

**Briefing Paper**

**Guidance for ABO Subtyping Organ Donors for Blood Groups A and AB**

*OPTN/UNOS Operations and Safety Committee*

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# Guidance for ABO Subtyping Organ Donors for Blood Groups A and AB

<i>Affected Policies:</i>	<i>N/A</i>
<i>Sponsoring Committee:</i>	<i>Operations and Safety</i>
<i>Public Comment Period:</i>	<i>January 22, 2018 –March 23, 2018</i>
<i>Board of Director's Date:</i>	<i>June 11-12, 2018</i>

## Executive Summary

The OPTN/UNOS Operations and Safety Committee (the Committee) has updated the Guidance for ABO Subtyping Organ Donors for Blood Groups A and AB, originally developed by the Committee and approved by the OPTN/UNOS Board of Directors in June 2011.

Since the original publication, the Committee sponsored major revisions to ABO policies that were approved by the OPTN/UNOS Board of Directors and were implemented in June 2016. During that process, the Committee identified the need to revise the subtyping guidance, as many questions emerged related to subtyping. Questions and identified issues include lab result nomenclature, results interpretation, and incomplete knowledge of policy requirements.

In addition, the revised Kidney Allocation System (KAS) went into effect in December 2014. It eliminated variances (including subtyping variances). KAS put use of subtyped deceased donors into policy to help promote greater access to kidneys for blood type B candidates. Allocation of kidneys using subtyped donors has increased. Pre-KAS there were 19 transplants (0.2% of all kidney transplants) using subtyped donors for blood type B candidates. Post-KAS (year 2) that number rose to 168 (1.4% of all kidney transplants).

The revised guidance document is one part of several educational efforts to assist members with subtyping. Nearly a quarter of OPOs had a subtyping issue cited on their last site survey. Professional Education developed a subtyping e-learning module in response to these concerns. The guidance document is cited as a resource. It needs to be updated to complement the efforts aimed at improving compliant subtyping practices and reporting.

Changes made to the guidance document include:

- Updated OPTN Policy references
- Amended information about special considerations such as neonates
- Updated additional complementary resources
- Revised structure and addition of key points
- Modified language to read more as a plain language document

## What problem will this resource address?

Guidance for ABO Subtyping Organ Donors for Blood Groups A and AB was developed and approved by the Board of Directors in June 2011. Since the original publication, the Committee sponsored major revisions to ABO policies that were approved by the OPTN/UNOS Board of Directors and were implemented in June 2016. During that process, the Committee identified the need to revise the subtyping guidance, as many questions emerged related to subtyping. Questions and identified issues include lab result nomenclature, results interpretation, and incomplete knowledge of policy requirements.

In addition, the revised Kidney Allocation System (KAS) went into effect in December 2014. It eliminated variances (including subtyping variances). KAS put use of subtyped deceased donors into policy to help promote greater access to kidneys for blood type B candidates. Allocation of kidneys using subtyped donors has increased. Pre-KAS there were 19 transplants (0.2% of all kidney transplants) using subtyped donors for blood type B candidates. Post-KAS (year 2) that number rose to 168 (1.4% of all kidney transplants).

The guidance document is still a valuable and requested resource. Members and UNOS staff identify subtyping issues. These issues include lab result nomenclature, results interpretation, and incomplete knowledge of policy requirements. Nearly a quarter of OPOs had a subtyping issue cited on their last site survey. Instructional Innovations developed a subtyping e-learning module in response to these concerns and the guidance document is cited as a resource in the module. It needs to be updated to support efforts to promote compliant subtyping practices and reporting.

The revisions also address questions that have recently been asked regarding other special circumstances such as subtyping neonates.

## Why should you support this resource?

This resource is being revised to address identified transplant community needs. It needs to be updated to remain relevant to the community. It was developed in consultation with relevant subject matter experts, stakeholders, and internal staff. It is a free resource to assist members with subtyping education and practices. The revised guidance is a tool that can assist with answering questions, reducing confusion, and promoting effective practices regarding subtyping requirements. The revised guidance also supports other efforts to increase subtyping and availability of organs to candidates with traditionally less access due to blood types. This resource augments other policy initiatives and resources such as ABO policy modifications, KAS, UNOS Connect e-learning modules, and the most recently approved Guidance for Transplant Program Participation in the Transplantation of Non-A1/Non-A1B (A2/A2B) Donor Kidneys into Blood Group B Candidates.

