

Serious Adverse Events and Reactions

1st Edition



World Marrow Donor Association
Clinical Working Group
www.worldmarrow.org

Summary from 2003 till 2010

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SERIOUS AND ADVERSE EVENT REGISTRY (SEAR 2003)

Reports collected in 2003: 3 after BM donation (31 participating registries representing 5,756,117 donors): 1 persistent low back pain, 1 BM donor with seizure and deep venous thrombosis after donation, 1 BM donor with reaction to G-CSF with swelling of tongue and palate.

3 reports did not fulfill the SEARs definition. Total of 6 reports in 3,427 donations (0.175%)



SERIOUS AND ADVERSE EVENT REGISTRY (SEAR 2004)

Summary of SEAR envelopes sent in the year 2004 to the WMDA Office

The WMDA Office received 20 SEAR envelopes reporting about the year 2004.

All these envelopes were sent to the Chair of the Clinical Working Group

Number of SEAR envelopes	Date received	Number of SEAR envelopes	Date Received
1	02-02-2004	1	23-11-2004
1	14-04-2004	3	03-12-2004
1	09-06-2004	1	03-12-2004
1	06-07-2004	1	17-12-2004
2	13-07-2004	1	17-12-2004
1	16-08-2004	2	06-01-2005*
1	18-10-2004	1	06-01-2005*
1	05-11-2004	1	11-01-2005*

* registry posted this envelope in 2004

Report from the Chair of the Clinical Working Group:

BONE MARROW

- 3 BM donors had lower back pain including one with osteomyelitis of the iliac crest.
- In 1 BM donor the joint of the trocar broke in the right iliac crest.
- 1 BM donor had lower back pain after her second donation.

PBSC

- 1 PBSC donor had testicular cancer three months after donation.
- 4 PBSC donors had to be hospitalised because of nausea, emesis, headaches or dehydration.
- 1 PBSC donor experienced tetany.
- 1 PBSC donor had to be hospitalised because of fever and rigors 2 days after donation.
- 1 PBSC donor experienced high intensity bone pain.

- 1 PBSC donor presented multiple infections including sinusitis and teeth infections.
- 1 PBSC donor had to be hospitalised because of bleeding after removal of the femoral venous catheter.
- 1 PBSC donor presented with brachial and popliteal thrombosis.
- 1 PBSC donor experienced severe pain in the foot consistent with a gout attack.
- 1 PBSC donor presented an asystoly for 20 to 30 seconds during leukapheresis and had a neurocardiogenic syncope. The donor recovered completely.
- 1 PBSC donor had tinnitus on day 4 of G-CSF stimulation

UNSTIMULATED LYMPHOCYTES

1 donor of unstimulated lymphocytes fainted, had paresthesia in both upper and lower extremities and diarrhoea after collection.



SERIOUS AND ADVERSE EVENT REGISTRY (SEAR 2004)

The WMDA Office sends a monthly SEAR Reminder to the WMDA Registries. Herewith information which stem cell registries participate. These registries reply to the monthly reminder.

44 registries participate in SEAR representing: 9,414,522 donors. These registries performed 2,965 bone marrow and 3,964 PBSC donations. The Chair of the Clinical Working Group reported about 5 bone marrow and 14 PBSC events.

SEAR PARTICIPANTS

Country	Donors	BM	PBSC	Total Donations
Argentina	11,276	0	0	0
Armenia	8,417	0	2	2
Australia	155,869	26	79	105
Belgium	48,859	2	36	38
Brazil	93,200	26	4	30
Canada	218,854	85	8	93
China Hong Kong	44,796	25	1	26
Croatia	143	0	0	0
Cyprus BMDR	92,250	0	23	23
Cyprus Par.	3,110	0	0	0
Czech BMDR	17,913	0	9	9
Czech Central	27,931	8	28	36
Denmark	14,333	5	8	13
Denmark BMDC	4,996	2	1	3
Finland	19,582	13	14	27
France	129,042	67	38	105
Germany	2,360,837	464	1,865	2,329
Greece	17,575	1	19	20
Ireland	18,436	5	1	6
Israel Hadassah	38,176	1	16	17
Israel Ezer	185,557	1	37	38
Italy	309,716	172	10	182
Japan	201,300	728	0	728
Mexico	3,815	1	0	1
Netherlands	34,117	37	13	50
New Zealand	7,220	1	0	1
Norway	22,972	4	13	17
Poland	3,227	0	7	7
Poland Warsaw	6,050	2	3	5
Poland POLTR	5,575	8	0	8
Slovenia	1,831	1	0	1
South Africa	56,071	0	6	6
Spain	50,705	5	22	27
Sweden	39,950	5	28	33
Switzerland	19,481	3	14	17
Taiwan	267,229	134	42	176
Turkey-Istanbul	29,011	0	0	0
UK Anthony Nolan	363,322	141	153	294
UK BBMR	237,755	45	53	98
UK Wales	39,563	34	11	45
USA ABMDR	51,955	0	0	0
USA CRIR	49,476	0	2	2
USA Gift of Life	83,941	13	48	61
USA NMDP	4,019,088	900	1,350	2,250
TOTAL	9,414,522	2,965	3,964	6,929

REGISTRIES NOT PARTICIPATE

Country	Donors	BM	PBSC	Total donations
Austria	52,951	2	17	19
Bulgaria	446	0	0	0
China	212,332	0	119	119
Hungary	4,449	0	0	0
India	2,400	0	0	0
Israel Sheba	1,332	0	0	0
Korea	67,022	146	16	162
Lithuania	85	0	0	0
Poland ALF	2,355	14	1	15
Poland FUJ	11,308	0	7	7
Portugal	22,178	0	3	3
Russia	16,604	0	0	0
San Marino	727	0	0	0
Singapore	36,780	3	2	5
Slovakia	462	0	0	0
Thailand	5,892	3	4	7
Turkey Ankara	1,908	0	0	0
Uruguay	22	0	0	0
TOTAL	439,253	168	169	337



