Instructions for Infectious Disease Markers Form (Form 2004 – Revision 4)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Infectious Disease Markers Form.

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: CIBMTRFormsManualComments@nmdp.org. Comments will be considered for future manual updates and revisions. For questions that require an immediate response, please contact your transplant center's CIBMTR CRC.

Infectious Disease Markers (IDMs) Data

Form 2004 will come due in the following instances:

- Non-NMDP unrelated donor (TED or CRF track)
- Non-NMDP unrelated cord blood (TED or CRF track)
- Related cord blood (TED or CRF track)

- HLA-identical sibling (CRF track or when consented for “Research Sample Repository” on TED track)
- HLA-matched other relative or HLA-mismatched relative (CRF track or when consented for “Research Sample Repository” on TED track)

If the donor or cord blood unit was secured through the NMDP, IDM test results will be reported by the donor center on NMDP Forms 24 and 50, or will be submitted by the cord blood bank through CORD Link®.

Infectious diseases result from pathogens that enter the human body and multiply. Examples of pathogens include viruses, bacteria, fungi, and parasites. Infectious diseases may be transmitted through liquids, food, body fluids, contaminated objects, or airborne particles.

An Infectious Disease Marker (IDM) indicates if an individual currently has, or previously has had, an infectious disease that could be transferred to another person.

- Antibody testing assesses whether an individual’s immune system recognizes an antigen presentation, which indicates previous exposure to the pathogen.
- Antigen testing, such as testing for the presence of the Hepatitis B surface antigen, assesses whether the individual has an active infection, where the pathogen is present in the blood. Antigen testing is done because the individual may not yet have developed antibodies against the pathogen at the time of infection.

The purpose of IDM testing is to assess the donor’s exposure to infectious diseases and the likelihood of their transmitting a disease to the recipient.

For a glossary of terms used in this section of the manual, see Appendix B.

Key Fields

Accuracy of the Key Fields is essential for ensuring that:

- Data are being reported for the correct recipient.
- Outcomes data accurately reflects appropriate transplant type and product for each transplant center.
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other agency.

The Key Fields precede the form body and are automatically populated in the FormsNet3℠ application based on information provided on the CRID Assignment Form 2804. If errors are noted in the key fields, correct Form 2804 and then review it for accuracy. After Form 2804 has been corrected, verify data has been updated on all completed forms. If the data has not been updated automatically, centers will need to

reprocess the completed forms to correct the key field data. If errors are noted in key fields for second or subsequent transplants, contact your CRC to make any necessary corrections to the transplant or product type. Transplant and product type will not be automatically populated on product or donor specific forms (Forms 2004, 2005, and 2006) and will need to be manually reported.

Donor/Cord Blood Unit Identification

Question 1: Specify non-NMDP donor
Indicate whether the reported IDMs are for a related donor (peripheral blood stem cells or bone marrow), an unrelated donor with product procured from a source other than the NMDP (peripheral blood stem cells or bone marrow), or a non-NMDP cord blood unit (report related or autologous cord blood units as non-NMDP cord blood units).

If the donor is related to the recipient, continue with question 4. If the donor is not related to the recipient and the donation is not an NMDP product, continue with question 2. If the product is a cord blood unit obtained from a non-NMDP bank, including related and autologous cord blood products, continue with question 3.

Question 2: Non-NMDP unrelated donor ID
Specify the unrelated donor identification number used by the donor registry to identify and track the [peripheral blood stem cell or bone marrow] donor. Continue with question 4.

Question 3: Non-NMDP cord blood unit ID
Specify the cord blood unit identification number used by the cord blood bank to identify and track the unit. Continue with question 4.

Questions 4-5: Date of birth (donor/infant)
Indicate whether the donor's or infant cord donor's date of birth is "known" or "unknown." If "known," report the donor's or infant cord donor's date of birth in question 5; if the date of birth is known, it is not necessary to complete questions 6-7 specifying the donor or infant cord donor age. If "unknown," continue with question 6.

