HTA policy on testing requirements for Human T-lymphotropic Virus, type I (HTLV-1) for donors of tissues and cells intended for human application

Background

The HTA has identified inconsistencies in the way in which licensed establishments apply the mandatory testing requirements for HTLV-1 testing.

These relate to the identification of donor populations to which the mandatory testing requirements apply, the timing at which an HTLV test may be performed and interpretation of the repeat testing requirements as they relate to HTLV-1.

In the absence of a Nucleic Acid Amplification Technique (NAT) test, establishments have also reported difficulties in conducting repeat testing for HTLV-1. This applies in particular to those establishments which use NAT testing for other infectious disease markers and do not routinely need to obtain a repeat serology sample for any other purposes.

The HTA has developed a policy on HTLV-1 testing in order to provide clarification to licensed establishments on the mandatory minimum testing requirements. The policy explains the scientific basis for repeat testing and the HTA's proposed approach to assure consistency in the way in which these requirements are interpreted.

In coming to its position, the HTA has aimed to develop a policy that is proportionate and risk-based, whilst providing clarification regarding the formal requirements for HTLV testing as set out in Annex II of Commission Directive 2006/17/EC.

Mandatory minimum testing requirements for HTLV-1

For all tissues and cells procured for human application, it is a requirement of Annex II of Commission Directive 2006/17/EC that HTLV-1 antibody testing must be performed for donors living in, or originating from high-prevalence areas, or with sexual partners originating from those areas or where the donor's parents originate from those areas.

Where living donors of allogeneic tissues and cells have been identified as fulfilling the above criteria, then repeat testing for HTLV-1 is required after an interval of 180 days, if the tissues and cells are stored for long periods. Repeat testing does not apply to donors of allogeneic bone marrow stem cells and peripheral blood stem cells[1]. Repeat testing does apply to cord blood donations for allogeneic use. These requirements relating to HTLV-1 testing are based on the EU Commission interpretation of EU Directive 2006/17/EC[2], rather than being requirements put in place by the HTA.

Identification of donor populations to which the mandatory testing requirements for HTLV-1 apply

Consistent application of the HTLV testing requirements relies on the use of a single and reliable data source, to determine HTLV-1 high-prevalence areas.

The European Centre for Disease Prevention and Control (ECDC), at the request of the EU Commission, has constructed a map indicating the HTLV-1 high prevalence areas in the world.

This map is intended to be used by those assessing the suitability of tissues and cells donors. Some areas were not classified as low or high prevalence because of unreliable or absent data.

Scientific basis for subjecting donors to repeat testing

HTLV-1 has been shown to be transmitted by mother-to-child transmission (breastfeeding), sexual contact and via transplantation of organs, tissues and leucocyte-rich blood components[3]. The HTA has been asked whether testing all donors for HTLV-1 at the point of donation would sufficiently mitigate the risk of transmission.

Testing a donor at the point of procurement would identify an existing, long standing infection and thus identify the risk of transmission posed by a donor, or a donor's parents, originating from an area with a high prevalence of HTLV-1 infection.

---

[1] The requirements for donor testing with respect to sampling time and repeat testing are different for these cell types as set out in Annex II of Commission Directive 2006/17/EC. This includes related products such as donor lymphocyte infusions.

[2] Legal opinion provided during June 2012 meeting of National Competent Authorities for Tissues and Cells.

[3] European Centre for Disease Prevention and Control. HTLV-I/II transmission by tissue/cell transplantation. Part 1: Epidemiological review. Stockholm: ECDC; 2012.

A theoretical risk of HTLV-1transmission would remain for those donors who have recently acquired infection from a sexual partner.

Use of alternative testing methods

Annex II of Commission Directive 2006/17/EC provides that if in a living donor, the 'donation sample' is additionally tested by the nucleic acid amplification technique (NAT) for HIV, HBV and HCV, testing of a repeat blood sample is not required.

The EU Commission has advised that where required, in the absence of NAT, a repeat blood sample would need to be obtained after an interval of180 days in order to carry out an HTLV-1 antibody test.

There is currently no commercially available CE-marked NAT test available for HTLV-1, and use of NAT for HTLV testing is not referred to as part of the provision for NAT testing within Annex II of Commission Directive 2006/17/EC.

There is potentially scope to allow the use of an appropriately validated testing method for HTLV, in place of repeat testing, in line with the provision of adaption to scientific and technical progress as outlined above.

The HTA's position on HTLV-1 testing requirements

Where HTLV-1 testing is mandatory (i.e. in donors identified as being part the high prevalence cohort), then HTLV-1 antibody testing is always required on a blood sample obtained at the time of donation.

HTLV prevalence data should be obtained from the ECDC Technical Report - Geographical distribution of areas with a high prevalence of HTLV-1 infection . Where an area is specified as having no data, or being of unknown risk, these donors should be managed in an equivalent way to donors associated with high prevalence areas.

The map should be considered as a guide for assessing the suitability of donors; it should be remembered that precise estimations of prevalence are difficult and donor responses are not always accurate. The testing of all donors would mitigate these uncertainties.

Testing all donors for HTLV-1 at the time of donation

As best practice, the HTA recommends that all donors of tissues and cells for human application are tested for HTLV-1 at the time of donation. This blood sample

must be obtained in accordance with the timeframes set out in Annex II of Commission Directive 2006/17/EC.

Where an establishment routinely tests all living donors of allogeneic tissues and cells for HTLV-1 at the time of donation, the HTA will not seek evidence of repeat testing providing the donors do not represent a risk of recently acquired infection[4].

This risk must be identified through the donor selection process. For example, this could be achieved by identifying any new risk factors such as recent sexual partners who represent a risk of HTLV-1 transmission. Where such a risk is identified, the HTA expects that repeat testing will be conducted.

Testing only donor populations to which the mandatory testing requirements for HTLV-1 apply at the time of donation

In the absence of routine HTLV testing for all donors, establishments must have robust donor selection processes in place to identify those donors which require testing for HTLV-1 based on the requirements set out in Annex II of Commission Directive 2006/17/EC.

The establishment's donor selection processes must be sufficiently robust to identify individuals at risk of existing, long standing infection (i.e. by virtue of the donor originating from, or having parents from, an area of high prevalence) and those at risk of a recently acquired infection. In the case of the former, the HTA expects that donors will be tested at the time of donation in line with the requirements of Annex II of Commission Directive 2006/17/EC. Where such testing is carried out, the HTA will not seek evidence of repeat testing in line with the approach set out in the preceding section. For donors at risk of a recently acquired infection, the HTA expects that testing at the time of donation and repeat testing after an interval of180 days will be carried out.

The HTA expects establishments to formally risk assess this approach to HTLV testing and to have robust and well-documented procedures in place to support a donor selection process that identifies different types of HTLV infection risks.

NAT testing

In the absence of a CE marked NAT test for HTLV, an HTLV-1 NAT test developed in house would be acceptable if supported by appropriate validation data. When performed on the donation sample this would replace the repeat testing requirement for HTLV-1 (as applies to NAT testing for HIV, HBV & HCV).

[4] A recently acquired infection in this context is one acquired within a time period that would preclude the detection of infectivity by the screening assay employed i.e. within the ‘window period’.

Conclusion

In coming to this position the HTA has looked for a proportionate and risk-based approach to the regulation of this activity. It remains the responsibility of each establishment to ensure that the risk of infection from donated tissues and cells is assessed as accurately as possible.