## How was this resource developed?

In 2008, a kidney donated from a living donor, whose ABO subtyping completed prior to the donation was reported as non-A<sub>1</sub> (e.g. A<sub>2</sub>), was transplanted into a blood type O recipient resulting in immediate graft rejection and organ failure. Repeat subtype testing of the donor indicated the actual subtype to be A<sub>1</sub>. In response to this event, the Membership and Professional Standards Committee (MPSC) requested that the Committee examine current OPTN policies to evaluate whether they are adequate to ensure that subtyping of both deceased and living donors is accurately determined and verified.

In April 2010, after data review and discussion, the Committee requested that a group of experts in the field of ABO typing and subtyping be formed to assist with the task. The ABO Subtyping Work Group was created and included representation from American Association of Blood Banks (AABB), a histocompatibility laboratory supervisor, a blood bank medical director, the OPTN/UNOS Histocompatibility Committee, representatives from OSC, and other transplant center and OPO personnel familiar with processes related to allocation of organs based on ABO subtyping. The OSC requested the Work Group to assist the Committee with understanding the current practice of laboratories performing subtype testing and centers requesting completion of such tests. They were also asked to assist in proposing requirements that would be consistent with current laboratory and transplant community practice for ABO subtype testing.

This group developed the guidance as part of their overall work on subtyping issues to address community education needs. Their work also resulted in a policy proposal approved by the OPTN/UNOS Board of Directors in November 2011. Policy changes were made to require two separate specimens and tests for subtyping as well as requiring two-person verification of results prior to reporting results to the OPTN Contractor.

The revised guidance was developed by a work group including members of the Committee. The revision efforts also included three additional subject matter experts: two members who have served on the Histocompatibility Committee and are currently lab directors, as well as one member who is a blood bank expert. The work group met monthly to review the current guidance, research content, discuss current issues, and review new developments in the field.

Support staff to the Operations and Safety Committee contributed to the review. Member Quality staff provided updated feedback on issues that they might still uncover during site surveys such as the need to emphasize that two out of three subtyping results cannot be reported or used for allocation. All tests must indicate the same result in order for use in allocation; otherwise, the donor must be allocated on primary blood type. Other internal support staff reviewed the document and made suggestions to incorporate more plain language.

The workgroup solicited pre-public comment feedback from the Minority Affairs, Kidney, and Organ Procurement Organization (OPO) Committees. The Kidney Committee provided suggestions to improve readability and organization. As a result, the key points are listed at the beginning of the document for those that might not read the entire guidance. The guidance was presented to the Minority Affairs Committee. No suggestions were made at their monthly call. OPO leadership received an advance copy but did not have pre-public comment feedback. The Operations and Safety Committee will continue to consult with these stakeholders during the public comment process as needed. A revised document was developed and submitted for full Committee consideration. The Operations and Safety Committee voted at their November 2017 monthly conference call to send the revised guidance document for January 2018 public comment consideration.

## **How well does this resource address the problem statement?**

This resource addresses the issues identified in the problem statement by doing the following:

1. Updated OPTN Policy references

The revised guidance removes language on kidney variance policy that is no longer in effect following the implementation of the new KAS. It also references organ-specific policies (e.g. kidney, kidney-paired donation, and liver). It also cites specific requirements from revised ABO policies that were amended for clarity.

2. Amended information about special considerations such as neonates

Questions have arisen about special yet rare circumstances. For example, members have asked how far back in time does the rule apply requiring a pre-red blood cell transfusion specimen. The Committee has discussed this question but has decided not to specify a timeline in policy or guidance but the guidance offers information on the red blood cell life cycle. It also raises other considerations such as subtyping in neonates. Neonates do not immediately express red blood cell antigens. Members are encouraged to develop relationships and consult with their blood bank. When there is concern that subtyping cannot be accurately conducted, the reasons must be documented and allocation must be based on primary blood type. Other issues known from site surveys are highlighted such as not using two out of three results to determine subtype.

3. Updated additional complementary resources

In 2011, this guidance was the sole OPTN resource. Since then, two UNOS Connect modules that include significant interactive content on subtyping requirements have been developed and released. These are referenced, as well as the recently approved guidance for transplant programs on managing the candidate side of titer monitoring.

4. Revised structure and addition of key points

The guidance has been reformatted to put the most important information first and move the more technical information towards the back. All key points are put in a summary statement up front. This is done to capture those who may have limited time or ability to read the entire document.

