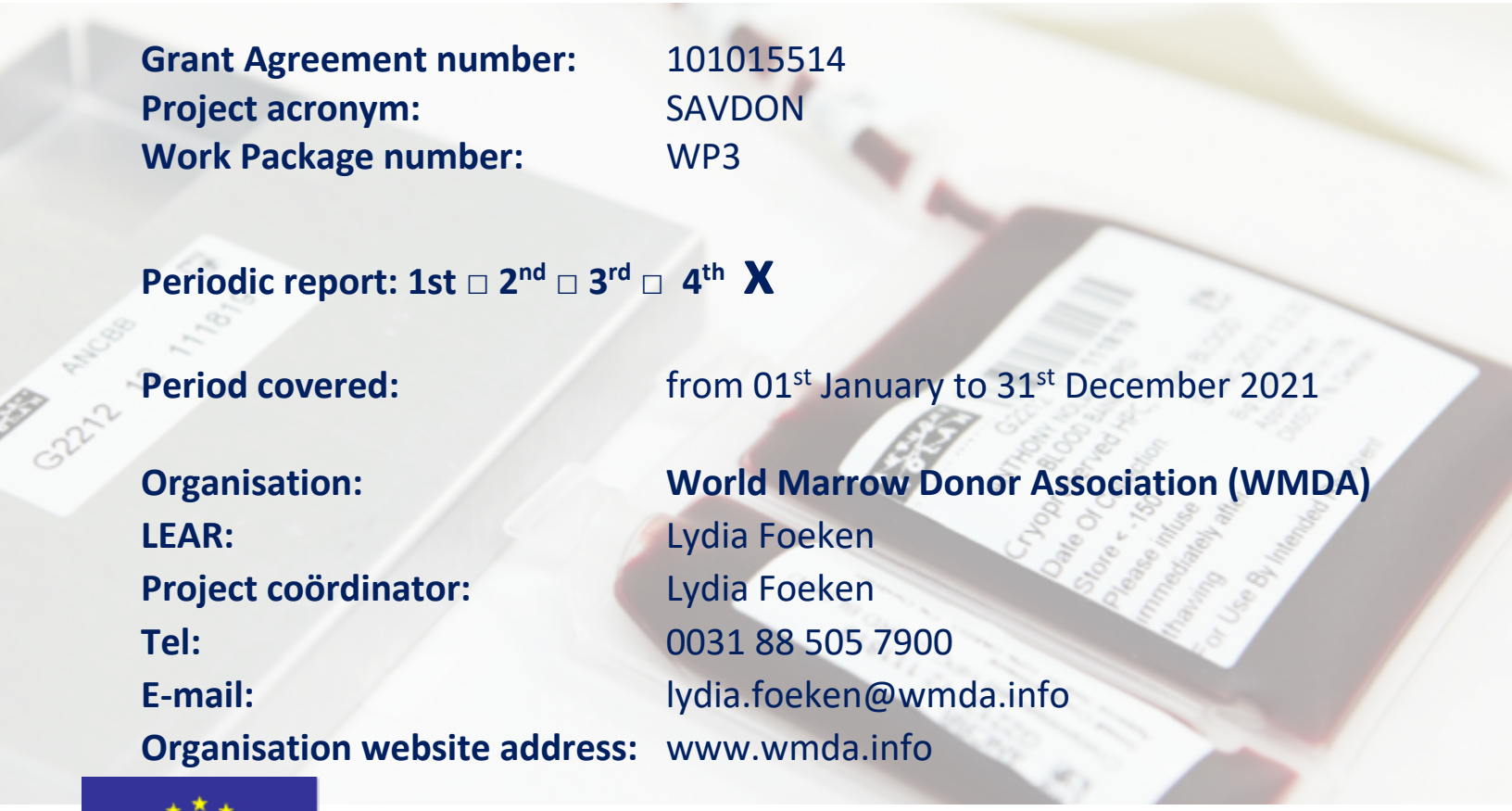
D3.2 WMDA 2020 annual report from the S(P)EAR committee