SERIOUS EVENTS AND ADVERSE EFFECTS REGISTRY (SEAR 2005)

Summary of SEAR envelopes sent in the year 2005 to the WMDA Office

Number of SEAR envelopes	Date Received
1	11-01-2005
1	17-01-2005
1	21-01-2005
1	15-03-2005
2	12-04-2005
3	13-05-2005
1	10-06-2005
1	13-06-2005
1	11-07-2005
1	19-07-2005
1	05-09-2005
1	04-10-2005
1	24-10-2005
1	21-11-2005
1	01-12-2005

All these envelopes were sent to the Chair of the Clinical Working Group. From the 18 reports only 15 can be considered to fulfil the criteria of SEARS as previously defined. They include the following:

5 after BM donation:

- 3 BM donors had persistent lower back pain after donation.
- 1 BM donor had low grade osteomyelitis of the iliac crest.
- 1 BM donor, a 47 year old man experienced 10 days post-donation a non haemorrhagic stroke with hemiparesis, had a dysplasia and platelet counts of 40 000 /ul. It was assumed that he had an unproven viral encephalitis and thrombotic microangiopathy. This donor remained disabled (wheelchair).

9 after PBSC donation:

- 1 PBSC donor presented multiple infections including sinusitis and teeth infections.
- 1 PBSC donor was hospitalised because of a bleeding episode after removal of the femoral venous catheter.
- 1 PBSC donor had an asystoly for 20 to 30 seconds during leukapheresis and had a neurocardiogenic syncope. The donor recovered completely.
- 1 PBSC donor presented a tinnitus on day 4 of G-CSF stimulation.
- 4 PBSC donors were hospitalised because of nausea, sacral pain, severe headache, chest pain and/or emesis.
- 1 PBSC donor had a viral pericarditis 4 days after donation, was hospitalised and recovered after 63 days.



1 after unstimulated lymphocyte donation:

- 1 donor fainted, had paresthesia in both upper and lower extremities and diarrhoea.

The following reports did not fulfil the criteria of SEARs:

- 1 PBSC donor had a fibrocystic change of her breast tissue 363 days after donation.
- 1 PBSC donor had hives on the arms and the stomach area, an allergic reaction to G-CSF was suspected.
- In 1 BM donor marrow morphology after donation revealed evidence of a malignancy with a B-CLL marker profile. This donor was referred to a haematologist.

In summary:

In 2005, 46 of 63 stem cell donor registries participated in reporting SEARs representing 10,105,581 donors. These registries performed 2,947 bone marrow and 4,553 PBSC donations, which is 95% of all stem cell donations.

Fourteen (0.19% of the stem cell donations) serious events and adverse effects after bone marrow, peripheral blood stem cell donations were reported. One DLI donation (0.17% of the DLI donations) were reported to SEAR>



SERIOUS EVENTS AND ADVERSE EFFECTS REGISTRY (SEAR 2005)

SEAR PARTICIPANTS					REGISTRIES NOT PARTICIPATING IN SEAR				
Country	Donors	BM	PBSC	Total	Country	Donors	BM	PBSC	Total
				Donations					Donations
Argentina	18,330	0	0	0	Austria	54,079	3	14	17
Armenia	10,061	0	0	0	Bulgaria	556	0	1	1
Australia	154,479	46	122	168	Bulgaria	92	0	0	0
Belgium	47,441	0	30	30	China	365,130	0	168	168
Brazil	135,351	38	4	42	India	2,800	0	0	0
Canada	221,248	54	26	80	Israel Sheba	1,387	0	0	0
China Hong Kong	50,202	22	14	36	Korea	83,875	159	29	188
Croatia	143	0	0	0	Lithuania	348	0	1	1
Cyprus BMDR	94,156	2	16	18	Poland ALF	3,209	9	8	17
Cyprus Par.	4,064	0	0	0	Poland FUJ	11,336	1	6	7
Czech BMDR	18,538	0	5	5	Portugal	44,744	0	14	14
Czech Central	29,773	22	73	95	Russia	17,122	0	0	0
Denmark	18,775	0	1	1	San Marino	802	1	0	1
Denmark BMDC	7,463	0	2	2	Singapore	36,780	5	2	7
Finland	21,029	6	16	22	Slovakia	500	0	0	0
France	134,578	72	66	138	Turkey Ankara	2,326	0	0	0
Germany	2,601,609	535	2,221	2,756	Uruguay	55	0	0	0
Greece	19,533	2	2	4	TOTAL	625,141	178	243	421
Hungary	4,626	0	0	0					
Ireland	19,043	5	3	8					
Israel Ezer	228,440	2	38	40					
Israel Hadassah	39,495	0	10	10					
Italy	315,921	132	56	188					
Japan	232,565	907	0	907					
Mexico	4,588	0	6	6					
Netherlands	35,357	23	28	51					
New Zealand	7,589	1	0	1					
Norway	23,424	1	15	16					
Poland PL1	5,701	5	4	9					
Poland PL2	6,186	1	0	1					
Poland PL5	7,898	5	11	16					
Slovenia	5,010	0	3	3					
South Africa	58,838	0	4	4					
Spain	54,517	10	20	30					
Sweden	40,083	9	36	45					
Switzerland	19,798	6	27	33					
Taiwan	281,551	143	67	210					
Thailand	9,198	1	3	4					
Turkey-Istanbul	30,724	0	2	2					
UK Anthony Nolan	370,050	130	199	329					
UK BBMR	275,477	57	90	147					
UK Wales	44,440	50	12	62					
USA ABMDR	48,078	0	0	0					
USA CRIR	53,754	0	0	0					
USA Gift of Life	97,222	15	67	82					
USA NMDP	4,199,235	645	1,254	1,899					
TOTAL	10,105,581	2,947	4,553	7,500					



SERIOUS EVENTS AND ADVERSE EFFECTS REGISTRY (SEAR 2006)

Summary of SEAR envelopes sent in the year 2006 to the WMDA Office (N=20)

