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D4.2 Progress report on the gathering, analysis and provision of data, insight and resources that support members to safeguard the rights and safety of stem cell donors

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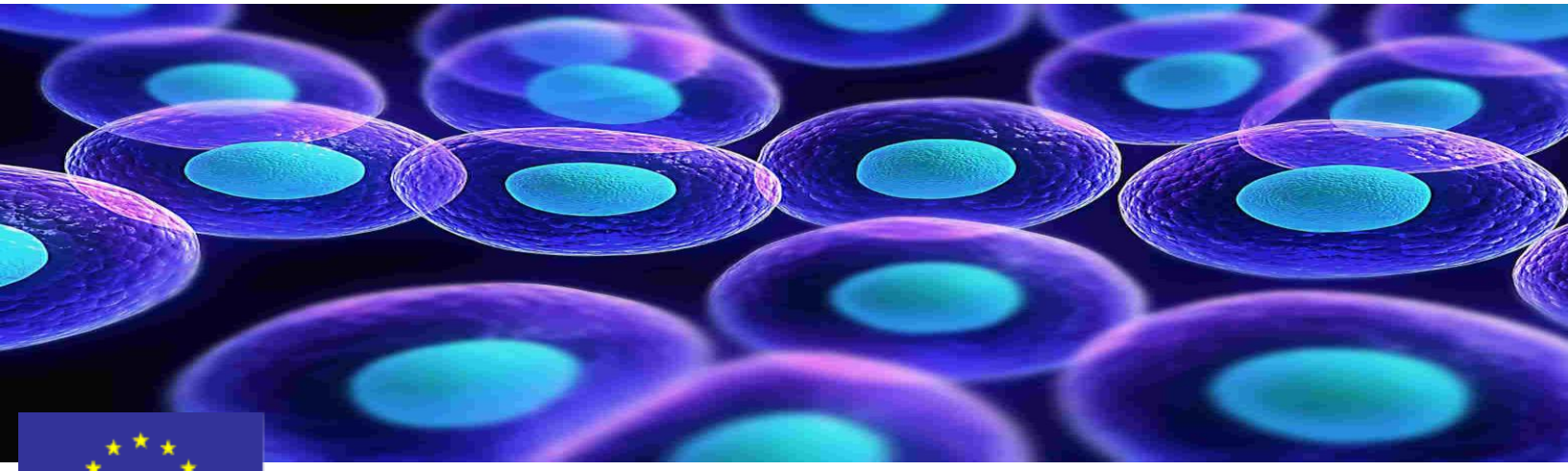

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Publishable Summary

WMDA aims to create a new infrastructure to collect serious adverse events and reactions occurring after a donation of hematopoietic stem cells in either the donor, the product or the recipient.

Since 2002, WMDA is collecting this type of information. The number of reports is increasing annually, because of the growth in the number of donations and the long-term follow up. This makes it logistically complicated to analyse the data received and to trace the communication between the reporting organisation and the WMDA.

At the beginning of 2018 the journey started to develop a new infrastructure. It intends to:

- Become a unique system for reporting serious adverse events and reactions to the WMDA
- Expansible to accommodate the reports for related donors as well
- Traceable to track and trace communication and clarification
- Run statistics on the reports received
- Send out rapid alerts to designated reporters

The old S(P)EAR questionnaire for submitting SEAR/SPEAR incidents is available via the WMDA member page on Share. The new S(P)EAR reporting system is still under construction. This new and improved version will make it possible to prepare informative annual reports, analyse this important data more extensively, and improve communication between WMDA and the organisation reporting the incident. The changes in this new questionnaire will be applied to make it more friendly and complete. The improvement is still ongoing, and the new reporting form should be available in June 2019.

Abbreviations

MVP	=	Minimal Viable Product
RFI	=	Request For Information.
SEAR	=	Serious Event Adverse Reactions
SPEAR	=	Serious Product Event Adverse Reactions
SCM	=	Stem Cell Matters
TRIP	=	Transfusion and Transplantation Reactions in Patients
WMDA	=	World Marrow Donor Association

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1. Introduction to S(P)EAR

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. Because almost half of the blood stem cells collected from volunteer donors for transplantation cross international borders, optimal donor safety requires global strategies.

Since 2006, Transfusion and Transplantation Reactions in Patients (TRIP) collects data on adverse reactions and events related to the application of human tissues and cells in the Netherlands. Their mission is to receive and analyse reports of adverse events associated with blood transfusion or with the application of human tissues or cells. TRIP also promotes biovigilance in the widest sense, throughout the chain from donor to recipient, in order to contribute to improved safety of transfusion and transplantation. (1, 2). In addition to this, WMDA focusses on biovigilance worldwide.

Biovigilance is the systematic monitoring of serious adverse reactions and incidents in the transplantation chain of substances of human origin, with the objective of making the application of tissues, cells and organs safer and more effective.

