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Traceability

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Abstract The importance of effective and timely traceability in both the recall of substances of human origin (blood, cells, tissues and organs) implicated in infectious transmission, and in the prevention of inappropriate use of substances of human origin is now well recognised. However, traceability remains poorly understood and inadequately controlled in many cases. In particular there is: a lack of appreciation of the complexity of the traceability pathway; a fragmented approach to traceability; and, an assumption that traceability data is static. The traceability path for a single tissue donor may involve dozens or even hundreds of different organizations, each responsible for one segment of the path. Whilst responsibility within each organization may be clearly defined, responsibility for maintaining the interfaces between organizations is often less clear. Traceability is seldom regarded in a holistic manner, the assumption being made that if each segment of the pathway is correctly maintained then the full path will be intact. End to end traceability audits are not routinely performed, and the only true test of the trail occurs when recall is required—often with inadequate results.

Keywords Traceability · Tracking · Biovigilance · Unique identification · Patient safety

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Introduction

Traceability in the field of transplantation is generally defined as the ability to trace the path of a transplantation product from the donor to the recipient, and vice versa.

Incidents involving transmission of HCV through transplantation, and the subsequent follow up investigations, have highlighted the importance of traceability both in the prevention of infection and the appropriate follow up of infected individuals. Incomplete or inaccurate traceability records can prevent effective tracking of recipients and have been shown to result in patients receiving tissue transplants from infected donors that could have been avoided. (Tugwell et al. 2005).

Policy makers are now recognising the importance of traceability. In the most recent version of the World Health Organizations Guiding Principles on Organ and Tissue Transplantation (World Health Organization 2010), guiding principle 10 states that: "The level of safety, efficacy and quality of human cells, tissues and organs for transplantation, as health products of an exceptional nature, must be maintained and optimized on an ongoing basis. This requires implementation of quality systems including traceability and vigilance, with adverse events and reactions reported, both nationally and for exported human products".

Within European Directive 2004/EC/23 there is a responsibility placed on Member States to ensure that

"all tissues and cells procured, processed, stored or distributed on their territory can be traced from the donor to the recipient and vice versa. This traceability shall also apply to all relevant data relating to products and materials coming into contact with these tissues and cells". (European Commission 2004).

In 2007 US agencies including Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA) and Centers for Medicair and Medicaid Services (CMS) held a workshop on Organ and Tissue Safety which recognised the importance of timely tracking in order to identify and expedite treatment for other recipients possibly impacted by infected tissue (Fishman et al. 2009). A report of the US Department of Health and Human Services recognises that "A unique donor identifier that links all of the organs and tissues from a common donor may facilitate the rapid identification of all allografts from that donor in the event of a public safety concern". This same report also recognises the importance of ensuring a comprehensive system of tracking and vigilance for all biologics (blood, cells tissues and organs) (US Department of Health and Human Services 2009).

Despite such recognition, traceability remains poorly understood and inadequately controlled in many countries, and does not provide the necessary responsiveness, reliability and longevity to ensure patient safety.

There are three key reasons for this:

- there is a lack of appreciation of the complexity of the information trail;
- traceability tends to be viewed in a fragmented rather than holistic manner with the assumption that joining together the links at the time of information retrieval will result in a full traceability chain;
- traceability data tends to be regarded as static rather than dynamic with the assumption that if the traceability path is intact today it will be so in the future.

Complexity of the information trail

The concept of 'a traceability path from donor to recipient' implies a one-to-one pathway, but this is an oversimplification of the real life situation. The pathway between patient and donor is rarely one to one. Most tissue donors donate a range of tissues that will be divided and processed to produce multiple grafts for use in many patients. Tissue procurement may be performed by multiple teams with the recovered tissue going to different tissue banks.

A single tissue product may pass through several different organizations on its journey from donor to recipient. These may all be in the same country and within the purview of a single regulatory authority, or may span multiple countries and regulators.

Figure 1 illustrates a very simplified example of organ and tissue recovery from a deceased donor, but even with this simple model there are likely to be between 12 and 20 different organizations involved in the traceability trail. Where many hundreds of tissue products are prepared, and where distributors are involved as well as tissue banks, the number of organization could easily run into the hundreds. Such a situation may exist where highly processed bone is produced in a large number of small packs for dentistry applications.

Adding to the complexity is the fact that there is generally no unique identification of tissues from a single donation event, hence the organ procurement organization will use one identifier, the eye bank a second and the tissue bank a third. A lack of cross-referencing between the procurement organization identifiers means there is no formal traceability across the different types of donation (in this case, organs, eyes and musculoskeletal tissue).

