Lantana
CONSULTING GROUP

Extended Blood Product Genotyping Information Exchange

An Initiative to Develop an HL7 FHIR® Standard Implementation Guide

A White Paper Supported by:*

Bruce A. Beckwith, MD, FCAP	Chairman of Pathology	North Shore Medical Center, Salem, MA
Mark Edmunds, MD	Medical Director	San Diego Blood Bank
Jeanne Hendrickson, MD	Professor of Laboratory Medicine and Pediatrics, Medical Director of Apheresis, and Associate Medical Director of Transfusion Medicine Service	Yale University School of Medicine, Department of Laboratory Medicine
Doug Morton	Chief Operating Officer	San Diego Blood Bank
Anders Nygren, PhD	Chief Executive Officer	HaploGNX
Mandy Flannery O'Leary, MD, MPH	Associate Member of the Department of Pathology at Moffitt Medical Group and Associate Professor of the Department of Oncologic Sciences at University of South Florida	Moffitt Cancer Center
Robert Rainer MD, MBA	Medical Director	The Blood Connection
John Spinosa, MD, PhD	Chief Medical Consultant	Lantana Consulting Group
David Wellis, PhD	Chief Executive Officer	San Diego Blood Bank

*Affiliation listed for individual identification, does not imply organizational endorsement.

Last revised: January 14, 2022

Introduction

Every year blood product transfusions benefit millions of patients–but not without risk. Significant risks include adverse immunologic reactions and delays in obtaining specialized products. Fast, accurate blood product and patient phenotype information exchange between donor centers and blood banks is the first defense in reducing these risks.

Blood donor centers and blood banks, however, have no bidirectional digital interfaces between their regulated information management applications. Critical information is often not shared, or if shared, is re-keyed and stored in inconsistent formats making it error-prone and difficult or impossible to access electronically. This lack of a bidirectional, electronic interface is a rate limiting step in improving transfusion medicine procedures, improving utilization of blood products, and most importantly, increasing patient safety.

This white paper outlines the challenges facing blood product information exchange and recommends a standards-based solution to overcome these challenges and conserve resources through better data representation and integration.

Background

- **Donor centers collect and process blood products for transfusion.** Donor centers use blood establishment computer systems (BECS), which are regulated and geared toward safely manufacturing blood products (whole blood, packed RBC, platelets, plasma). These donor centers are frequently the source for specialized RBC patient genotyping tests–the results of which must be returned to the requesting institution.
- **Blood banks transfuse manufactured blood products received/purchased from donor centers into patients.** Blood bank laboratory information systems (BBLIS) are also regulated and geared toward the critical steps of safely transfusing manufactured blood products via compatibility checks, provenance, and patient monitoring.
- **The missing link:** The commonality between these two systems are the blood products themselves, their associated metadata (unique ID, product description), and the metadata describing the patient's blood type. The missing link? These systems do not represent this critical information in the consistent, standard form required for digital interfaces.

Challenges

Three common information-exchange challenges shared by donor centers and blood banks are described below.

Manual Information Exchange

Presently, much of the metadata associated with a blood product must be rekeyed into the BBLIS upon receipt from the donor center.

Blood banks communicate special circumstances or individual patient needs by phone or fax to blood donor centers. Manufactured blood products arrive with a barcode containing a unique identifier and other basic information, while other metadata is printed on a label and must be rekeyed into the BBLIS upon receipt. The amount of information generated about blood product phenotypes is increasing, especially in genetic predictors of RBC phenotypes (genotyping or genetic sequencing-based phenotyping), along with a concomitant increase in patient blood type information (more patient RBC phenotyping information). This increased data load is straining these labor-intensive information-sharing processes, leading to decreased efficiency and potential sources of error. Finding compatible blood

for a patient with a low incidence antigen or one or more alloantibodies is becoming increasingly time consuming.