Questions 6-7: Age
Indicate whether the donor's or infant cord donor's age at the time of product collection is "known" or "unknown." If "known," report the donor or infant cord donor's age at the time of product collection in question 7. If donor is less than one year old, report age in months rounded to the nearest whole month. If the product was collected at birth, report "0" months. If "unknown," continue with question 8.

Question 8: Sex (donor/infant)
Indicate the biological sex of the product donor or infant cord donor.

Question 9: Who is being tested for IDMs?
Indicate whether the donor (for peripheral blood stem cells and/or bone marrow products), mother of an infant cord donor, or cord blood *unit* itself is being tested for IDMs. Maternal IDMs and cord blood unit IDMs apply only to cord blood products; if both maternal and cord blood IDMs are available, report the results from cord blood unit testing. Cord blood banks send documentation accompanying the cord that will specify IDM results and the source of the specimen sent for IDM testing; most cord blood banks perform IDM testing on maternal serum due to the limited volume and cell count of cord blood units.

Infectious Disease Markers

Report the final test results. Final test results could refer to either the initial screening test or the confirmatory test. If a screening test is negative, a confirmatory test might not be done. In this case, use the screening test as the final test result. However, if a screening test is positive, a confirmatory test may be done. In this case, use the confirmatory test as the final test result.

When reporting inconclusive or indeterminate test results, leave the results data field blank in the FormsNet 3^{SM} application and override the error as "unknown."

Hepatitis B Virus (HBV)

Hepatitis B infection is caused by the hepatitis B virus (HBV). Hepatitis B is spread through infected blood and other body fluids. Signs and symptoms of infection generally occur 60-150 days after exposure and include fever, fatigue, nausea, vomiting, and jaundice (secondary to liver inflammation). Patients with an acute hepatitis B infection generally do not require treatment; approximately 95% of adults who get acute hepatitis B will recover without developing chronic hepatitis B infection. Chronic hepatitis B infection is generally monitored for progression or evidence of liver damage, at which point patients may be treated with antiviral drugs. Chronic hepatitis B infection can lead to liver scarring (cirrhosis) and liver cancer (hepatocellular carcinoma). In the United States, the hepatitis B vaccine is now part of the routine childhood vaccination schedule.

Question 10: Hepatitis B surface antigen (HBsAg)
The hepatitis B surface antigen is a protein expressed on the surface of the hepatitis B virus. Its presence in the blood serum indicates acute or active chronic infection. In acutely infected patients, blood will test HBsAg positive within one to nine weeks of exposure to the virus. Patients who do not go on to develop chronic infection will be surface antigen negative by 15 weeks after the onset of symptoms. Chemiluminescent immunoassay (CIA), electrochemiluminescent immunoassay (ECLIA), or enzyme-linked immunosorbent assay (ELISA) are used to test for the presence of hepatitis B surface antigens; research indicates CIA and ECLIA may be more sensitive for detecting low

levels of HBsAg.[1] Positive HBsAg results require confirmation with specific antigen neutralization.

Report the laboratory result as "reactive" (positive) or "non-reactive" (negative), and continue with question 11.
If HBsAg testing was not done, indicate "not done" and continue with question 12.

[1]Fei CR, Ye AQ, Zhang J. (2011). Evaluation of different methods in determination of low level HBsAg. *Zhejiang Da Xue Xue Bao Yi Xue Ban, 40(4):436-439.*

Question 11: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Question 12: Hepatitis B core antibody (Anti-HBc)
The total hepatitis B core antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of the core antigen by liver cells. Since core antigen is present only in infected liver cells and cannot be detected in the blood of an infected individual, only core antibody is tested, since it circulates in the peripheral blood. After infection, total core antibodies will persist for life. Presence of core antibodies can indicate active and/or prior infection, but hepatitis core antibodies will not be present in individuals with no history of natural infection with HBV. This means that vaccinated individuals will not be anti-HBc positive because vaccination results in the body developing antibodies to the hepatitis B *surface* antigen. Chemiluminescent immunoassay (CIA), enzyme-linked immunosorbent assay (ELISA), or Elecsys anti-HBc is used to test for the presence of hepatitis B core antibodies. Currently, there is no licensed confirmatory test for anti-HBc in the United States; confirmation of antibody presence is done by performing a second anti-HBc test using a different manufacturer's test kit.

