Vox Sanguinis (2002) **83**, 110–118

ORIGINAL PAPER

Value of central analysis of leucocyte depletion quality control data within the National Blood Service, England

N. Beckman,[1] R. Cardigan,[1] T. Wallington[1] & L. M. Williamson[1,2]

[1]*National Blood Service, Birmingham, UK*

[2]*Department of Haematology, University of Cambridge, Cambridge, UK*

On behalf of the National Blood Service Leucodepletion Project Implementation Board

Vox Sanguinis

Background and Objectives The results of quality monitoring leucocyte counts were analysed nationally for the first 2 years of universal leucocyte depletion (LD), spanning the time-period before and after standardization of the counting and LD methods. The objectives were twofold: first to determine whether the implementation strategy was effective in achieving the LD specification ($< 5 \times 10^6$ leucocytes in 99% of components with 95% statistical confidence); and second, whether quality monitoring was able to detect potential non-conformance.

Materials and Methods Residual leucocytes were counted using Beckman Coulter or Becton Dickinson (BD) flow cytometers and reagents. Data were collected into standardized analysis software (NWA Quality Analyst) for local trend analysis and checks for conformance to process specification, and collated centrally. Analysis was performed for six time-periods between January 1999 and March 2001. Specification failures were analysed to determine the likelihood of extreme failure. Statistical process monitoring was adjusted to suit LD processes.

Results Data from red cells in optimal additive solution (OAS), filtered either as whole blood or red cell concentrates, and platelet pools improved significantly over the 2-year period with specification failures falling from 0·35%, 0·48% and 0·56%, respectively, in January–June 1999 to 0·06%, 0·01% and 0·04% in January–March 2001. Specification failures in red cells in OAS LD for the period January–December 2000 showed only 0·02% with a leucocyte count of $> 30 \times 10^6$/unit. Extreme failures are now very rare. Monitoring methods have been effective in detecting process change and drift.

Conclusion LD performance varies between different LD systems, but monitoring has proved sufficiently robust to detect processes that perform poorly. The chosen specification has been both achievable and appropriate to the systems in use. Standardization of the counting method is central to the ability to monitor and analyse results effectively across the whole service.

Received: 12 November 2001, revised 13 May 2002, accepted 20 May 2002

Key words: leucocyte depletion, monitoring, specification, standardization.

Introduction

Prior to 1998, leucocyte depletion (LD) of blood components in the UK was limited to specific clinical indications [1]. LD was carried out either by bedside filtration or by postproduction prerelease filtration performed by Blood Centres using sterile connection 'dock-on' red cell or platelet filters. In July 1998, the UK Department of Health mandated the implementation of universal LD by the UK Transfusion Services as a precaution against transmission of variant Creutzfeldt–Jakob disease (vCJD).

The National Blood Service (NBS) in England, which produces 3 million components from 2·5 million donations/year

Correspondence: Neil Beckman, National Blood Service, Vincent Drive, Edgbaston, Birmingham, B15 2SG, UK.
E-mail: GRO-C

in 11 processing centres, proceeded to universal LD implementation. A major challenge was the quality monitoring of LD processes and components. An appraisal of available methods quickly determined that, with the exception of components manufactured in small quantities, 100% testing of components for residual leucocyte levels was not feasible. Hence, LD would have to be defined in terms that allowed statistical process control. Experimental evidence on the possible role of leucocytes in vCJD transmission did not suggest any critical leucocyte level which had to be achieved to confer vCJD safety. Leucocyte counts as low as possible were therefore the objective. It was agreed that LD to 5×10^6 leucocytes/unit would be the minimum level acceptable and for monitoring purposes no more than 1% would fail this specification with 95% confidence. The 5×10^6 leucocytes/unit specification, which was already in place, had originally derived from studies to prevent human leucocyte antigen (HLA) alloimmunization [2,3].

The assessment of relative performance between Centres and processes could not be achieved without the standardization of leucocyte counting equipment, procedures and reagents. Beckman Coulter and Becton-Dickinson (BD) flow cytometers and the IMAGN 2000 microfluorimeter were evaluated before the adoption of flow cytometry at all processing centres using standard procedures and reagents [4].

