WMDA	Reporting Serious Adverse Events and Reactions to the WMDA			
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1. PURPOSE & SCOPE

To collect and analyse information on recipient and donor Serious Adverse Events (SAE) and Severe Adverse Reactions (SAR) which affect donors and/or products from all WMDA regular member organisations.

To follow a rapid alert system for disseminating information on SAE/R to all WMDA regular members of the international community in contact with allogeneic donors and patients.

2. ABBREVIATIONS

WGME	Working Group Medical
SEAR	Serious Events and Adverse Reactions
SPEAR	Serious Product Events and Adverse Reactions

3. TERMINOLOGY

SAE	Serious Adverse Event: 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.
SAR	Serious Adverse Reaction: 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.
Imputability	An assessment of the likelihood that an adverse event/reaction in a donor or recipient is related to the process of donation or to a safety or quality defect in the transplanted tissue or cells. Defined as: Definite, Probable, Possible, Unlikely, Excluded, or Not Assessable.
Definite	Conclusive evidence beyond reasonable doubt of relatedness to the adverse event/reaction.
Probable	Evidence in favour of attributing relatedness to the adverse event/reaction.
Possible	Evidence suggests possible relatedness but alternative explanations are also reasonably likely.
Unlikely	Evidence is clearly in favour of attributing relatedness to the adverse event/reaction to other causes.
Excluded	Conclusive evidence beyond reasonable doubt of unrelatedness.
Not Assessable	Insufficient data for imputability assessment.
Impact	The potential consequences and probability of recurrence of an adverse event or reaction, taking into account consequences for donors or recipients, for the transplant system in general and for tissue or cell supply.
Initial reviewer	A trained physician assigned by WMDA, with experience in online reporting and assessment of SAE reports and biovigilance.
Medical consultant	A trained physician with training and experience in hematopoietic stem cell donation and transplantation.
Reporter	A staff member of a registry who sends the report to the WMDA

4. PROCEDURE

4.1 Reporting of Events and Reactions

4.1.1 Registry responsibility

4.1.1.1 Each WMDA regular member assigns a reporter in their organisation.

4.1.1.2 The procedure and an electronic link for reporting S(P)EAR are available on the WMDA website (www.wmda.info).

4.1.1.3 The WMDA should be notified of reportable S(P)EAR within fifteen (15) working days of becoming known to the registry/cord blood bank, except in the case of a donor death that shall be reported within seventy-two (72) hours.

4.1.1.4 All appropriate data fields must be completed in a comprehensive and clear manner, including an assessment of imputability.

4.1.1.5 The reporting organisation may be requested to provide further information if requested by the WMDA office/S(P)EAR subcommittee.

4.1.1.6 Participation in S(P)EAR reporting in no way replaces or removes the need for organisations to comply with the legal reporting requirements of their national/competent authorities or other regulatory or pharmaceutical bodies.

4.1.2 Events to report (type and timing)

4.1.2.1 If an event/reaction is deemed to be one of the following it should be reported: serious/unexpected/medically relevant/previously unknown.
Hospitalisation *per se* should NOT be reported, unless for an event that is life-threatening or fatal or unexpected. Expected events (*e.g*. nausea/pain) should NOT be reported unless life-threatening or fatal (reference 5.6).

4.1.2.2 Early: Any S(P)EAR from the initiation of donation until thirty (30) days after the completion of the donation. These S(P)EAR should be referred to using CTCAE/ICD-10 terminology (reference 5.4 and 5.5).

4.1.2.3 Late: Any S(P)EAR with onset more than thirty (30) days after completion of the donation. These S(P)EAR should be referred to using ICD-10 terminology (reference 5.5).

4.1.3 WMDA workflow regarding reported S(P)EARs

4.1.3.1 The WMDA has established a workflow to review the reported S(P)EAR reports. To review all reports an initial reviewer, a medical consultant and the members of the S(P)EAR Committee are involved.

4.1.3.2 The initial reviewer reviews all reports for completeness, accuracy and contacts the reporter if clarification is needed. The reporter receives either a confirmation of acceptance or a request for additional information or a request for modification within six weeks after reporting.

4.1.3.3 The chair of the S(P)EAR subcommittee reviews the reports, identified as serious by the reporting organisation, to decide on the need for a rapid alert (current grade 4/5).

4.1.3.4 The initial reviewer reviews all reports with the medical consultant on a monthly base. The medical consultant in collaboration with the initial reviewer:

- check the classification of the reports based on the predefined classification
- tag complicated, educational or otherwise important reports
- draft the quarterly an educational event for Stem Cell Matters in collaboration with the reporting organisation
- prepare the annual report
- support the S(P)EAR subcommittee meeting

4.1.3.5 The responsibility of the S(P)EAR subcommittee is defined as:

- perform final review of all reports according to predefined classification
- meet twice a year to discuss trends and debate difficult issues

- identify trends or quality issues that necessitate additional WMDA recommendations or task forces.

4.1.3.6 Individual registry participation in S(P)EAR reporting (or lack thereof) will be communicated to the WMDA accreditation steering subcommittee.

4.2 Rapid alert system

4.2.1 In the case of a donor death, or if the chair of the S(P)EAR subcommittee (or in his/her absence, their designee) deems a S(P)EAR report to require expedited reporting, an ad-hoc meeting of the S(P)EAR subcommittee will be called to review the event. This should be done within five (5) working days of the event being reported to the WMDA.

4.2.2 If the S(P)EAR subcommittee judges the impact of the S(P)EAR to be high, it will prepare a communication to be sent to the WMDA member organisations and relevant members of the international community in contact with allogeneic (related and unrelated) donors and patients. This must be done in a timely manner, but may require investigation and thus a time scale is not specified.

4.2.3 The WMDA board must agree and approve the communication sent out.

5. Associated documentation/references/websites

5.1 20170517-SEAR-S(P)EAR Operating
5.2 www.wmda.info to 'tools' under professionals
5.3 http://www.notifylibrary.org
5.4 http://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcaev3.pdf
5.5 http://apps.who.int/classifications/apps/icd/icd10online/
5.6 20141209-SEAR-INFO-S(P)EAR Examples