CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Instructions for Infectious Disease Markers Form 2004

All transplant centers (both TED-only and Comprehensive Report Form) must complete the Form 2004 for all non-NMDP allogeneic or syngeneic donors and non-NMDP cord blood units. If the donor or cord blood unit was secured through the NMDP, IDM test results will be reported on NMDP Forms 24 and 50 by the donor center 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 but are not limited to: viruses, bacteria, fungi, and parasites. Infectious diseases may be transmitted through liquids, food, body fluids, contaminated objects, or airborne inhalation.

An Infectious Disease Marker (IDM) indicates if an individual currently has, or previously had, an infectious disease that could be transferred to another person. The purpose of IDM testing is to assess the donor's exposure to infectious diseases and the likelihood of transmitting a disease to the recipient.

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

Key Fields

For instructions regarding the completion of the Key Fields, see appendix K.

Infectious Disease Markers (report final test results)

The term *final test results* could refer to either the initial screening test or the confirmatory test. When the screening test is negative, a confirmatory test might not be done; in this case the screening test would be considered the *final test result.* However, when the screening test is *positive*, a confirmatory test might be completed; in this case the confirmatory test would be considered the *final test result.*

NOTE: Test Date

For the purposes of this manual, the term "test date" is defined as: **the date the laboratory conducted testing on the collected blood sample.** Report the date documented on the laboratory report that best fits this definition (e.g., report date, performed date, result date, accessioned date, received date, or document date).

NOTE: Reporting *inconclusive* and/or *indeterminate* test results

For paper form submission, draw a single line through the data field, write "unknown" in the margin, date, and initial. Using the FormsNet™2 application, leave the data field blank, override the error, and add "inconclusive or indeterminate result" in the override comment box.

Question 1: Who is being tested for IDMs?
Indicate whether a donor, the mother of a cord blood unit, or the cord blood unit itself is being tested for IDMs. Ensure that this corresponds with the product type specified in the key fields for this Form.

Hepatitis B Virus (HBV)

Hepatitis B is caused by the hepatitis B virus (HBV). Infection with this virus can cause scarring of the liver, liver failure, liver cancer, and even death. Hepatitis B is spread through infected blood and other body fluids. Acute hepatitis B infection does not usually require treatment because most adults clear the infection spontaneously. Treatment of chronic infection may be necessary to reduce the risk of cirrhosis and liver cancer.

Question 2: HBsAG (hepatitis B surface antigen)
The enzyme-linked immunosorbent assay (ELISA) or enzyme immunoassay (EIA) techniques test for the presence of proteins produced by the hepatitis B virus. Confirmatory testing is done using a neutralization test. The first marker appears approximately 3 weeks following infection, and disappears approximately 6 months later.

Report the laboratory result as "reactive" or "non-reactive" and continue with question 3.

If HBsAG testing was not done, check "testing not performed" and continue with question 4.

Question 3: HBsAG Test Date
Report the HBsAG test date as documented on the laboratory report.

Question 4: Anti-HBc (hepatitis B core antibody) (*no confirmatory test available*)
The ELISA technique tests for the antibody directed against the hepatitis B virus core proteins. The hepatitis B core antibody test can indicate previous HBV infection. Currently there is no licensed confirmatory test for Anti-HBc. If the screening test is reactive, a second Anti-HBc test is performed using a different manufacturer's test kit.

Report the laboratory result as "reactive" or "non-reactive" and continue with question 5.

If Anti-HBc testing was not done, check “testing not performed” and continue with question 6.

Question 5: Anti-HBc Test Date
Report the Anti-HBc test date as documented on the laboratory report.

Hepatitis C Virus (HCV)

Hepatitis C is a serious infection caused by the hepatitis C virus (HCV) which attacks the liver and may cause life-long infection. HCV is considered the most serious hepatitis infection because of its significant long-term health consequences. The infection is often asymptomatic, but once established, chronic infection can cause inflammation of the liver. This condition can progress to fibrosis and cirrhosis. In some cases, those with cirrhosis will go on to develop liver failure or liver cancer. Presence of the antibody in the blood represents exposure to hepatitis C virus, which is most often spread by blood-to-blood contact. No vaccine against hepatitis C is available.

Question 6: Anti-HCV (hepatitis C antibody)
The ELISA or EIA techniques test for antibodies to the hepatitis C virus. Confirmatory testing is done using the recombinant immunoblot assay (RIBA) test. These tests can determine past exposure to the hepatitis C virus, but not current viral load.

Report the laboratory result as “reactive” or “non-reactive” and continue with question 7.

