

Oct 13, 2015

IMPORTANT PRODUCT CORRECTION NOTIFICATION

Additional Limitation for Visual Reference Guide for ORTHO BioVue® System Cassettes

Please distribute this information to the appropriate personnel at your facility

Dear Valued Customer,

This is to inform you of an Important Product Correction Notification involving the following:

Name	Publication No.	Publication Date
<i>Visual Reference Guide for ORTHO BioVue® System Cassettes</i>	J39791	2012-01-04

List of Product Codes for ORTHO BioVue® Cassettes Affected

Product Codes-ORTHOBioVue® Cassettes
6901906 – Newborn
6904485 – ABD Confirmation Cassette (RUM1)
707100 – ABO/Rh Reverse
707101 – ABO/Rh Reverse – China
707117 – Anti-K
707119 – ABODD
707135 – ABD Confirmation
707136 – ABD Confirmation China
707150 – ABO-Rh
707155 – ABO/Rh Reverse
707156 – ABO/Rh Reverse – China
707165 – DAT-IDAT
707190 – ABO-Rh
707250 – Rh/K
707255 – Rh-hr
707270 – ADK
707280 – Rh/K
707300 – AHG Poly Specific
707301 – AHG Poly Specific China
707310 – AHG Poly/Neutral
707350 – AHG Poly Specific

707351 – AHG Poly Specific China
707355 – AHG Poly/Neutral
707400 – AHG Anti-IgG
707401 – AHG Anti-IgG China
707450 – AHG Anti-IgG
707451 – AHG Anti-IgG China
707550 – Reverse Diluent
707580 – Reverse Diluent
707650 – Neutral
707680 – Neutral

The purpose of this notification is to inform you regarding unexpected results due to aspiration of transfused donor cells in a recently transfused patient sample may lead to the need for additional troubleshooting and testing. Automated pipetting systems (such as ORTHO ProVue, ORTHO AutoVue and ORTHO VISION for BioVue Cassettes and ORTHO VISION for MTS Gel) may contribute to the sample containing a predominant population of donor cells. On this basis, when cells are aspirated from the centrifuged packed cells in the bottom of the sample tube (per the design of each ORTHO automated systems), the potential for unexpected results exists.

Summary of Anomaly

Transfusion, disease states and cellular therapies that affect cellular production can influence the characteristics of a patient's red cell population. Such patient-specific situations can affect test results, depending on the quantity of red cells transfused, the impact of the disease state on autologous red cell production and/or the therapy employed (e.g. bone marrow transplant). (Please see reference information in the Question and Answer).

Due to differences in the specific gravity of donor cells vs. autologous (patient) red cells, unexpected results may potentially be obtained when blood samples drawn from recently transfused patients are tested by a variety of test methods used in immunohematology, including antigen typing using ORTHO BioVue® System Cassettes. Automated pipetting systems may contribute to the sample containing a predominant population of donor cells. On this basis, when cells are aspirated from the centrifuged packed cells in the bottom of the sample tube (per the design of ORTHO automated immunohematology systems), the potential for unexpected results exists. Ortho Clinical Diagnostics (OCD) will be providing information about the testing of recently transfused patients in the Visual Reference Guide for ORTHO BioVue® System Cassettes at a future date.

Impact to Patient Results

Unexpected results due to aspiration of transfused donor cells in a recently transfused patient sample may lead to the need for additional troubleshooting and testing.

Evaluation of patient clinical history and transfusion status is critical to interpretation of all immunohematology tests before making final interpretation of test results.

Ortho Clinical Diagnostics

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Please see the Question and Answer section for sample scenarios that can potentially produce unexpected results due to differences in specific gravity of donor vs. patient red cells.

Actions Required from You

1. Include the Publication Update information on Page 3 of this letter with your current Visual Reference Guide for ORTHO BioVue® System Cassettes until the updated guide is distributed to your facility.
2. Complete and return the **Customer Acknowledgement Form** within **(2) two business days** to acknowledge your reading and understanding of this notice.
3. Please contact an Ortho Clinical Diagnostics representative if you experience this phenomenon.

Rate of Occurrence

Please see the Question and Answer section for sample scenarios that can potentially produce unexpected results due to differences in specific gravity of donor vs. patient red cells.