Number of SEAR envelopes	Date Received
1	10-01-2006
2	17-01-2006
1	07-02-2006
1	07-03-2006
1	07-03-2006
1	04-07-2006
1	04-07-2006
1	18-07-2006*
1	02-10-2006
1	09-10-2006
1	25-10-2006
1	07-11-2006
1	07-11-2006
1	27-11-2006
1	28-11-2006
1	11-2006
1	04-12-2006
1	06-12-2006

* The envelop received on July 18th 2006 contained retrospective SEAR incidents which appeared in 2003 (2), 2004 (1) and 2005 (6)

- **8 after BM donation**
 - 4 respiratory
 - 1 fever
 - 1 first degree heart block during anesthesia
 - 1 severe pain in right leg
 - 1 reversible paralysis of facial nerve
- **11 after PBSC donation**
 - 1 arteriovenous fistula
 - 1 acute hepatitis
 - 1 perianal bleeding and neurodermitis-like exanthema
 - 1 lymphoma (after 16 months)
 - 1 haemoptoe and diffuse interstitial edema
 - 2 hospitalizations with pneumonia
 - 2 hospitalizations with severe headache +/-vomiting
 - 1 anxiety, shortness of breath caused by viral infection
 - 1 deep venous thrombosis
- **1 after DLI**
 - 1 polyarthritis (shoulders, hands) after 13 months/25 months after G-CSF



SERIOUS EVENTS AND ADVERSE EFFECTS REGISTRY (SEAR 2006)

SEAR PARTICIPANTS					REGISTRIES NOT PARTICIPATING IN SEAR				
Country	Donors	BM	PBSC	Total	Country	Donors	BM	PBSC	Total
				Donations					Donations
Argentina	24,772	0	0	0	Bulgaria	588	0	2	2
Armenia	11,452	0	0	0	Bulgaria	143	0	0	0
Australia	153,902	15	60	75	Croatia	143	0	0	0
Austria	56,194	2	21	23	China	554,495	0	215	215
Belgium	46,152	2	20	22	Korea	13,157	128	92	220
Brazil	314,496	34	3	37	Korea	32,237	17	24	41
Canada	222,672	41	53	94	Lithuania	937	0	0	0
China Hong Kong	58,470	17	14	31	Poland FUJ	11,952	0	5	5
Cyprus BMDR	96,070	0	34	34	Portugal	57,746	1	14	15
Cyprus Par.	4,950	0	0	0	Russia	17,102	0	0	0
Czech BMDR	19,098	1	8	9	Serbia	244	0	0	0
Czech Central	30,780	10	15	25	Slovakia	523	0	0	0
Denmark	18,421	6	7	13	United Arab Em	45	0	0	0
Denmark BMDC	9,445	0	0	0	Uruguay	70	0	0	0
Finland	21,062	13	16	29	TOTAL	689,382	146	352	498
France	141,375	66	88	154					
Germany	2,861,728	547	2,492	3,039					
Greece	26,573	0	0	0					
Hungary	4,837	0	1	1					
India	0	0	0	0					
Ireland	21,249	3	1	4					
Israel Ezer	263,656	6	73	79					
Israel Hadassah	57,563	1	20	21					
Israel Sheba	1,491	0	0	0					
Italy	320,709	138	91	229					
Japan	269,614	943	0	943					
Mexico	5,096	0	0	0					
Netherlands	37,131	31	23	54					
New Zealand	7,828	2	1	3					
Norway	25,169	9	19	28					
Poland PL1	6,436	0	1	1					
Poland PL2	6,793	0	1	1					
Poland PL3	3,906	3	11	14					
Poland PL5	10,371	6	7	13					
Russia Karelian	1,992	0	0	0					
San Marino	803	0	0	0					
Singapore	40,642	4	12	16					
Slovenia	7,694	0	2	2					
South Africa	61,414	0	6	6					
Spain	58,151	8	33	41					
Sweden	40,053	2	14	16					
Switzerland	20,733	9	11	20					
Taiwan	295,077	78	130	208					
Thailand	16,060	4	3	7					
Turkey Ankara	2,734	0	0	0					
Turkey-Istanbul	31,253	0	2	2					
UK Anthony Nolan	381,905	80	223	303					
UK BBMR	298,260	52	108	160					
UK Wales	48,583	50	11	61					
USA ABMDR	59,675	0	1	1					
USA CRIR	64,126	0	3	3					
USA Gift of Life	108,580	13	52	65					
USA NMDP	4,435,686	659	1,374	2,033					
TOTAL	11,132,882	2,855	5,065	7,920					



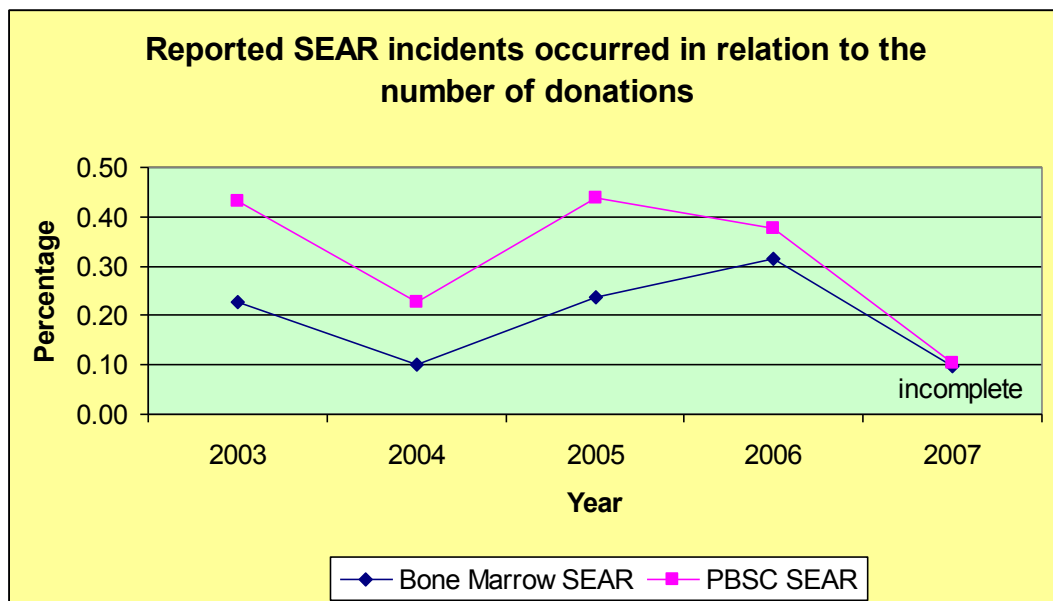
SERIOUS EVENTS AND ADVERSE EFFECTS REGISTRY (SEAR 2007)

