Reported by:
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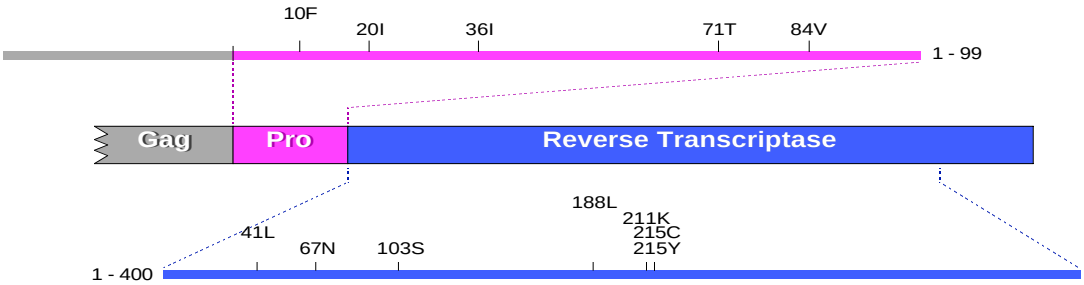
FOR INTERNAL USE ONLY

# *Virtual*Phenotype™

**Genotype with quantitative phenotypic analysis**

| Patient/Sample Details | | Test Details | | Physician Details |
|---|---|---|---|---|
| Patient Name | PATIENT_LAST_NAME, FIRST | Sample Type | SAMPLE | Hospital X |
| Subject ID | SUBJECT ID | Collection Date | Apr 14, 2003 15:22 | Address |
| Sample ID | SAMPLE ID | Receipt Date | Apr 14, 2003 | City ZIP |
| Patient ID | PATIENT_ID | Session | SESSION | State |
| Birth Date | DATE OF BIRTH | Report Date | Apr 24, 2003 | |
| Gender | X | Virco ID | VIRCO ID | |
| | | Lab ID | | |

## Resistance-associated mutations identified:




| Subtype analysis [1] |
|---|
| |

| Drug | | Matches in database | Proportion of matched samples: within normal susceptible range [2] / above normal susceptible range [2] / above normal susceptible range but below clinical cut-off [2, 3, 4] | Fold change in $IC_{50}$ (Cut-off for normal susceptible range) | Ref. |
|---|---|---|---|---|---|
| **Trade name** | **Generic name** | | 25 50 75 (%) | | |
| **NRTI** | | | | | |
| Retrovir® | Zidovudine | 98 | | 13.6 (4.0) | |
| Epivir® | Lamivudine | 879 | | 3.1 (4.5) | |
| Videx® | Didanosine | 490 | | 1.0 (2.0) | |
| Hivid® | Zalcitabine | 491 | | 0.9 (2.0) | |
| Zerit® | Stavudine | 568 | | 1.4 (1.75) | |
| Ziagen® | Abacavir | 467 | | 1.6 (3.0) | |
| **NtRTI** | | | | | |
| Viread™ | Tenofovir DF | 54 | | 2.0 (3.0) | 4 |
| **NNRTI** | | | | | |
| Viramune® | Nevirapine | 34 | | 63.9 (8.0) | |
| Rescriptor® | Delavirdine | 49 | | 31.6 (10.0) | |
| Sustiva®, Stocrin® | Efavirenz | 67 | | 135.3 (6.0) | |
| **PI** | | | | | |
| Crixivan® | Indinavir | 25 | | 5.3 (3.0) | |
| Norvir® | Ritonavir | 24 | | 11.9 (3.5) | |
| Viracept® | Nelfinavir | 25 | | 10.6 (4.0) | |
| Invirase®, Fortovase® | Saquinavir | 25 | | 7.0 (2.5) | |
| Agenerase® | Amprenavir | 23 | | 3.6 (2.0) | |
| A component of Kaletra® | Lopinavir | 5 | | 3.8 (2.5) | 3 |

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# *Virtual* Phenotype™

## Virco ID VIRCO ID - Subject ID SUBJECT ID

Details about patient and sample as well as the test results are printed on the previous page.