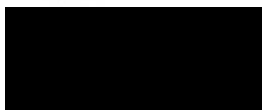
Resolution

To clarify this potential for unexpected results, Ortho Clinical Diagnostics (OCD) is adding the following information to Visual Reference Guide for ORTHO BioVue® System Cassettes:

“Following centrifugation of a freshly collected patient sample drawn from a recently transfused patient, the potential exists for the donor’s transfused red cells, which are denser and heavier, to concentrate at the bottom of the sample tube in a layer below the patient’s own red cells, which are less dense and lighter. If the cell suspension used for testing contains a majority of transfused donor cells, unexpected patient results could be observed due to the patient cells being an absent or minor population in the prepared cell suspension. The unexpected patient result could be a result associated with the transfused donor cells, or it could be due to a mix of patient and donor cell populations.”

We apologize for the inconvenience this may cause your laboratory. We have anticipated some questions you may have in the following Question and Answer section. If you have any additional questions, please contact Customer Technical Services at **1800 5646 766** at any time.

Yours sincerely,



Lee, Ching Hwee
Senior Regulatory Affairs Specialist

Questions and Answers

1. Is it only the specific gravity (density) of donor red cells blood that is different than patient red cells?

No, it is more the age of the red cells that contributes to the density differences. A fresh sample of blood will contain a range of cells of various ages. Initially, the same holds true of a unit of blood. As the unit ages, despite being supported biochemically to meet the therapeutic expectations of a stored unit of blood, all cells progressively age without new cells being added to the overall cell population that exists in the unit. Conversely, in most normal circumstances, the red cells in a patient's body are being renewed and replace cells that are being removed because of their age. Based on these factors, the majority of red cells in a transfused red cell sample have a greater age/density when compared to a patient sample, where the cell population has a wider range of age and densities. Therefore, older cells, whether of the donor or patient red cell population, are found at the bottom of a centrifuged blood sample, while younger cells are distributed further up the red cell layers of a centrifuged blood sample.

2. Under which conditions might unexpected results be obtained?

Below are examples of scenarios where unexpected results could occur:

Trauma

1. As the result of trauma, a patient has had their entire blood volume exchanged with donor blood several times. Because of this, the red cells in the patient are representative of the donor blood that was transfused to the patient. Depending on policy and process, the patient may have received ABO compatible, but not type-specific blood (i.e., Type A blood receives units of blood group Type O).
2. One or two days later, new samples for pre-transfusion testing are tested. Upon centrifugation of the sample, predominantly transfused cells, due to their greater density, migrate to the bottom of the sample tube, while the upper layers of cells in the sample tube are a majority of patient's own cells, which have lower specific gravity.
3. Based on where red cells are aspirated from the tube, the testing may demonstrate a range of test reactions or results representative of the mixture in the layer accessed by the pipette.
4. The patient's blood group antigen status may therefore be representative of the donor blood transfused rather than the patient's actual blood group antigen status.

Aplastic Anemia

- Any disease state in which reticulocyte production is dramatically depressed or nonexistent often involves constant transfusion support to maintain the patient. The patient who is chronically transfused concurrent with their poor red cell production typically will have predominant concentrations of donor cells versus the patient cells, no matter which layer of the red cell column is evaluated.

- Similar to the Trauma scenario above, the admixture of donor and patient cells is dependent on the amount of red cells transfused, the production of red cells in the patient, and the aspirated layer of red cells. Therefore, similar challenges to understanding true (patient) antigen blood group status exist.

3. What are the available sources of information regarding the specific gravity of donor cells vs. autologous (patient) cells?

The following sources provide information regarding autologous (patient) red cells in a blood sample from recently transfused patients:

1. AABB (American Association of Blood Banks) *Technical Manual*, 18th edition; Method 2-22: 1-2; 2014.
2. Judd W John. Section V: Cell Separation Methods, *Methods in Immunohematology*, 2nd Edition (Montgomery Scientific Publications): 119; 1994.
3. Reactivity of Reticulocyte-Enriched Cell Populations with Selected Commercial Antisera Abstract, *Transfusion*, Vol. 54: Supplement: 159A; 2014.
4. Renton PH and Hancock Jeanne A, A Simple Method of Separating Erythrocytes of Different Ages, *Vox Sang.* 9: 183-186; 1964.
5. Branch Donald R, Sy Siok Hian Anita L, Carlson Fumiko, Maslow William C, Petz Lawrence D, Erythrocyte Age-fractionation Using a Percol™- Renografin® Density Gradient: Application to Autologous Red Cell Antigen Determinations in Recently Transfused Patients, *AJCP* Vol. 10; 1981.
6. Reid Marion E, Toy Pearl TCY, Simplified Method for Recovery of Autologous Red Blood Cells from Transfused Patients, *AJCP*; March 1983.