Before the start of the implementation of universal LD, the Biomedical Excellence for Safer Transfusion (BEST) Working Party of the International Society of Blood Transfusion (ISBT) had produced a guideline paper which detailed methods of monitoring based on parametric or non-parametric analysis [5]. The parametric analysis method utilized established principles of process control charts [6–8]. Process stability monitoring was adopted using parametric analysis by control charts, process capability measurement and newly developed statistical process monitoring (SPM) methodology specific to the requirement for LD quality monitoring.

The NBS completed the introduction of universal LD by November 1999. From April 1999, data on the performance of leucodepletion processes was collected by individual processing centres and collated centrally, including data gathered since January 1999. This allowed a national review of all the data, which was performed in addition to the routine local check of control charts for each process and the monthly assessment of process conformance to specification. There was therefore an opportunity to analyse large numbers of results from all production processes used across the NBS.

This article reports results obtained during the evaluation of different LD systems, and on the performance of these systems during the first 2 years spanning pre- and post full implementation.

Methods

Whole blood, red cell, plasma, platelet pool and apheresis LD systems were assessed during and after the project (Table 1). Systems were validated subsequently as new products became available. Systems already in routine use were not further validated although routine monitoring data was collated and is given. These included the Pall Autostop platelet pool filter and the Gambro Cobe LRS/Turbo apheresis system. Data given is for systems in routine use at the time of writing.

Whole blood and red cell filters, where manufacturers' instructions allowed, were validated both for filtration on the day of collection (day 0) after ambient storage and after a 4 °C overnight hold (day 1).

Red cell bottom-and-top/top-and-bottom (BAT/TAB) processing involved centrifugation of the whole-blood

Table 1 Systems evaluated for leucocyte depletion (LD) performance during implementation of universal LD in the National Blood Service (NBS), England

	Whole blood filter		Red cell filter		Plasma filter	Platelet pool filter	Apheresis system
Manufacturer	Day 0[a]	Day 1[a]	Day 0[a]	Day 1[a]	Day 0[a]	Day 1[a]	(platelets)
Baxter	R7490	R7455 R7490 R8435	R7489	R7223 R7481 R7489 R8435	FGR7014	R7103	Amicus
Gambro Cobe Haemonetics							Trima MCS+
Macopharma	FQF 6261B	FQF 6261B	6260PB-NPE	6260PB-NPE			
NPBI	T2926	T2926	T2916 T2961	T2916 T2961			
Pall	780-44U WBT410CU	780-44U WBT410CU	789-24U		LPS1B1U LPS1B2U		

[a]Day of filtration.

donation followed by separation to red cells, buffy coat and plasma. The red cells were subsequently filtered after the addition of optimal additive solution (OAS). Plasma was either discarded or was filtered using a dock-on plasma filter. Four buffy coat units were pooled with autologous plasma and centrifuged. The platelet-rich plasma was then expressed through a LD filter to give leucocyte-depleted pooled platelets.

Standardization of leucocyte counting

The comparison of quality control (QC) data from specific centres required national standardization of flow cytometry procedures for counting residual leucocytes, to ensure comparability of results. The NBS has performed considerable validation work, which has led to standardized flow cytometry protocols, a decrease in intersite variability [4] and resulted in Beckman Coulter and BD reagents passing validation criteria on both Beckman Coulter and BD flow cytometry equipment.

The results reported here for 2000/2001 were from flow cytometry using BD LeucoCount reagents with either Beckman Coulter Epics XL or BD FacsCalibur flow cytometers and standard methodologies. Full details of the standard methods adopted have been reported previously [4]. Prior to 2000, results were obtained using validated methods by flow cytometry using BD or Beckman Coulter reagents or by using the IMAGN microfluorimeter, a possible cause of variation in the data.

The flow cytometry histograms used for residual leucocyte counting excluded apparent 'fragments' that could not be conclusively identified as leucocyte derived.

External quality assessment exercises were established across the NBS sites. Within the NBS this was achieved using fresh LD components for platelets and red cells, and externally by the UK National External Quality Assessment Scheme (NEQAS) using stabilized mononuclear cell preparations [9].