## [1] Subtype analysis

Sequence analysis of polymerase region generated for resistance testing purpose suggests that the virus is a member of HIV-1

## [2] Cut-offs and definitions

HIV-1 evaluated by any of the tests in the Virco HIV drug resistance monitoring range is categorised as either 'within the normal range of susceptible virus' or 'above the normal range of susceptible virus - reduced susceptibility'. The normal range of susceptible virus has been determined by performing phenotypic resistance tests on 1,000 untreated HIV-positive individuals and for several thousand samples of genetically wild type virus. The results are different for different drugs, highly concordant between the two analyses and form the basis on which the cut-offs below were derived. The cut-offs for the **Antivirogram®** phenotypic test are set at 2 standard deviations above the mean value for untreated or wild type virus. This means that any $IC_{50}$ value above this point is interpreted as being above the normal susceptible range (within the 97.5% confidence interval). The cut-offs for the *Virtual* **Phenotype™** are very similar to those for the **Antivirogram®.**

[3] Lopinavir is a component of Kaletra®. According to the FDA label, after 24 weeks of treatment of PI-experienced/NNRTI-naïve patients with Kaletra®, efavirenz and nucleoside reverse transcriptase inhibitors, a plasma HIV RNA ≤400 copies/mL was observed in 93% (27/29) and 65% (15/23) of patients with <10-fold and ≥10-fold reduced susceptibility to lopinavir at baseline, respectively. This 10-fold value may, therefore, represent a clinical cut-off above which the probability of a response to Kaletra® is reduced.

[4] According to studies cited in the FDA label, after 24 weeks of treatment of antiretroviral-experienced patients with Viread™ in combination with other antiretroviral agents, a mean reduction in plasma HIV RNA of 0.61 log10 copies/ml was observed for patients (n=91) with virus having ≤4-fold reduced susceptibility to Viread™ at baseline. Patients with virus having a greater than 4-fold reduced susceptibility had a mean reduction in plasma HIV RNA of 0.12 log10 copies/ml (n=9). This 4-fold value may, therefore, represent a clinical cut-off above which the probability of a response to Viread™ is reduced.

- The results printed on this report are based upon an HIV sequence provided to Virco for *Virtual* **Phenotype™** analysis only (information regarding the length of the submitted sequence is given on the front page of the report). Virco is not responsible for the quality, integrity or accuracy of the submitted sequence, nor for the accuracy of patient demographic data added to this report.
  Alternative sequencing methods that do not cover the whole of the protease gene (codons 1-99) and codons 1-400 of the reverse transcriptase gene, may not include all known resistance-associated mutations. This may result in a less accurate *Virtual* **Phenotype™** analysis.
- This is a complete report. The test result relates only to the items tested.
- The report shall not be reproduced except in full without the written approval of the testing laboratory.
- A patient's response to therapy depends on multiple factors including the percentage of a patient's viral population that is resistant, drug pharmacokinetics, and medication compliance. Therefore this test result should be interpreted in conjunction with the patient's antiretroviral treatment history, viral load count, and clinical status when making therapeutic decisions.
  This test may be unsuccessful if the plasma HIV RNA viral load is < 1000 copies of virus per ml of plasma, measured with Roche Amplicor Monitor assay™ (Roche Diagnostic Systems, Branchburg NJ).
- The sequencing assay was developed and its performance characteristics determined by Virco. It has not been cleared or approved by the U.S.Food and Drug Administration. Such FDA clearance or approval is not required.
- For NY State only: 'This test result is confidential HIV information and may not be redisclosed except as outlined by NY State Law (art. 27F).'
- VirtualPhenotype is a trade mark of Virco Central Virological Laboratory (Ireland) Ltd.
- Antivirogram is a trade mark of Virco BVBA and is registered in a number of countries.

**Molecular Biology Laboratory**

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**Interpretation and Final Approval**

Technical validation by JSM on Apr 24, 2003

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