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Content

Abbreviations

- DLI = donor lymphocyte infusion
- HPC-apheresis = haematopoietic progenitor cell - apheresis
- HPC-cord = haematopoietic progenitor cell - cord
- HPC-marrow = haematopoietic progenitor cell – marrow
- S(P)EAR = Serious (Product) Events and Adverse Reactions
- WMDA = World Marrow Donor Association

Introduction

The WMDA facilitates reporting of Serious (Product) Events and Adverse Reactions (S(P)EARs) via a global online reporting tool. The S(P)EAR tool allows for reporting on adverse events and reactions in relation to cell donation, collection and/or processing from related and unrelated donors. By systematically collecting and analyzing the data on submitted S(P)EARs, the World Marrow Donor Association (WMDA) aims to gain insight in the occurrence of S(P)EARs and to share this knowledge with the global community.

The data received via the online reporting tool is used in an anonymized manner to publish the S(P)EAR Annual Report. The 2020 S(P)EAR annual report is used in this deliverable D3.2 publication to present the data and to highlight the importance of serious adverse events reporting as part of the 2020 work programme of the World Marrow Donor Association for the EU Third Health Programme (2014-2020).

The complete WMDA S(P)EAR Annual Report 2020 is freely accessible for WMDA members and available on request for people interested in the data.

1. Overview of submitted S(P)EAR reports in 2020

In 2020, a total of 474 S(P)EAR reports were accepted by the S(P)EAR Committee[1]. Table 1 outlines the details of the received reports. In 2020, 32 different organisations submitted reports, compared to 27 in 2019 and 18 reporting organisations in 2018.

2020 Key facts

- The committee accepted **474 S(P)EAR incident reports** in 2020, compared to 210 in 2019.
- Reports were received from **32 different organisations**, compared to 27 reporting organisations in 2019.
- **54 reports** were classified as **COVID-related**.
- **Two rapid alert notifications** were sent in 2020 to all members of the international community.
- The online central S(P)EAR reporting system and data structure now allows for **deeper analysis** including **benchmarking** reporting behavior.

1.1 Report categorisation

S(PEAR) reports are categorised into three different categories: harm to recipient, harm to donor and risk of harm. Harm to donor reports accounted for 80,1% of total reports (n=367), of which 41,3% (n=151) occurred within 6 months within donation (short term harm) and 58,7% (n=216) occurred 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 36 times, amounting to 7,8% of the total reports received. More information on harm to recipient reports can be found in chapter 3. Risk of harm reports accounted for 12% of the total, with 55 reports that were classified as such. More information on the risk of harm reports can be found in chapter 4.

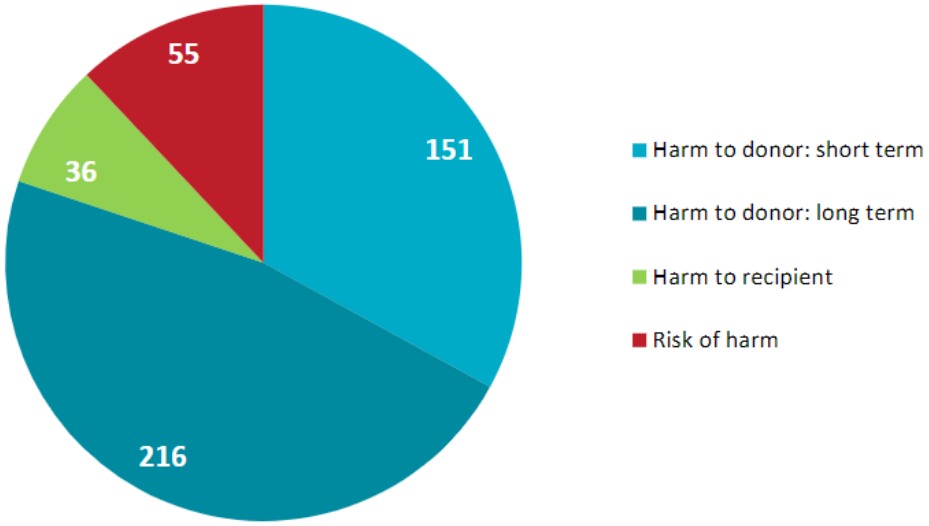


Figure 1: Type of report

[1] 15 reports were *accepted*, but categorized as NOT A SEAR by the Committee, and are excluded from further analysis. The same applies to one duplicate report.

