Editorial Commentary

The use of routine hematology analyzers for quality management of leukocyte depletion in blood transfusion products: a comment

Albert Huisman

University Medical Center Utrecht, Central Diagnostic Laboratory, Utrecht, the Netherlands
Correspondence to: Albert Huisman. University Medical Center Utrecht, Central Diagnostic Laboratory, Utrecht, the Netherlands.
Email: a.huisman@umcutrecht.nl.

Comment on: Blanco RA, Cavagnetto C, Willmott L, *et al.* The use of a hematology analyzer with a new generation of software as an alternative to flow cytometry for enumerating residual white blood cells in blood components. Transfusion 2020;60:155-64.

This is a commentary on a recently published paper concerning the use of hematology analyzers to quantify residual white blood cells (rWBCs) in blood components (1).

Leukocytes that are present in blood products (i.e., red blood cell concentrates "packed cells" or platelet (thrombocyte) concentrate transfusion products) have no therapeutic value, but can theoretically give rise to adverse events. Therefore, currently leukocyte reduction or leukocyte depletion is an integral part of the preparation of blood products. Leukocyte reduction is believed to lead to a reduction in adverse events associated with transfusion such as febrile reactions and human leukocyte antigen (HLA) alloimmunization. Whether the reduction in adverse events is actually the case has not yet been demonstrated. A recent Cochrane review shows no demonstrable benefit (or harm) from this process; however, the overall quality of the included studies was low and the studies included in the review generally included too few patients to provide definitive answers (2). Nevertheless, it is nowadays common practice to apply leukocyte depletion for blood products intended for human transfusion. A guide (3) prepared by the Council of Europe states that the number of leukocytes per unit of transfusion product should be $<1.0\times10^{6}$, which is a stricter standard compared to applicable standard in the USA ($<5.0\times10^{6}$) (4). To monitor the number of leukocytes in the blood products, flow cytometry analyzers using leukocyte specific monoclonal antibodies are used, generally leading to a robust leukocyte count (5). A drawback of this analytical technique is that it is relatively time consuming and the use of the monoclonal antibodies and flow cytometry equipment involves significant financial costs.

Hematology analyzers used for the complete blood count (CBC) have undergone enormous technological development and improvements (6-8). There are now also special settings for these analyzers where it is possible to determine very low numbers of leukocytes in body fluids, like cerebrospinal fluid (CSF) (9). The authors of the discussed paper (1) have investigated whether a hematology analyzer is suitable for monitoring the leukocyte depletion process in the preparation of blood products for human transfusion. The hematology analyzer described in this paper uses a "Blood Bank" mode in which the gating strategy (i.e., the detection of WBC's using fluorescence flow cytometry and light scatter) is modified in order to detect rWBCs in blood products. They have performed this research in a robust manner and have indeed been able to demonstrate that the type of hematology analyzer (in "Blood Bank" mode) discussed in their paper is suitable for this process. The European standard states: "*For quality control, an appropriate validated method must be used for counting leucocytes*" (3). As discussed above, it is necessary that the analyzer can reliably enumerate a very low leukocyte count. The limit of quantitation (LoQ) is the most commonly used parameter for this purpose. The LoQ is the lowest cell number that can still be reliably measured. In general, the LoQ is defined as the cell count where the CV <20%. In the paper that is discussed here, the authors show that this is approximately 2 WBC/μL (0.002×10^{9}/L); the limit of detection (LoD) is approximately 1 WBC/μL (0.001×10^{9}/L). In a series of robust and elegant experiments,

the authors subsequently demonstrate that the intended hematology analyzer (in "Blood Bank" mode) is suitable for the purpose described above and can thus be used in the quality management and quality control of leukocyte depletion of blood transfusion products. However, it should be noted that the detection limit required for this purpose is at the lower limit of what is achievable with this particular hematology analyzer (in this mode). The hematology analyzer in the paper discussed here has only been tested for the standards that apply in the UK, additional studies should be conducted for other standards. When the standards become stricter (lower number of rWBCs allowed), the question is (given the LoQ) whether hematology analyzers are suitable for the intended purpose. Because the hematology analyzer used in this paper uses a special "Blood Bank" mode for the quantification of rWBCs, is unclear whether quantification of rWBCs is possible with hematology analyzers from other manufacturers. Other hematology analyzers may for instance require software modifications or sample preprocessing. Therefore, when a different type of hematology analyzer is used for quantification of rWBCs in blood products it should be demonstrated that it is suitable for the intended purpose.

The use of a hematology analyzer in the quality management process (more in particular the detection of rWBCs) of the production of blood products for human use has a number of advantages; these including the shorter processing time and a cost reduction. The paper discussed above shows that it is indeed possible to use a hematology analyzer for this purpose. This paper can therefore be seen as a step forward in the use of hematology analyzers in quality management process of the production of blood products for human use.

Acknowledgments

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Blood*. The article did not undergo external peer review.

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at http://dx. doi. org/10. 21037/aob-20-40). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Blanco RA, Cavagnetto C, Willmott L, et al. The use of a hematology analyzer with a new generation of software as an alternative to flow cytometry for enumerating residual white blood cells in blood components. Transfusion 2020;60:155-64.
2. Simancas-Racines D, Osorio D, Martí-Carvajal AJ, et al. Leukoreduction for the prevention of adverse reactions from allogeneic blood transfusion. Cochrane Database Syst Rev 2015;(12):CD009745.
3. Guide to the preparation, use and quality assurance of blood components. Recommendation No. R (95) 15. 20th ed. Strasbourg: Council of Europe: European Directorate for the Quality of Medicines & HealthCare, 2020.
4. Pre-storage leukocyte reduction of whole blood and blood components intended for transfusion. Rockville: U.S. Department of Health and Human Services; Food and Drug Administration, 2012.
5. Zeng Y, Dabay M, George V, et al. Comparison of flow cytometric methods for the enumeration of residual leucocytes in leucoreduced blood products: a multicenter study. Cytometry A 2018;93:420-6.
6. Green R, Wachsmann-Hogiu S. Development, history, and future of automated cell counters. Clin Lab Med 2015;35:1-10.
7. Vis JY, Huisman A. Verification and quality control of routine hematology analyzers. Int J Lab Hematol 2016;38

Suppl 1:100-9.

8. Verbrugge SE, Huisman A. Verification and standardization of blood cell counters for routine clinical

laboratory tests. Clin Lab Med 2015;35:183-96.

9. Sandhaus LM. Body fluid cell counts by automated methods. Clin Lab Med 2015;35:93-103.