

Joint UKBTS Professional Advisory Committee ⁽¹⁾ Summary Sheet

1. Paper for the JPAC meeting on:	Thursday 17 July 2014
2. Date submitted:	7 th July 2014
3. Title (including version no.):	Concessionary Release Limits for Leucocyte Depletion
4. Author(s):	Graham Rowe, Jonathan Wallis and Rebecca Cardigan for SACBC
5. Brief summary:	A question was raised at the MHRA inspection at SNBTS in January 2014 as to why units with $> 1 \times 10^6$ leucocytes were not being discarded & the UK services were employing a discard limit of $> 5 \times 10^6$. It was agreed a paper would be prepared for discussion at the MHRA Blood Consultative Committee following review by SACBC and JPAC. This paper reviews the current specifications for LD and data on the risks associated with non-LD components.
6. Action required by JPAC: (What do you want JPAC to do in response to this paper?) e.g.	Endorse the recommendation that the concessionary release limit for LD is set at $>5 \times 10^6$ leucocytes per component and that this is clarified in section 7.1 of the Red Book.
<ul style="list-style-type: none"> • endorse a specific recommendation • advise where there is a choice of possible actions • advise on priorities within the work plan • provide a steer on policy 	
7. Any other relevant information:	

⁽¹⁾ Joint United Kingdom Blood Transfusion Services Professional Advisory Committee

Concessionary Release Limits for Leucocyte Depletion

Graham Rowe, Jonathan Wallis and Rebecca Cardigan for SACBC

7th July 2014

Background:

A question was raised at the MHRA inspection at SNBTS in January 2014 as to why units with $> 1 \times 10^6$ leucocytes were not being discarded & the UK services were employing a discard limit of $> 5 \times 10^6$. It was agreed a paper would be prepared for discussion at the MHRA Blood Consultative Committee following review by SACBC and JPAC.

Current specifications for leucocyte depletion (LD)

Universal LD of the blood supply was introduced in the UK in 1999 as part of a series of measures to reduce the potential risks of vCJD being transmitted by blood. At that time, data from animal models suggested that any infectivity present in blood may be distributed between leucocytes and plasma. Other countries have adopted universal LD for the other benefits it may bring including reduction in the risk of viruses contained within leucocytes such as HTLV and CMV and reduction in febrile transfusion reactions.

The specification for LD blood components reflect the current capability of LD systems, the fact that only a fraction of components are tested for residual leucocytes, and that the limit of sensitivity of current counting methods by flow cytometry is around $0.3 \times 10^6/U$.

Current specifications for LD

Component	Red cells in AS, LD	Platelets Apheresis, LD	Platelets derived from WB (4 donors), LD
BSQR 2005 ¹	$< 1 \times 10^6$	$< 1 \times 10^6$	$< 1 \times 10^6$
Council of Europe 17 th edn ²	$< 1 \times 10^6$	$< 1 \times 10^6$	$< 1 \times 10^6$
Red Book 8 th edn ³	$>95\% < 5 \times 10^6$ and $>90\% < 1 \times 10^6$	$>95\% < 5 \times 10^6$ and $>90\% < 1 \times 10^6$	$>95\% < 5 \times 10^6$ and $>90\% < 1 \times 10^6$
AABB 27 th Ed	$>95\% < 5 \times 10^6$	$>95\% < 5 \times 10^6$	⁴ $>95\% < 8.3 \times 10^5$

- 1 The required frequency of sampling for all measurements shall be determined using statistical process control:
2. These requirements are deemed to have been met if 90 per cent of the tested units fall within the values indicated
3. Process performance should be assessed against the 1×10^6 limit when using statistical process control (statistical process monitoring) measurements.
4. For a single PRP unit, not pooled.

In requiring SPC to be used the confidence levels & conformance required should be stated to permit appropriate control of such a process especially with the unit to unit biological human variations involved. Also due to the donor variability it would be appropriate to define the process as being monitored using SPM rather than SPC since the latter is designed to reflect routine controllable manufacturing processes. It should also be noted that there is no statement regarding this to be a discard limit.