If Anti-HCV testing was not done, check “testing not performed” and continue with question 8.

Question 7: Anti-HCV Test Date
Report the Anti-HCV test date as documented on the laboratory report.

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

The Human T-Lymphotropic virus I/II (HTLV I/II) is a retrovirus in the same class as HIV. HTLV I/II is associated with certain leukemias and lymphomas, as well as demyelinating diseases such as multiple sclerosis.

Question 8: Anti-HTLV I/II
Testing is done using combination ELISA or Chemiluminescent Immunoassay (ChLIA) which detects antibodies to the HTLV I/II viruses. There is no licensed confirmatory test for HTLV I/II. If the screening test is reactive, a second HTLV I/II test is performed using a different manufacturer’s test kit.

Report the laboratory result as “reactive” or “non-reactive” and continue with question 9.

If Anti-HTLV I/II testing was not done, check “testing not performed” and continue with question 10.

Question 9: Anti-HTLV I/II Test Date
Report the Anti-HTLV I/II test date as documented on the laboratory report.

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 lymphocytes, which 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. Infection with HIV occurs by the transfer of bodily fluids and is present as both free-virus particles and virus within infected immune cells.

Question 10: HIV-1 p24 antigen

The p24 antigen test detects the presence of a major core protein of HIV. Confirmatory testing is done using a neutralization test. Because the p24 protein is only detectable during a short window of time and the test is not effective once the body begins to produce antibodies, the p24 antigen test is no longer frequently used.

Report the laboratory result as “reactive” or “non-reactive” and continue with question 11.

If HIV-1 p24 antigen testing was performed but results are not being reported to CIBMTR, check “not reported” and continue with question 12.

If HIV-1 p24 antigen testing was not done, check “not performed, HIV NAT testing performed” and continue with question 12.

Question 11: HIV-1 p24 antigen Test Date
Report the HIV-1 p24 antigen test date as documented on the laboratory report.

Question 12: 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 (both HIV-1 and HCV RNA) rather than antigens or antibodies. This test allows earlier detection and provides more sensitivity than previously used tests.

If the test kit used also includes results for HBV NAT, report these results under question 25, *Other Infectious Disease Markers.*

If a non-FDA-licensed NAT test was used, results should be reported under question 25.

If FDA-licensed NAT testing was used to detect the presence of HIV-1/HCV, check “yes” and continue with question 13.

If FDA-licensed NAT testing was not used to detect the presence of HIV-1/HCV, check “no” and continue with question 17.

Question 13: HIV-1
Report the laboratory result as “reactive” or “non-reactive” and continue with question 14.

If NAT testing was performed but results are not being reported to CIBMTR, check “not reported” and continue with question 15.

Question 14: HIV-1 Test Date
Report the HIV-1 test date as documented on the laboratory report.

Question 15: HCV
Report the laboratory result as “reactive” or “non-reactive” and continue with question 16.

Question 16: HCV Test Date
Report the HCV test date as documented on the laboratory report.

Question 17: Anti-HIV 1 and anti-HIV 2* (antibodies to HIV)
*Testing for both HIV antibodies is required. This testing may be performed as separate tests or as a combined assay.

Testing is done using combination EIA which detects antibodies to the HIV-1 and HIV-2 viruses. HIV-1 is confirmed by Western Blot, which detects specific proteins using gel electrophoresis. There is currently no licensed confirmatory test for HIV-2. If the screening test is reactive, HIV-2 is confirmed by specific ELISA.

Report the laboratory result as “reactive” or “non-reactive” and continue with question 18.

If anti-HIV-1 and anti-HIV-2 testing was not done, check “testing not performed” and continue with question 19.

If anti-HIV-1 and anti-HIV-2 testing was performed but results are not being reported to CIBMTR, check “not reported” and continue with question 19.

Question 18: Anti-HIV 1 and anti-HIV 2: Test Date
Report the anti-HIV 1 and anti-HIV 2 test date as documented on the laboratory report.

If the anti-HIV 1 and anti-HIV 2 tests were not completed on the same day, report the first test date as documented on the laboratory report.

Syphilis

Syphilis is caused by the bacterium *Treponema pallidum* which usually enters the body through the mucous membranes. The infection alternates periods of activity with periods of inactivity. Syphilis (unless antibiotic-resistant) can be treated with antibiotics. If not treated, syphilis can cause serious effects such as damage to the heart, aorta, brain, eyes, and bones.