The Clinical Working Group of the WMDA started to encourage registries to send their SEAR reports to the central database in 2002. It took some time to set up the system within the registries. In 2007 53 registries participated in the SEAR project (these registries provided 93.5% of the stem cell products worldwide, 8,877 donations).

The WMDA Office received 31 SEAR envelopes in the year 2007.

- 14 envelopes reported SEAR incidents from donations before 2007
- 9 envelopes reported SEAR incidents from donations before 2007, but SEARs occurred in 2007
- 8 envelopes reported SEAR incidents from donations performed in 2007 (8,756 donations)

The Chair of the Clinical WG received many SEARs concerning donations in previous years. Therefore the number of SEARs/year has been constantly changing. The WMDA Office and the Chair of the Clinical WG decided to update the previous years and correlate the updated SEARs with the number of harvests of the respective year.





Find here a description of the SEAR incidents that occurred in 2007 and were reported to the WMDA Office.

- **6 after BM donation**

BM DONATIONS BEFORE 2007

- 2 AML (two years and nine years after donation)
- 1 septic right sacroiliac joint with abscess from β -hemolytic streptococci (4 months after donation)

IMMEDIATELY after BM donation in 2007 (3,068 BM donations in 2007)

- 1 hospitalization for vaso-vagal syncope, vomiting
- 1 hospitalization for shortness of breath, nausea, vomiting, dehydration, anemia
- 1 edema and inflammation of musculus gluteus

- **11 after PBSC donation**

DONATIONS BEFORE 2007

- 2 seminoma (three and four years after donation)
- 1 breast cancer (13 months after donation)
- 1 gastric carcinoma (one year after donation)
- 1 tumor of pituitary gland (1.5 years after donation)
- 1 Graves' disease (1 year after donation)

IMMEDIATELY after PBSC donation in 2007 (5,809 PBSC donations in 2007)

- 1 macrohematuria, microvascular ischemia, acute tubular necrosis
- 1 hospitalization for chest pain during leukocytosis
- 1 dysesthesia left face, arm and leg
- 1 hospitalization for pain, vomiting, swollen neck lymph nodes
- 1 scleroderma (six months after donation)



SERIOUS (PRODUCT) EVENTS AND ADVERSE EFFECTS REGISTRY (S[P]EAR 2007)

S(P)EAR PARTICIPANTS					REGISTRIES NOT PARTICIPATING IN S(P)EAR			
Country	Donors	BM	PBSC	Total	Country	Donors	BM	PBSC
				Donations				
Argentina	31,841	0	0	0	Bulgaria	168	0	0
Armenia	13,522	0	2	2	Bulgaria	624	0	1
Australia	151,910	25	79	104	Croatia	143	0	0
Austria	58,574	5	26	31	China	769,372	0	259
Belgium	44,935	3	13	16	Ghana	1,017	0	0
Brazil	554,371	50	5	55	Korea Catholic+KMDP	152,370	87	228
Canada	231,075	36	44	80	Lithuania	2,250	0	5
China Hong Kong	63,047	17	16	33	Poland FUJ	12,350	0	1
Cyprus BMDR	101,283	1	19	20	Portugal	106,846	2	24
Cyprus Par.	5,379	0	0	0	Russia Moscow	17,276	0	0
Czech SCR	19,178	0	1	1	Russia St. Petersburg	1,577	0	0
Czech Central	32,118	20	22	42	Serbia	325	0	0
Denmark	19,993	6	5	11	Slovakia	550	0	0
Denmark BMDC	10,527	0	1	1	United Arab Emirates	45	0	0
Finland	21,341	13	14	27	Uruguay	113	0	0
France	154,689	77	109	186	TOTAL	1,065,026	89	518
Germany	3,107,485	715	2,997	3,712				
Greece	27,606	0	2	2				
Hungary	4,983	0	2	2				
India	3,250	0	0	0				
Ireland	22,511	1	4	5				
Israel Ezer	323,187	5	85	90				
Israel Hadassah	60,183	3	24	27				
Israel Sheba	1,533	0	0	0				
Italy	325,097	113	107	220				
Japan	299,777	993	0	993				
Mexico	7,848	0	3	3				
Netherlands	37,272	27	21	48				
New Zealand	7,951	1	2	3				
Norway	26,889	6	18	24				
Poland PL1	7,227	1	2	3				
Poland PL2	6,854	0	3	3				
Poland PL3	4,536	7	1	8				
Poland PL5	13,537	5	7	12				
Russia Karelian	2,080	0	0	0				
San Marino	803	0	0	0				
Singapore	42,144	1	7	8				
Slovenia	9,069	1	6	7				
South Africa	63,123	0	3	3				
Spain	65,438	9	31	40				
Sweden	40,189	2	22	24				
Switzerland	21,203	6	10	16				
Taiwan	307,527	76	183	259				
Thailand	8,656	3	2	5				
Turkey Ankara	2,624	0	0	0				
Turkey-Istanbul	31,253	0	5	5				
UK Anthony Nolan	389,199	100	268	368				
UK BBMR	305,574	38	97	135				
UK Wales	52,832	43	4	47				
USA ABMDR	60,040	0	0	0				
USA CRIR	71,520	3	4	7				
USA Gift of Life	121,023	15	72	87				
USA NMDP	4,750,472	641	1,461	2,102				
TOTAL	12,146,278	3,068	5,809	8,877				



SERIOUS PRODUCT EVENTS AND ADVERSE EFFECTS REGISTRY (SPEAR 2007)

Find here a description of the SPEAR incidents that occurred in 2007 and were reported to the WMDA Office.