Since the beginning of 2018, WMDA has set up a new global online reporting system for WMDA member organisations to report Serious (Product) Events and Adverse Reactions – S(P)EARs – to the WMDA. The EU definitions of a serious adverse event or reaction are as follows (3):

EU definition of a serious adverse event DIRECTIVE 2004/23/EC, article 3 (m)	**EU definition of a serious adverse reaction** DIRECTIVE 2004/23/EC, article 3 (n)
'serious adverse event' means 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, hospitalisation or morbidity	*'serious adverse reaction' means 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, hospitalisation or morbidity*

WMDA collects and analyses information on recipient and donor S(P)EARs which affect donors and/or products from the WMDA stem cell donor registries and cord blood banks. Furthermore, they follow a rapid alert system for disseminating information on S(PEAR) to all members of the international community in contact with allogeneic donors and patients. (4) On WMDA Share an Imputability Assessment Tool is available which specifies the adverse reaction severity grades, the adverse reaction imputabilities and the criteria for serious adverse events.

A collaboration with CoGapp, a system provider, was established at the beginning of 2018 to develop the system for S(P)EAR. CoGapp is an innovative digital media agency. They are industry-leaders in producing software for online archives and they were chosen after an outstanding respond to the Request For Information (RFI) for a new reporting system and solution provider. In addition, WMDA has worked with CoGapp in the past on the successful Search & Match system.

2. Project objectives, highlights and achievements for the period

The overall objective of the global reporting system for WMDA member organisations is to have a system to quickly and easily gain insight in the occurrence of serious events and adverse effects in relation to blood stem cell donation by unrelated donors and blood stem cell collection, processing and donation from unrelated donors. WMDA aims to collect and analyse information on recipient and donor serious adverse events and reactions which affect donors and/or products from al WMDA stem cell donor registries and cord blood banks. In addition, WMDA intent to follow a rapid alert system for disseminating information on SAE/R to all members of the international community in contact with allogeneic donors and patients. The current form will be revised and improved, guided by medical professionals.

For the new reporting system, WMDA aims to achieve a good defined questionnaire, along with those from the Competent Authorities, in order to reduce redundancy in reporting of serious adverse events and reactions.

The project activities are grouped according to four principal issues, all of them coordinated and monitored by the board of WMDA. The issues are the following:

1. WMDA office takes care of the financial issues, legal status & user access policies and contract with the selected software vendor
2. S(P)EAR Committee takes care of the definition of the questionnaire and the workflow in the new infrastructure
3. WMDA and S(P)EAR Committee take care of the dissemination and outreach
4. Product owner takes care of the services to the users, technical design of the product and the infrastructure

The aim for 2018 is to develop a questionnaire (considering the work being done on GRID as well) that can be used for reporting the serious adverse events and reactions to the WMDA and to define a workload how reports can be handled if they are reported to the WMDA.

At the start of 2018, when the project kicked off, the plan and timeline for delivery was as shown below:

Schedule plan	Audience	Provisional Dates
Develop new questionnaire	WMDA project manager and S(P)EAR committee	5th Jan
Showcase recent developments	S(P)EAR committee	11th July
Meeting to review what outstanding issues remain and triage	Software developer and WMDA project manager	13th July
Ensure all functional behaviour ready in preparation for August 22nd meeting	Software developer and	22nd August

	WMDA project manager	
Internally work though all the use cases scenarios and fix any issues as a result of testing	WMDA project manager	22nd Aug - 2nd Sept
Identify and invite specific user group for testing	WMDA project manager and sponsor	1st August
User group testing with bi-weekly meeting update on feedback	WMDA members organisations	3rd Sep - 30th Sep
Review feedback and make changes and test in preparation for user group testing	Software developer and WMDA project manager	1st Oct - 12th Oct
User group pre-Minneapolis showcase testing	WMDA members organisations	15th Oct - 26th Oct
Present system in Minneapolis	S(P)EAR committee	Nov
Invite pilot users for system pilot phase approval	WMDA project manager and sponsor	Nov post Minneapolis
Specific pilot user's system test and submission of the forms	WMDA members organisations	Nov - Dec 2018
Correct any issues during this period	Software developer and WMDA project manager	Nov - Dec 2018
Roll out to all users for Jan 1st 2019	Software developer and WMDA project manager	Jan 2019

Cogapp started building the new system in April 2018. This lasted until June 2018. After the demo to test the new reporting system, the S(P)EAR Committee was not satisfied with the result. During summer holidays, the project was shut down. In September and October, Cogapp worked partly to get a demo ready for the November meeting in Minneapolis (USA). This deadline was not met due to disagreement within the S(P)EAR Committee and lack of resources at Cogapp. In December, the construction work was continued by Cogapp.

One of the achievements of 2018 is the new and improved questionnaire. This revised questionnaire can be found via:

2018 revised questionnaire with updates to some new questions, logic and additional re-instating feature	WMDA questionnaire form v3.0.xlsx

The new system will be ready by the end of 2018. Although the system is not ready yet, currently WMDA members who send in their S(P)EAR reports are already asked for additional information.

Furthermore, follow ups are performed by a medical specialist. The plan is to launch the questionnaire in June 2019 to the WMDA member organisations.