The identifiers assigned will be unique within the organization assigning them, but most likely not once they leave the organization. As an example, some US Tissue Banks may use the convention of identifying a donor by the year of procurement followed by a sequence number, thus 2010–001 is the first donation in 2010. This means that there may be many different donors whose tissue is identified by the reference 2010–001, one from each tissue bank using this convention. The identifier alone is therefore not sufficient to uniquely identify the donor and it becomes necessary to identify the supplying tissue bank throughout the information trail. However, in many cases there will be no uniform means of identifying the individual tissue banks making such a system cumbersome, error-prone and poorly suited to computerisation. In order

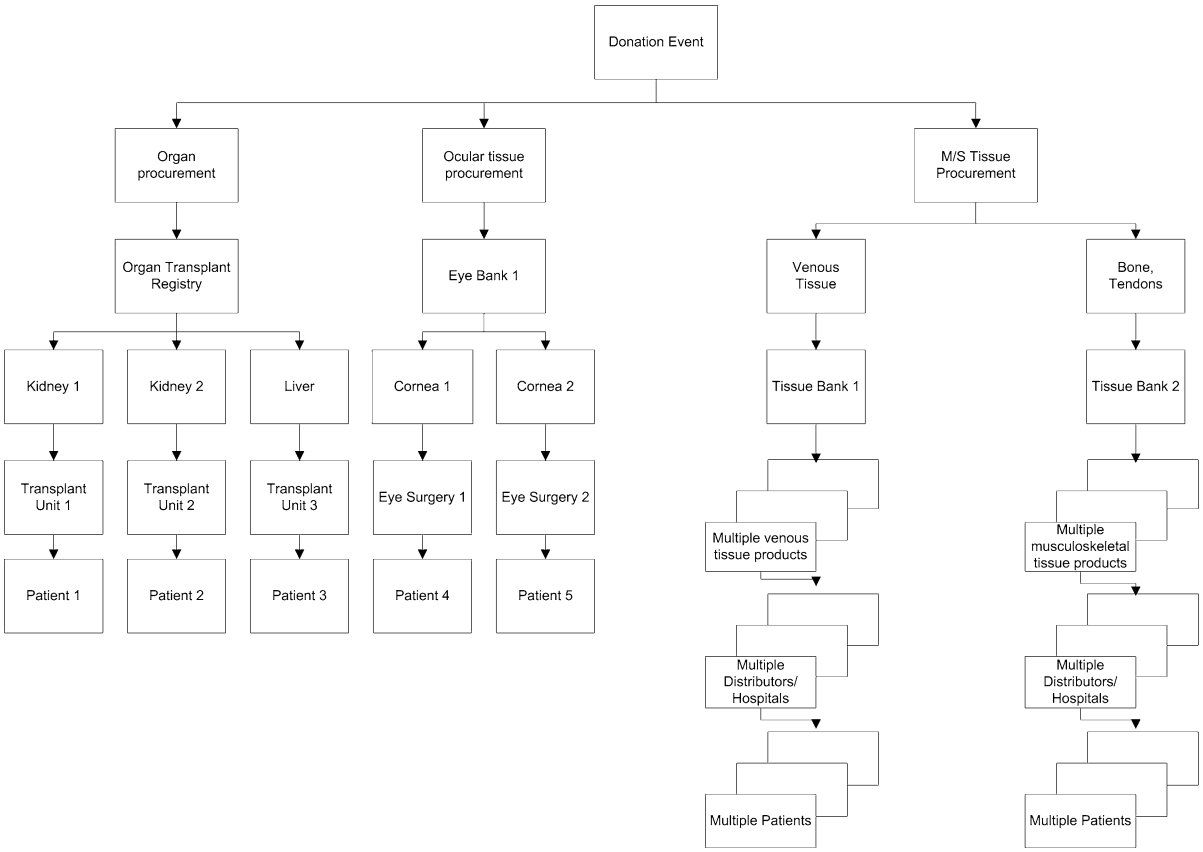

Fig. 1 Simplified example of organ and tissue recovery from a single donor

to address this type of issue in the US a transplantation transmission sentinel network (TTSN) has been proposed and a pilot implementation has been performed and evaluated (Joyce et al. 2010). The pilot was successful and informative and further evaluation is now under way.

Further complications can arise when a tissue is transferred from one tissue bank to another, maybe for additional specialised processing. In this case, the number assigned by the first bank is unlikely to be compatible with the receiving bank's system and thus re-numbering of the tissue will occur.

By the time tissue grafts reach the operating room, products from a single donation may be identified by many different identifiers and supplied from many different sources.

Because of the lack of unique identification the traceability pathway is very fragile. A single break in the chain becomes a dead end with no alternative means of picking up the trail.

Fragmented responsibility

The most common approach to traceability is to make each organization that receives donor tissue responsible for the traceability trail from the point of receipt to the point of distribution. This scope will generally include maintaining 'pointers' to the organization the tissue was received from, and the organizations the tissue was distributed to. Theoretically this ensures that there is a complete traceability path regardless of how many organizations the tissue passes through between donor and recipient.

