2024

Alloantibody Exchange

Sharing patient's transfusion histories makes blood transfusion safer.

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2 EXECUTIVE SUMMARY

Transfusion medicine experts, commercial ventures, and national blood systems agree on the need for a national alloantibody registry to share blood transfusion history and prevent delayed hemolytic transfusion reactions. Less discussion has occurred around the increase in efficiency an alloantibody registry would offer to blood banks. Currently, blood banks share transfusion histories over the telephone in a non-uniform manner (e.g., a technologist at one blood bank may call hospitals in the area near a patient's home address to see if they have any blood bank history on a patient). In most cases, a patient's transfusion history remains unknown to the treating hospital. An electronic exchange would increase transfusion safety and eliminate the need for phone calls by providing a more secure, complete, accurate, reliable, faster, and less expensive conduit to transfusion histories. These benefits will provide value to blood banks who enroll in the Alloantibody Exchange, while systems without access could be perceived as outdated and a liability to patient safety.

We have created an Alloantibody Exchange that blood banks can access free of charge. It is owned by a 501(c)(3) non-profit corporation and public charity, Transfusion Antibody Exchange Inc. These business designations require Transfusion Antibody Exchange Inc. to provide a public service and prohibit the distribution of money to owners or shareholders. The Alloantibody Exchange operates in Microsoft's cloud computing platform, Azure. It operates with many modern security features including end-to-end encryption, Azure AD authentication credentials, role memberships, object-level authorizations, IP firewalls, requirements for application registration, SQL database auditing, and geo-redundant backup storage.

Blood bank clinicians and staff may provide clinical rationale to the health system. But they have limited involvement in its security review, contracting, or implementation.

Blood banks who wish to participate in the Alloantibody Exchange can choose the "Sign Up" button at the top of the alloantibody.org website. We have taken great care to build a succinct yet thorough project management plan for health systems to follow. It details the project's tasks, timeline, and communication plan.

Summary: Advantages of the Alloantibody Exchange

1. Improved patient care by shared knowledge of evanescent antibodies which are otherwise undetectable and may cause delayed hemolytic transfusion reactions.
2. Improved blood bank efficiency from time saved in acquiring special requirements for transfusion such as patient alloantibody and antigen histories
3. More thorough patient histories made possible by electronic query across a network of multiple blood banks
4. Secure transmission of patient histories in contrast to telephone communications

3 BACKGROUND

Many of the volunteers in our group have witnessed or have been emotionally moved by accounts of delayed hemolytic transfusion reactions. These transfusion reactions can lead to death and may be preventable. According to the Food and Drug Administration (FDA), delayed hemolytic transfusion reactions, a type of non-ABO hemolytic reaction, are a leading cause of transfusion-associated death. Tests performed by blood banks to assess the compatibility of blood between the donor unit and recipient may not prevent delayed hemolytic transfusion reactions because they cannot detect the antibodies that cause the reactions (Figure 1). The best way to prevent delayed hemolytic transfusion reactions is for all blood banks to know the antibodies that other blood banks have detected in their patients.

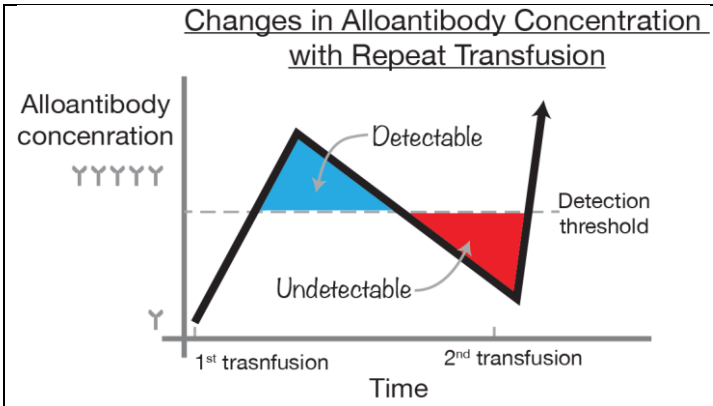


Figure 1A. A blood transfusion, like a vaccine, can trigger the formation of an antibody (x-axis: 1st transfusion). Over time, the amount of antibody declines and may become undetectable (red triangle). Re-exposure to blood, like a booster vaccine, can trigger further antibody production (x-axis: 2nd transfusion). This causes a delayed hemolytic transfusion reaction.