5. Modified language to read more as a plain language document

Concerns were expressed that of the information might be more technical than helpful to assist one of the intended audiences of front line OPO staff. Efforts were put in to make the language simpler. Both work group members as well as communication and policy staff reviewed and revised the content to incorporate plain language wherever possible.

The updates, additional guidance, plain language, and reformatting should benefit the transplant community and help increase compliance with subtyping policies as well as promote effective practices. This resource, along with others discussed, should help answer community questions and ultimately help promote application of allocation subtyping policies that aim to increase organ access for certain blood type candidates.

## **Was this resource changed in response to public comment?**

Yes, this proposed guidance was amended slightly post public comment. Some changes were made to the document organization and terms used. Other edits were made for clarity and to address further issues that have been observed with interpreting subtyping results.

This proposal went out for public comment during a 60-day period from January 22, 2018 to March 23, 2018. The OPTN/UNOS Kidney Transplantation and MPSC provided comments and supported the guidance document. The proposal passed on the consent agenda in all eleven regions with no additional comments. Other comments were posted by the Association of Organ Procurement Organizations (AOPO); American Society for Histocompatibility and Immunogenetics (ASHI); American Society of Transplantation (AST); American Society of Transplant Surgeons (ASTS) and North American Transplant Coordinators Organization (NATCO). All of these organizations supported the proposal.

The MPSC felt the actual variability between blood banks is not likely to change as a result of this guidance document, so the community may continue to be confused and commit errors when interpreting and reporting donor subtyping results. MPSC members who discussed the guidance did not have any consensus recommendations on some of the issues that cause questions (e.g. red blood cell transfusions). While the Committee felt that having more specifics or timelines might be helpful for OPOs to adopt into their protocols, they ultimately decided that the data do not exist to give more affirmative guidance and that it seemed appropriate to leave those decisions to OPOs, the blood banks, and the labs that they work with.

The Committee requested specific public comment feedback on the following:

*Is guidance sufficient for special considerations (red blood cell transfusions, neonates)? Do you need more detail or policy?*

- Comment: ASHI responded that the AABB technical manual states, “adult levels of ABO expression are generally present by age 2 to 4” (page 268, 19th edition). They are concerned that the proposal states that typing for non-A<sub>1</sub> based on lectin is sufficient after age 1. That discrepancy could be significant; however, if the blood bank representatives involved in drafting this proposal have no concerns, then ASHI would defer to their experience.

Response: The work group which included two laboratory directors and one blood bank subject matter expert had debated this exact recommendation during guidance development. Ultimately, it was decided not to use this recommendation due to varying interpretations, concerns over eliminating donor subtype ability by routinely using an upper age limit, and differing standards on manufacturer package inserts for anti-A<sub>1</sub> lectin. The guidance does not contain a definitive age limit for neonates but advises OPOs to consult with their blood banks and laboratories. Two examples of the package inserts are shown to demonstrate the variability in advice.

- Comment: The AST felt there are times when ABO subtyping is not considered accurate enough and should be avoided. These include after a blood transfusion is given to a particular donor and in neonates. The guidance is sufficient in this regard and provides an appropriate amount of information. It may be helpful, though, to spell out what should NOT be done, based on specific circumstances and label the section of the text as something similar to, “Do not perform ABO subtyping in the following conditions...” Sufficient detail and policy are not present, and we recommend greater clarification about what NOT to do rather than merely suggesting that one should consult a blood banking specialist in those circumstances, because then you open the door for heterogeneous recommendations.

The pediatric transplant community has particular interest regarding ABO guidance in determining subtyping methods for neonates. There is not consensus regarding testing timelines, interpretation of test results, or clinical decision algorithms.

Response: The Committee agreed with the AST suggestion to emphasize what not to do in subtyping. The content was edited and reorganized to highlight these points.

*Did we fail to address any other concerns?*

- The Kidney Committee unanimously agreed that there were no deficiencies in the guidance document, and that all updates were evidence-supported and well-organized.
- AOPO commented, “We have no related concerns that are not addressed in the updated guidance document.”
- NATCO commented, “The update is clear and no further detail is indicated.”

The Committee also received a question following a presentation of the guidance during a national webinar. A transplant hospital attendee mentioned a situation where subtyping had been performed post-allocation by a transplant hospital. This was after the OPO had reported subtyping to the OPTN and allocated an organ based upon two results did not conflict and were performed in accordance with OPTN subtyping policies. The OPO had obtained a non-A<sub>1</sub> result, however the transplant hospital obtained an A<sub>1</sub> result. It has been clarified by the OPTN that the third result would be considered a conflicting result and that subtype should not be used for allocation when this occurs. This issue was referred to the Committee for further evaluation.