Statistical handling of data

SPM was performed using commercially available software (NWA Quality Analyst) and standardized software formatting. This included the use of calculations, analysis and display ranges, reports and charts. The use of Individual/Moving Range (MR) or x-bar/Range (R) $\log_{10}$ control charts and 100% testing was defined for product types depending on the numbers produced and the identified risk of an upper specified limit (5×10^6 leucocytes/unit) LD failure. Individual/MR charts displayed single results and the difference between the current and previous results, and were used where production numbers were low but the process was performed routinely. x-bar/R charts displayed the mean of a subgroup of five results and the range within the subgroup, and were used where production numbers were sufficient for subgroups to be analysed.

The data obtained from initial testing was used to calculate upper control limits (UCL) on control charts prior to the introduction of fixed control limits later in the project (see below).

x-bar/R and individual control charts were formatted to indicate points above the UCL or trends of seven rising points or seven consecutive points above the centre line (CL). Sampling, by a validated method, occurred during each production run for a process. Individual/MR charts required a single sample/day or per machine/day in the case of apheresis systems. x-bar/R charts required two subgroups of five samples per process per day.

Control charts were reviewed immediately upon entering results from leucocyte testing into the database. Control chart subgroups or individual results lying above the calculated UCL or which gave a trend warning or specification failure, required further samples to be taken from the process. If these also gave control chart warnings or further specification failure(s), an investigation was initiated into the probable cause and remedial action put in place, where counting or production problems could be identified.

Conformance to national process specification (at least 99% of units produced by a given method having $< 5 \times 10^6$ leucocytes/unit with 95% confidence) was assessed monthly as part of the routine quality review using an automated, validated spreadsheet.

Analysis of national results was performed by merging the relevant NWA Quality Analyst files from all processing centres and generating capability reports and charts.

Results

The results between January 1999 and March 2001 are shown in (Table 2).

There was a general improvement in the pass rate of red cells in OAS with time such that in the period January–June 2000, 99·85% and in January–March 2001 99·95%, of all red cells in OAS units had a leucocyte count of $< 5 \times 10^6$/unit. The specification failure rate for red cells in OAS, produced by red cell filtration for the period January–March 2001 was 0·01%, markedly better than the 0·06% for red cells in OAS derived directly from whole-blood filtration, a process that was more susceptible to unpredictable failure.

The Gambro Cobe LRS/Turbo process was already well established within the NBS before the start of the leucodepletion project. The Haemonetics MCS+ apheresis system began with an unacceptably high failure rate (2·12%) and the products were therefore 100% leucocyte counted prior to release. Changes to the filtration method have significantly reduced the specification failure rate, which has plateaued between 0·5% and 0·8%.

Table 2 Collated national leucocyte depletion results using combined data for all processes for each product, showing the percentage of products > 5×10^6 leucocytes/unit

	% of components with leucocyte counts > 5×10^6/unit					
Product	**Jan–April 1999**	**Jan–Dec 1999**	**Oct–Dec 1999**	**Jan–June 2000**	**Jun–Dec 2000**	**Jan–Mar 2001**
Cobe LRS/Turbo Apheresis[d]	0·16	0·30	0·51	0·27	0·10	0·30
(no. tested)	(1213)	(6568)	(2756)	(6728)	(6057)	(4705)
Haemonetics MCS+ Apheresis	2·12	0·68	0·49	0·56	0·78	0·64
(no. tested)	(1985)	(7228)	(4467)	(12 382)	(5288)	(6905)
Pooled platelets	0	0·56	0·28	0·11[a]	0·03	0·04
(no. tested)	(2194)	(14 595)	(5992)	(10 625)	(13 130)	(8087)
Fresh-frozen plasma	0	0	0	0·01	Not collated	0
(no. tested)	(562)	(5186)	(3561)	(9466)		(7161)
Red cells in additive solution	0–0·70[e]	0·35	0·35	0·15	0·14	0·06
whole-blood filtered (no. tested)	(6176)	(17 352)	(10 496)	(16 497)	(25 484)	(17 212)
Red cells in additive solution	0–1·74[e]	0·48	0·23	0·16	0·06[b]	0·01[c]
red cell filtered (no. tested)	(1442)	(9935)	(5125)	(10 142)	(10 164)	(7833)

[a]Excludes the results from a single centre. Analysis of all data gives a failure rate of 0·88%.

[b]Excludes NPBI T2916 results, which were being intensively monitored owing to a process failure.

[c]Excludes noted production anomalies such as non-'wetted' filters.

[d]Includes results from components 'flagged' by apheresis equipment as requiring leucocyte counting.