<u>Mission statement</u>: The Alloantibody Exchange works to facilitate the sharing of a patient's RBC antibody and antigen history between hospital blood banks. Sharing of this information can save lives and reduce transfusion-associated morbidity.

We have the technology to build a national transfusion antibody exchange in the United States. Storage space is not an issue: the RBC antibody history for the entire United States could fit on a thumb drive. Secure data transfer is not an issue: the internet was invented in the United States and secure financial data is routinely exchanged on mobile devices. Other countries, like the Netherlands, have an operational RBC antibody registry (TRIX). TRIX has identified thousands of instances where antibodies were present in their national registry and yet were undetectable by the blood bank. Since the national adoption of TRIX in 2011 the number of delayed hemolytic transfusion reactions has dropped by 50%.

No exchange in the United States has attempted to deploy the TRIX model, which relies on blood bank information system (BBIS) vendors. Prior failed attempts to establish an exchange in the United States targeted the blood suppliers instead of the blood banks (National Patient Antibody Registry, NPAR). They required manual entry of RBC antibodies into the registry instead of leveraging automated computer uploads (Community Blood Center of Greater Kansas City). Additionally, all previous attempts in the United States have built software separate and distinct from the BBIS, requiring technologist to allocate their time in counter-productive ways. None have attempted a BBIS vendor collaboration.

Based on the TRIX model, we envision a national exchange that seamlessly integrates with the BBIS. Blood bank technologists enter newly identified antibodies as they do now. Automated routines send these antibodies to the registry. When a new patient enters the BBIS, a computer program queries the

registry and presents the data to the technologist. The exchange becomes part of the technologist's workflow, without extra effort spent to maintain or search for new patient's history.

Staff at separate blood banks currently communicate a patient's transfusion history over the telephone. But importantly, they have no means to determine who has information about a patient's transfusion history before telephoning each other (Figure 2). The equivalent of a database search in our registry requires a blood bank to call many other blood banks to find those with whom they share a patient. Staff must be available to dial and answer the phone, verify the identity of the person on the other end of the line, lookup, and then verbally communicate a patient's record. In stark contrast to an electronic data exchange, telephone communication is less secure, prone to errors in patient identification and antibody specificity, costs more, cannot search nationally, and, most importantly in situations of emergent blood needs, it takes longer. Blood bank concerned with security may not provide patient records over the phone. Many previously detected antibodies are never known to the blood banks that issue these patient's potentially incompatible blood.

Figure 2. Time is money. To obtain transfusion records, blood bank staff call other blood banks, not knowing if they even have the patient's transfusion records. This is a waste time.

The creation of a national transfusion medicine exchange with the support of BBIS vendors will increase the speed, accuracy, reliability, and security of transfusion medicine. These factors will promote safety and efficiency in America's blood banks. The cost of maintenance and deployment for blood banks will likely approach zero. We have requested the major BBIS vendors in the United States to participate in the registry: Cerner, Haemonetics, Soft, Sunquest, Meditech, and WellSky (formerly Mediware). Through detailed project management, test-driven software design, and the collaboration of shared efforts across vendors, we will reduce the development costs for the BBIS vendors. For interested vendors, we have outlined a simple timeline to follow for adoption of the registry, welcome feedback, and will share it, as permitted, with all vendors.

4 SCOPE OF PROJECT

The Alloantibody Exchange applies to a small proportion of a health system's patient population (1%), namely those with special requirements for blood transfusion. Estimates include approximately 1% of patients with a hospital admission and a smaller proportion of outpatients. (See PMID: 29675950/, Fig. 1.) For patients with special requirements for blood transfusion, the Alloantibody Exchange collects limited information, namely alloantibody and blood group antigen histories. Overall, relative to the PHI available in the health system, the Alloantibody Exchange involves a small fraction of the total patients, and for these patients, a smaller fraction of health information. This limits the project scope and risks.