Question 19: STS
The term Serologic Test for Syphilis (STS) includes several different tests for syphilis, e.g., Venereal Disease Research Laboratory (VDRL), Rapid Plasma Reagin (RPR), and Fluorescent Treponemal Antibody Absorption (FTA-ABS).

The ability to detect syphilis depends on the stage of the disease. STS testing is nearly 100% accurate if used in the middle stages of the disease, but is less sensitive during the earlier and later stages. STS is sensitive, but is not specific for syphilis because it does not detect antibodies against the actual bacterium, but detects antibodies against substances released by cells when damaged by T. pallidum. Some conditions that may cause a false positive result are: HIV, Lyme disease, pneumonia, and malaria.

Other types of syphilis tests include: Treponema pallidum particle agglutination assay (TPPA) and Microhemagglutination assay – Treponema pallidum (MHA-TP). Any reactive RPR or VDRL test result should be confirmed by FTA-ABS or TPPA.

Report the laboratory result as “reactive” or “non-reactive” and continue with question “non-reactive” and continue with question 20.

If STS testing was not done, check “testing not performed” and continue with question 21.

Question 20: STS Test Date
Report the STS test date as documented on the laboratory report.

Cytomegalovirus (CMV)

CMV is a common virus that infects 50-90% of adults worldwide, and is transmitted from person to person through bodily fluids. The virus that causes CMV is part of the herpes virus family and, like other herpes viruses, CMV may be dormant for a period of time before the virus is activated in the host. CMV infections are usually harmless in a healthy immune system and typically cause only mild symptoms, if any. However, if a person's immune system is seriously weakened (as in an immunosuppressed stem cell recipient) the virus can have serious consequences such as pneumonia, liver failure, and even death.

Testing for CMV is often done using ELISA, which detects antibodies to the CMV virus. A titer of less than 0.91 indicates absence of infection. Agglutination testing is also a commonly used testing method for the presence of the CMV virus. There is no confirmatory test available for CMV.

Question 21: Anti-CMV (IgG or total)

The quantity of CMV antibodies in the blood indicates either a positive or negative test. If the exposure/infection was recent, it is usually detected with IgM antibodies. Past exposure/infection is usually detected with IgG antibodies; once exposed to CMV, an individual will likely have a measurable amount of IgG antibody in the blood for the rest of his or her life. For the purposes of this manual, either a positive IgM or a positive IgG test qualifies the result as "positive."

Report the laboratory result as "reactive" or "non-reactive" and continue with question 22.

If previous Anti-CMV testing was reported as reactive, check "previously reported reactive, not tested" and continue with question 23.

If CMV testing was not done, check "testing not performed" and continue with question 23.

Question 22: Anti-CMV Test Date

Report the Anti-CMV test date as documented on the laboratory report.

West Nile Virus (WNV)

WNV is a virus of the family *Flaviviridae.* WNV can infect birds, humans, and other mammals. The most common route of human infection is from the bite of an infected mosquito; however human-to-human transmission is possible through methods such as: occupational exposure, blood transfusions, organ transplant, etc. 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 23: WNV-NAT testing
Testing is done using the NAT (PCR) test which detects the presence of WNV RNA. There is no readily available confirmatory test for WNV.

Report the laboratory result as “reactive” or “non-reactive” and continue with question 24.

If WNV-NAT testing was not done, check “testing not performed” and continue with question 25.

If WNV-NAT testing was not required, check “not applicable” and continue with question 25.

Question 24: WNV-NAT Test Date
Report the WNV-NAT test date as documented on the laboratory report.

Other Infectious Disease Marker

Common tests that are often reported under the “other infectious disease marker, specify” field include, but are not limited to:

- Chagas
- Epstein-Barr Virus
- Herpes Simplex Virus
- Toxoplasmosis
- Sickle Cell Screen
- Varicella Zoster Virus
- Anti-HBs
- Anti-HBe
- WNV done by ELISA

Questions 25: Other infectious disease marker, specify (e.g., EBV)
If the donor was tested for an IDM other than those listed, check “yes” and continue with question 26.

If the donor was not tested for any other IDMs, check “no” and continue with question 37.

Questions 26: Specify date performed
Report the test date as documented on the laboratory report.

Questions 27: Specify test and method

Specify the test and method used to detect the IDM.

Questions 28: Specify test results
Report the laboratory results of the IDM.

Questions 29-32: Other infectious disease marker, specify (e.g., EBV)
See instructions for questions 25-28

Questions 33-36: Other infectious disease marker, specify (e.g., EBV)
See instructions for questions 25-28

Question 37: Contact information of person completing the form
Enter the name, phone number, fax number, and e-mail address of the person completing the form.