[e]Represents the minimum and maximum failure rates for the process, by Centre.

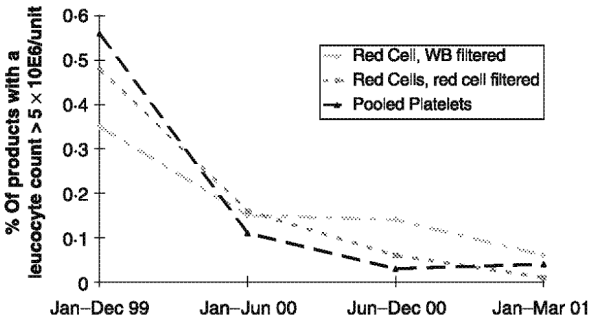

Fig. 1 National leucocyte depletion specification component failure rates for analyses periods. WB, whole blood.

Fresh-frozen plasma has given only a single specification failure during the entire period of monitoring, following whole-blood filtration. The red cell unit associated with this unit of plasma gave a leucocyte count of 457×10^6/unit, suggesting a filter manufacturing fault.

Improvement in the specification pass rate over time was demonstrable for pooled platelet products and red cells in OAS, whether filtered as whole blood or red cells, and showed a downward trend (Fig. 1) for non-overlapping analysis periods.

A review of the individual processes for the period January–June 2000 revealed variation in leucocyte contamination levels within products, which was dependent on the process used (Table 3). Leucocyte contamination results of > 30×10^6/unit were viewed as outliers, which significantly skewed the overall results for some processes. All processes gave > 99% of products with a leucocyte count of < 5×10^6/unit during this monitoring period. For red cells in OAS, the process-associated failure rate varied from 0·02% to 0·65% of total units tested.

Red cells in OAS units showed ≈ 1 : 6250 units giving failures of > 100×10^6 leucocytes/unit during the January–June 2000 period of review. Two exceptionally high failures (> 2000×10^6 leucocytes/unit) were detected in this period, both coming from the Baxter whole-blood filter RS2000 (R7455 pack), which was subsequently replaced with the RZ2000 filter (R7490 pack), the specification failure rate of which was 0·02% for the January–June 2000 analysis with a maximum count of $51{\cdot}8 \times 10^6$ leucocytes/unit.

In addition to the failure rate, consideration has been given to the magnitude of the failures within a process. Table 4 shows the distribution of specification failures for the period January–June 2000 for all components produced.

As data became available, it was apparent that because calculated control limits for processes performing well were very close to the CL, minor changes within the process resulted in a control limit violation, even where all results were < 1×10^6 leucocytes/unit. It was concluded that extra monitoring was not justified in these situations, and therefore fixed control limits were introduced. These were set

Table 3 Collated national leucocyte depletion results, January–June 2000, analysed by manufacturer

	Mean and max. values are leucocyte counts (× 10E6/u)	All Data				Excluding results > 30			%		
		No. tested	Mean (× 10E6/u)	SD	Max.	Mean (× 10E6/u)	Max. (× 10E6/u)	SD	> 1 (× 10E6/u)	> 5 (× 10E6/u)	> 30 (× 10E6/u)
Apheresis platelets	Cobe LRS/Turbo[a]	6728	0.77	22·37	1167·3	0·19	0·51	26·7	1·01	0·27	0·10
	Haemonetics MCS+	12 382	0.29	1·00	42·4	0·29	0·92	25·7	3·46	0·56	0·01
Pooled platelets	Pall Autostop[b]	10 625	0·24	0·43	16·8				1·44	0·11	0
Plasma											
FFP	All methods	9466	0·17	0·12	10·0				0.02	0.01	0
Red cells											
Exchange	All methods	3100	0·42	0·99	33·4	0·41	0·79	17·6	4·74	0·68	0·03
CPD	All methods	7595	0·34	1·26	71·7	0·33	0·58	21·6	5·21	0·13	0·03
	Baxter R7223	5557	0·38	1·47	71·7	0·36	0·67	21·6	6·55	0·18	0·04
	Baxter R7224	728	0·20	0·28	2·8				2·48	0	0
	Baxter R7490	1310	0·25	0·19	3·9				1·07	0	0
Red Cells OAS	All methods	29 707	0·48	19·35	2363·2	0·30	0·47	22·5	2·94	0·13	0·02
Red Cells OAS/WB filter	Baxter R7455	1454	3·50	86·43	2363·2	0·29	0·48	7·6	3·58	0·34	0·14
	Baxter R7490	9994	0·27	0·58	51·8	0·26	0·27	5·1	1·95	0·02	0·01
	NPBI T2926	1161	0·82	13·40	457·4	0·43	0·41	6·3	4·91	0·17	0·09
	Macopharma 6261	1989	0·53	0·98	19·0				7·19	0·65	0
	Pall T20019	1899	0·36	2·04	88·0	0·32	0·37	5·7	3·37	0·11	0·05
Red Cells OAS/RC filter	Baxter R7481	1515	0·37	0·97	22·5				4·88	0·40	0
	Baxter R7489	4606	0·32	2·57	171·2	0·46	0·29	12·9	3·82	0·20	0·02
	NPBI T2916	4021	0·19	0·18	5·2				0·50	0·02	0
	Total	79 603									