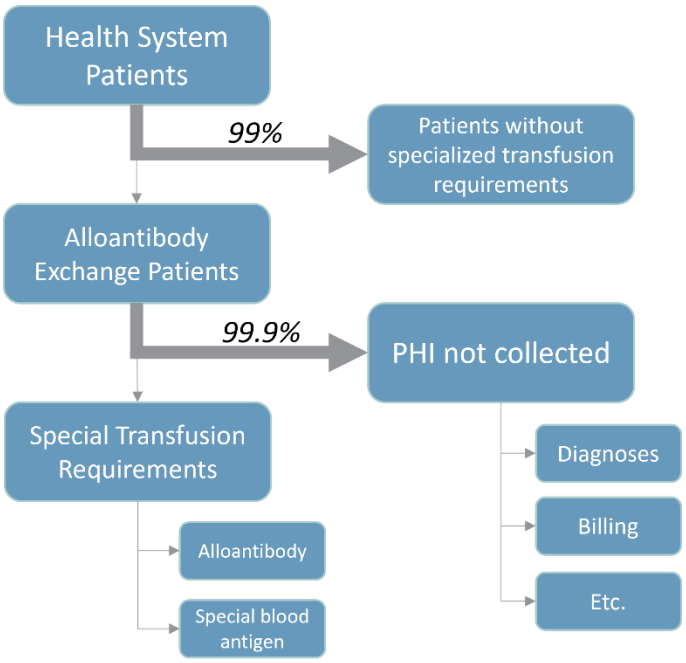


Figure. The Alloantibody Exchange provides potentially life-saving special transfusion requirements to a narrow patient population, and for these patients, limited data is collected.

5 Question and Answer

5.1 How does the Alloantibody Exchange handle patient data privacy?

Patient data privacy is primary concern for us as well. Patient data privacy is primary concern for us as well. We will work with your health system IT to perform a security review. This does not involve blood bank staff. It is also helpful to remember the scope of this project only includes information relative to providing appropriately matched blood products. Patients with special transfusion requirements generally make up 1% of a health system's patient population, and the information collected from this 1% includes only alloantibody, antigen, and special transfusion requirements. We do not collection information on a patient simply because they had a type and screen. We do not collect diagnoses, medications, or billing information. Our focus is very narrow.

5.2 Does the Alloantibody Exchange comply with the security standards specified in HIPAA?

We have read and annotated the HIPAA regulations line-by-line to ensure we comply fully. Read our documentation here. Sharing patient information is allowed under HIPAA. It does not require informed consent for the treatment of patients. See HIPAA 165.506(c)(2) on page 84, "A covered entity may disclose PHI for treatment activities of a healthcare provider". We will work with your health system IT to review HIPAA requirements. This does not involve blood bank staff.

5.3 What does the registry use to identify a patient?

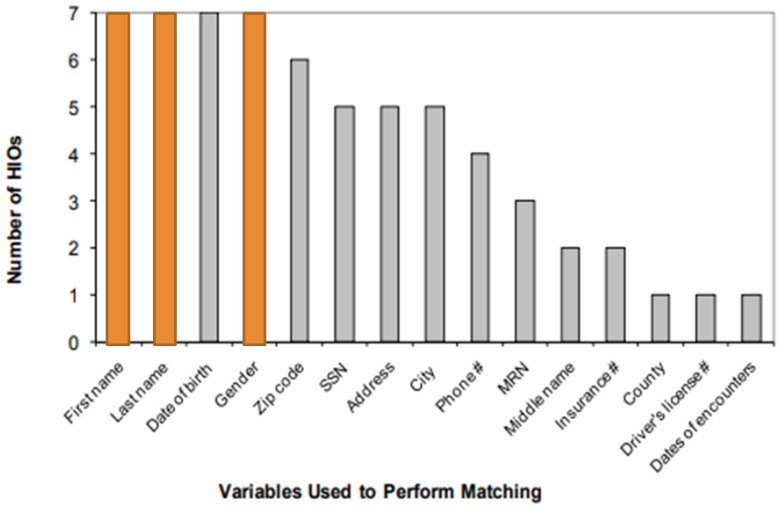
We employ automated procedures developed by a review of health information exchanges to identify patients across systems. We use six patient identifiers: first name, last name, date of birth, birth sex, ABO, and Rh. Although imperfect without a unique national medical identifier, health information exchanges do function successfully in many states. For each patient's transfusion requirements, we do provide the origin of the information, allowing further dialogue as needed.

As shown in the Figure, a review of health information organizations (HIOs) recognized three identifiers (first name, last name, gender) used by all HIOs surveys with some HIOs using up to two additional variables. We have included these three identifiers (first name, last name, gender), two additional identifiers used by the Kansas City Alloantibody Registry (ABO/Rh) and added birth sex.