The following specific changes have been made to the guidance document, post public comment:

- The term “type” replaces the term “group” throughout the document when referring to blood type because that is the term largely used in OPTN Policy and OPO discussions
- All of the “key points” remain at the beginning of the document but are not repeated throughout the various sections
  - The last key point is bolded and reworded to emphasize “what not to do” in response to public comment
  - An additional key point regarding caution not to confuse Rh results with subtype results is added following an OPO member suggestion
- Additional bullets on common issues are included for clarity
- An additional package insert language and citations are included to demonstrate variability
- Language to address “weak” results is edited for clarity
- A sentence is added to address when a transplant hospital conducts its own subtyping and obtains different results. This is considered a conflicting result and allocation must be performed on primary blood type.

The Committee met on April 11, 2018 in Richmond, Virginia, and briefly discussed the issue with an OPO and transplant hospital obtaining conflicting subtype results. The OPO subtyping policy was not written with this situation in mind. This situation will be further discussed by the Operations and Safety Committee’s Patient Safety Advisory Group. They will develop recommendations regarding needs for further guidance, education, operational instructions and policy clarification.

The Committee reviewed all public comments and made minor edits. The Committee voted unanimously (17 in favor-0 opposed) to send the guidance to the OPTN/UNOS Board of Directors for consideration at their June 2018 meeting.

## **Which populations are impacted by this resource?**

This guidance document augments existing efforts to promote sound subtyping practices that can widen organ offer access to some blood type B and blood type O candidates.

## **How does this resource impact the OPTN Strategic Plan?**

1. *Increase the number of transplants:* There is no impact to this goal.
2. *Improve equity in access to transplants:* There is no impact to this goal.
3. *Improve waitlisted patient, living donor, and transplant recipient outcomes:* There is no impact to this goal.
4. *Promote living donor and transplant recipient safety:* This guidance document originally developed and published in 2011 helps the transplant community understand the fundamentals of subtyping practices and terminology. The revisions will improve the transplant community's abilities to understand the importance of subtyping and to avoid incorrect results reporting.
5. *Promote the efficient management of the OPTN:* The revised guidance could help decrease questions and therefore decrease member and staff efforts involved in answering questions.

## **How will the OPTN implement this resource?**

This proposal will not require programming in UNet<sup>SM</sup>

Professional Education will monitor this proposal for educational needs. The impact to members suggests that an educational offering may not be necessary.

Updated guidance will be posted on the OPTN website.

## **How will members implement this resource?**

The overall fiscal impact will be minimal to all member types as this is a guidance document that might be used for staff training.

### **Transplant Hospitals**

The fiscal impact to transplant hospitals will be minimal. They might use the updated tool as part of staff training.

### **OPOs**

The fiscal impact to OPOs will be minimal. They might use the updated tool as part of staff training.

### **Histocompatibility Laboratories**

The fiscal impact to histocompatibility laboratories will be minimal. They might use the updated tool as part of staff training.

## **Will this resource require members to submit additional data?**

No, this proposal is a guidance document and does not require additional data collection.

## **How will members be evaluated for compliance with this resource?**

This proposal is a guidance document does not require evaluation for compliance.

## **How will the sponsoring Committee evaluate whether this resource was successful post implementation?**

Although the Committee will not formally monitor this guidance document, support staff will be queried regarding the frequency and type of observed subtyping questions and issues among members. Staff will also review data from the subtyping course available on UNOS Connect as well as monitor website hits accessing the guidance. This will help determine whether the existing resources are being used, whether they are helpful, or whether additional steps need to be taken to assist with subtyping requirements and promotion of increasing access to disadvantaged blood type candidates.



## Guidance Document

All the language in the guidance document below is proposed new language; underlines have been omitted for easier reading.

1 **RESOLVED**, that the guidance document entitled *Guidance for ABO Subtyping of Organ Donors*  
2 *for Blood Types A and AB*, as set forth below, is hereby approved, effective June 12, 2018.