The UKBTS have already introduced discard limits to a number of components. The rationale is that units tested and found to be out with these limits are not considered as suitable for clinical use because they may pose a risk in terms of quality or safety to the recipient, or indicate that there is a problem with the manufacturing process. UKBTS have adopted a UK wide discard limit for LD components of $>5 \times 10^6$ leucocytes, however this is currently not stated in the red book.

SACBC have considered the main risks associated with issuing a non-leucocyte depleted component and whether there is any evidence as to whether a residual leucocyte content of 5×10^6 or 1×10^6 alters this risk.

What are the risks of receiving non-LD blood?

a) transmission of cytomegalovirus (CMV)

Blood monocytes are an important reservoir of CMV in the asymptomatic carrier, and transmission by cellular blood components is well documented. In an immunocompetent recipient, this can result in no clinical sequelae, or at worst an acute self-limiting primary CMV infection. However, the importance of CMV in transfusion medicine lies in its capability to cause devastating and even fatal systemic infection in immunosuppressed individuals, including premature neonates.

For some years, it has been standard practice to provide such recipients with cellular components (red cells and platelets) from unexposed CMV sero-negative donors, but this places a perpetual strain on supplies of CMV sero-negative platelets, particularly if HLA matching is also required. In 2011, SaBTO considered whether whether LD could provide an equivalent level of safety to that established for antibody testing.

The outcome of this review was published as a position statement (SaBTO 2012) identifying which patients would require serologically tested units negative for antibodies to CMV & which patients were considered suitable to receive leucodepleted blood as CMV "safe". The Leucocyte depletion standard used to assess the risks was as follows:

"Universal leucodepletion was implemented by all four UK Blood Services in 1999, primarily as a vCJD risk reduction measure. The UK specification for leucodepletion of $< 5 \times 10^6$ white cells per unit (3 log depletion, of 99% of components, with 95% confidence) is generally accepted as the level which renders components "CMV safe" (Vamvakas, 2005;Lipson et al, 2001;Drew & Roback, 2007)." However the paper also acknowledged: "a precise threshold level has not been identified"

Recent studies suggest that residual CMV transmission rates of LD blood probably arise from free virus/viral DNA in plasma during the window period for seronegative patients, and during the first year following infection for sero-positive patients (reviewed in Zeimann et al 2014). Given the very low rates of transmission now seen with LD blood to current standards, it would be very difficult to show a further improvement given this residual non white cell related route of transmission.

b) transmission of Human T cell leukaemia virus (HTLV) I and II

HTLV is a white cell associated virus. HTLV testing was implemented in the UK in 2002 in mini pooled samples as a cost effective risk reduction measure at the request of the Department of Health. The 2012 SHOT report identified 2 transmissions; 1 in

2000-01 & one in 2001-02 with none over the next 10 years of reporting. Indicating it is a rare complication of transfusion & that current testing regimes & 100% leucodepletion of blood components have ensured this remains a very low risk of transmission.

c) Transfusion-associated graft versus host disease (Ta-GVHD)

Ta-GvHD is a rare but invariably fatal complication of transfusion, due to contaminating lymphocytes in cellular blood components. Cellular components for at risk recipients are therefore irradiated to reduce this risk and currently LD is not considered as an alternative to irradiation. The minimum number of transfused lymphocytes necessary to cause Ta-GvHD is unknown and may vary by clinical setting (Treleaven et al 2011).

There have been no cases of TaGvHD in immunocompetent individuals who do not receive irradiated blood on protocol since the introduction of universal LD in the UK. Prior to this there were quite a few such cases and they were common in Japan prior to the introduction of irradiation. As such we can with some confidence state that LD to the current standards appears to have prevented TaGvHD in immunocompetent individuals all be it that the numbers were small before 1999.