However, the 'pointers' are themselves vulnerable, particularly over time as we will see when we look at the dynamic nature of traceability data. In addition, to work up the traceability trail from a product implicated in an adverse reaction to the donor, and then back down the trail to all other tissue products from that donation will involve many organizations and may take considerable time.

Where the traceability path moves across national boundaries the reliability of the traceability trail in practice may be doubtful.

There are some notable exceptions to the situation described above. For example, in Italy the regulator (competent authority) is informed of all donation events and assigns a single donation identifier that is used to identify all organs and tissue procured from the donor. A centralized system receives input from all parties involved in handling the tissue from donor to recipient and maintains a central database of the entire information chain within the country (CEN European Committee for Standardization Workshop Agreement 2008). Such an approach addresses at a national level many of the concerns regarding fragmentation of the information trail, however there still remain interfaces to be maintained at the point of import to, and export from, the country.

Dynamic data

If, despite the challenges identified above, we are confident that an intact traceability trail has been formed, is it reasonable to assume this will always be the case? European legislation requires that the traceability trail be maintained for 30 years from the point of graft usage. As some products have long shelf lives, and organizations involved in the early part of the chain may have no information on what the date of usage was, this effectively means permanent retention. But is simply keeping the data equivalent to maintaining the traceability trail?

Whilst the data trail within the organization is likely to remain static, the vulnerability is in the 'pointers' to the supplying and receiving organizations. As an example (in which all the names used are fictitious) assume a tissue bank received bone product with reference number 2002/002/0143 from Wellbrook Tissue Services in 2002. Wellbrook changed its name in 2005 to New Hope Tissue Foundation, and in 2008 was purchased by Severnside Tissue Services. The traceability trail now points to a non-existent organization and the traceability trail is broken. It may be possible to trace the new holders of the data, but this can only be done by accessing information that falls outside the traceability information set, and indeed outside the control of the tissue bank community and its regulators. The traceability trail itself is compromised simply because the data stored has been treated as static.

A further problem with the timescales involved is technologies obsolescence and media degradation. Electronic media is frequently used to provide long term storage of traceability data, but the technologies involved are in a constant state of change and today's "state-of-the-art" storage system is likely to be obsolete in less than 10 years. Even if systems are maintained, media can degrade. Traceability may still be possible but it is likely to take a long time. An effective traceability strategy must include regular data management reviews to assess data storage needs and to implement timely data transfer to avoid the obsolescence trap.

Effective traceability

With all of the above factors impacting upon the traceability trail, the question has to be asked as to how reliable traceability information really is. Where audits are performed they are usually within one organization and only verify the internal elements of the trail. Holistic, end-to-end, audit is essential to demonstrate the effectiveness of traceability, but is rarely performed. Thus the only real test of effectiveness tends to be in the live situation when an adverse situation has occurred and tissue needs to be withdrawn urgently. In such situations traceability systems have often been found wanting with long delays in tracing products and identifying recipients, and some products and recipients never being located.

Is there any way to improve this situation? By far the most effective means of improving recall would be the introduction of a globally unique donation identification number that is used on all tissue from a single donor. Such an identifier provides a rapid alerting tool that can be used to help prevent the use of compromised tissue. When deemed appropriate an alert could be issued to the transplantation community to suspend use of all, or a specific supplier subset of, tissue bearing the specified unique identifier.

Globally unique identification also strengthens the traceability trail as any single points of failure in the traceability chain are far more likely to be overcome if the reference number used in every organization is

the same. Moreover, if the unique identifier can identify the assigning tissue bank responsible for procurement, a 'short-cut' exists from the recipient back to the donor allowing much more rapid tracing.

Even if a single identifier for all organs and tissues is not practical in the first instance, use of globally unique identifiers assigned to each group of tissue is still a big step forward, as long as these initial identifiers are carried on all tissue grafts prepared from the procurement (e.g. in the scenario from Fig. 1 distinct, but globally unique, identifiers are issued by organ procurement, eye procurement and tissue procurement teams). In this situation there should ideally be a mechanism for cross-referencing the identifiers assigned by each recovery team.

The second urgently required step is to introduce end-to-end audit for traceability so that weaknesses can be identified and rectified. Regulators and professional bodies need to work together to determine the most appropriate means of achieving such audits, and there needs to be clarity over where the responsibility for traceability lies throughout the entire pathway, and in particular over the management of the interfaces between organizations. Audit should also ensure that the long term viability of the traceability trail is assured through regular review of the data management strategy.

These two actions will not solve all the challenges of effective traceability, but will go a long way to improving the reliability of the traceability chain. They will allow much more rapid recall thus shortening the 'window period' between risk identification and product withdrawal, hence increasing patient safety.

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