3

## 4 **Guidance for ABO Subtyping Organ Donors for Blood Types** 5 **A and AB**

6

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## 26 Summary

27 The “Guidance for ABO Subtyping Organ Donors for Blood Groups A and AB” was originally developed in  
 28 2011. This revised guidance contains updates to OPTN Policy references and additional resources. It  
 29 provides amended information about special considerations such as neonates. The guidance document is  
 30 one of several resources to assist OPTN members with subtyping questions and practices. The goal is to  
 31 continue expanding organ access for candidates through transplanting non-A<sub>1</sub> donors.

## 32 Key Points

- 33 • Persons who are in primary blood groups (also known as blood type) A and AB can be further  
 34 tested to determine a more specific subgroup (also known as a subtype).
- 35 • Subtypes for blood type A include A<sub>1</sub>, A<sub>2</sub>, A<sub>x</sub>, A<sub>int</sub> and others, but the most common is A<sub>1</sub>.
- 36 • If the donor is **not** subtype A<sub>1</sub>, it means they have less A antigen on their red blood cells (RBCs)  
 37 and organs, which allows them to donate to recipients outside of their primary blood type.
- 38 • OPTN Policies refer to all subtypes that are not A<sub>1</sub> as non-A<sub>1</sub>. Therefore, a donor who is primary  
 39 blood type A and subtyping results show that the donor does not have the A<sub>1</sub> subtype is referred  
 40 to as having blood type A, non-A<sub>1</sub>.
- 41 • When reporting to the OPTN Contractor, A<sub>2</sub> is used as shorthand for any blood type A subtype  
 42 other than A<sub>1</sub> (i.e. non-A<sub>1</sub>, negative for A<sub>1</sub>). A<sub>2</sub>B is used as shorthand for any blood type AB  
 43 subtype other than A<sub>1</sub>B (i.e. non-A<sub>1</sub>B, negative for A<sub>1</sub>B).
- 44 • Perform subtyping before the donor receives any RBC transfusions.
- 45 • **Any** blood transfusion can affect the accuracy of subtyping results despite the donor's  
 46 hemodilution status.
- 47 • OPOs and transplant hospitals should consult with their blood banks to consider special issues  
 48 that might impact results (such as RBC transfusion and neonates) and follow their  
 49 recommendations.
- 50 • It is never acceptable to use two out of three results for a subtype determination. If there are any  
 51 discrepant results, then *only* primary type can be used for allocation.
- 52 • There are no standards for how laboratories should report ABO subtypes. The International  
 53 Society for Blood Transfusion Committee on Terminology for Red Cell Surface Antigens has  
 54 created a standardized numerical format for reporting red cell subtypes, but this is not suitable for  
 55 everyday communication. Popular terminology often uses terms: A<sub>1</sub>, A<sub>2</sub>, A<sub>1</sub>B, and A<sub>2</sub>B. OPTN  
 56 Policies use the term non-A<sub>1</sub> for any subtype that is not A<sub>1</sub>.
- 57
- 58 • When reviewing results, be cautious not to confuse the Rh factor result with the ABO subtype  
 59 result.
- 60
- 61 • Routine testing determines the presence or absence of the A<sub>1</sub> antigen only. It does not determine  
 62 the actual sub-type. Typing is either positive for A<sub>1</sub> or negative for A<sub>1</sub>. This is why the term A, non-  
 63 A<sub>1</sub> is used for a donor that does not have the A<sub>1</sub> antigen.
- 64
- 65 • The absence of A<sub>1</sub> does not necessarily equal A<sub>2</sub> due to the existence of multiple subtypes.
- 66 • **Subtyping results must not be reported to the OPTN Contractor or used for organ**  
 67 **allocation when:**

68 The results do not match or indicate the same result. It is never acceptable to use two out of three results.  
 69 If one result is different, then only primary type must be reported and used for allocation.

- 70           • Pre-RBC transfusion specimens are not available for initial and/or confirmatory testing of  
71           subtyping.

## 72    **What is required by OPTN Policy?**

73    The OPTN has several policies that allow the transplantation of donors who have a non-A<sub>1</sub> subtype into  
74    candidates of other blood types. These policies include:

- 75           • *Policy 9.7.B: Points Assigned by Blood Type*  
76           • *Policy 8.5.D: Allocation of Kidneys by Blood Type*  
77           • *Policy 13.7: OPTN KPD Screening Criteria*