TABLE 1: OVERVIEW OF 2020 S(P)EAR REPORTS	HARM TO DONOR	HARM TO RECIPIENT	RISK OF HARM	TOTAL
TOTAL REPORTED	367	36	55	458[1]
• Short term harm (=<6 months)	151			151
• Long term harm (>6 months)	216			216
PHASE INCIDENT OCCURRED IN[2]				
• Mobilisation	28 / 4[3]	1	5	38
• Collection	19 / 6		14	39
• Distribution	-	1	1	2
• Processing	- / 4	6	6	16
• Transport	-	3	10	13
• Transplant	-		5	5
• =<30 days after collection	71			71
• >30 days after collection	35			35
• Donor aftercare	- / 9		2	11
• Donor assessment	- / 1	1	4	6
• Donor search and selection	- / 2	1		3
• Other/unsure	- / 5	2	8	15
• Unknown/not specified	(214[2])			(214[2])
TYPE OF (INTENDED) PRODUCT				
• HPC-apheresis	296	29	40	365
• HPC-marrow	68	7	10	85
• MNC-apheresis	3		2	5
• HPC-cord			3	3
PRODUCT CRYOPRESERVED				
• Yes		22	30	52
• No	2	8	17	27
• Unknown/not specified	365	6	8	379
DONOR DETAILS				
• Sex: male	214	2	32	248
• Sex: female	153	2	20	175
• Sex: not specified	-	32	3	35
• Average age [range] at donation	33.8 [18-67]	23.8 [19-30]	31.4 [1-80]	33.4 [1-80][4]

[1] 15 reports were *accepted*, but categorized as NOT A SEAR by the Committee, and are excluded from further analysis. The same applies to one duplicate report (see Chapter 5 for details)
[2] Only needed to specify for harm to a donor incidents =<6 months after donation
[3] Second figure describes contributing incident / Risk of harm
[4] 2 CB units and 12 related donors included

1.2 Imputability

The reporting registry makes an assessment of the causation for each harm to donor incident that occurs within six months and in harm to recipient reports. The committee then reviews the imputability and proposes changes where necessary. Below, the final imputability scores for short term harm to donor reports are displayed (for long term harm imputability does not have to be reported).

The imputability of (see Figure 2) 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 (60,2%) were classified as possible/probably (n=47; 31,1%) or definite (n=44; 29,1%). Harm to recipient reports most often (75%%) received an imputability score of definite (n=18; 50%) or possible (n=9; 25%).