3. Project management

3.1 Governance and capacity building

The members of the S(P)EAR committee are medically trained with experience in biovigilance and donor care. They come from different organisations around the world which brings in a balanced knowledge. The responsibility of the S(P)EAR committee is monitoring the quality of the project as it develops, providing advice about changes to the project. In addition, they provide support, guidance and oversight of progress to the member organisations. Furthermore, the governance consists of:

1. Project chair from WMDA, to lead the S(P)EAR committee.
2. Project manager from WMDA, responsible for developing and managing this specific project and the cost, time and scope. In addition, initially testing the new system.
3. Software developer CoGapp, responsible for defining, designing, unit testing and eventually implement the software application.
   The S(P)EAR committee in collaboration with the WMDA office defined a Request For Information (RFI) that has been sent to three selected software vendors. In appendix 1 the RFI is provided. Following the results of this, the outcome was that CoGapp was assigned to develop and maintain update the system for S(P)EAR.
4. WMDA appointed a medical advisor who has experience in reporting of serious adverse events and reactions occurring in donors after stem cell donation.
5. A collaboration has been established with the Dutch Biovigilance Office (TRIP). TRIP is appointed by the Dutch health authorities to report serious adverse events and reactions. TRIP is well-known as one of the leading organisations in the field of biovigilance.
6. The DKMS group is the world's largest international network of donor centres and 41% of all stem cell donations worldwide are enabled by DKMS. As they have a lot of experience in reporting they bring in medical and operational expertise.

3.2 Consortium management tasks and achievements

- The responsibility of the S(P)EAR committee is monitoring the quality of the project while providing advice and making decisions about changes to the project as it develops. The role of this team is to provide support, guidance and oversight of progress. This is still ongoing.
- The definition of the questionnaire is coordinated by the WMDA Office and was started in the beginning of 2018. As planned, WMDA is elaborating a draft version to it members. The first draft will be a starting point for comments and discussions with the members. With the information collected a final version of the questionnaire can be defined.
- The kick-off meeting with the software vendor CoGapp was in April and the different collaborators agreed on the scope of the project. The goal was to clarify the requirements for the system.
- The role of the development team is to define, design, unit test and eventually implement the software application. They are working on a new and improved version of this system.

- The product owner will initially perform a system test and later on a test team is assembled to perform in-depth testing. In the end the goal is to assign a test team to check the system in Minneapolis.
- Internal communication, see Share for meeting notes

3.2.1 Changes in the consortium

There have been no changes in the consortium this year.

3.2.2 Problems and envisaged solutions

One of the major risks at the key stage of the project was around CoGapp's availability. Due to lack of capacity in October and November the Minimal Viable Product (MVP) was not ready for the test team in Minneapolis. This could have been solved if the S(P)EAR Committee did agree sooner on the content of the Questionnaire or by planning earlier or more time in CoGapp's schedule.

3.3 Dissemination and outreach

The S(P)EAR committee have weekly international calls, apart from the continuous email trafficking. In addition, there have been several face to face meetings throughout the year. The last one was in Munich, during the annual WMDA Spring Meeting. In addition, there are regularly phone calls with CoGapp and ongoing email conversations.
Furthermore, on the WMDA Share website there is a restricted area for the S(P)EAR committee.

3.4 Communication between S(P)EAR Committee and the listing organisations

Every year, a report of Serious (Product) Events and Adverse Reactions is published to the public. These reports, including the WMDA S(P)EAR report 2017, can be found HERE

- Stem Cell Matters (SCM). Inform the public about S(P)EAR updates. Every quarter of a year, an educational S(P)EAR is discussed in SCM. SCM can be found HERE
- The WMDA Share website provides a guidance to reporting S(P)EAR. The online portal is to be launched next year with questionnaire, information and FAQs.
- International meetings:

WMDA Spring Meeting 2018, Munich DE	**WMDA November Meeting 2018, Minneapolis USA**
The Medical Working Group gave a talk about Donor Suitability.	The chair of the WMDA S(P)EAR Committee gave an overview of the S(P)EAR reports submitted in 2018.
	The chair of the WMDA S(P)EAR Committee presented the road to the new S(P)EAR Online Reporting System.

4. Project planning and status 2019

The previous timeline was revised, and the stakeholders changed the planning for 2019 into:

Currently, CoGap is working on developing the new online reporting system. The plan is to finish this of by the end of the year or the beginning of next year, depending on any issues we might encounter. At the beginning of next year, the system will be tested by 2 or 3 people from the S(P)EAR Committee. In addition, CoGapp will integrate the suggested changes. The new system will then be tested by a larger group, consisting of WMDA members, in March/April. At this stage, S(P)EAR reports from 2018 will be added to the system, for both testing and completion. At the Spring meeting in Noordwijk (The Netherlands), celebrating the 25th year anniversary of WMDA, a workshop will be organised to inform the listing organisations about the new S(P)EAR system and they can practise how to use it. In addition, the pre-launch of the system will be finalised and eventually the launch of the new online reporting system is scheduled for June.

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