[a]Includes results from components 'flagged' by apheresis equipment as requiring leucocyte counting.

[b]Exclude the results from a single Centre. Analysis of all data gives a failure rate of 0·88%.

CPD, citrate-phosphate-dextrose; FFP, fresh-frozen plasma; OAS, optimal additive solution; RC, red cell; WB, whole blood.

Table 4 Number of LD specification failures occurring nationally for the period January to June 2000

Process/product	Failure range ($\times 10^6$/unit) 5–10	10–30	30–100	> 100
Cobe LRS/Turbo Apheresis[a] (no. tested = 6728)	7	4	2	5
% of total tested	0·10	0·06	0·03	0·07
Haemonetics MCS+ Apheresis (no. tested = 12 382)	42	26	1	0
% of total tested	0·34	0·21	0·01	0
Pooled platelets[b] (no. tested = 12 469)	70	37	3	0
% of total tested	0·56	0·30	0·02	0
Fresh-frozen plasma (no. tested = 9466)	1	0	0	0
% of total tested	0·01	0	0	0
Red cells OAS (no. tested = 29 707)	24	10	2	4
% of total tested	0·08	0·03	0·01	0·01

[a]Includes results from components 'flagged' by apheresis equipment as requiring leucocyte counting.
[b]Includes all results.

at a level where a single product with a count of $> 5 \times 10^6$ leucocytes/unit in a subgroup of five, where other products had counts of $0{\cdot}5 \times 10^6$ leucocytes/unit, would cause a control limit violation (UCL log5·89 for x-bar and UCL log0·99 for Range charts). These UCL were also used for Individual/MR charts where a specification failure would also result in a control limit violation on at least one chart. The control chart examples were given after the introduction of fixed control limits.

Example 1

Pooled platelets produced using the Pall Autostop filter showed a reduction in failure rate towards the end of 1999 (Fig. 2). This was, however, followed by a marked increase in the failure rate in the January–June 2000 data. In this time-period, 110 platelet pools nationally were found to have a leucocyte count of $> 5 \times 10^6$/unit, of which 98 had been produced at a single centre in a 4-month period. Local investigations revealed that the automated presses used during filtration were exerting too much pressure, forcing leucocytes through the filter into the final product. The remedial action involved corrective maintenance by an engineer and resulted in the process returning to a controlled state.