Report the laboratory result as "reactive" (positive) or "non-reactive" (negative), and continue with question 13.

If anti-HBc testing was not done, indicate "not done" and continue with question 14.

Centers for Disease Control & Prevention. (2012). *CDC Hepatitis B Information for Health Professionals.* Retrieved from http://www.cdc.gov/hepatitis/HBV/HBVfaq.htm

Question 13: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Hepatitis C Virus (HCV)

Hepatitis C infection is caused by the hepatitis C virus (HCV). Hepatitis C is generally spread through infected blood. Newly infected individuals are generally asymptomatic, though signs and symptoms of infection, similar to those seen in other viral hepatitis infections, can develop. Since acute hepatitis C infection is generally asymptomatic, it is rarely identified or treated during the acute infection stage. Approximately 15-25% of infected individuals will clear the virus without treatment, and will not develop chronic

hepatitis C infection. Chronic hepatitis C infection can lead to chronic liver disease and/or scarring of the liver (cirrhosis); chronic HCV is the leading indication for liver transplant in the United States. Currently no approved vaccination for hepatitis C exists.

Question 14: Hepatitis C antibody (Anti-HCV)

The total hepatitis C antibody refers to both IgG and IgM antibodies produced by the body in response to the presentation of antigens by the hepatitis C virus. Antibodies can generally be detected as soon as four weeks after exposure and will persist for life. Enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA) is used to screen for hepatitis C antibodies; confirmatory testing is done by recombinant immunoblot assay (RIBA). A positive ELISA or CIA result without confirmation by RIBA is considered an indeterminate result, unless HCV RNA is detected in the blood by PCR.

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 15.

If anti-HCV testing was not done, indicate “not done” and continue with question 16.

Question 15: Date sample collected

Indicate the date the sample was collected for infectious disease marker testing.

Human T-Lymphotropic Virus (Anti-HTLV I/II)

Human T-lymphotropic viruses include two distinct and separate retroviruses, HTLV-1 and HTLV-2. In 2005 two additional HTLV virus types (HTLV-3 and HTLV-4) were discovered and found to be closely related to the two originally known lymphotropic viruses. The mechanism of transmission of HTLV-1 and HTLV-2 is somewhat uncertain, but believed to be through exposure to blood or other body fluids, or through vertical transmission (maternal-fetal transmission). Patients infected with HTLV-1 or HTLV-2 are generally asymptomatic, and there is currently no treatment or vaccine. Infection with HTLV-1 is associated with an increased risk of T-cell leukemia/lymphoma. Patients with HTLV-1 or HTLV-2 are also at risk for HTLV-associated myelopathy, also known as tropical spastic paraparesis, a progressive and permanent disease of the central nervous system.

Question 16: Human T-Lymphotropic Virus antibody (Anti-HTLV I/II)

Testing for antibodies to HTLV is typically done by enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). The immunoassays are typically combined and will detect antibodies to HTLV-1 and HTLV-2. There is no way to determine if a positive result is due to antibodies to HTLV-1, HTLV-2, or both. Currently, there is no licensed confirmatory test for anti-HTLV I/II in the United States; confirmation of antibody presence is done by performing a second anti-HTLV I/II test using a different manufacturer’s test kit.

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 17.
If anti-HTLV I/II testing was not done, indicate “not done” and continue with question 18.

Question 17: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Human Immunodeficiency Virus (HIV)

HIV infection is caused by exposure to one of two viruses, either HIV-1 or HIV-2. HIV-2 is less virulent and has a longer incubation period than HIV-1. Both types of HIV progressively destroy CD4+ cells, which include T-helper cells, monocytes, and their derivatives (macrophages and dendritic cells), and are an important part of the body’s immune defense. HIV can lead to acquired immunodeficiency syndrome (AIDS), a condition in which the immune system begins to fail, leading to life-threatening opportunistic infections. Mechanism of HIV transmission is through exposure to blood or other body fluids, or through vertical transmission (maternal-fetal transmission).