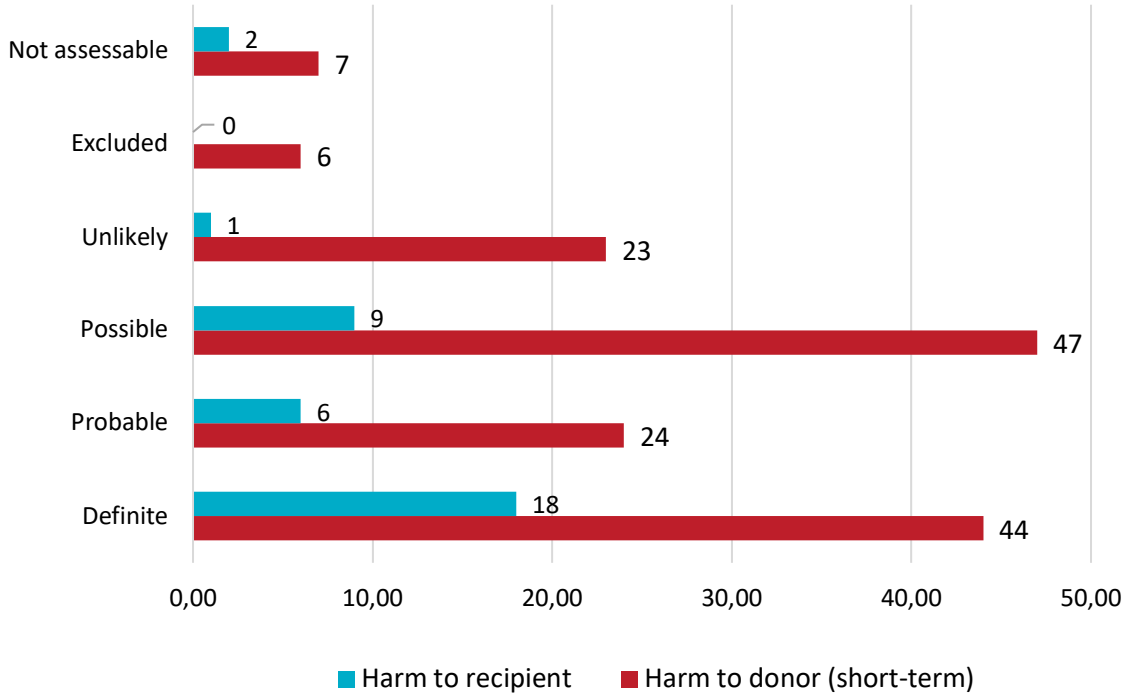


*Figure 2: Imputability**

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

1.3 Transplant performed as planned

When a report is submitted as a harm to recipient (n=36) or a risk of harm (n=55) type of report, the reporter is asked to specify if the transplant was performed as planned.

In 38,5% of cases the transplant did take place as planned. This is a significant change to the 60% of transplants preformed as planned in 2019. One could speculate this is due to COVID-19 regulations put in place, but no cause has been identified. Of the 24 transplantations not performed in Risk of Harm reports, in 17 cases a relation to COVID was indicated by the reporter. This can be, for example, a donor that tests positive which results in the cancellation of donation or issues regarding the increased use of cryopreservation due to travel restrictions.

TRANSPLANT PREFORMED AS PLANNED?	HARM TO RECIPIENT	RISK OF HARM
Transplantation performed as planned	17	18
Transplantation performed on later date than planned	5[1]	7
Transplantation performed using different product	1	4
Transplantation not performed	9	24[2]
Unknown	4	2
TOTAL	36	55

1 Discrepancy to 3.1: not all reports confirm if transplant from a BU donor / alternative product was performed

2 Of the 24 transplantations not performed, 17 relate to COVID, thereof 11 to cryopreservation and 6 to donors tested positive for SARS-CoV-2.

2. Harm to donor reports

Harm to donor reports describe 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 reports, 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 more than 6 months after donation.

A total of 367 harm to donor incidents were reported in 2020. Short term harm was reported in 41.3% of the cases (n=151) and 58.7% (n=216) of cases were long term harm. This is a remarkable difference to 2019, when 56.6% of reports related to short term harm. In 295 harm to donor reports, the type of (intended) product was HPC-Apheresis (80.6%), 69 were HPC-marrow (18.9%), and 3 reports of MNC (intended) products (0.8%).

2.1 Type of harm to donor (2020 vs 2019)

	N (2019)	% OF TOTAL (2019)	N (2020)	% OF TOTAL (2020)
Acute systemic toxicity during mobilization or collection	12	7,7%	7	1,9%
Allergic reaction	11	7,1%	9	2,5%
Autoimmune disease	19	12,3%	113	30,8%
- Long term	11	7,1%	85	23,2%
- Short term	8	5,2%	28	7,6%
Haematological malignancy / neoplasia	10	6,5%	15	4,1%
- Long term	8	5,2%	15	4,1%
- Short term	2	1,3%	-	-
Infection	11	7,1%	25	6,2%
Mechanical damage	4	2,6%	7	1,9%
Non-haematological malignancy / neoplasia	43	27,7%	102	27,8%
- Long term	39	25,2%	99	27,0%
- Short term	4	2,6%	3	0,8%
Thrombotic / embolic	3	1,9%	10	2,7%
None of these categories are applicable:	42	-	72	-
- Cardiovascular and cerebrovascular disease	2	1,3%	8	2,2%
- Psychiatric / psychogenic disorder	2	1,3%	4	1,1%
- Musculoskeletal / joint affection	2	1,3%	3	0,8%
- Neurological disease	4	2,6%	11	3,0%
- Unnecessary donor burden	2	1,3%	21	5,7%
- Other[2]	30	19,4%	25	6,8%
TOTAL	**155**	100%	**367**	100%

