Imputability Assessment Tool

Definition serious adverse reaction (SAR):

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.

Adverse reaction severity grade

Grade 0	Nil: no harm, no risk, donor or patient not informed as there was no risk of harm
Grade 1	Non-serious: mild clinical/psychological consequences. No hospitalisation. No anticipated long term consequences/disability
Grade 2	Serious: hospitalisation or prolongation of hospitalisation and/or persistent or significant disability or incapacity, intervention to preclude permanent damage. Evidence of a serious transmitted infection.
Grade 3	Life-threatening: the living donor or recipient needed major medical or surgical intervention following donation or transfusion respectively to prevent death (vasopressors, intubation, IC admission). Evidence of life-threatening transmitted infection.
Grade 4	Death: following an adverse reaction after donation or transfusion. Grade 4 does not apply if the patient recovers to the clinical situation before transfusion and later dies of an unrelated cause.

Adverse reaction imputability:

Definite, certain	Conclusive evidence beyond reasonable doubt for attribution to donation or infusion of the cell product
Probably, likely	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
Not Assessable	Insufficient data for imputability assessment

Definition serious adverse event (SAE):

Any untoward occurrence associated with the procurement, storage and distrubution of tissues and cells that might lead to the transmission of a communicable disease, to death or life-greatening, disabling or incapacitating conditions for donors or patients or which might result in, or prolong, hospitalisation or morbidity.

Criteria for serious adverse event (SAE):

The event (could have) led to inappropriate use of tissues or cells

The event (could have) resulted in loss of the complete or significant quantity of irreplaceable cells

The event (could have) led to a serious adverse reaction (grade 2, 3 or 4)

The event (could have) led to misidentification or an unintended switch of cells

The event (could have) led to (an unforeseen) transmission of disease from donor to recipient

IMPACT: A product of the the likelihood of recurrence and severity of (potential) reaction on donor/patient, the system and the cell supply. A method to determine what the urgency is and what type of action is warranted.

	Likelyhood of recurrence	
1	Rare	Difficult to believe it could happen again
2	Unlikely	Not expected to happen again
3	Possible	May occur occasionally
4	Likely	Expected to happen again but not persistent
5	Probably	Expected to happen again on many occasions

	Severity	On donor/patient; potential in case of SAE, actual in case of SAR	On system	On cell supply
0	Insignificant	Nil	No effect	Insignificant
1	Minor	Non-serious	Minor change	Some applications postponed
2	Moderate	Serious	Damage for a short period	Many cancellations or postponements
3	Major	Life threatening	Major damage to system-significant delay to repair	Significant cancellations-importation required
4	Catastrophic	Death	System destroyed - need to rebuild	All allogeneic applications cancelled

IMPACT MATRIX: grades from 0 to 20

Likelihood of recurrence from left to right Severity grade from top to bottom	Rare 1	Unlikely 2	Possible 3	Likely 4	Probable 5
Insignificant 0	0	0	0	0	0
Minor 1	1	2	3	4	5
Moderate 2	2	4	6	8	10
Major 3	3	6	9	12	15
Catastrophic 4	4	8	12	16	20

IMPACT and the necessity of actions: to be discussed.

0-3	The registry manages the corrective and preventive actions. Voluntary reporting to WMDA is encouraged.
4-9	Report to health authority which may request an inspection and corrective and preventive actions to be followed up. Reporting to WMDA is required for accredited registries.
10-20	Health authority will generally designate representatives to participate in corrective and preventive action plan. Reporting to WMDA is required for accredited registries within 24 hours after registry is informed.

IMPUTABILITY ASSESSMENT of SAR: WMDA examples

Imputability	Definite	Probable	Possible	Unlikely	Excluded

0-30 days after donation	Anemia occurring immediately after bone marrow donation Local trauma as a result of Central Venous Catheter placement Anaphylactic reaction occurring 10 minutes after first G-CSF administration Pulmonary edema during intubation for bone marrow collection Transmission of rare chromosomal abnormalitity found in donor and recipient Severe rejection of graft after unintended infusion of completely mismatched stem cells.	Exacerbation of psoriasis 2 days after G-CSF administration Hematuria due to IgA nephropathy during mobilization Back pain lasting 2 weeks after bone marrow harvest	Varicella zoster occuring 3 weeks post PBSC donation.	Rheumatoid Arthritis Car accident 1 week post donation	
long-term follow up			Back pain lasting more than 6 weeks	Colorectal cancer, 2 years after PBSC donation First symptoms of Rheumatoid Arthritis 3 months post PBSC	Breast carcinoma 3 years post bone marrow harvest