Question 18: Human Immunodeficiency Virus p24 antigen (HIV-1 p24 antigen)
The HIV p24 antigen is a viral core protein that is detectable in the blood during acute infection; it is detectable earlier than HIV antibody. The p24 antigen appears approximately two weeks after exposure and will be present in the blood for three to five months. Once antibodies to HIV are detectable in the blood, p24 antigen is usually no longer detectable by immunoassay due to antigen-antibody binding. Enzyme-linked immunosorbent assay (ELISA) is used to test for the presence of p24 antigen; it may be done in conjunction with antibody testing in order to detect the virus in all stages of infection. Positive p24 antigen results require confirmation with specific antigen neutralization.

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 19.

If HIV-1 p24 antigen testing was not done, indicate “not done” and continue with question 20.

If HIV-1 p24 testing was performed but results are not being reported to CIBMTR (for example, donor declines to release results), indicate “not reported” and continue with question 20.

University of California, San Francisco. (n.d.) *HIV InSite Knowledge Base.* Retrieved January 15, 2013, from http://hivinsite.ucsf.edu/InSite?page=KB

Question 19: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Question 20: Was FDA licensed NAT testing for HIV-1/HCV performed?
Nucleic acid testing (NAT) is a combination PCR test that detects the presence of viral genes rather than antigens or antibodies. This test allows earlier detection and provides more sensitivity than previously used tests.

If the test results include HBV NAT testing or if a non-FDA licensed NAT test was used, report these results under question 43, *Other Infectious Disease Marker.*

If FDA-licensed NAT testing was used to assess the patient for presence of HIV-1 and/or HCV RNA, check "yes" and continue with question 21. If no FDA-licensed NAT testing was used to assess the patient for presence of HIV-1 or HCV RNA, check "no" and continue with question 25.

Question 21: Human Immunodeficiency Virus-1 (HIV-1) NAT
Report the laboratory result as "positive" or "negative," and continue with question 22.

If HIV-1 NAT testing was performed but results are not being reported to CIBMTR (for example, donor declines to release results), indicate "not reported" and continue with question 23.

Question 22: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Question 23: Hepatitis C (HCV) NAT
Report the laboratory result as "positive" or "negative," and continue with question 24.

Question 24: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Question 25: Anti-HIV 1 and anti-HIV 2
The HIV-1 and HIV-2 antibodies are produced by the body in response to the antigens presented by the HIV-1 and HIV-2 viruses, such as p24 (HIV-1) core antigen and p26 (HIV-2) core antigen. Antibodies are not detectable as early during the course of infection as the viral antigens, but will persist for the patient's lifetime once developed. Enzyme-linked immunosorbent assay (ELISA) is used to test for the presence of HIV-1 and HIV-2 antibodies. Most laboratories will utilize a combined assay that detects both viral antibodies, but in some cases they will be done as separate tests. Positive HIV-1 antibody results require confirmation by western blot, which uses gel electrophoresis to detect specific proteins. Currently, there is no licensed confirmatory test for anti HIV-2 in the United States; confirmation of antibody presence is done by performing a second anti HIV-2 test using a different manufacturer's test kit.

Report the laboratory result as "reactive" (positive) or "non-reactive" (negative) only if the patient was evaluated for antibodies to ***both*** HIV-1 and HIV-2. Continue with question 26.

If the patient was only assessed for antibodies to one virus, report “not done” and continue with question 27.

If no anti HIV-1 and anti HIV-2 testing was done, indicate “not done” and continue with question 27.
If anti HIV-1 and anti HIV-2 testing was performed but results are not being reported to CIBMTR (for example, donor declines to release results), indicate “not reported,” and continue with question 27.

Question 26: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Syphilis

Syphilis is a bacterial disease that spreads by contact with open syphilis sores that generally occur on the external genitalia and anus. It can also be spread through transmission from mother to fetus, also known as “vertical transmission.” It is caused by *Treponema pallidum* bacterium and can be treated with antibiotics; in the early stages of disease, syphilis is generally curable. Late stage syphilis—generally untreated or resistant disease—can cause permanent damage to internal organs or lead to neurosyphilis, where the bacterium invades the central nervous system.

