Guidelines for the Blood Transfusion Services

9.3: Specific screening targets

http://www.transfusionguidelines.org/red-book/chapter-9-microbiology-tests-for-donors-and-donations-general-specifications-for-laboratory-test-procedures/9-3-specific-assays

9.3: Specific screening targets

9.3.1: HBsAg

- The UK specification for the minimum level of sensitivity for the performance of HBsAg screening is 0.2 IU/mL. A UK HBsAg working standard (07/288 or equivalent) containing 0.2 IU/mL HBsAg is available from the National Institute for Biological Standards and Control (NIBSC). Laboratories using an assay of high analytical or dilutional sensitivity where the working standard reacts too strongly are advised to utilise the NIBSC HBsAg monitoring standard (07/286 or equivalent) set at 0.05 IU/mL in place of the working standard.

- In addition to the assay manufacturer's controls, the UK working standard must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.2: anti-HIV 1+2 or HIV 1+2 Ag/Ab combination

- Screening for both HIV p24 antigen and antibody to HIV 1+2+O in a combination assay is recommended as the serological screening approach for HIV within the UK Blood Services.

- The UK requirement for the minimum level of sensitivity for the performance of HIV 1+2 serological screening is that a positive result should be obtained with the UK anti-HIV 1 working standard, available from NIBSC (99/750 or equivalent). Laboratories using an assay of higher analytical or dilutional sensitivity where the working standard reacts too strongly are advised to utilise the NIBSC HIV working standard 1/5 dilution (99/710 or equivalent) in place of the working standard. There is no specific requirement to demonstrate individual anti-HIV 2 or HIV p24 Ag reactivity.

- In addition to the assay manufacturer's controls, the UK working standard must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.3: anti-HCV

- The UK requirement for the minimum level of sensitivity for the performance of anti-HCV screening is that a positive result should be obtained with the UK anti-HCV working standard (19/240 or equivalent), available from NIBSC. Laboratories using HCV assays of higher analytical or dilutional sensitivity where the working standard reacts too strongly are advised to utilise an alternative UKCA

or CE marked material intended for such use which may be used in place of the working standard if the material has been fully validated by the UK Blood and Tissue Establishment using the material.

- In addition to the assay manufacturer's controls, the UK working standard must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.4: anti-HTLV I/II

- The UK requirement for the minimum level of sensitivity for the performance of anti-HTLV I/II screening is that a positive result should be obtained with the UK anti-HTLV working standard, available from NIBSC (03/104 or equivalent).

- In addition to the assay manufacturer's controls, the UK working standard must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.5: Syphilis antibody

- The UK requirement for the minimum level of sensitivity for the performance of syphilis (specific treponemal antibody) screening is that a positive result should be obtained with the appropriate syphilis Ab standard available from NIBSC (QCRSYPHQC1 (20/B767), QCRSYPHQC2 (17 /B713) or equivalent).

- In addition to the assay manufacturer's controls, the NIBSC syphilis antibody quality control preparation must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.6: Malarial antibody

Donations collected from donors with an identified malarial risk may be released if the donation has been collected following the exclusion period set out in the Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) Donor Selection Guidelines[3] and malarial antibody is not detected on screening. These guidelines also identify specific situations when donations may be released if malarial antibody is detected and additional testing for malarial DNA is then performed and malarial DNA not detected, and situations when donations may be collected at a timepoint within the standard exclusion period.

- The UK requirement for the minimum level of sensitivity for the performance of malarial antibody (anti-*P.falciparum/vivax*) screening is that a positive result should be obtained with the malarial Ab standard available from NIBSC (QCRMALQC1 (13/B627) or equivalent).

- In addition to the assay manufacturer's controls, the NIBSC malaria antibody quality control preparation must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.7: *T.cruzi* antibody

The deferral criteria for donors from *T. cruzi* endemic areas are given in the JPAC Donor Selection Guidelines[3]. Donors at risk of *T. cruzi* must be tested for anti-*T.cruzi* and negative results obtained prior to the release of any donation for clinical use.