## 78    **Requirements for Blood Type Determination**

79    Clinical policies and information about how to perform transplants that are primary blood type  
80    incompatible but are done with certain subtyping results are determined by the transplant program. When  
81    these types of transplants are planned, the OPTN has policies about how to determine a subtype for a  
82    deceased donor (*Policy 2.6.B: Deceased Donor Blood Subtype Determination*) or a living donor (*Policy*  
83    *14.5.B: Living Donor Blood Subtype Determination*). OPTN policies mandate that all deceased and living  
84    donors, as well as candidates, be blood typed on two separate occasions, and these rules apply to  
85    subtyping as well. By definition, this means the blood must:

- 86           1. Be drawn on two separate occasions  
87           2. Have different collection times  
88           3. Be submitted as separate samples  
89           4. Have results indicating the same blood type

## 90    **Requirements for Blood Subtype Determination**

91    If testing determines that a deceased donor's primary blood type is A, then you must also subtype that  
92    donor. The only exception to this rule is when no blood samples are available before the donor is given  
93    red blood cell (RBC) products. Subtyping is optional for living donors and blood type AB deceased  
94    donors. If the donor is found to be blood type A, non-A<sub>1</sub>, a second subtype must be drawn (different draw  
95    time, different draw occasion) for confirmation. It is important to note that:

96    ***All subtyping for deceased or living donors must be completed before the donor receives any red***  
97    ***blood cell transfusions.***

## 98    **What is a Subtype?**

99    We are all familiar with the blood types A, B, O and AB.

100   Enzymes that add sugars to form either the type A or the type B antigens determine the blood type.  
101   Individuals who are blood type O lack the enzyme to add those sugars and have an H precursor  
102   substance that gives them their O blood type. You can find blood type antigens on many cells, including  
103   RBCs and cells inside blood vessels of all vascular organs that are routinely transplanted. The reason  
104   these blood type antigens are clinically important in transplantation and blood transfusion is that  
105   individuals have naturally occurring antibodies to blood type antigens they do not have. Those antibodies  
106   are termed isoagglutinins. Isoagglutinins are antibodies that can react with the blood type antigens on the  
107   cells of the organ being transplanted. For instance, blood type O individuals have A and B isoagglutinins,  
108   blood type B individuals have A, blood type A individuals have B, and blood type AB individuals have no  
109   isoagglutinins.

110   When an incompatible transplantation takes place, such as transplanting a blood type B organ into a  
111   blood type O individual, that organ would likely be rejected immediately. The rejection occurs because the  
112   B isoagglutinins in the blood type O recipient react with the B antigens on the vessels of the transplanted  
113   organ.

114 Eighty percent of blood type A and AB persons are subtype A<sub>1</sub> and A<sub>1</sub>B, respectively. The other 20% of  
115 these blood types are subtype non-A<sub>1</sub>. Most often the subtype is A<sub>2</sub> (or A<sub>2</sub>B), but occasionally it may be a  
116 more rare subtype like A<sub>3</sub>, A<sub>int</sub>, etc. Blood type A, non-A<sub>1</sub> individuals express only about 20% of the  
117 normal level of type A antigen on their RBCs and organs. A<sub>1</sub> subtyping is not routinely performed in  
118 compatibility testing; however, some patients and donors may be identified as A, non-A<sub>1</sub> or AB, non-A<sub>1</sub>B  
119 in the course of routine blood bank typing because they have anti-A<sub>1</sub> antibody in their plasma (1-8% of  
120 type “A, non-A<sub>1</sub>” and 25% of type “AB, non-A<sub>1</sub>B” persons<sup>1</sup>).

## 121 Why does it matter?

122 An ABO subtype (A<sub>1</sub> vs. A, non-A<sub>1</sub>) allows organs to be allocated to additional candidates for both  
123 deceased and living donor transplants. A person who is primary blood type A normally could not donate  
124 their organ to a candidate who is blood type B. If the person who is blood type A also has a non-A<sub>1</sub>  
125 subtype, then they could possibly donate a kidney to a person who is primary blood type B (or O),  
126 depending on other factors.

## 127 When should we use and not use subtyping results for allocation?

128 Subtyping results can only be used when both samples were obtained before any RBC transfusions, and  
129 subtype testing results (both initial and confirmatory) are clear, valid, and match each other. You must not  
130 use subtype testing if you question the validity or interrelation of the ABO subtype testing results or if pre-  
131 transfusion specimens are not available for both initial and confirmatory subtyping testing. In these  
132 situations, the safest approach is to allocate the organs based on the donor’s primary blood type only. It is  
133 inconsistent with OPTN Policy to use two out of three results if even one of the results does not indicate  
134 the same subtype. Conflicting results include those from transplant hospital or another lab if reported to  
135 the OPO prior to or during allocation.