- **1 SPEAR before PBSC donation 2007**
 - 1 wrong tube sent for quality control

- **1 SPEAR 24 hours after BM donation**
 - DONATIONS BEFORE 2007 (2005)**
 - B-CLL in donor

- **3 SPEAR Immediately after donation in 2007**
 - 1 MRSA in marrow culture
 - 1 Staph capitis in marrow culture
 - 1 Leakage of CB tube at TX centre



SERIOUS (PRODUCTS) EVENTS AND ADVERSE EFFECTS REGISTRY (S[P]EAR 2008)

The Clinical Working Group remains responsible for the inspection of serious events and adverse effects (SEAR) and serious product events and adverse effects (SPEAR). The WMDA Office collects the SEAR and SPEAR reports. Registries are encouraged to report such events to the WMDA Office as soon as they come to light.

In total 62 S(P)EAR were reported to the WMDA in 2008. Below is a brief description of the SEAR and SPEAR incidents that were reported.

Serious events and adverse effects (SEAR)

14 after BM donation

BM DONATIONS BEFORE 2008 (n=5)

- 1 Non-Hodgkin's lymphoma
- 1 Breast cancer
- 1 CML
- 1 Benign brain tumor
- 1 Prolonged pain at harvest site

BM DONATION IN 2008 (n=9)

- 1 hospitalization for severe chest pain, anxiety related
- 1 transfusion of ABO-compatible RBCs from another donor
- 1 central chest pain, non-cardiac
- 1 abdominal thrombosis, urinary tract infection
- 1 wound infection, staphylococcus epidermidis bacteremia
- 1 vasovagal reaction or second degree AV block and asystole secondary to ondansetron
- 1 deep venous thrombosis
- 1 sacral puncture, cauda equina hematoma
- 1 commotio cerebri after collapse

36 after PBSC donation

PBSC DONATIONS BEFORE 2008 (n=21)

- 2 Breast cancer
- 1 CLL after second PBSC
- 2 Prostate cancer
- 1 Thyroid cancer
- 1 Metastatic testicular cancer
- 2 Melanoma
- 2 Hodgkin's lymphoma
- 2 Colorectal cancer
- 2 Carcinoma (thymus, appendix)
- 1 Hepatoma
- 1 Lung cancer



1 Myeloma

1 Graves' disease

1 Urticaria for several months

1 heart failure requiring heart transplant

PBSC DONATION IN 2008 (n=15)

2 during G-CSF

1 supraventricular tachycardia 16 hrs after 2nd dose

1 anaphylactic reaction to first dose

8 during PBSC collection

1 supraventricular tachycardia during CVC insertion

1 severe migraine

1 hospitalization for pneumonia 4 days after collection

1 subdural hematoma 1 day after collection

1 vasovagal reaction

1 asthmatic reaction during leukapheresis

1 hypotensive reaction after rupture of bag

1 bleeding at CVC site inguinal

5 after collection

1 MS

1 Breast cancer

1 Colorectal cancer

1 Lyme arthritis

1 Paraesthesias of toes for 6 weeks

Serious product events and adverse effects (SPEAR) (n=12)

1 loss of viability of PBSC after cryopreservation

1 leakage of PBSC bag at TC

1 failure of registry to clearly communicate change in product (from PBSC to BMT) to TC

1 PBSC arrived partially frozen at TC after transport by courier on dry ice, 66% viability

1 Wrong SC product given to courier at collection center

1 decrease of viability after transport and processing

2 contaminations of product without clinical infection

1 clotting of product during transplant, 45 hours after harvest

1 CB partially thawed by arrival at TC

1 clots in first apheresis bag at TC

1 rupture of tubing of cell separator during first apheresis



SERIOUS (PRODUCT) EVENTS AND ADVERSE EFFECTS REGISTRY (S[P]EAR 2008)

SEAR PARTICIPANTS					REGISTRIES NOT PARTICIPATING IN SEAR				
Country	Donors	BM	PBSC	Total	Country	Donors	BM	PBSC	Total
				Donations					Donations
Argentina	20,076	1	0	1	Bulgaria	210	0	0	0
Armenia	13,950	0	0	0	Bulgaria	644	0	1	1
Australia	172,859	10	75	85	Croatia	8,899	0	0	0
Austria	60,640	5	32	37	China	963,894	0	275	275
Belgium	47,466	0	15	15	Ghana	1,017	0	0	0
Brazil	939,128	43	10	53	India Bangalore	1,916	0	0	0
Canada	241,069	21	48	69	India	3,500	0	0	0
China Hong Kong	68,703	12	28	40	Israel Ezer	401,440	3	111	114
Cyprus BMDR	102,389	0	28	28	Korea Catholic	KONOS	35	90	125
Cyprus Par.	5,790	0	0	0	Korea KMDP	166,547	19	194	213
Czech SCR	19,206	2	8	10	Lithuania	3,001	0	1	1
Czech Central	33,344	31	12	43	Poland PL1	8,126	3	3	6
Denmark	22,407	5	3	8	Poland PL4	12,502	0	1	1
Denmark BMDC	11,371	3	2	5	Poland PL5	19,245	6	11	17
Finland	21,156	6	9	15	Portugal	142,691	3	46	49
France	163,765	80	124	204	Romania	328	0	0	0
Germany	3,357,693	746	3,420	4,166	Russia Moscow	17,276	0	0	0
Greece	21,255	0	0	0	Russia St. Petersburg	3,744	0	0	0
Hungary	5,011	0	0	0	Serbia	1,322	0	0	0
Ireland	18,963	0	5	5	Slovakia	670	0	0	0
Israel Hadassah	66,506	2	27	29	Turkey-Istanbul	26,808	0	2	2
Israel Sheba	1,546	0	0	0	United Arab Emirates	69	0	0	0
Italy	328,523	106	109	215	Uruguay	188	0	0	0
Japan	329,247	1,100	0	1,100	TOTAL	1,784,037	69	735	804
Mexico	9,926	1	4	5					
Netherlands	37,594	18	27	45					
New Zealand	8,079	3	3	6					
Norway	27,771	10	20	30					
Poland PL2	8,246	0	2	2					
Poland PL3	5,525	2	3	5					
Russia Karelian	2,458	0	0	0					
San Marino	800	0	0	0					
Singapore	44,800	1	4	5					
Slovenia	10,777	2	5	7					
South Africa	64,182	0	5	5					
Spain	72,157	8	28	36					
Sweden	40,702	7	25	32					
Switzerland	22,033	5	12	17					
Taiwan	319,295	73	252	325					
Thailand	35,530	3	2	5					
Turkey Ankara	3,037	1	2	3					
UK Anthony Nolan	394,910	91	292	383					
UK BBMR	310,576	40	111	151					
UK Wales	56,414	33	9	42					
USA ABMDR	34,621	0	0	0					
USA CRIR	80,064	2	8	10					
USA Gift of Life	128,165	23	66	89					
USA NMDP	5,047,169	656	1,690	2,346					
TOTAL	12,836,894	3,152	6,525	9,677					