[2] Other: e.g. COVID, lasting pain, anaemia

2.1.1 Malignancies

	N	TIME AFTER DONATION, YEARS [MEDIAN]	AGE[1] AT DIAGNOSIS, YEARS [MEDIAN]
Haematological malignancy	**15**	**4.5**	**42.8**
Breast cancer	17	3.5	44
Testicular cancer	15	2.5	33
Melanoma	10	5	39
Prostate cancer	10	5.5	55.5
Colorectal cancer	8	5.5	37
Thyroid cancer	7	4	47
Lung cancer	5	5	52
Cervix, uterus and ovarian cancer	5	6.5	53
Renal cancer	5	2	47
Oral cavity and oesophageal cancer	4	7.5	49
Intracranial neoplasia	4	5.5	36.5
Bile duct and pancreatic cancer	3	3	54.75
Connective tissue (liposarcoma)	3	7	36
Other[2]	6	3	51.5
TOTAL	**117**		

1 Calculated from age at donation and reported interval to diagnosis
2 Other: 2x non-melanoma skin cancer, 2x ocular cancer, 1x laryngeal cancer, 1x unspecified

2.1.2 Haematological malignancy / neoplasia

	TYPE OF PRODUCT	TIME AFTER DONATION, YEARS (UNLESS STATED)	AGE[1] AT DIAGNOSIS, YEARS
Lymphoma, NOS (cervical and mandibular lymphadenopathy)	PBSC	10 months	42
B-CLL	BM	1	37
Diffuse large B-cell lymphoma	PBSC	1	39
Essential thrombocythemia	PBSC	2	38
Myeloproliferative Disease	PBSC	4	67
Hodgkin lymphoma	PBSC	4	62
Acute lymphatic leukaemia (ALL)	PBSC	4	24
CD30+ Lymphoma	PBSC	5	48
Indolent systemic mastocytosis	BM	5	36

Mycosis fungoides	BM	6	41
Gastric MALT lymphoma	PBSC	7	59
Chronic myeloid leukaemia (CML)	PBSC	7	36
Hodgkin lymphoma	PBSC	8	56
Non-Hodgkin lymphoma	PBSC	8	53
Diffuse large B-cell lymphoma	PBSC	9	47
TOTAL	**15**		