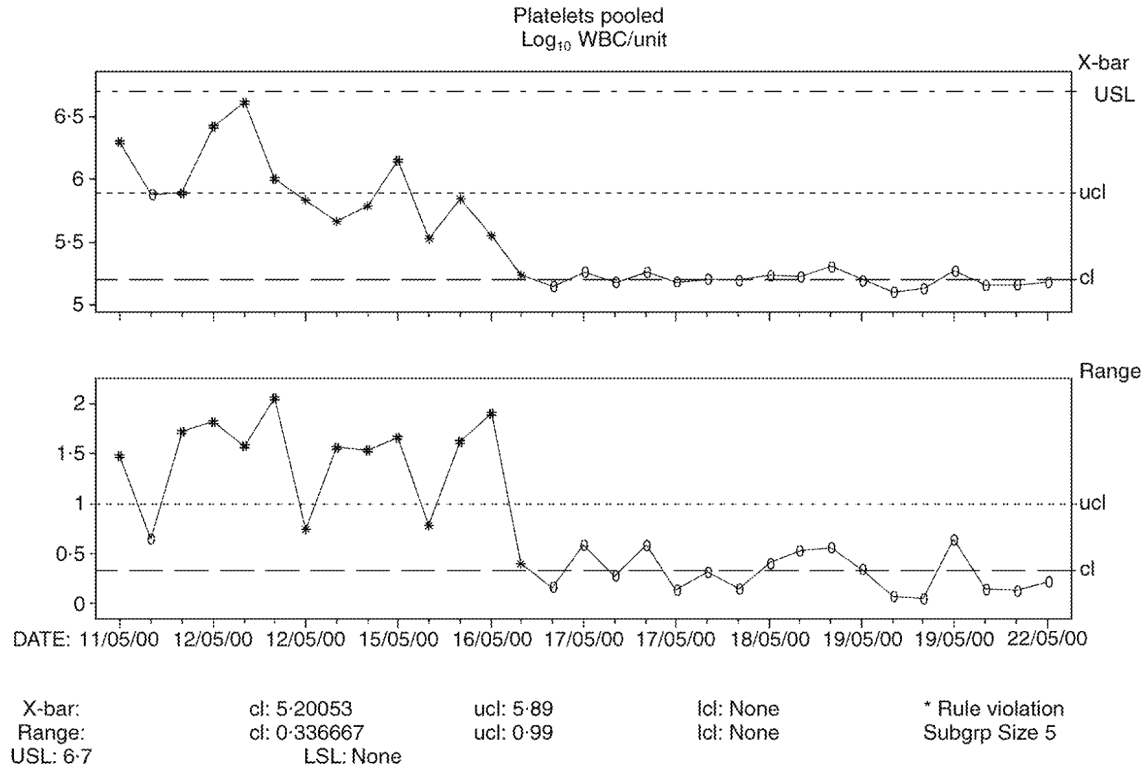

Fig. 2 x-bar and Range control chart of the $\log_{10}$ residual leucocyte contamination of pooled platelet process, showing a return to a controlled state following remedial action to incorrectly set up automated press equipment. WBC, white blood cells.