- The UK requirement for the minimum level of sensitivity for the performance of anti-*T.cruzi* screening is that, in the absence of a specifically defined UK working standard produced by NIBSC, a positive result should be obtained with a formally validated in-house *anti-T.cruzi* quality control preparation. *T. cruzi* international standards are available from NIBSC (09/188 and 09/186 or equivalent).

- In addition to the assay manufacturer's controls, the anti-*T.cruzi* quality control preparation must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.8: anti-HBc

The exclusion period for blood donors who have had body piercing, acupuncture etc. are given in the JPAC Donor Selection Guidelines[3].

All blood donors are to be screened for anti-HBc at their first donation or their donation after the introduction of anti-HBc screening. Anti-HBc screening to be repeated if a donor lapses (over 2 years) or has a new HBV risk. Tissue and stem cell donations have anti-HBc screening as a mandatory requirement.

- The UK requirement for the minimum level of sensitivity for the performance of anti-HBc screening is that a positive result should be obtained with the appropriate anti-HBc standard available from NIBSC (QCRTHBcQC1 (16/B704) and QCRTHBcQC2 (14/B651) or equivalent).

- In addition to the assay manufacturer's controls, the NIBSC anti-HBc quality control preparation must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

- Blood donations which are confirmed positive for anti-HBc should be tested for anti-HBs; Tissue and stem cell donations found to be reactive for anti-HBc alone may not require additional anti-HBs testing (see section 9.3.10).

9.3.9: anti-HCMV

- The UK requirement for the minimum level of sensitivity for the performance of anti-HCMV screening is that a positive result should be obtained with the anti-CMV standard available from NIBSC (QCRCMVQC1 (18/B731) or equivalent).

- In addition to the assay manufacturer's controls, the NIBSC anti-HCMV quality control preparation must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.10: anti-HBs

Blood donations confirmed positive for anti-HBc with anti-HBs <100 mIU/mL are deemed unsuitable for release whereas blood donations confirmed positive for anti-HBc with anti-HBs levels >=100 mIU/mLtested in the past 24 months by a UK Blood Service, can be considered suitable for release if HBsAg and ID HBV DNA negative.

In the case of tissue and stem cell donations ONLY, there is no requirement for an anti-HBs level of >=100 mIU/ml if both HBsAg and HBV DNA negative on individual donation [non-pooled] screening.

- The UK requirement for the minimum level of sensitivity for the performance of anti-HBs testing is that a positive result should be obtained with the anti-HBs standard available from NIBSC (QCRHBsQC1 or equivalent).

- In addition to the assay manufacturer's controls, the NIBSC anti-HBs quality control preparation must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down.

9.3.11: Hepatitis C virus RNA

- The UK requirement for the minimum level of sensitivity for the performance of HCV RNA screening is 5000 IU/mL in an individual donation. A multiplex working reagent (HBV DNA, HCV RNA, HIV RNA) is available from NIBSC (14/198 or equivalent).

- The assay must include a specific internal control for each sample tested.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and any additional quality control samples have satisfied the criteria laid down.

9.3.12: Hepatitis B virus DNA

- There is currently no specific UK requirement for the minimum level of sensitivity for the performance of HBV DNA screening. A multiplex working reagent (HBV DNA, HCV RNA, HIV RNA) is available from NIBSC (14/198 or equivalent).

- The assay must include a specific internal control for each sample tested.

- No series of tests should be considered acceptable unless the result of the assay manufacturer's and any additional quality control samples have satisfied the criteria laid down.