Question 27: Serologic test for syphilis (STS)
Serologic testing for syphilis includes several testing methods which are either nontreponemal or treponemal. Examples of nontreponemal testing are Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) testing. Nontreponemal testing includes any evaluation done to detect antiphospholipid antibodies that are created by the body in response to syphilis infection; however, these antibodies are not specific for *Treponema pallidum*, and may also be created as response to HIV, malaria, pneumonia, or Lyme disease. Confirmatory testing must be done with treponemal methods for any positive result. Treponemal testing utilizes *Treponema pallidum* or its components to test for antibodies specific to syphilis infection. Treponemal testing includes fluorescent treponemal antibody absorption (FTA-ABS), microhemagglutination assay for antibodies to *Treponema pallidum* (MHA-TP), and *Treponema pallidum* hemagglutination assay (TPHA).

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 28.

If STS testing was not done, indicate “not done” and continue with question 29.

Question 28: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Cytomegalovirus (CMV)

Cytomegalovirus (CMV), also known as human herpes virus 5 (HHV5), is one of the *Herpesviridae* family and is very common. It is estimated that 50-80% of people in the United States are infected by age 40. In healthy individuals, infection with CMV may not lead to any symptoms; however, the virus will lay dormant in the body after initial infection and can reoccur. In immunocompromised patients, such as immunosuppressed transplant recipients or HIV/AIDS patients, the virus can have serious consequences such as pneumonia, liver failure, and death.

Question 29: Cytomegalovirus antibody (Anti-CMV) (IgG or Total)

Testing for antibodies to CMV is typically done by enzyme-linked immunosorbent assay (ELISA) or latex agglutination testing. These test methods can be used to detect IgM and/or IgG, which are both antibodies to CMV. The presence of IgM antibodies indicates a recent or current infection, usually within the past six months. The presence of IgG antibodies indicates a previous infection and confers a long-term immune response to the virus. All other factors being equal, CMV-negative products are generally preferred for CMV-naïve recipients. Results may be expressed as quantified antibody titer. In this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative.

Report the laboratory result as “reactive” (positive) or “non-reactive” (negative), and continue with question 30. A positive IgM or IgG assay is considered a “positive” or “reactive” result. Any previous history of positive antibody assay can be reported as a “positive” or “reactive” test result, even if the donor was not retested. All CMV testing on cord blood units should be reported as “non-reactive.” If IDM testing for a cord blood unit was done on maternal serum, report the documented testing result.

If anti-CMV testing was not done, indicate “not done” and continue with question 31.

Centers for Disease Control & Prevention. (2012). *CDC CMV Homepage.* Retrieved from http://www.cdc.gov/cmv/index.html

Question 30: Date sample collected

Indicate the date the sample was collected for infectious disease marker testing.

West Nile Virus (WNV)

West Nile Virus (WNV) is part of the *Flaviviridae* family and can infect birds, humans, and other mammals. It is spread by exposure to infected blood, most commonly through a mosquito vector. It can also be spread through transmission from mother to fetus (also known as “vertical transmission”), blood transfusions, organ transplant, or needlesticks. Mild or moderate symptoms of WNV may include fever, tiredness, headache and body aches, skin rash, and swollen lymph nodes. Severe symptoms of WNV include encephalitis, myelitis, and meningitis.

Question 31: West Nile Virus NAT (WNV-NAT)
Nucleic acid testing (NAT) is a PCR test that detects the presence of viral genes (WNV RNA) rather than antigens or antibodies. This test allows earlier detection and is more sensitive than antibody testing.

Report the laboratory result as "positive" or "negative," and continue with question 32. Do not report WNV enzyme-linked immunosorbent assay (ELISA) testing results; report this or any other WNV or anti-WNV testing under "Other Infectious Disease Marker" in questions 43-46.

If WNV-NAT testing was not done, indicate "not done" and continue with question 33. Do not use the "not applicable" option; "not done" is the most appropriate response for all situations in which WNV-NAT testing was not done.