## 136 What can interfere with test results?

137 If a donor recently received an RBC transfusion, the A<sub>1</sub> subtyping result may be inaccurate and therefore  
138 you should obtain all subtyping samples before RBC transfusions occur. Plasma and platelet transfusions  
139 do not affect RBC typing results.

140 For example, if you gave an organ donor an emergency blood type O RBC transfusion before you  
141 collected the subtyping specimen, then the A<sub>1</sub> typing could be inaccurate. Experiments with *in-vitro*  
142 mixtures of blood type O and A<sub>1</sub> RBCs suggest that A<sub>1</sub> typing could become falsely negative if more than  
143 75% of the RBCs are type O<sup>2</sup>. Since it is difficult to estimate precisely how many units of blood type O  
144 RBCs need to be given to affect the efficacy of the test (as this depends on the patient’s size, amount and  
145 rate of blood loss, timing of the transfusions and intravascular volume status) you must obtain all samples  
146 before RBC transfusion.

147 In the event that the potential donor received a RBC transfusion in the past (as opposed to the current  
148 hospitalization), then OPOs and transplant hospitals must determine the time, if any, since transfusion  
149 that they consider safe to perform subtype testing. Currently no data identifies how many blood type A  
150 RBC transfusions it may take to change the subtyping result from non-A<sub>1</sub> (A<sub>1</sub> negative) to A<sub>1</sub>. Transfused  
151 RBCs have a half-life of 30 days and the “youngest” RBCs in the blood bag would circulate for up to 120  
152 days.

## 153 Infants and Neonates

154 Neonates and infants do not fully express their ABO antigens. Manufacturers of anti-A<sub>1</sub> lectin also have  
155 varying warnings in their package inserts such as “results should be interpreted with caution in infants

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<sup>1</sup> John Roback et al., eds., AABB Technical Manual 17th edition (Bethesda, MD: AABB, 2008).

<sup>2</sup> Glenn Ramsey et al., “Abstract Presentations from the AABB Annual Meeting and CTTXPO, Baltimore, MD, October 9-12, 2010,” Transfusion 50 (2010): 168A.

156 less than one year of age”<sup>3</sup> and “cord blood and specimens from infants cannot be accurately typed with  
157 anti-A1 lectin since the A1 antigen is not fully developed on red blood cells until the age of six months”<sup>4</sup>.

158 Umbilical cord blood is another consideration for neonates and it is generally recommended that you not  
159 use cord blood cells to determine primary ABO or subtype. OPO and transplant programs should consult  
160 with their blood banks to consider this issue and adjust practices accordingly.

## 161 What do the results say?

162 The wide range of terminologies used by blood banks and manufacturers to describe subtyping results is  
163 confusing. It is particularly confusing when transplant programs or OPOs need to identify the accurate  
164 subtyping for transplant compatibility. As mentioned earlier, the actual subtype test looks for whether a  
165 blood type A or AB donor’s RBCs react with anti-A<sub>1</sub> lectin. The following tables provide subtype  
166 terminology used by the OPTN, along with synonymous terms that you may also see on typing results.

### 167 Blood Type A Subtype Reporting Terminology:

OPTN	A <sub>1</sub>	A, non-A <sub>1</sub>
Other terms used	A <sub>1</sub> positive	A <sub>1</sub> negative
	A <sub>1</sub> reactive	Non A <sub>1</sub>
	-	A <sub>2</sub>

168

### 169 Blood Type AB Subtype Reporting Terminology:

OPTN	A <sub>1</sub> B	AB, non-A <sub>1</sub> B
Other terms used	AB, A <sub>1</sub> positive	AB, A <sub>1</sub> negative
	AB, A <sub>1</sub> reactive	AB, A <sub>1</sub> non-reactive
		A <sub>2</sub> B

170

171 When reporting to the OPTN Contractor, A<sub>2</sub> is used as shorthand for any blood type A subtype other than  
172 A<sub>1</sub> (i.e. non-A<sub>1</sub>, negative for A<sub>1</sub>). A<sub>2</sub>B is used as shorthand for any blood type AB subtype other than A<sub>1</sub>B  
173 (i.e. non-A<sub>1</sub>B, negative for A<sub>1</sub>B).