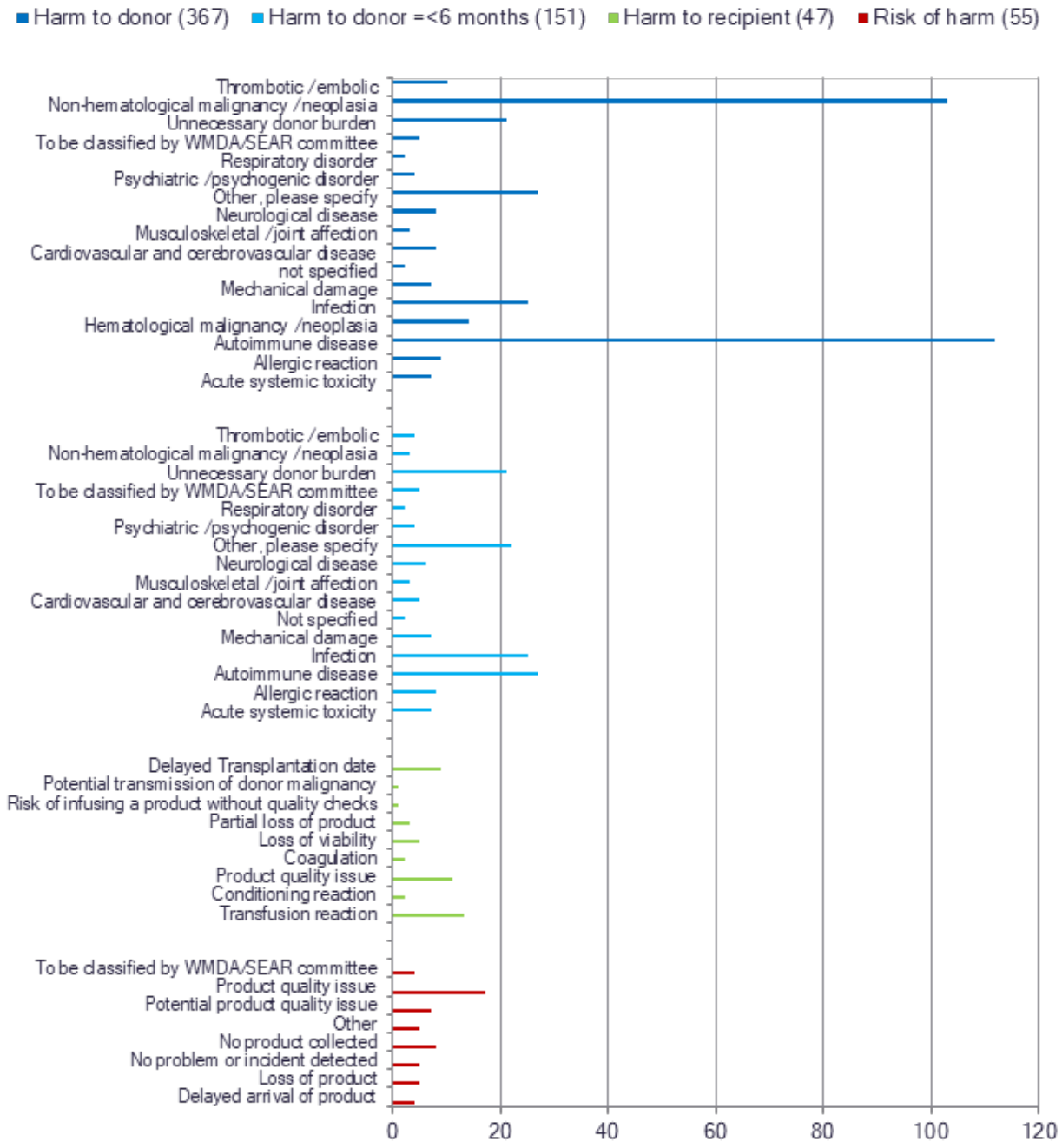
1 Calculated from age at donation and reported interval to diagnosis

2.1.3 Autoimmune disorders

	N	TIME AFTER DONATION, YEARS [MEDIAN]	AGE[1] AT DIAGNOSIS, YEARS [MEDIAN]
IBD	21	2	27
Multiple sclerosis &transverse myelitis	15	4	33
Rheumatoid arthritis	12	2	47.5
Hypo- and hyperthyroidism	10	2	29.5
Connective tissue disease, granulomatosis, Raynauds	10	3.5	27.5
Ankylosing spondylitis	7	1	30.4
Sarcoidosis	5	1	33
Atopic dermatitis	5	7 days	27
Psoriasis	5	1 month	24.1
Purpura	3	1	27.3
Iritis, uveitis	3	1	25
Alopecia areata, vitiligo	3	7 days	23
Glomerulonephritis	3	28 days	36
Other[2]	10	-	-
TOTAL	**112**		

1 Calculated from age at donation and reported interval to diagnosis
2 Other: diabetes, lichen planus, eosinophile oesophagitis, autoimmune hepatitis, Pemphigus vulgaris, Erythema nodosum, suspected SLE, autoimmune pancreatitis

2.2 Chart: Type of harm/problem



3. Harm to recipient reports

S(P)EAR reports that are classified as "Harm to recipient" are to describe 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 demonstrated consequence of product quality issues, delay in delivery and others.

A total of 36 harm to recipient incidents were reported in 2020. The majority of incidents occurred in the context of HPC-Apheresis (80.6% (n=29)), 7 after HPC-Marrow transplants (19.4% (n=7)). WMDA received no reports on harm to recipient related to HPC-Cord or MNC in 2020.

In 22 cases, the product was cryopreserved, 7 were not, 4 unknown, and in 3 reports there was no product collected. For only 2 out of the 22 cryopreservations, a causal connection can be ruled out. In 12 reports, processing or manipulation to the product may have contributed (including 8 cryopreservations).