In the 2012 SHOT report a total of 14 cases of TA-GvHD have now been reported since 1996; all were fatal. Only two cases have been reported to SHOT in recipients of non-irradiated, leucodepleted components; One in the 1998-99 report (a patient with myeloma) and one in the 2000-2001 report (a patient with acute lymphoblastic leukaemia). No case of TA-GvHD has been reported to SHOT in any recipient of a leucodepleted component prepared by the UK blood services since the 2000/2001 report, despite the fact that in error, over 400 recipients that should have received irradiated components did not.

d) Febrile reactions

An added benefit to removing leucocytes has been to reduce Febrile non Haemolytic Transfusion Reactions (FNHTR) precipitated due to the release of cytokines as leucocytes die during storage. Collection of these complications have not been routinely reported to SHOT so this data is based on the reduction in referrals for serological investigations of potential transfusion reactions.

However, allergic/febrile reactions still occur with cellular and non-cellular products (Ibojie et al 2002). Residual plasma proteins, peptides and other chemicals, not leucocyte derived, are often considered as a cause of these reactions. There seems no rationale for increasing the level of leucodepletion for this purpose given the lack of evidence of benefit and the lack of primary intent of the process.

e) Prion infectivity

This indication for LD applies predominantly in the UK and not elsewhere. European standards are therefore not designed for this purpose. When LD was introduced in 1999 evidence from animal models at that time indicated that any infectivity present in blood would likely be contained either by leucocytes or in plasma. Little has changed in this respect. A level of 5×10^6 residual leucocytes per unit was set as the specified limit with >99% of components required to meet that specification with 95% statistical confidence. This was based on a level required to prevent HLA alloimmunisation, the capability of LD processes, and a desire that the maximum

level specified was not exceeded in as high a proportion of components as possible. Data from animal models suggests that LD is only partly effective in removing infectivity in blood (Gregori et al 2004 and McCutcheon et al 2011) and it is not known whether the level of LD is important in this respect. Since the introduction of universal LD in the UK there have been no documented cases of TavCJD, whereas there are 4 cases linked to transfusion of non-LD red cells. The level of infection in donors did not subside until after 2000 and as such it would appear that the measure did reduce the risk of transmission. Subsequently there has been a substantial decline in dietary associated cases of vCJD with no deaths in 2011, one death in 2012 and no deaths to date in 2014. There are no patients currently alive with probable vCJD disease. The prevalence of possible carriers without disease is uncertain. The most recent appendix survey (Gill et al, 2013) suggest that this is as high as 1 in 2000 population, and as high as 1 in 1000 of those with the valine/valine genotype. We have no information as to whether these possible carriers, if donors, would be a risk for transmission of vCJD or other prion disease. We do not know whether carrier rates are similar or different to the rest of Europe. We can not speculate meaningfully as to the benefit of a tighter standard for LD given these huge uncertainties. We do know that since the introduction of the current standards of LD there has been no documented transmission of disease for 15 years during which time we will have transfused over 30 million individual components in the UK. If we anticipate a transfusion to disease time of 7 years (based on the pre-LD cases) we still have nearly 15 million individual exposures without disease. We cannot mandate any tightening of the LD standards based on these data.

f) Alloimmunisation to leucocyte antigens

Allo-immunisation to white cell antigens (HLA) remains a significant risk for a small group of patients awaiting a solid organ transplant. There is evidence that LD does not prevent alloimmunisation, though it may reduce the frequency, strength and duration of antibody response. We do not know whether the immunisation still seen after LD is due to residual leucocytes, soluble antigens in plasma or red cell bound antigens (HLA class 1 only). It is possible that a lower number of residual leucocytes will further reduce this problem but what limits would be needed to prevent it entirely are simply not known. The problem is most evident in patients awaiting renal transplant. At present avoidance of transfusion wherever possible is the strategy used. Studies are being planned to look at the best options for prevention. Less than one percent of blood is used for these patients. Better LD may possibly benefit them but would not be of benefit to most other individuals receiving transfusion.

g) Other immunomodulatory effects

There is no convincing evidence of a significant immunomodulatory effect of residual white cells after current LD standards. The only prior evidence relates again to renal transplants where some degree of desensitisation may be seen in patients having a renal transplant (Opelz et al). This work related to leucocyte rich components and previous policy of deliberate pre-transplant transfusion has long been replaced by a policy of avoiding transfusion based on better and newer data on graft survival with modern immunosuppressives.