Question 32: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Chagas (*T. cruzi*)

Chagas disease is caused by the parasitic protozoan *Trypanosoma cruzi* (*T. cruzi)*, which is endemic in South America, Central America, and the Caribbean. Chagas is spread through exposure to infected blood, most commonly through an insect vector such as triatomine bugs. It can also be spread through transmission from mother to fetus (also known as "vertical transmission"), blood transfusions, organ transplant, or needlesticks. In acute infection, there are rarely severe symptoms; most cases are asymptomatic or will exhibit generalized, non-specific symptoms. Treatment with anti-parasitic drugs during the acute phase is often curative. Of the individuals who are untreated and enter the chronic phase of infection, only 20-40% will ever have signs and symptoms related to Chagas disease. Symptomatic Chagas disease can affect the nervous, digestive, and cardiac systems and can be very severe, even resulting in death.

Question 33: Chagas
Testing for antibodies to *T. cruzi* is generally done by enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). If active infection is suspected, another evaluation, such as PCR, may be done to confirm and identify the strain of infection. In 2011, the FDA approved a more specific immunoassay that evaluates the donor for antibodies to specific excreted-secreted antigens presented by the *T. cruzi* pathogen. This assessment is intended to be a supplemental test for individuals who have been repeatedly reactive to the previously approved immunoassays.

Report the laboratory result as "positive" or "negative," and continue with question 34.

If Chagas testing was not done, indicate "not done" and continue with question 35.

Question 34: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Herpes Simplex Virus (HSV)

Herpes Simplex Virus includes two viruses, HSV-1 and HSV-2, which are two of the human herpes viruses (*Herpesviridae* family). Other human herpes viruses include cytomegalovirus (CMV), Epstein-Barr virus (EBV), and varicella zoster virus (VZV). HSV-1 is typically manifested as skin lesions or lesions of the oral mucous membranes; it may also infect the genitalia, but this is less common. HSV-2 is typically manifested as lesions of the external genitalia. Both HSV-1 and HSV-2 are spread through contact with lesions during active infection; HSV-1 can be spread through saliva. After initial infection, the virus will lay dormant in the body and can reoccur. Stress, fatigue, and infection can all cause the virus to be reactivated. According to data from 1999-2004, the seroprevalence of HSV-1 in individuals in the United States between ages 14-49 is estimated at 57.7%, while the seroprevalence of HSV-2 for the same population is estimated at 17.2%.[2]

[2]Xu F, Sternberg MR, Kottiri BJ, et al. (2006). Trends in Herpes Simplex Virus Type 1 and 2 Seroprevalence in the United States. *J Am Med Assoc, 296(8).*

Question 35: Herpes simplex virus antibody (Anti-HSV)
Testing for antibodies to HSV is typically done by enzyme-linked immunosorbent assay (ELISA), glycoprotein G-specific immunoblot assay, or Western Blot. These immunoassays detect antibodies to both HSV-1 and HSV-2, though the results will specify whether detected antibodies are specific to HSV-1 or HSV-2 (or both). Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative.

Report the laboratory result as “positive” or “negative,” and continue with question 36. If ***either*** HSV-1 or HSV-2 antibodies are detected, report “positive.”

If anti-HSV testing was not done, indicate “not done” and continue with question 37.

Question 36: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Epstein-Barr Virus (EBV)

Epstein-Barr Virus (EBV) is one of the human herpes viruses (*Herpesviridae* family). EBV infection may cause infectious mononucleosis, particularly in young adults. Infectious mononucleosis symptoms include fever, sore throat, lymphadenopathy, and fatigue. After initial infection, the virus will lay dormant in the body and can reoccur; recurrence of EBV is often subclinical. Late events associated with prior EBV infection

include Burkitt's lymphoma, post-transplant lymphoproliferative disorder (PTLD), and nasopharyngeal carcinoma.

Question 37: Epstein-Barr virus antibody (Anti-EBV)
Testing for antibodies to EBV is typically done by enzyme-linked immunosorbent assay (ELISA). This immunoassay can be used to detect IgM and/or IgG antibodies to EBV. The presence of IgM antibodies indicates a recent or current infection, usually within the past four to six months. Presence of IgG antibodies indicates a previous infection and confers long-term immune response to the virus. Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative.