Required by all HIOs surveyed (3)

Optionally used (up to 2 additional variables)

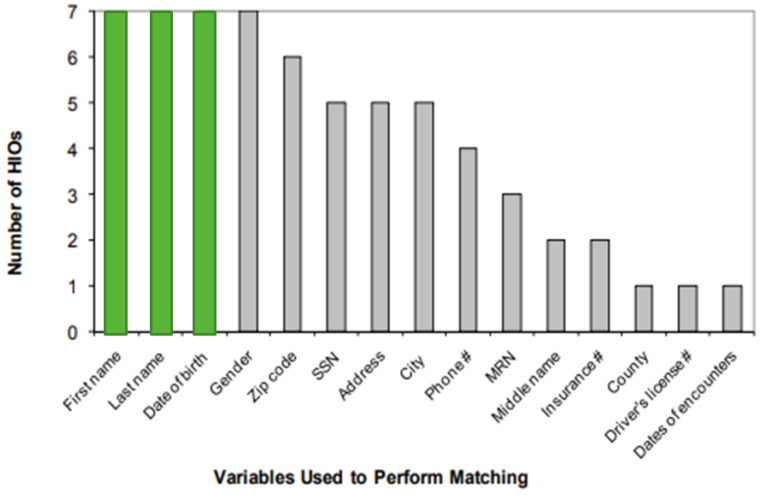
Figure 6-1. Frequency of Use of Matching Variables Across HIOs



NOTE: MRN = medical record number; SSN = social security number.

Kansas City Registry (+ABO/Rh)

Figure 6-1. Frequency of Use of Matching Variables Across HIOs



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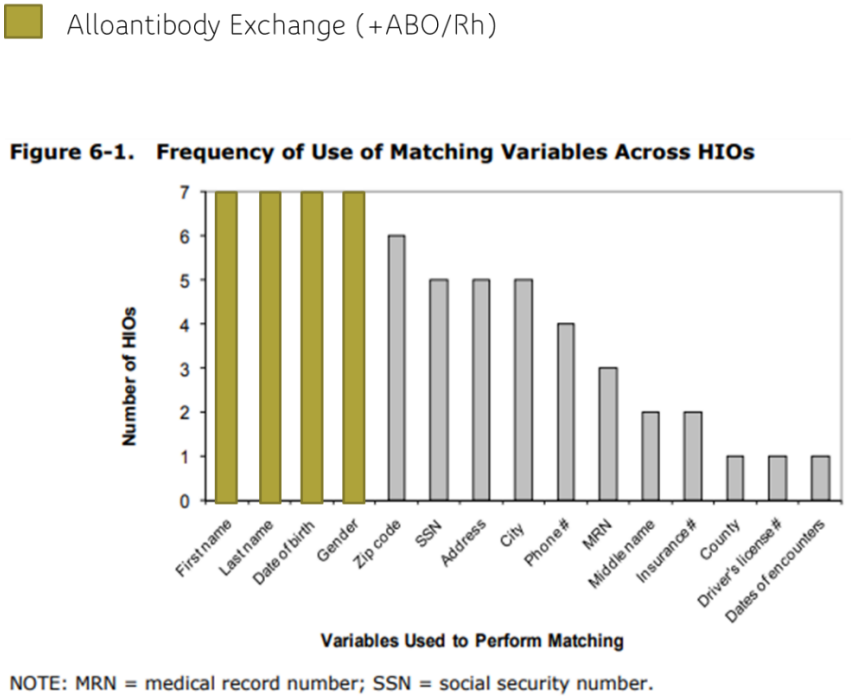

Figure. List of patient identifiers used in (top) surveyed health information organizations (HIOs), (middle) Kansas City Alloantibody Registry, (bottom) Alloantibody Exchange. See https://archive.healthit.gov/sites/default/files/patient-matching-white-paper-final-2.pdf

Linkage between patients occurs in the Alloantibody Exchange through automated and manual processes. Automated linkage of patients occurs with input from the six identifiers. Manual linkage is permitted by authorized individuals. This manual process is helpful in cases where patients may change ABO/Rh (e.g., bone marrow transplant) status or last name (e.g., marriage), for example.

Health systems may have a unified patient medical record with individual sites employing multiple blood bank information systems. In this situation, shared medical record numbers will also automatically link patients. The Alloantibody Exchange will setup this condition for patient linking with the health system.