Inventory Management

The process for finding rare blood units is cumbersome, and can encompass local, regional, national, and (infrequently) international searches. The same applies to determining the best units to screen for hospital inventories to serve, for example, chronically transfused patients such as those with sickle cell disease (SCD) with or without an identified alloantibody. ***Chronically transfused patients, especially those with sickle cell anemia, are particularly at risk. Patients living with SCD not only form alloantibodies more frequently than other chronically transfused groups,***[1] ***but alloantibodies in patients with SCD are associated with increased mortality and morbidity.***[2] These outdated sourcing and inventory practices impair the transmission of more granular phenotyping information, indirectly contributing to avoidable adverse reactions.

Limited Scalability

The current manual processes between BBLIS and BEC systems do not scale, which may be delaying the implementation and use of more detailed genotyping information. At population levels, efficiently managing and exchanging this additional information would allow for more precise blood compatibility determination (through computational methods), better allocation of rare blood phenotypes (via better inventory management), and improved understanding of the long-term sequelae of blood transfusions (by more granular and extensive phenotyping information in patient follow-up).

Solution: HL7® FHIR® Standard

The development of a transparent, open standard describing blood product and patient RBC phenotypes will encourage industry innovation in digital interfaces for blood product information exchange. We recommend a Health Level 7 (HL7) Fast Healthcare Interoperability Resources (FHIR)[3] Implementation Guide (IG) framework for this initiative. FHIR is a flexible, scalable interoperability standard that streamlines information exchange between healthcare systems. (See Figure 1: FHIR-enabled Blood Product Information Exchange for details.)

The goals of this initiative are to:

- Convene a group to launch this work and support it throughout with domain expertise.
- Develop a FHIR IG for exchange of blood product and patient genotyping and phenotyping information.

What is an open standard?

Open standards are discipline-specific and are developed, approved, and maintained through a voluntary, collaborative, consensus-driven process.

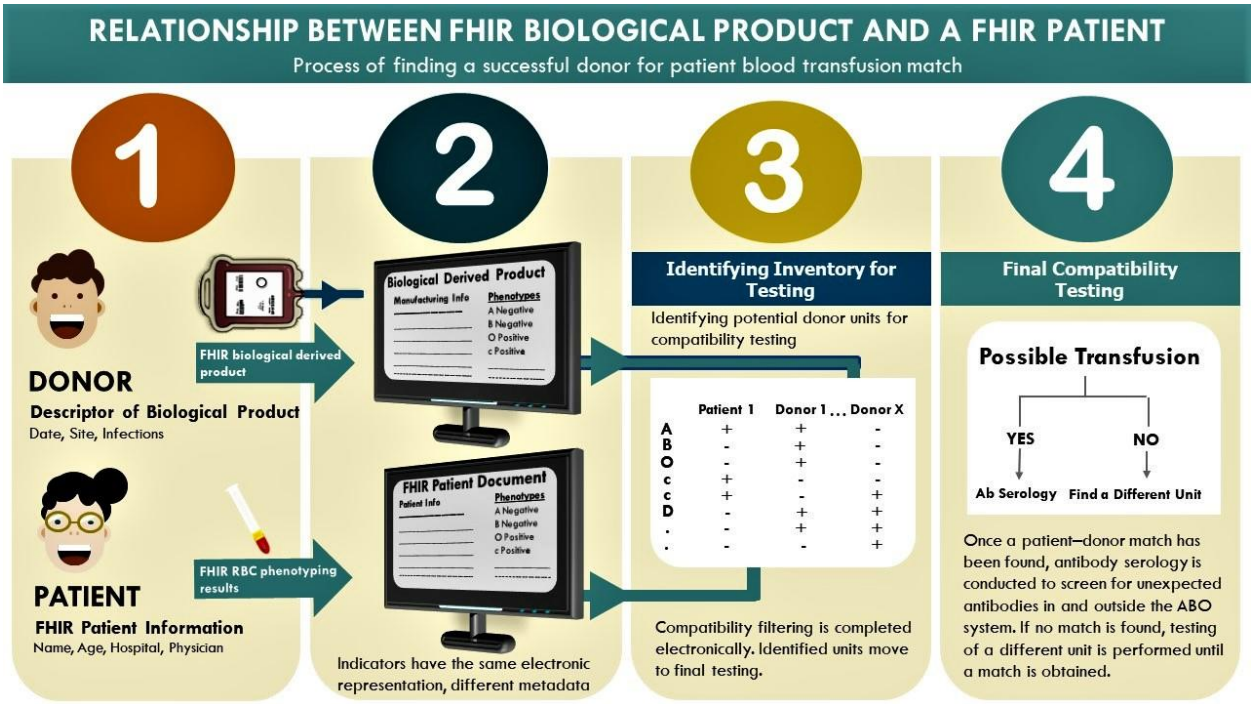
Open standards are the basis for interoperability among products or services, creating a common specification to share information.