Conclusions

The Guidelines for the Blood transfusion services in the UK recommend use of SPM of the LD process ensuring that at least 90% of components tested by flow cytometry are $< 1 \times 10^6$ per unit by count meeting the Council of Europe guidelines & that more than 99% of components should contain $< 5 \times 10^6$ leucocytes, both within 95% confidence. Process performance should be assessed against the 1×10^6 limit when using statistical process control (statistical process monitoring) measurements. Personal communication from Dirk de Korte of Sanguin Blood Service is attached as appendix 3 demonstrating a similar approach as the UK services.

Implementing a discard level of $>1 \times 10^6$ leucocytes of units tested would result in the unnecessary disposal of blood components with no evidence to confirm why the donations were considered unsuitable for transfusion (See table 1). Discarding all components with a count $>1 \times 10^6$ leucocytes may compromise availability of some components.

Current performance for 2013, in appendix 1, demonstrates a wide range of performance dependent on manufacturing process & manufacturer. LD performance is collated in the UK for review at SACBC & JPAC, which was reviewed by JPAC in March 2013. The latest figures by process & supplier are shown in appendix 1 with appendix 2 for comparison showing performance from 2010 - 2012.

Table 1 Potential number of tested units discarded in 2013 @ $>1 \times 10^6$ UK wide

Component	Total Number of units $>1 \times 10^6$	Percent of tested components discarded
Apheresis Platelets	558	0.94
Buffy coat derived pooled platelets	932	6.82
SAG-M red cells	854	1.28

Recommendation

That a concessionary release limit for LD is set at $>5 \times 10^6$ leucocytes per component. This should be made clear in section 7.1 of the Red Book that relates to LD by changing the existing text from:

'Where SPM methodology is not judged appropriate due to an inability to control the process or the production of small numbers of components, all components routinely issued to stock must have been shown to contain less than 1×10^6 leucocytes.

Issue (to stock) of components, which do not meet the leucocyte depletion specified limit, must follow a concessionary release procedure (see Section 7.9). '

To

'Where SPM methodology is not judged appropriate due to an inability to control the process or the production of small numbers of components, all components routinely issued to stock must have been shown to contain less than 5×10^6 leucocytes.

Issue (to stock) of components, which do not meet the leucocyte depletion specified limit of 5×10^6 /unit, must follow a concessionary release procedure (see Section 7.9).

Appendix 1

Cumulative UK LD performance by manufacturer 2013														
Component	Process	No. Issued	No. tested	Number			Percent			Failure/testing Ratio (expressed as 1 in n)			Corrected residual Risk (expressed as 1 in n)	
				>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>1x10 ⁶ Per Unit
Apheresis platelets	Amicus Fresenius	9,117	8,723	86	9	1	0.986	0.103	0.011	101	969	8,723	22,427	2,347
	Trima Terumo	121603	50860	435	24	3	0.855	0.047	0.006	117	2,119	16,953	3,643	201
	Combined	130730	59583	521	33	4	0.874	0.055	0.007	114	1,806	14,896	3,318	210
Pooled platelets	Autostop haemonetics	49,348	8,753	342	30	0	3.907	0.343	0	26	292	0	355	31
	Composelect Fresenius	5,909	4,920	478	82	0	9.715	1.667	0	10	60	0	358	61
	Combined	55257	13673	820	112	0	5.997	0.819	0	17	122	0	162	22
SAG-M RBC's	Haemonetics WB	428756	6,707	22	0	0	0.328	0	0	305	0	0	0	310
	Macopharma WB	1083071	27607	272	18	0	0.985	0.065	0	101	1,534	0	1,574	104
	Haemonetics RC	97414	4,730	6	0	0	0.127	0	0	788	0	0	0	829
	Macopharma RC	421948	26162	483	52	1	1.846	0.199	0.004	54	503	26,162	536	58
	Fresenius WB	7,203	644	0	0	0	0	0	0	0	0	0	0	0
	Fresenius RC	5,635	680	0	0	0	0							
Combined	2044026	66530	783	70	1	1.177	0.105	0.002	85	950	66,530	982	88	