An important consideration for the evaluation of patient linkage includes the consequences of false positive and false negative linkage. False positives linkages occur when two records belonging to different patients are linked. In this scenario, a patient has the potential to receive over-matched blood, which is generally not harmful. The Alloantibody Exchange will provide the source of the alloantibody, allowing users to contact their blood bank colleagues as needed. False negative linkages occur when two records belong to the same patient, but they are not linked in the Alloantibody Exchange. In this scenario, the Alloantibody Exchange is no worse than the current system.

5.4 Does HIPAA permit the disclosure of PHI to the registry?

Yes. HIPAA permits the disclosure of protected health information (PHI) for the treatment activities of a healthcare provider according to 165.506(c)(2), “A covered entity may disclose PHI for treatment activities of a healthcare provider”. This quote is taken from HIPAA Administrative

Simplification – Regulation text as amended through March 26, 2013, page 84.) Also see "Be the Match", a non-profit organization involved in bone marrow donations including PHI related to HLA data.

5.5 Do patients need to sign informed consent to enter the registry?

Patients do not need to sign a separate informed consent to have their antibody data shared with the registry. Patients have already consented for treatment/transfusion at the care site. Implicit in this consent is that the care site will provide a safe blood product for transfusion. The safest blood product cannot be provided without knowledge of the patient's red blood cell antibody history.

5.6 Will standardized antibody identities be used?

The Alloantibody Exchange supports the ISBT antibody standard. This standard is also used in TRIX, a European antibody exchange. The list of antibodies is available on request or through the API.

We can help sites to map their alloantibodies to the ISBT standard if they do not already. We have significant experience in data mapping within our team including large scale laboratory result mapping and the mapping of alloantibodies for multi-site projects.

- https://pubmed.ncbi.nlm.nih.gov/28505339/
- https://pubmed.ncbi.nlm.nih.gov/32061102/
- https://pubmed.ncbi.nlm.nih.gov/35713605/
- https://pubmed.ncbi.nlm.nih.gov/34871342/
- https://pubmed.ncbi.nlm.nih.gov/30427537/

5.7 Do accreditation organizations (e.g., CAP) require blood banks to review a patient's historical alloantibodies (e.g., antibody screen results)?

Yes. The College of American Pathologist (CAP) checklist item TRM 40300 (Historical Record Check) states ABO, Rh, and antibody screen test results are compared against results of the same tests recorded previously to detect discrepancies and identify patients requiring specially selected units. This checklist item can be carried out by a validated computer system, which typically reviews records internal to a healthcare system. Alternatively, qualified personnel can perform a manual review. The ability of the check to be performed by a computer was viewed by the CAP Transfusion Medicine Checklist committee as a time saver for blood banks.

5.8 How did this project begin?

Our project started from conversations between Dr. Karen Quillen (Boston University), Dr. Christopher Tormey (Yale), and Dr. Jeanne Hendrickson (Yale) to reduce delayed hemolytic transfusion reactions. They contacted Dr. Ronald "George" Hauser to consult on the project. He incorporated "Transfusion Antibody Exchange Inc." in January 2017. In April of 2017 they received 501(c)(3) non-profit status. At that time, they conceived of a system like NPAR, which they realized later that year would be difficult to implement. In late May of 2019, Dr. Tormey reviewed a paper on TRIX, and in a subsequent review article, Dr. Tormey and Dr. Hauser elaborated in an editorial on how to improve upon that system for a

United States audience. Unlike TRIX, our integrated blood bank design does not need standalone software to interact with the registry. Additional software is a barrier to adoption by blood banks. Our editorial was published in *Transfusion* in August of 2019.

5.9 Will the Food and Drug Administration (FDA) require a product review?

To our knowledge, the FDA does not require an unsolicited review of this project prior to vendor implementation of compatibility with the Alloantibody Exchange. The FDA may, at any time, ask for further information.

Vendor concern about the potential review appears to vary. The registry is willing to assist in the preparation of documents for such a review.

5.10 Do you support interfaces with Common Well Health Alliance and Care Quality?

We currently do not have an interface to these health information exchanges. CommonWell exchanges clinical notes in Consolidated-Clinical Document Architecture (CCDA) format. It also appears to contain significant fees associated with its use including a one-time Certification and Onboarding fee of $50,000, membership dues ($2,500), and service adopter fees ($20,000).

5.11 How often will the system update?

We update at data at least once a day.

5.12 How can we get started?

Click “Schedule a Meeting at the top of alloantibody.org.

6 About the Authors

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