SERIOUS (PRODUCTS) EVENTS AND ADVERSE EFFECTS REGISTRY (S[P]EAR 2009)

The Clinical WG is responsible for the collection and discussion of serious events and adverse effects (SEAR) and serious product events and adverse effects (SPEAR). Registries are encouraged to report such events to the WMDA as soon as they come to light.

In total 45 S(P)EAR were reported to the WMDA in 2009. Below is a brief description of the SEAR and SPEAR incidents that were reported.

Serious events and adverse effects (SEAR) (n=28)

13 in 2009 (7 - 2008, 2 – 2007, 3 - 2006, 1 – 2004, 1 - 2003, 1-1997)

Following PBSC

- 1 allergic reaction to first dose of GCSF (required oxygen and steroids). Did not donate
- 1 Horner's syndrome following cervical line insertion
- 1 faint following tubing rupture during PBSC (target dose collected on second day)
- 1 bilateral episcleritis responded to steroid eye drops
- 1 superficial thrombophlebitis on GCSF
- 1 acute hearing loss D5 GCSF. Persistent.
- 1 severe headache D3 GCSF. Hospitalised. Recovered.
- 2 high BP during collection. 1- TIA 6/52 later. 1-intracranial haemorrhage 1/12 later.
- 2 severe reaction to ACD. Collection stopped. Enough cells
- 1 nausea and headache on machine
- 1 neck pain ?vasculitis (post collection). Normal investigations and recovered
- 1 pain related to BM site as part of medical
- 1 death from stroke (ICH) - 3 years post donation
- 4 cancers
 - Lung/ hepatoma (hepatoma had 3 doses of GCSF – PBSC not collected due to patient factors)/ meningioma/oesophageal cancer

Following BM donation

- 2 persistent back pain
- 1 SVT in theatre
- 1 fat embolism post GA and BM harvest - full recovery
- 1 cauda equina syndrome post BM
- 3 cancers
 - Breast/ brain (benign)/NHL

Following DLI

- 1 severe groin bruising post groin line for DLI



Serious product events and adverse effects (SPEAR) (n=17)

9 - 2009 (4 - 2008, 1-2007, 1 - 2006, 1 - 1996)

- 1 Donor blood group incorrect on label (all other identifiers correct)
- 1 Donor ID incorrect on bag (other identifiers correct)
- 1 Incorrect product collected by courier (2 harvested on same day). Identified and rectified before courier left airport
- 1 Cord unit arrived partially thawed. 28% viability in segment. Not infused.
- 2 Clots in apheresis bag – engrafted
- 1 Clotting in transfusion lines
- 1 Rupture of tubing on cell separator. Collection abandoned. Target achieved on day 2
- 1 of 3 bags ruptured at insertion point (cord). Not detected at pre-thaw
- 1 Damaged cord bag (1 of 2)
- 4 Severe reactions to double cord infusion (“shocked heart”)
- 2 donor derived malignancies
 - Patient with MDS (Transplanted in 2006). Diagnosed with CML in November 2008. Donor diagnosed with CML May 2008
 - Patient with CML (Transplanted in 1996) diagnosed with mantle cell lymphoma in May 2008. Donor diagnosed with MCL September 2008



SERIOUS (PRODUCT) EVENTS AND ADVERSE EFFECTS REGISTRY (S[P]EAR 2009)

SEAR PARTICIPANTS

Country	Donors	BM	PBSC	Total
				Donations
Armenia	14,650	0	1	1
Australia	173,257	23	99	122
Belgium	47,518	0	11	11
Canada	251,877	39	55	94
China Hong Kong	74,762	15	13	28
Croatia	12,096	0	2	2
Cyprus BMDR	109,167	0	29	29
Cyprus Par.	6,048	0	1	1
Czech SCR	20,015	3	3	6
Czech Central	34,476	20	14	34
Denmark	24,350	5	8	13
Denmark BMDC	12,260	1	5	6
Finland	20,796	12	7	19
France	176,364	84	147	231
Germany	3,721,273	877	3,963	4,840
Greece	21,255	0	0	0
Hungary	4,914	0	2	2
Ireland	19,926	7	7	14
Israel Ezer	503,135	5	125	130
Israel Hadassah	69,604	8	40	48
Israel Sheba	1,678	0	0	0
Italy	329,737	78	93	171
Japan	353,361	1,211	0	1,211
Mexico	10,824	2	3	5
Netherlands	38,161	31	22	53
New Zealand	8,864	0	4	4
Norway	28,323	5	28	33
Poland PL2	8,246	0	2	2
Russia Karelian	2,701	0	0	0
San Marino	800	0	0	0
Singapore	42,824	10	15	25
Slovenia	14,029	1	6	7
South Africa	63,852	0	8	8
Spain	80,314	9	32	41
Sweden	40,645	4	21	25
Switzerland	22,787	4	19	23
Taiwan	330,155	14	261	275
Thailand	58,175	1	7	8
Turkey Ankara	3,189	0	0	0
UK Anthony Nolan	404,888	75	288	363
UK BBMR	309,258	36	90	126
UK Wales	59,696	30	16	46
USA ABMDR	34,571	0	0	0
USA CRIR	103,104	9	15	24
USA Gift of Life	153,838	20	70	90
USA NMDP	5,496,679	659	1,816	2,475
TOTAL	13,318,442	3,298	7,348	10,646