Appendix 2LD results by manufacturer and process stream by year 2010 to 2012

Cumulative by Manufacturer All UK Services Year 2012				Number			Percent			Failure/Testing Ratio (expressed as 1 in n)			Corrected Residual Risk (expressed as 1 in n)	Corrected Residual Risk (expressed as 1 in n)
Component	Process	No. Issued	No. tested	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>1x10 ⁶ Per Unit
Apheresis Platelets	Fenwal	7967	7872	58	1	0	0.737	0.013	0.000	136	7872	#DIV/0!	660171	11382
	Gambro Trima	192036	70932	792	79	40	1.117	0.111	0.056	90	898	1773	1424	142
	All	200003	78804	850	80	40	1.079	0.102	0.051	93	985	1970	1626	153
Pooled Platelets	Pall Autostop	39193	6717	82	3	0	1.221	0.045	0.000	82	2239	#DIV/0!	2702	99
	NPBI (Fresenius) Composelect	5790	3595	346	48	0	9.624	1.335	0.000	10	75	#DIV/0!	198	27
	All	44983	10312	428	51	0	4.151	0.495	0.000	24	202	#DIV/0!	262	31
FFP ONLY NHSBT test	All	61	61	0	0	0	0.000	0.000	0.000	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
SAGM Red Cells	Pall WB	926827	17640	69	1	0	0.391	0.006	0.000	256	17640	#DIV/0!	17982	261
	MacoPharma WB	760467	20639	331	23	0	1.604	0.111	0.000	62	897	#DIV/0!	922	64
	Pall RC	151063	6059	5	1	0	0.083	0.017	0.000	1212	6059	#DIV/0!	6312	1262
	MacoPharma RC	294668	20598	440	66	3	2.136	0.320	0.015	47	312	6866	336	50
	NPBI RC	7912	930	0	0	1	0.000	0.000	0.108	#DIV/0!	#DIV/0!	930	#DIV/0!	#DIV/0!
	All	2133025	64936	845	91	3	1.301	0.140	0.005	77	714	21645	736	79

Cumulative by Manufacturer All UK Services Year 2011				Number			Percent			Failure/Testing Ratio (expressed as 1 in n)			Corrected Residual Risk (expressed as 1 in n)	Corrected Residual Risk (expressed as 1 in n)
Component	Process	No. Issued	No. tested	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>1x10 ⁶ Per Unit

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Apheresis Platelets	Fenwal	7760	7528	44	5	0	0.584	0.066	0.000	171	1506	#DIV/0!	50360	5723
	Gambro Trima	241316	58754	782	66	13	1.331	0.112	0.022	75	890	4520	1177	99
	All	249076	66282	826	71	13	1.246	0.107	0.020	80	934	5099	1272	109
Pooled Platelets	Pall Autostop	47759	6710	195	23	0	2.906	0.343	0.000	34	292	#DIV/0!	339	40
	NPBI (Fresenius) Composelect	7067	2730	232	12	0	8.498	0.440	0.000	12	228	#DIV/0!	371	19
	All	54826	9440	427	35	0	4.523	0.371	0.000	22	270	#DIV/0!	326	27
FFP ONLY NHSBT test	All	678	422	1	0	0	0.237	0.000	0.000	422	#DIV/0!	#DIV/0!	#DIV/0!	1118
SAGM Red Cells	Pall WB	941347	17695	60	1	0	0.339	0.006	0.000	295	17695	#DIV/0!	18034	301
	MacoPharma WB	734397	20734	131	12	0	0.632	0.058	0.000	158	1728	#DIV/0!	1778	163
	Pall RC	160835	6908	4	1	0	0.058	0.014	0.000	1727	6908	#DIV/0!	7218	1805
	MacoPharma RC	354091	21541	249	19	0	1.156	0.088	0.000	87	1134	#DIV/0!	1207	92
	NPBI RC	6025	737	0	0	0	0.000	0.000	0.000	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!
	All	2190670	66878	444	33	0	0.664	0.049	0.000	151	2027	#DIV/0!	2090	155

