Change Notification for the UK Blood Transfusion Services

Date of Issue: 23 May 2025 **Implementation:** to be determined by each Service

No. 11 – 2025

Chapter 9.3: Specific screening targets

Please note this document supersedes CN 11-2025 (v1.0) previously circulated on 23.05.25.

Two errors have been corrected in which text was incorrectly omitted in v1.0.
These corrections are highlighted on **page 2** and **page 10**.

This notification includes the following changes:

	BM-DSG Bone Marrow & Peripheral Blood Stem Cell	CB-DSG Cord Blood	GDRI Geographical Disease Risk Index	TD-DSG Tissue - Deceased Donors	TL-DSG Tissue - Live Donors	WB-DSG Whole Blood & Components	Red Book Guidelines for the BTS in the UK
1. Chapter 9.3	○	○	○	○	○	○	●
2. Annexe 1	○	○	○	○	○	○	●

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Changes are indicated using the key below. This formatting will not appear in the final entry.

original text	«inserted text»	~~deleted text~~

1. Changes apply to the **Red Book**

Chapter 9:

Microbiology tests for donors and donations: general specifications for laboratory test procedures

(no changes to 9.1 – 9.2)

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. «This level of sensitivity can be demonstrated during assay evaluation/validation/verification through the use of a quality control calibrated to the World Health Organisation (WHO) International Standard. If the WHO International Standard is withdrawn or otherwise unavailable, an alternative quality control reagent can be used that must be validated for use by the UK Blood Service using that reagent.» ~~*A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 a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. This control must have a unitage of 0.2 IU/mL or less. If the unitage is not defined by the manufacturer it can be validated by at least one of the UK Blood Services. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~*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 «controls» and the additional quality control sample~~*s*~~ have satisfied the criteria laid down.

9.3.2: anti-HIV 1+2 or HIV 1+2 Ab/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 «during assay evaluation/validation/verification with a quality control calibrated to the WHO International Reference reagent. There is no specific requirement to demonstrate individual anti-HIV 2 or HIV p24 Ag reactivity. If the WHO International

Reference reagent is withdrawn or otherwise unavailable, an alternative quality control reagent can be used that must be validated for use by the UK Blood Service using that reagent.» ~~*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 a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~*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 «controls» and the additional quality control sample~~*s*~~ 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 «during assay evaluation/validation/verification with a quality control calibrated to the WHO International Standard. In the absence of standardisation against a WHO International Standard, the reagent must be validated for use by the UK Blood Service using the reagent.» ~~*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 a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~*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 «controls» and the additional quality control sample~~*s*~~ 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 «during assay evaluation/validation/verification with a quality control reagent calibrated to the WHO International Standard. In the absence of standardisation against a WHO International Standard, the quality control must be validated for use by the UK Blood Service using the reagent.» ~~*with the UK anti-HTLV working standard, available from NIBSC (03/104 or equivalent).*~~

- «In addition to the assay manufacturer's controls a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.»

~~*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 «controls» and the additional quality control sample~~s~~ 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 «during assay evaluation/validation/verification with a quality control reagent calibrated to the WHO International Standard. In the absence of standardisation against a WHO International Standard for enzyme immunoassays, the quality control must be validated for use by the UK Blood Service using the reagent.» ~~*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 a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~*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 «controls» and the additional quality control sample~~s~~ 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 «JPAC» ~~*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* «as a minimum») screening is that a positive result should be obtained «during assay evaluation/validation/verification with a quality control calibrated to the WHO International Reference reagent. If the WHO International Reference reagent is withdrawn or otherwise unavailable, an alternative quality control reagent can be used that must be validated for use by the UK Blood Service using that reagent.» ~~*with the malarial Ab standard available from NIBSC (QCRMALQC1 (13/B627) or equivalent).*~~

- «In addition to the assay manufacturer's controls a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~*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 «controls» and the additional quality control sample~~s~~ 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 «during assay evaluation/validation/verification with a quality control calibrated to the WHO International Standard. If the WHO International Standard is withdrawn or otherwise unavailable, an alternative quality control reagent can be used that must be validated for use by the UK Blood Service using that reagent.» ~~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 a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~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 «controls» and the additional quality control sample~~s~~ have satisfied the criteria laid down.

9.3.8: anti-HBc

The exclusion period for blood donors who have had body piercing, «which includes derma-rolling, ear and body piercing, permanent and semi-permanent make-up, tattooing, platelet rich plasma facial, ritual self-flagellation and» 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 «at each donation».