Report the laboratory result as "positive," "negative," or "inconclusive," and continue with question 38.

If anti-EBV testing was not done, indicate "not done" and continue with question 39.

Question 38: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Varicella Zoster Virus (VZV)

Varicella zoster virus (VZV) is one of the human herpes viruses (*Herpesviridae* family). VZV, known as chickenpox with its initial presentation, manifests as pruritic skin blisters and typically first presents in childhood. After the initial infection, the virus will lay dormant in the body and can reoccur. Recurrence results in herpes zoster, more commonly known as shingles, which manifests as a painful, blistering skin rash.

Question 39: Varicella zoster virus antibody (Anti-VZV)
Testing for antibodies to VZV is generally done by fluorescent-antibody-to-membrane-antigen (FAMA), enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). These immunoassays can be used to detect IgM and/or IgG antibodies to VZV. Presence of IgM antibodies indicates a recent or current infection, usually within the past four to six months. Presence of IgG antibodies indicates a previous infection and confers a long-term immune response to the virus. Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative.

Report the laboratory result as "positive" or "negative," and continue with question 40.

If anti-VZV testing was not done, indicate "not done" and continue with question 41.

Question 40: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Toxoplasmosis

Toxoplasmosis is caused by the parasitic protozoan *Toxoplasma gondii*, or *T. gondii.* Toxoplasmosis is spread through ingestion of contaminated food or water, or contact with infected cat feces. *T. gondii* infection is usually subclinical in healthy individuals, but infection can cause serious symptoms in pregnant women and immunocompromised individuals. Chronic, dormant *T. gondii* infection may follow initial exposure, and can then reoccur. Severe toxoplasmosis can affect the brain, eyes, and other organs and can cause permanent organ damage.

Question 41: Toxoplasmosis
Testing for antibodies to *T. gondii* is generally done by enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA). These immunoassays can be used to detect IgM and/or IgG antibodies to *T. gondii*. The presence of IgM antibodies indicates a recent or current infection, usually within the past four to six months. The presence of IgG antibodies indicates a previous infection and confers a long-term immune response to the virus. Results may be expressed as quantified antibody titer; in this case, the laboratory or test kit manufacturer will provide reference ranges to determine if the result is considered positive, indeterminate, or negative. Confirmatory testing is available to verify a positive serological result; this is done by Toxoplasma Serological Profile (TSP), which is a panel of multiple antibody ELISAs and agglutination testing.

Report the laboratory result as “positive” or “negative,” and continue with question 42.

If Toxoplasmosis testing was not done, indicate “not done” and continue with question 43.

Question 42: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Other Infectious Disease Marker

Testing may be done for antibodies to pathogens other than those already listed on this form. If the donor was tested for any other infectious disease markers, report in questions 43-46. Questions 44-46 can be duplicated to report multiple additional IDM results.

Examples of other testing that may be reported as an “other infectious disease marker” include:

- Anti-HBs
- Anti-HBe

- WNV by ELISA
- Lyme disease

Question 43: Other infectious disease marker
Indicate if the donor was tested for an IDM other than those already listed on this form; do not report PCR results. If the donor was tested for other IDMs, check “yes” and continue with question 44. If the donor was not tested for any other IDMs, check “no” and continue with signature section.

Question 44: Date sample collected
Indicate the date the sample was collected for infectious disease marker testing.

Question 45: Specify test and method
Specify the pathogen(s) evaluated, the immunoassay or other test used, and the immunoglobulins measured.

Question 46: Specify test results
Report the qualitative laboratory results of the IDM (ex: reactive/non-reactive); do not report quantified titer levels.

Signature
The FormsNet3^{SM} application will automatically populate the signature data fields, including name and email address of person completing the form, and date upon submission of the form.

Manual Update History

Version Number	Date of Change	Type of Change (Add / Remove / Modify)	Description of Change
2.1	01/15/2015	Modify	Updated to meet CIBMTR brand standards
2.1	01/15/2015	Modify	Bolded in Infectious Disease Markers section: ***When reporting inconclusive or indeterminate test results, leave the results data field blank in the FormsNet 3^{SM} application and override the error as "unknown."***