HL7® standards are available under a licensing agreement by which HL7 retains its copyright with specific terms and no cost is incurred to stakeholders.

[1] Hendrickson, J.E. https://aob.amegroups.com/article/view/6143/html
[2] Telen et al. https://pubmed.ncbi.nlm.nih.gov/25444611/
[3] HL7 FHIR http://www.hl7.org/documentcenter/public/standards/FHIR/FHIR%20for%20the%20C-Suite.4Sep19.pdf

- Specify genomic data structures and phenotyping data structures for BECS, BBLIS incorporation.
- Support and encourage implementation across the blood transfusion industry.
- Create a common set of resource profiles compatible with the Biologically Derived Products FHIR resource[4,5] in development by the FDA.

Figure 1: FHIR-enabled Blood Product Information Exchange



Conclusion

We believe now is the time to put in place standardized representations of blood bank genotype and phenotype information as a first step in bidirectional digital interface development. A recent paper[6] recognizes the benefits of electronic blood product information exchange and discusses how the International Council for Commonality in Blood Banking Automation (ICCBBA) is ensuring that existing ISBT 128[7] standard terminology and reference tables can be used in electronic messaging.

Implementing the open HL7 FHIR specification would modernize blood product information exchange and transfusion medicine procedures, increase patient safety, and decrease administrative burden.

The first step is to convene a group of industry stakeholders to initiate this work. Key stakeholders include blood donor centers, health systems, reagent vendors (both serology and array-based; phenotyping and genotyping tests), BBLIS and BECS vendors, professional groups, and

[4] http://hl7.org/fhir/biologicallyderivedproduct.html
[5] https://www.healthit.gov/isa/uscdi-data-class/biologically-derived-product#level-1
[6] Ashford and Moniz https://onlinelibrary.wiley.com/doi/full/10.1111/trf.16294
[7] ISBT 128, developed by the ICCBBA, is the global standard for the terminology, identification, coding and labeling of medical products of human origin

pathologists. The cover page signatories have indicated their support and we are continuing outreach to increase awareness and engagement.

About This Initiative

The Blood Bank Implementation Guide is an unfunded volunteer effort, initiated by Lantana Consulting Group[8] under the direction of John Spinosa, MD, PhD, Chief Medical Consultant. For more information, contact john.spinosa@lantanagroup.com.

References

- Hendrickson JE. Red blood cell alloimmunization and sickle cell disease: a narrative review on antibody induction. *Annals of Blood.* 2020;5:33. doi: 10.21037/aob-2020-scd-01
- Telen MJ, Afenyi-Annan A, Garrett ME, Combs MR, Orringer EP, Ashley-Koch AE. Alloimmunization in sickle cell disease: changing antibody specificities and association with chronic pain and decreased survival. *Transfusion*. 2015 Jun;55(6 Pt 2):1378-87. doi: 10.1111/trf.12940. Epub 2014 Dec 1. PMID: 25444611; PMCID: PMC4451450.
- Ashford, P. and Moniz, K. (2021), Standardized electronic transfer of blood product information. Transfusion, 61: 1324-1328. https://doi.org/10.1111/trf.16294

[8] https://www.lantanagroup.com/