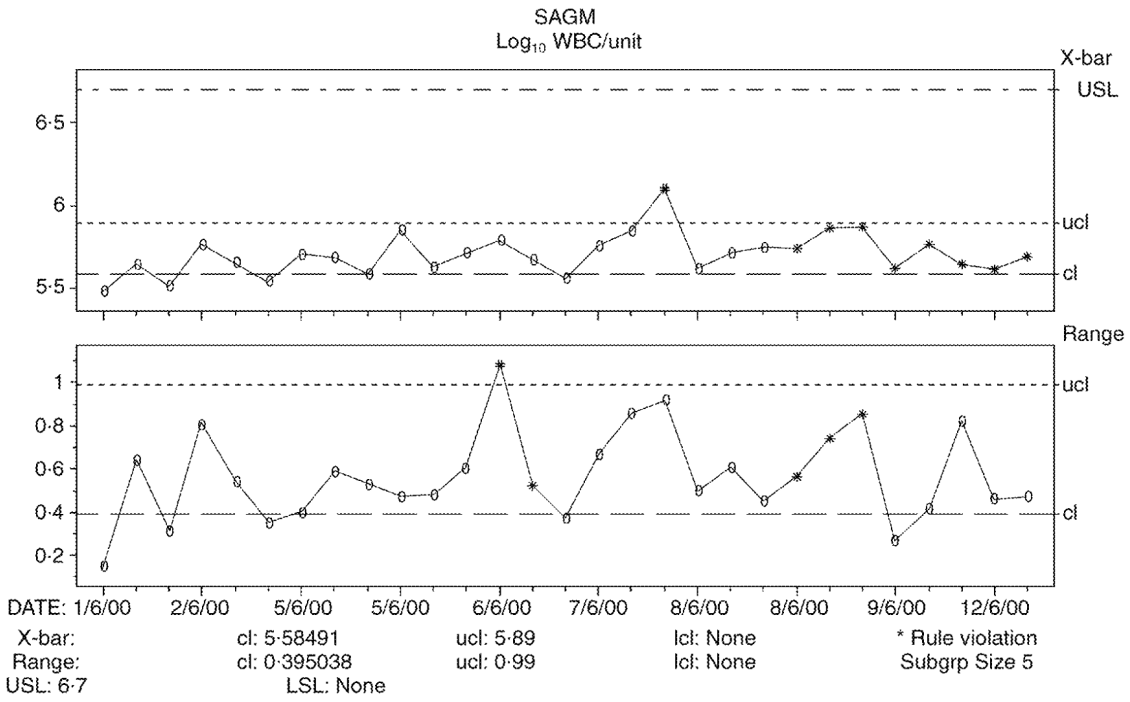

Fig. 3 x-bar and Range chart of the $\log_{10}$ residual leucocyte contamination of a red cell process demonstrating trend warnings caused by a process change. WBC, white blood cells.

Example 2

During a period of 5 weeks, the mean weekly leucocyte count of red cells in an OAS process in one centre increased from $0{\cdot}48 \times 10^6$/unit to $0{\cdot}93 \times 10^6$/unit, while the confidence level that at least 95% of units contained $< 5 \times 10^6$ leucocytes, decreased from 99% to not proven at 75% (Fig. 3). An investigation of the production process was undertaken in conjunction with the filter manufacturer, which identified problems in mixing of the unit during donation. When altered, there was an improvement in the results. Monitoring was increased during the poor performance period.

Discussion

Control charts have successfully detected drift as a result of process change and sudden alterations in the results of leucodepletion, using both calculated and fixed control limits. Calculated control limits have the disadvantage that LD processes with good conformance to specification give more than the predicted number of control chart warnings. The distribution of LD data 'approximates' to log normal [5], but our results were sufficiently skewed to make estimates of the frequency of control chart warnings based on a normal distribution of the $\log_{10}$ values less than were actually observed. The introduction of fixed control limits, as described above, removed the need for additional monitoring of processes that were performing well. However, it was recognized that a single failure of $> 5 \times 10^6$ would not necessarily cause an x-bar control limit violation where other units within the subgroup had leucocyte counts of $< 0{\cdot}5 \times 10^6$/unit, although a Range chart violation would be present. It has not been necessary to detect small changes in processes that perform well, as, in our hands, these were not associated with specification failures. These small changes have, where significant, led to trend warnings which themselves required action. The reduction in sensitivity as a result of higher fixed UCL has not resulted in specification failures being missed as these were detected by a review of the raw results, control charts being used to detect significant changes in the process. All specification failures resulted in increased testing, with a review of the process if further failures or control chart violations were noted. The 'fixed' control limits resulted in much reduced testing consequent to control chart violations, while having no adverse impact on the identification of major changes in the processes. These fixed control limits were not applied to processes that were performing poorly where an original calculated method was used to derive control limits.

As both of the above examples show, control charts can be used successfully to detect changes within processes. An investigation of process failure needs to examine every stage in the process, from blood donation through to leucocyte counting.

The nationally adopted specification in the UK (at least 99% of products $< 5 \times 10^6$ leucocytes/unit with 95% confidence)

has proved to be achievable within the estimated accuracy of the counting technology. The Council of Europe specification [10] of at least 90% of units $< 1 \times 10^6$ leucocytes/unit in tested products has also been achieved for all processes (Table 3). Both whole-blood and red cell filtration processes can be realistically expected to give these pass rates consistently once production staff are experienced, provided the choice of filtration method is based on extended trial or routine production data.

Failures to meet specification fell broadly into two categories: systematic failures, where the upper end of the data distribution straddled the specified limit; or rare sporadic failures as a result of filter production error or possibly donor-related problems. In the former, most failures were close to the specified limit of 5×10^6 leucocytes/unit, with fewer units giving higher values. It has become clear that processes which initially struggle to achieve conformance to specification are more likely to prove problematic when used routinely, leading to considerable increases in leucocyte counting and discard rates.

In the case of sporadic failures, the magnitude of the failure cannot be predicted. It can be expected that any red cell filtration process will give the occasional sporadic outlier ($> 30 \times 10^6$ leucocytes/unit). All whole-blood filters, red cell filters and platelet leucodepletion methods used within the NBS have given at least one product of $> 30 \times 10^6$ leucocytes/unit during the period January 1999–June 2000. Fresh-frozen plasma has not given a leucocyte count of $> 10 \times 10^6$/unit to date. Extreme failures in any product type are very rare.