3.1 Type of harm to recipient

	N	SUBCATEGORY / COMMENT	
Delayed Transplantation date	9	(loss of the intended product)	
Transfusion reaction	13	(1 fatal, 7 after cryo)	
Conditioning reaction	2	(to ATG)	
Product quality issue	11	Coagulation	2
		Partial loss of product	3
		Loss of viability	5
		Risk of transmission of other disease	1
Potential transmission of donor haematological malignancy	1		
TOTAL	**36**		

4. Risk of harm reports

A S(P)EAR "Risk of harm" report 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.

Fifty-five (55) risk of harm incidents were reported. Forty (40) incidents took place during or after HPC-Apheresis, 2 during MNC-Apheresis, 10 following HPC-Marrow and 3 following HPC-Cord. Risk of harm incidents occurred during various phases of the procedure, but mainly during collection (n=14) and transport (n=10). In 30 reports, the product was cryopreserved, in 17 it was not, and in 8 cases no matching product was collected.

Eighteen (18) transplantations were performed as planned, twenty-four (24) transplantations were not performed, 7 were performed on a later date than planned, 4 transplants were performed using different product and for 2 incidents it was not specified, or it was unknown. Of the 24 transplantations not performed, 17 relate to COVID, thereof 11 to cryopreservation and 6 to donors tested positive for SARS-CoV-2.

4.1 Type of risk of harm

	N	SUBCATEGORY	
Delayed arrival of product	4		
Loss of product	5		
No product collected	8		
Product quality issue	17	Bacterially contaminated product	2
		Incorrect label and/or samples	3
		Low viability	6
		Other	4
		Risk of transmission of other disease	1
		To be classified by WMDA/SEAR committee	1
Potential product quality issue[1]	5		
Other	5		
Risk of harm to donor	9	Incorrect donor health screening	3
		Potentially unnecessary donation procedure	6
TOTAL	**55**		

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

4.2 Phase of procedure where event occurred

A risk of harm can occur in different phases of the donation or transplantation procedure. The table below provides an overview of the phases and the corresponding number of reports.

	N
Collection	14
Distribution	1
Donor aftercare	2
Donor assessment (health screening)	4
Mobilisation	5
Processing	6
Transplant	5
Transport	10
Other or unsure	8
TOTAL	**55**

5. COVID-19 related reports

At the time of the data analysis, fifty-four (54) reports were classified as COVID-related reports. An incident was either an effect of an infection (suspected/confirmed) with SARS-CoV-2, or directly caused by mitigation measures such as travel restrictions, quarantine, or cryopreservation of HSC products.

Due to this new and very specific situation especially at the beginning of the SARS-CoV-2 pandemic, consistent and unambiguous categorization of COVID-19 related incidents within the existing categories of the reporting tool was often not feasible. For example, a bone marrow product not transfused due to loss of viability during cryopreservation after prolonged shipping time and expected low cell counts because of weight ratio can be classified as Risk of harm (recipient, best product not available), Risk of harm (transport), Risk of harm (product quality issue), or Harm to donor (unnecessary donor burden). An in-depth analysis of the COVID-19 related cases is outside the scope of this Annual Report, but is currently in preparation with the intention to publish together with the COVID survey results.

5.1 Overview COVID-19 related incidents

(categorization subject to change)

	N
A1 - Donor, infection during collection	3
A2 - Unnecessary donor burden	18
A3 - Donor, product not infused after donor tests positive	5
A4 - Donor, other	2
B2 - Recipient, no product from original donor after start of conditioning	4
B3 - Recipient, relevant delay for start of conditioning	1
B4 - Recipient, other	4
C1 - Technical problem, low cell dose/viability	10
C2 - Technical problem, equipment, procedure or validation (Controlled rate freezer)	1
C2 - Technical problem, equipment, procedure or validation (dry shipper)	2
C3 - Technical problem, material, procedure or validation (bags)	2
C4 - Technical problem, lack of coordination	1
D2 - Transport issues, prolonged shipping	1
TOTAL	**54**

6. Excluded reports

Reports will be accepted as long as they contain relevant information. Nevertheless, 15 reports have been categorized as NOT A SEAR after review by the Committee, since they did not fulfil the defined criteria for a SEAR / SPEAR incident. In addition, for one event reports were submitted from both the receiving as well as the sending registry and therefore 1 report was marked as a double report.