- The UK requirement for the minimum level of sensitivity for the performance of anti-HBc screening is that a positive result should be obtained «during assay evaluation/validation/verification with a quality control calibrated to the WHO International Standard. If the WHO International Standard is withdrawn or otherwise unavailable, an alternative quality control reagent can be used that must be validated for use by the UK Blood Service using that reagent.» ~~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 a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~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 «controls» and the additional quality control sample~~s~~ 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 «during assay evaluation/validation/verification with a quality control reagent calibrated to the WHO International Standard. In the absence of standardisation against a WHO International Standard, the quality control must be validated for use by the UK Blood Service using the material.» ~~*with the anti-CMV standard available from NIBSC (QCRCMVQC1 (18/B731) or equivalent).*~~

- «In addition to the assay manufacturer's controls a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~*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 «controls» and the additional quality control sample~~s~~ 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 «during assay evaluation/validation/verification with a quality control reagent calibrated to the WHO International Standard. In the absence of standardisation against a WHO International Standard, the quality control must be validated for use by the UK Blood Service using the material.» ~~*with the anti-HBs standard available from NIBSC (QCRHBsQC1 or equivalent).*~~

- «In addition to the assay manufacturer's controls a quality control suitable for the purposes of monitoring the performance of *in-vitro* assays must be included at least once in each series of tests to demonstrate acceptable sensitivity of the test method. Where available, the quality control should be CE or UKCA marked. The quality control must be manufactured by a different manufacturer to that of the assay.» ~~*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 «controls» and the additional quality control sample~~s~~ 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 «controls» and any additional quality control sample~~s~~ have satisfied the criteria laid down.
- «If an additional quality control is run on each series of tests, it should be a CE or UKCA marked quality control where available and suitable for the purposes of monitoring the performance of *in-vitro* assays and manufactured by a different manufacturer to that of the assay.»

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 «controls» and any additional quality control sample~~s~~ have satisfied the criteria laid down.
- «If an additional quality control is run on each series of tests, it should be a CE or UKCA marked quality control where available and suitable for the purposes of monitoring the performance of *in-vitro* assays and manufactured by a different manufacturer to that of the assay.»

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 «controls» and any additional quality control sample~~s~~ have satisfied the criteria laid down.
- «If an additional quality control is run on each series of tests, it should be a CE or UKCA marked quality control where available and suitable for the purposes of monitoring the performance of *in-vitro* assays and manufactured by a different manufacturer to that of the assay.»

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 «controls» and any additional quality control sample~~s~~ have satisfied the criteria laid down.
- «If an additional quality control is run on each series of tests, it should be a CE or UKCA marked quality control where available and suitable for the purposes of monitoring the performance of *in-vitro* assays and manufactured by a different manufacturer to that of the assay.»

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 «controls» and any additional quality control sample~~s~~ have satisfied the criteria laid down.
- «If an additional quality control is run on each series of tests, it should be a CE or UKCA marked quality control where available and suitable for the purposes of monitoring the performance of *in-vitro* assays and manufactured by a different manufacturer to that of the assay.»

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 «controls» and the additional quality control sample~~s~~ 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 «Pharmacopoeia» ~~*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 «the result of the assay» manufacturer's «controls and» ~~*QC requirements in the IFU have been met, and*~~ the results of any additional quality control sample~~*s*~~ used have satisfied the criteria laid down.

- «If an additional quality control is run on each series of tests, it should be a CE or UKCA marked quality control where available and suitable for the purposes of monitoring the performance of *in-vitro* assays and manufactured by a different manufacturer to that of the assay.»

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 «result of the assay» manufacturer's «controls and» ~~*QC requirements in the IFU have been met, and*~~ the results of any additional quality control sample~~*s*~~ used have satisfied the criteria laid down.

- «If an additional quality control is run on each series of tests, it should be a CE or UKCA marked quality control where available and suitable for the purposes of monitoring the performance of *in-vitro* assays and manufactured by a different manufacturer to that of the assay.»

«**Note** – International Standards or Reference Reagents do not need to be CE or UKCA marked.»

(no changes to 9.4 – 9.9)

2. Changes apply to the **Red Book**

Annexe 1:

NIBSC standards available from MHRA South Mimms Laboratories

MHRA South Mimms Laboratories, formerly the National Institute for Biological Standards and Control (NIBSC), produces a wide range of standard materials, available as World Health Organisation (WHO) international standards, WHO reference reagents~~, *Conformité Européene (CE) marked standards*~~ and NIBSC brand standards. Many are pertinent to transfusion medicine such as serological, virological, bacteriological and coagulation standard preparations.

A list of available standards is available at www.nibsc.org/products.

Please note that alternative preparations may be available from other manufacturers.