## 174 Common issues in subtype reporting:

175

176 Some of the most common issues found in reviewing and reporting subtype results include:

- 177 • Unclear subtyping results
- 178 • Uncertainty whether the term negative or positive refers to Rh factor or subtype
- 179 • Discordant results (results that do not seem to indicate the same subtype)
- 180 • Not knowing the time of the last transfusion
- 181 • Not knowing if the donor had a transfusion at a prior health care facility or in transit

## 182 What should I do when I am not sure how to report results?

183 A patient’s age, transfusion status, and testing methods of the laboratory can all affect the efficacy of the  
184 test. If you have questions about how to interpret subtyping results or whether testing was performed

<sup>3</sup> Anti-A1 Lectin Package Insert, Core Diagnostics LTD.

<sup>4</sup> IFY H241Dolichos-A1 Lectin Anti-A1 Ver 1.0 2015, Hemo Bioscience

185 accurately, your safest approach is to report and allocate the organs based on the donor’s primary blood  
186 type and not to consider subtyping. For all blood type A donors, the host OPO must document either that  
187 subtyping was completed or the reason it could not be completed.

## 188 **More technical information about subtyping**

189 Determination of a donor’s A<sub>1</sub> RBC subtype is performed with anti-A<sub>1</sub> lectin, an FDA-approved test  
190 reagent. Lectins are non-antibody proteins, which bind with high specificity to a particular carbohydrate  
191 structure. Anti-A<sub>1</sub> lectin is extracted from the lentil-like seeds of the plant *Dolichus biflorus* (horse gram).  
192 Anti-A<sub>1</sub> lectin binds to the A<sub>1</sub> carbohydrate and agglutinates A<sub>1</sub> or A<sub>1</sub>B RBCs in a suspension. When type  
193 A or AB RBCs are not agglutinated by anti-A<sub>1</sub> lectin, the RBCs are negative for A<sub>1</sub>.

194 Strictly speaking, there is no (non-DNA) test for the A<sub>2</sub> antigen— only a test for whether the A<sub>1</sub> antigen is  
195 present or not. Therefore, when a blood type A donor does not test positive for A<sub>1</sub> the result is called an  
196 A, non-A<sub>1</sub>. Other type A variants exist. One type A variant called A<sub>int</sub> (intermediate) is partway between A<sub>1</sub>  
197 and A<sub>2</sub> in strength and can give weak reactions in A<sub>1</sub> typing. A<sub>int</sub> is found most often in blood type A  
198 African-Americans (5-8%). All of the other type A variants, such as A<sub>3</sub>, A<sub>end</sub>, and A<sub>x</sub>, are rarely seen  
199 (<1:1000 type A persons) and are much weaker in expression overall than type A, non-A<sub>1</sub>, and therefore  
200 presumably would be equivalent to non-A<sub>1</sub> for organ-transplant purposes. Laboratories using anti-A<sub>1</sub> lectin  
201 testing should follow the manufacturer’s directions carefully.

202 From the perspective of transplant safety, **any** reaction with anti-A<sub>1</sub> lectin, when performed according to  
203 the manufacturer’s directions, should be regarded as positive or reactive for A<sub>1</sub>. This would not be  
204 considered safe for potential use as a non-A<sub>1</sub> donor by the transplant program, unless proven otherwise.  
205 OPO and transplant programs should consult with their blood banks if needed regarding guidance or  
206 additional questions.

## 207 **Who can help?**

208 Your local blood bank is a great resource. OPOs and transplant hospitals should establish a relationship  
209 with them as they can advise on protocol development and answer questions. Other national groups such  
210 as the American Association of Blood Banks (AABB) (<http://www.aabb.org/Pages/default.aspx>) have  
211 additional resources.

## 212 **Resources to learn more**

- 213 • UNOS Connect, the location for all your transplant education materials, is available at:

214 <https://unosconnect.unos.org/>

215 Two courses are available on UNOS Connect that relate to subtyping:

- 216 • ABO Subtyping (SFT 116)
- 217 • ABO Typing and Subtyping (SYS104)

- 219 • OPTN/UNOS “Guidance for Transplant Program Participation in the Transplantation of Non-A1/Non-  
220 A1B (A2/A2B) Donor Kidneys into Blood Group B Candidates” is available at:

221 <https://optn.transplant.hrsa.gov/resources/guidance/>

- 222 • You can also find resources organized by specific organ types:

223 [Kidney and pancreas](#)

224 [Liver and intestine](#)

225 [Heart and lung](#)

226 [Vascularized composite allograft](#)

227 #