These reports are included in the submission statistics, but excluded from data analysis.

REPORTS EXCLUDED FROM ANALYSIS	N	REASON FOR EXCLUSION
Time incident occurred	3	Regular incident more than 10 years after donation
		Incident before start of donation / conditioning procedure
	2	
'Expected' non-critical events	5	ABO incompatibility, coagulation, X-ray, increased shipping temperature (all products could be transfused)
		Poor mobilization (scheduled cryopreservation)
	1	
Differing practice / standards for package or labelling between CC and TC	2	Product shipped w/o incident, and identifiable
Genetic findings in donor cells	2	
2 reports for 1 incident	1	
TOTAL	**16**	

7. Rapid alerts

Two rapid alerts were sent out in 2020. In May 2020 (see 7.1) a rapid alert following the reports of several issues surrounding the cryopreservation of products was sent out to the community. Due to prolonged travel times in light of the travel restrictions imposed by SARS-CoV-2 regulations, cryopreservation was recommended to ensure the safe arrival of a product. Therefore you could see an increase in the exchange of cryopreserved products, and this resulted in the demand of the use of cryopreservation of parties that had little prior experience with the techniques. The rapid alert shared with the community some best practices in line with FACT-JACIE and AABB standards.

The second rapid alert (see 7.2) was disseminated within the community following three separate cases in which the patient's extended and/or verification HLA-typing was done after final donor selection. This is something to avoid as it can lead to unnecessary donations and thereby unnecessary burden for a donor if there's a discrepancy in the results. Therefore the rapid alert focused on sharing the S(P)EAR committees' recommendation on finalizing the recipient's eligibility checks before starting the donation procedure on the donor's side.

7.1 Rapid alert 1 (May 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

7.2 Rapid alert 2 (July 2020): Timely Patient Verification and Extended Typing

WMDA	**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)

8. Future directions – lessons learnt

The online serious adverse event reporting infrastructure developed by the WMDA was originally set up to report adverse events and reactions in the *unrelated* donor setting. The WMDA believes that the rights and safety of related donors should be protected as much as the rights and safety of unrelated donors. Therefore, in 2020 the WMDA focused on encouraging transplant centres to report their related donor events to the WMDA. For this, a new member joined the S(P)EAR committee in 2020 who was specifically responsible for assessing related donor reports. In 2020, we received 12 reports of adverse events in related donors, compared to 2 reports submitted in 2019 on related donors this is a 500% increase in reported cases. We will continue to focus our efforts on including transplant centres in 2021 by ensuring we're known to them and to ensure their reporting needs are met in the WMDA S(P)EAR reporting system.

The current S(P)EAR reporting tool was released in 2019. Although it's been fulfilling its purpose of allowing for reporters to submit adverse event and incident reports in a user-friendly manner and for the WDMA office to carry out data analysis, amongst other things, the current tool is lacking the flexibility to add on new requirements. Therefore, In the late fall of 2020 a project was started to rebuild the SPEAR system. Following a survey to assess the needs of S(P)EAR reporters and committee members, a team of IT experts started building the new tool in 2021. More on the rebuild of the S(P)EAR online reporting tool can be found in the 2021 publication on D3.1 '*Progress report on the WMDA online tool for reporting Serious Adverse Events and Reactions (S(P)EARs)*'.

The SARS-CoV-2 pandemic highlighted the importance of global collaboration and the sharing of knowledge and expertise. The WMDA has been pro-active in bringing key messages to the donation and transplantation community to ensure high quality products remain available for patients urgently needing a transplant even in challenging times, as is demonstrated by the rapid alert notifications sent in 2020. The S(P)EAR reporting system in this regard has worked adequately in allowing for the WMDA to alert the community on potential harm. The tool has also proven its power in allowing for a detailed data analysis on adverse event and incident reports that are possibly related to COVID-19.