REGISTRIES NOT PARTICIPATING IN SEAR

Country	Donors	BM	PBSC	Total
				Donations
Argentina	27,165	0	2	2
Austria	60,551	5	20	25
Brazil	1,372,931	65	12	77
Bulgaria Central Lab	286	0	0	0
Bulgaria Pirogov	655	0	1	1
China	1,124,052	0	343	343
China Sunshine	2,407	0	0	0
Ghana	1,017	0	0	0
India Bangalore	4,218	0	0	0
India	3,698	0	0	0
India MDR	2,170	0	0	0
Iran	570	0	0	0
Korea Catholic	KONOS	16	82	98
Korea KMDP	188,516	37	252	289
Lithuania	3,976	0	3	3
Macedonia	220	0	0	0
Poland PL1	9,688	3	1	4
Poland PL3	8,905	4	15	19
Poland PL4	12,602	0	0	0
Poland PL5	24,871	7	30	37
Poland PL6	26,566	0	4	4
Portugal	182,445	8	47	55
Romania	649	0	0	0
Russia Moscow	17,270	0	0	0
Russia St. Petersburg	3,744	0	0	0
Serbia	1,705	1	0	1
Slovakia	1,229	0	0	0
Turkey-Istanbul	27,861	1	2	3
United Arab Emirates	9	0	0	0
Uruguay	417	0	0	0
TOTAL	3,110,393	147	814	961

* KONOS = the Korean donors are listed in the Korea Network of Organ Sharing



SERIOUS (PRODUCTS) EVENTS AND ADVERSE EFFECTS REGISTRY (S[P]EAR 2010)

The Clinical WG is responsible for the collection and discussion of serious events and adverse effects (SEAR) and serious product events and adverse effects (SPEAR). Registries are encouraged to report such events to the WMDA as soon as they come to light.

Serious events and adverse effects (SEAR) and serious product events and adverse effects (SPEAR) – events reported in 2010

In total 144 S(P)EAR were reported to the WMDA in 2010. Below is a brief description of the SEAR and SPEAR incidents that were reported.

Serious Events and Adverse effects Registry (SEAR) (n=126)

PBSC

- 3 MS (family history in 1)
- 4 rheumatoid arthritis (1 seroneg, 1 seropos, 2?)
- 1 Ankylosing spondylitis (B27 +)
- 1 De Quervain thyroiditis
- 1 alopecia areata monocularis, scalp - recovering

- 4 breast cancer
- 4 prostate cancer
- 6 testicular cancer
- 1 thyroid cancer
- 4 melanoma
- 1 GI stromal tumour
- 1 giant cell tumour of elbow (benign)
- 2 bladder cancer
- 1 gall bladder cancer
- 1 adenocarcinoma of lung
- 1 cancer of the thyroglossal duct
- 1 cancer of pancreas/liver
- 1 oesophageal cancer
- 1 cancer of cervix/uterus
- 1 amyloidosis
- 1 MDS (4 years post donation)
- 2 NHL (1 Burkitts like, 1 year post donation; 1 was 9 years post donation)
- 1 HD (may have been present pre-donation as 1 enlarged LN documented)
- 1 AML
- 1 Ph+ CML

- 4 splenic bleeds requiring hospitalization and investigation
- 1 serious arrhythmias a few months post donation (probably longstanding)
- 1 venous thrombosis requiring 3 months anticoagulation
- 1 nervous breakdown with suicidal ideation requiring hospitalization
- 1 elevated liver enzymes for 2 months
- 1 transplant centre found short telomeres in the product



- 1 cauda equina syndrome 6 months post donation
- 1 pain L foot requiring surgical decompression of 2/4 metatarsal, pain free post surgery
- 1 wheezing/SOB/hypoxia - unresolved at time of report (known cat allergy)
- 1 Nausea and ecg changes. 1 night in hospital, uncomplicated and resolved
- 1 scleritis posterior
- 1 1 night in ICU due to retrosternal chest pain. Full recovery
- 1 bacterial pneumonia, recovered 45 days
- 2 acute hearing loss (1 on D3 of GCSF, 1 ?) – both resolved
- 2 allergic reaction to GCSF (1 minor, donated; 1 no collection)
- 1 widespread oedema post collection. No cause found. Resolved
- 2 drop in platelet count (<100). No harvest in either. Antibodies shown in 1
- 1 PE (2 months post)
- 1 swollen calf after injection. No DVT. Resolved
- 1 cholecystitis 1 day after collection requiring surgery
- 1 chest pain 1 day after donation. No cause found
- 1 pseudo-aneurysm in femoral artery following line insertion
- 1 tonic-clonic seizure during apheresis
- 1 asystole during apheresis (required CPR)
- 1 tricuspid valve endocarditis 2 months post donation
- 1 paroxysmal vertigo on D3 of GCSF
- 1 serious transfusion reaction following platelet transfusion
- 1 bilateral hyposphagma on D4 of GCSF
- 1 acute mononucleosis (post medical and pre-harvest infection)
- 1 persistent pain and disability at cannula site (wrist)
- 1 burst vein during apheresis, donor refused to be re-cannulated
- 1 donor refused second collection (traumatic procedure)
- 1 dyspnoea and chest pain
- 1 severe hypocalcaemia with bradycardia