Cumulative by Manufacturer All UK Services	Year 2010		Number			Percent			Failure/Testing Ratio			Corrected Residual Risk	Corrected Residual Risk	
									(expressed as 1 in n)			(expressed as 1 in n)	(expressed as 1 in n)	
Component	Process	No. Issued	No. tested	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>1x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>100x10 ⁶ Per Unit	>5x10 ⁶ Per Unit	>1x10 ⁶ Per Unit

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Apheresis Platelets	Fenwal	12344	11395	41	8	0	0.360	0.070	0.000	278	1424	#DIV/0!	18527	3615
	Gambro Trima	206750	51208	579	45	11	1.131	0.088	0.021	88	1138	4655	1513	118
	All	219094	62603	620	53	11	0.990	0.085	0.018	101	1181	5691	1654	141
Pooled Platelets	Pall Autostop	53677	8188	75	3	0	0.916	0.037	0.000	109	2729	#DIV/0!	3221	129
	NPBI (Fresenius) Composelect	10050	2836	147	17	0	5.183	0.599	0.000	19	167	#DIV/0!	232	27
	All	63727	11024	222	20	0	2.014	0.181	0.000	50	551	#DIV/0!	666	60
FFP ONLY NHSBT test	All	196665	1147	1	0	0	0.087	0.000	0.000	1147	#DIV/0!	#DIV/0!	#DIV/0!	1154
CPD Red Cells Maco CPD-A1 PALL	MacoPharma & PALL	1650	1209	11	2	0	0.910	0.165	0.000	110	605	#DIV/0!	2262	411
SAGM Red Cells	Pall WB	789200	19253	252	4	0	1.309	0.021	0.000	76	4813	#DIV/0!	4934	78
	NPBI WB	840670	19305	90	4	0	0.466	0.021	0.000	215	4826	#DIV/0!	4940	220
	Fenwall RC	8923	898	3	0	0	0.334	0.000	0.000	299	#DIV/0!	#DIV/0!	#DIV/0!	333
	Pall RC	174253	8600	47	1	1	0.547	0.012	0.012	183	8600	8600	9046	192
	MacoPharma RC	379247	21395	336	14	3	1.570	0.065	0.014	64	1528	7132	1620	67
	All	2192293	69451	728	23	4	1.048	0.033	0.006	95	3020	17363	3118	99

Appendix 3

With the introduction in the Netherlands in 2002 of the general leukocyte removal for erythrocytes and platelets, as a maximum number of remaining leukocytes a number of $< 5 \times 10^6$ per unit was set. Gradually this is replaced in various texts (Dutch Guideline Blood Products, Council of Europe Guide) by a maximum of $< 1 \times 10^6$, however, with simultaneous introduction of statistical requirements for quality control (QC).

Based on, among others, the study of van Marwijk Kooij et al (Blood. 1991; 77:201-5) the limit of 5×10^6 was selected, which was actually applied to 100% of the products. This can be achieved by assessing the process against the standard of 1×10^6 per unit in 90 % of cases with the use of statistical process control (it should take account of the low accuracy of the counting in the leukocyte concentrations below $3 \times 10^6/L$). With a log - normal distribution (this is true for almost all filters) of the remaining number of leukocytes this approach equals to almost 100 % $< 5 \times 10^6$ per unit. Based on this, a unit in which a value between 1 and 5×10^6 is measured in the normal QC can be issued. This also applies to split products which are derived from such units. There is no evidence in the literature that the maximum residual value of 1×10^6 leukocytes per unit gives less allo - immunization compared to a maximum residual value of 5×10^6 .

Background:

In the US, a leukocyte-free product is labeled "leukocyte reduced" and this is defined as > 95 % of the products $< 5 \times 10^6$ with a 95 % confidence level. In the UK, the process of leukocyte depletion is marked "leukocyte depletion" and the specification for a leukocyte product is "at least 99 % of leukocyte components less than 5×10^6 leukocytes with 95% and more than 90 % less than 1×10^6 leukocytes. The process must be assessed against the standard of 1×10^6 using statistical process control.

Personal Communication from Dirk de Korte, Sanguin Blood Service 12/05/2014

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