Interpretation:

V3 loop region of gp120, within the HIV-1 genome is amplified and sequenced. The sequences are analyzed using geno2pheno software. The results are reported as R5, X4 or D/M tropism. Dual/Mixed virus population can use CXCR4 and/or CCR5 Co-receptors to enter the CD+4 cells.
Presence of mutation at the primer binging site may lead to PCR amplification failure in rare situation.

Clinical Background :

- Human immunodeficiency virus (HIV) enters cells by a complex process that involves attachment to the CD4 receptor followed by binding to either the chemokine receptor 5 (CCR5) or chemokine receptor 4 (CXCR4) molecules and fusion of the viral and cell membranes.
- Maraviroc (Selzentry™, Pfizer) is the first co-receptor antagonist to be approved by the U.S. Food and Drug Administration (FDA). Maraviroc is a selective, slowly reversible, small-molecule antagonist of the interaction between human cell surface CCR5 and HIV-1 gp120, necessary for HIV-1 cell infection. Blocking this interaction prevents CCR5-tropic HIV-1 entry into cells. However, CXCR4-tropic HIV-1 entry is not prevented.
- M-tropic strains of HIV often use the R5 co-receptor, whereas T-tropic strain uses X4. There also exists dual- or mixed-tropic (DM or R5/X4) strain capable of using both the co-receptors. At an early stage of infection, virus exhibit R5 tropism, and in about half of them X4 strain appear at a later stage.
- Due to potential adverse effects (hepatic and cardiotoxicity), maraviroc should only be indicated in patients showing R5 tropism and not for X4 or DM or R5/X4 tropic viruses.

Clinical Indication for Testing:
HIV-1 Coreceptor Tropism analysis is considered medically necessary in an HIV-1 infected individual for either of the following indications:

- Prior to initiating a combination antiretroviral drug regimen with a coreceptor antagonist (CCR5 inhibitor, i.e. maraviroc); or
- In an individual who has experienced virologic failure while receiving therapy that contains a CCR5 inhibitor
- Note: This test has been developed and its performance is validated at Metropolis Healthcare Ltd.

Limitation of the Assay:
Presence of PCR inhibitors in the sample may prevent DNA amplification. Paradoxical results may arise due selection of inappropriate specimens and contamination during specimen collection.

References:

- Gupta et al., 2014, J Acquir Immune Defic Syndr.; 65(4):397-404
- Swenson et al., 2011, The Journal of Infectious Diseases;203:237–245
- Gibson et al., 2014, Antimicrob. Agents Chemother., vol. 58 no. 4 2167-2185