9.3.13: Human immunodeficiency virus RNA

- There is currently no specific UK requirement for the minimum level of sensitivity for the performance of HIV RNA screening. A multiplex working reagent (HBV DNA, HCV RNA, HIV RNA) is available from NIBSC (14/198 or equivalent).
- The assay must include a specific internal control for each sample tested.
- The assay must utilise two separate targets within the HIV genome to minimise any risk of failure of detection due to sequence changes in the primer or probe binding regions.
- No series of tests should be considered acceptable unless the result of the assay manufacturer's and any additional quality control samples have satisfied the criteria laid down.

9.3.14: Hepatitis E virus RNA

- There is currently no specific UK requirement for the minimum level of sensitivity for the performance of HEV RNA screening. An HEV RNA international standard is available from the Paul Ehrlich Institute (PEI) (6329/10 or equivalent).
- The assay must include a specific internal control for each sample tested.
- No series of tests should be considered acceptable unless the result of the assay manufacturer's and any additional quality control samples have satisfied the criteria laid down.

9.3.15: West Nile virus RNA

The exclusion criteria for donors from a WNV risk area is given in the JPAC Donor Selection Guidelines[3]. These guidelines specify some situations where donations may only be released if a test for WNV RNA is negative. WNV RNA screening can be performed on donations provided by donors within the exclusion period and the donations released if WNV RNA negative.

- There is currently no specific UK requirement for the minimum level of sensitivity for the performance of WNV NAT. A WNV international standard is available from NIBSC (18/206 or equivalent).
- The assay must include a specific internal control for each sample tested.
- No series of tests should be considered acceptable unless the result of the assay manufacturer's and any additional quality control samples have satisfied the criteria laid down.

9.3.16: Other infectious agents

The JPAC Donor Selection Guidelines[3] may identify other infectious agents and specify some situations when screening may be applied in addition to donor deferral. In such situations any screening performed must:

- use assays specifically evaluated and validated for the screening of the donation type.
- identify and utilise an independent quality control in each series of tests in addition to the manufacturer's assay controls.

- ensure that the results of the assay manufacturer's and the additional quality control samples have satisfied the criteria laid down prior to release of the result**.**

9.3.17: Additional screening of plasma intended for fractionation

All plasma pools intended for the manufacture of medicines are subjected to microbiological screening as described in the current European Pharmacopoeia Monograph on Human Plasma for Fractionation. Dependent on which product the plasma pool is being used to produce, to limit the viral burden in-process screening of the first homogenous plasma pool for both hepatitis A Virus (HAV) RNA and human parvovirus B19 (B19V) DNA is performed. A maximum level for B19 DNA has been defined in the European Pharmocopoeia, but not for HAV RNA.

There is no mandatory requirement to screen donations for HAV and Human B19V, although UK Blood services may elect to screen donations in minipools to reduce the risk of discard of larger plasma pools.

9.3.17.1: Human parvovirus B19 DNA

- There is currently no specific UK requirement for the minimum level of sensitivity for the performance of human B19V DNA screening. If screening is performed in minipools, UK Blood Services must ensure that human B19V DNA can be detected at a level that will ensure less than 10^4 IU/mL of B19V DNA in the homogenous plasma pool. A clinical virology immunodeficiency multiplex working reagent including Human B19 DNA (2.4×10^4 IU/mL) is available from NIBSC (15/130 or equivalent).

- The assay must include a specific internal control for each test performed.

- No series of tests should be considered acceptable unless the manufacturer's QC requirements in the IFU have been met, and the results of any additional quality control samples used have satisfied the criteria laid down.

9.3.17.2: Hepatitis A virus RNA

There is currently no specific UK requirement for the minimum level of sensitivity for the performance of HAV NAT. If screening is performed in minipools, UK Blood Services must ensure that HAV RNA can be detected at a level that will ensure a negative HAV NAT in the homogenous plasma pool. Currently HAV RNA standardised run control material is not available from NIBSC or PEI.

- The assay must include a specific internal control for each test performed.

- No series of tests should be considered acceptable unless the manufacturer's QC requirements in the IFU have been met, and the results of any additional quality control samples used have satisfied the criteria laid down.