BM

- 8 breast cancer (1 SLE in addition)
- 1 thyroid cancer
- 1 renal cell carcinoma
- 6 melanoma (1 sarcoidosis in addition)
- 1 sarcoma
- 1 colorectal cancer
- 1 medulloblastoma
- 1 bladder cancer
- 1 prostate cancer
- 1 testicular cancer
- 1 myeloma
- 1 MGUS
- 1 liver/bowel cancer
- 1 AML (9 years later)
- 1 ph+ ALL

- 1 prolonged back pain (+ history, no intervention)
- 1 severe back pain with disc prolapse and cauda equina compression, began 70 days post donation
- 1 symptomatic drop of Hb – needed 'infusional therapy'
- 2 sacro-iliitis (1 MRI confirmed, required admission, IV treatment, resolved in 48 days; 1 staph epidermidis related – 60 days to resolve).
- 2 bone marrow needle broke – fragment retained



- 1 superficial wound infection
- 1 serious arrhythmias under anaesthetic

PBSC/BM

- 1 Testicular cancer
- 1 Prostate cancer

Following DLI

- 1 Breast cancer
- 1 1 hour into collection donor had desaturation, coughing and ventricular arrhythmia

Serious Product Events and Adverse effects Registry (SPEAR) (n=18)

PBSC

- 1 missing donor ID on bag
- 1 Xrayed product (engrafted)
- 1 chromosomal abnormality picked up at chimerism analysis (Robertsonian translocation)
- 2 product clotted

BM

- 2 positive culture (propionibacterium acines; coagulase negative staphylococcus)
- 1 Wrong 'luggage' picked up at airport
- 1 3 bags of BM sent, but only 1 retrieved by TC (others missed).

Cord

- 1 low TNC (compared to pre-thaw) and bacterial contamination. Patient did not engraft
- 5 double cord infusion related 'shocked-heart' syndrome
- 1 chromosomal abnormality picked up at chimerism analysis (Klinefelter's syndrome)
- 1 transported with no temperature monitor and bag torn
- 1 fractured bag



SERIOUS (PRODUCT) EVENTS AND ADVERSE EFFECTS REGISTRY (S[P]EAR 2010)

ORGANISATIONS PARTICIPATING IN SEAR

WMDA REGISTRY MEMBERS

Country	Donors	BM	PBSC	Total
Argentina	46,537	2	5	7
Armenia	18,764	0	1	1
Australia	173,491	23	96	119
Austria	62,452	1	28	29
Belgium	49,709	0	7	7
Canada	268,726	20	81	101
China Hong Kong	78,415	13	14	27
China Sunshine	2,414	0	0	0
Croatia	19,315	1	4	5
Cyprus BMDR	110,481	2	23	25
Cyprus Par.	6,058	0	0	0
Czech SCR	20,199	4	5	9
Czech Central	35,533	33	22	55
Denmark	24,925	4	4	8
Denmark BMDC	12,923	0	1	1
Finland	20,493	13	7	20
France	187,519	79	139	218
Germany	4,062,456	1,018	4,613	5,631
Greece	29,608	0	1	1
Hungary	4,962	0	1	1
Ireland	20,362	6	2	8
Israel Ezer	555,691	8	154	162
Israel Hadassah	75,160	7	24	31
Israel Sheba	1,765	0	0	0
Italy	331,544	70	106	176
Japan	376,237	1,208	0	1,208
Mexico	11,893	3	2	5
Netherlands	38,645	27	26	53
New Zealand	9,355	0	6	6
Norway	28,576	3	17	20
Poland PL2	9,016	0	0	0
Poland PL3	10,586	4	14	18
Russia Karelian	2,711	0	0	0
San Marino	845	0	0	0
Singapore	50,671	1	5	6
Slovakia	1,728	0	3	3
Slovenia	15,773	0	9	9
South Africa	65,501	0	13	13
Spain	86,361	6	33	39
Sweden	40,478	2	28	30
Switzerland	27,342	7	13	20
Taiwan	338,886	14	282	296
Turkey-Istanbul	27,422	0	1	1
Thailand	82,615	3	10	13
Turkey Ankara	5,013	0	0	0
UK Anthony Nolan	418,306	56	304	360
UK BBMR	320,018	41	83	124
UK Wales	61,193	14	27	41
USA ABMDR	30,454	0	0	0
USA CRIR	192,192	5	12	17
USA Gift of Life	176,407	19	74	93
USA NMDP	5,954,004	709	1,939	2,648
TOTAL	14,601,730	3,426	8,239	11,665

ORGANISATIONS NOT PARTICIPATING IN SEAR

WMDA REGISTRY MEMBERS

Country	Donors	BM	PBSC	Total
Brazil	1,973,842	93	3	96
Korea Catholic	KONOS	9	95	104
Korea KMDP	205,159	23	289	312
Poland PL1	11,262	1	4	5
Poland PL4	12,632	0	0	0
Poland PL5	31,281	8	26	34
Portugal	248,425	8	50	58
TOTAL	2,482,601	142	467	609

NON WMDA MEMBERS

Country	Donors	BM	PBSC	Total
Bulgaria BMDR	444	0	0	0
Bulgaria Pirogov	659	0	0	0
China	1,279,654	0	511	511
Ghana	1,017	0	0	0
India Bangalore	4,218	0	0	0
India Asian	3,740	0	0	0
India MDR	4,296	0	0	0
India Datri	9,882	0	0	0
Iran ISCDP	1,015	0	0	0
Iran ISCDR	201	0	0	0
Lithuania	5,169	0	7	7
Macedonia	81	0	0	0
Poland PL6	94,781	6	24	30
Romania	645	0	0	0
Russia Moscow	11,776	0	0	0
Russia St. Petersburg	3,173	0	0	0
Serbia	2,301	0	0	0
United Arab Emirates	6	0	0	0
Ukraine	5	0	0	0
Uruguay	479	0	0	0
TOTAL	1,423,542	6	542	548

* KONOS = the Korean donors are listed in the Korea Network of Organ Sharing