

Tissue Tracking Failures and Lessons Learned: Hope for the Future



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Note: The opinions expressed by the author in this manuscript are not necessarily representative of the membership of the AATB.

Introduction

Imagine you work in the surgical suite of a hospital, in a transfusion service that handles tissue, or possibly in an ambulatory surgery center or in a dentist's office. You are the health care professional receiving a few boxes containing a dozen tissue allografts. Some are refrigerated, some are frozen, and a few are shipped without coolant and stored at ambient temperature. You inspect the different shipping boxes for damage and there is none. You verify that the refrigerated and frozen shipments are received before the date and time posted on the external box label. This is the expected expiration of the refrigerant used to maintain the controlled environmental temperature required for those graft types during transport. Since this expiry was determined using a validated procedure and specific, qualified shipping boxes, you are not obligated to place a thermometer inside these shipments to check the temperature on arrival¹.

These two boxes are opened first. The contents are cold in the refrigerated shipment and you remove each graft and inspect the integrity of each individual allograft package. You grab your bar code scanner and move it briefly over each universal machine-readable label and, voilà, the grafts are checked in to your inventory and receiving steps are all documented in the facility's software data base. It's unique identifier is documented as well as what was received, when it was received, and by whom. An assurance of the contents good condition are also recorded as is the day and time when placement into your storage occurred. Similar steps are carried out for the frozen grafts and for the few shipped at ambient temperature. You are finished in a matter of a few short—but productive—minutes and you begin other work.

If cryopreserved allograft heart valves were received at a hospital, the same simple steps would be followed but you would need to wear protective thermal gloves when handling these tissue grafts. When any of these allograft types are retrieved from inventory for use, or when some other disposition occurs (i.e., re-distribution to another facility, appropriately discarded, returned), this simple scanning movement is performed again and steps related to tracking are automatically recorded after you activate the appropriate file. This process may also be linked to billing codes and/or reimbursement codes.

Imagine that this scenario can occur throughout the world. It involves allografts shipped from registered tissue establishments located in any nation. Is this a futuristic impossibility and only a vision from a Star-Trek episode? Hardly. Today, this easy check-in and tracking of tissue allografts is not currently possible in North America, even though universal machine-readable bar coding is used worldwide to purchase and track inventory, sales, and other movements of a variety of food and additional items (e.g., airline luggage, boarding passes, rental cars, mail, etc). One such system, known as ISBT 128 coding, is becoming commonplace for tracking human-derived transfusable products (i.e, red blood cells, platelets, cryoprecipitate, and plasma for transfusion) so why is it not being used for human-derived transplantable tissue grafts?

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Standards and Regulations

Standards abound and regulations exist to facilitate tracking cells and tissues for transplant, implant, infusion, or transfer from time of donation through use in a recipient or other final disposition. These will not be detailed here but the following standards-setting professional organizations provide guidelines to support a trace-forward and trace-backward system: AABB, AATB, AORN, CAP, EBAA, FACT/JACIE, NMDP, and The Joint Commission. A few other accreditation organizations in the United States (US), namely AAAASF and AAAHC, could address tracking allografts but have not yet included it in their standards; however, the latter organization is keen on adding it. Regulations provide a level of compliance to tracking but oversight can be limited.

The State of New York has laws for [tissue banks](#) that include transplant centers in the state so the chain of custody to final disposition is covered but is only applicable to their licensed facilities. Additionally, a dozen states have some laws for tissue banking but these laws are not as detailed in regard to tracking requirements so they offer little value. Federal regulations promulgated by US FDA/CBER are useful and require tracking by tissue establishments to the consignee (to whom the tissue graft was distributed) but only encourages tracking to the recipient. The reason is that the agency does not normally have jurisdiction over end users and to expect tissue banks to control compliance by end users to tracking is also not practical. FDA does have jurisdiction over end users and consignees in the event of a tissue recall when it becomes a public health safety concern. CMS could close this gap in the US if they required tracking allograft use to its recipients but this has yet to be proposed in rulemaking.

Health Canada's regulations require that every registered tissue establishment and transplant establishment must ensure tracking using the unique identification code of each allograft they handle. Notice that the Canadian regulations are applicable to stakeholders supplying the tissue as well as those entities using them. A full report on cell and tissue coding and traceability in North America will be available soon².

Tissue Tracking Failures during Recalls

There have been true tests of tracking systems during allograft tissue recall events. Significant improvements do not appear to have occurred over the past twenty years when the following examples are reviewed. In all events that follow, tissue banks were able to track 100 percent of the distributed allografts to the consignees to whom they were sent. Tracking by the consignees was good, but less effective. What is not being tracked is how quickly (or slowly) successful tracking was accomplished. Brief summaries are provided for five examples²:

- **#1: 1991 - HIV (HTLV-III)**
 - Discovery that 1985 donor tested seronegative but was infected with HIV
 - 53 tissue grafts (+ 4 organs) made available
 - 5 tissue grafts (> 9 percent) unaccounted for by hospitals that received them
- **#2: 1992 - HCV**
 - More sensitive HCV 2.0 Ab test made available in 1992 and 1,142 past donors retested by a tissue bank (471 deceased; 671 living); 2 donors tested repeat reactive; 3 recipient seroconversions traced to 1 donor
 - 33 grafts made available; 29 grafts were distributed
 - 2 grafts (≈ 7 percent) unaccounted for by 2 hospitals; these were skin grafts
- **#3: 2002 - Process Validation Related**
 - 2,661 donors; 7,856 tissues recalled
 - 359 (≈ 4.6 percent) were unaccounted for by hospitals or there was no response to recall notifications sent; 2,013 surgeon notifications, 764 hospital notifications were made
- **#4: 2005/2006 - BTS related***
 - ≈ 28,000 tissue grafts/devices made available from 6 tissue banks
 - ≈ 700 tissue grafts (2.5 percent) unaccounted for by end users

- ≈ 1,300 tissue devices (4.6 percent) unaccounted for by distributors & end users US FDA/CDRH tissue device recall = Class III - little risk to public health
- *numbers improved over time until recalls closed
- **#5:** 2006 - Chryseobacterium meningosepticum
 - 4,805 soft tissue grafts (tendons/ligaments) recalled
 - Six grafts unaccounted for at four facilities until FDA assisted with resolve resulting in 100 percent disposition of grafts (0 percent)
 - Involved ≈ 750 hospitals in Canada, Mexico, and US

Initiatives

There are a number of initiatives in place or in development to address universal coding of cells and tissues to enhance traceability and recipient safety. In the US, the AATB formed the North America Tissue Technical Advisory Group (NATTAG) in 2005. NATTAG was a combination of AATB and ICCBBA (International Council for Commonality in Blood Banking Automation, Inc.) working together to evaluate ISBT 128 use in the US. The purpose of NATTAG was to advise ICCBBA of the ongoing development of the ISBT 128 standard, to provide a focus for standardization of terminology, to design label templates that meet regulatory requirements, to produce a consensus document, and to provide advice and support to facilities introducing ISBT 128. The membership is composed of representatives from [tissue banks](#) across the US and Canada, and liaisons from FDA, Health Canada, Korea, and the European Association of Tissue Banks (EATB). The benefits of standardization are identified as: 1) improved safety (users understand products despite language barriers); 2) enhancement to traceability (disparate computer systems can read the same labels); and, 3) marketability (labels may be read and interpreted globally)². In Europe, Directive 2004/23/EC of the European Parliament and of the Council (31 March 2004) describes in Article 25 coding of information, that: “1) Member States shall establish a system for the identification of human tissues and cells, in order to ensure the traceability of all human tissues and cells; and 2) the Commission, in cooperation with the Member States, shall design a single European coding system to provide information on the main characteristics and properties of tissues and cells.”³

Since this publication, coding of tissues and cells has been extensively considered. At this stage no final decision on the shape and management of the coding system has been made. It’s been described that the shaping of the European single coding system should make good use of already established initiatives and tools, and integrate these where possible⁴. ISBT 128 is being considered but is not the only system⁵. National and international cellular therapy product associations (AABB, FACT, JACIE, and NMDP) now require the use of ISBT 128 terminology but there have been discussions regarding the use of the labeling/bar codes. These tissue- and cell-related advisory groups to ICCBBA have been deliberating over the ISBT 128 terminology and coding in hopes of universal agreement and standardization: International Cellular Therapy Coding and Labeling Advisory Group (CTCLAG), Europe Tissue Technical Advisory Group (ETTAG), Eye Bank Technical Advisory Group (EBTAG), and NATTAG⁶. The World Health Organization (WHO) also endorses the “implementation of quality systems including traceability and vigilance, with adverse events and reactions reported, both nationally and for exported human products” and further describes in commentary regarding this Guiding Principle that “Internationally agreed means of coding to identify tissues and cells used in transplantation are essential for full traceability.”⁷

In May of this year, the World Health Assembly endorsed the “WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation” and urged all Member States “to encourage the implementation of globally consistent coding systems for human cells, tissues and organs as such in order to facilitate national and international traceability of materials of human origin for transplantation.”⁸ If implemented globally, universal coding/traceability can thwart efforts by those who participate in trafficking organs, tissues and cells, or the trafficking of human beings for the purpose of the removal of organs⁹.

Today

Current configurations of alphanumeric identifiers assigned to transplantable tissue allografts are primarily designed to be used internally by the tissue establishment processing (manufacturing) them. Systems like this can overlap with duplicate identifiers for allografts from different establishments and even if bar coding is visible on the labeling of a tissue graft, it is only “machine-readable” within that tissue bank. Today, more than 3,500 facility identifiers for the use of ISBT 128 have been assigned to organizations in 67 countries on six continents⁶. These numbers are growing substantially with more

health care facilities signing on to use of this software and system every year. Since there are a large number of donation and transplantation professionals working on initiatives with goals towards commonality for coding and traceability of cells, tissue, and organs, it's logical that this system's popularity will continue to increase.

Conclusion

For the future, machine-readable universal coding is a must if we wish to enhance patient safety by optimizing tissue allograft traceability. This can hopefully be accomplished on a global scale but we should first consider changes on a national level. Each stakeholder involved in the chain of custody of allografts needs to look beyond the limit of their own professional lifetime for this to develop to its full potential. The time to begin the process is now but everyone involved needs to communicate better with each other. End users should voice support for the universal implementation of ISBT 128 if this system meets your needs. You should make your desires known.

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