National standardization in process validation, leucocyte counting and statistical analysis was central to the ability to introduce universal LD. Protocols adopted for assessing different manufacturers and products identified pack types that could be used, while rejecting those that may lead to a process performing poorly, or where the quality of manufacture or robustness of supply were in doubt. Differences in process performance resulted from filter performance, manufacturer production quality issues, and variations in storage time/temperature and processing. Differences as a result of counting technology variability have reduced dramatically following the introduction of standardized processes nationally [4], with a leucocyte enumeration intersite coefficient of variation (CV) in red cell samples down from 36% to 9%. It is anticipated that this trend will continue. Variation within the data collected prior to 2000 owing to the differing leucocyte enumeration methods employed, cannot be excluded.

The results of the monitoring reviews suggest that processes improve after initial introduction until procedures are established and staff are experienced. Once processes have stabilized, an estimate of the process failure rate can be made. Further improvements within a process beyond this are difficult to achieve. Specific problems in a single processing centre can account for a significant proportion of the specification failures that are identified nationally, and as such must be dealt with effectively at a local level while ensuring that information is available to other processing centres on the nature of the problem.

The SPM used has developed in the light of experience to suit the requirements of the NBS.

Other quality monitoring and release options have been developed and are in routine use in other countries, including non-parametric batch release [11] and the use of Kolmogorov-Smirnov process mapping. It is not clear at this point which strategy is most beneficial for patients, or which is most cost effective.

Contingency measures have been developed to minimize the risks of process failure and procedures introduced for reviewing manufacturer production and supply capabilities.

Implementation of universal LD in the NBS has been achieved according to agreed timescales and specifications while maintaining the blood supply.

Acknowledgements

The authors would like to acknowledge the other members of the Leucodepletion Project Implementation Board: Dr Angela Robinson, Peter Garwood, Nick Tandy, Terry Male, Richard Bedford, Michelle Ashford, Gordon Nicholson, Alison Kruse and Steve Morgan, and all staff within the National Blood Service whose hard work has led to the improvements seen.

References

1 British Committee for Standards in Haematology Blood Transfusion Task Force: Murphy MF, Kinsey S, Murphy W, Pamphilon D, Warwick R, Williamson LM, Wood JK. Guidelines on the clinical use of leucocyte-depleted blood components. *Transfus Med* 1998; **8**:59–71

2 Claas FHJ, Smeenk RJT, Schmidt R, van Steenbrugge GJ, Ernisse JG: Alloimmunisation against the MHC antigens after platelet transfusions is due to contaminating leucocytes in the platelet suspension. *Exp Hematol* 1981; **9**:84–89

3 Fisher M, Chapman JF, Ting A, Morris PJ: Alloimmunisation to HLA antigens following transfusion with leucocyte-poor and purified platelet suspensions. *Vox Sang* 1985; **49**:331–335

4 Cardigan R, Phipps A, Seghatchian J, Bashir S, Aynsley S, Beckman N, Barnett D, Reilly JT, Williamson LM: The development of a National standardised approach to the enumeration of residual leucocytes in blood components. *Vox Sang* 2002; **83**:100–109

5 Practical guidelines for process validation and process control of white cell-reduced blood components: report of the Biomedical Excellence for Safer Transfusion (BEST) Working Party of the International Society of Blood Transfusion (ISBT). *Transfusion* 1996; **36**:11–20

6 Grant EL, Leavenworth RS: *Statistical Quality Control*, edn 5. New York, McGraw–Hill, 1980

7 Shewhart WA: *Statistical Method from the Viewpoint of Quality Control*. Washington, Department of Agriculture Graduate School, 1939

8 Levey S, Jennings ER: The use of control charts in the clinical laboratory. *Am J Clin Pathol* 1950; **20**:1059–66

9 Barnett D, Granger V, Mayr P, Reilly JT: Preparation and stabilisation of leucocytes: UK Patent Number 2279653. London, The Patent Office, 1998, 1–40

10 *Guide to the Preparation Use and Quality Assurance of Blood Components*. Strasbourg, Council of Europe Press, edn 7, 2000

11 Barclay GR, Walker B, Gibson J, McColl K, Turner ML: Quality assurance by a commercial flow cytometry method of leucodepletion of whole blood donations: initial application of universal testing and proposals for a batch-release sampling plan. *Transfus Med* 2000; **10**:37