Reviewer’s report

Title: DR_SEQAN: a PC/Windows-based software to evaluate drug resistance using human immunodeficiency virus type 1 genotypes

Version: 2 Date: 10 October 2005

Reviewer: John E Mittler

Reviewer’s report:

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The authors must modify the program so that information on the accuracy of their algorithm is included in their resistance prediction report. The simplest way to address this would be to include information from Table 1 just to the right of their predictions.

The authors should modify the program so that information on when their algorithm was last updated is displayed on the screen.

In some cases their two reports (the “resistance prediction” report on the left side of the screen and “fold-increase of IC50 relative to wild-type” report on the right side of the screen) gave conflicting predictions. For example, for protease L90M the resistance prediction was “partial resistance” even though the IC50 report indicted a fold increase of 1.0. This could confuse users. The authors should alter the program so that users can quickly grasp what these two reports are doing and why they may sometimes give different results.

There are already several other programs that perform similar functions, including some (such as SVM approach by Berenwinkel et al. 2003 and the linear regression model of Wang et al. 2004) that are based on objective quantitative modeling. The authors should comment on why rules-based algorithms should continue to be used when more quantitative methods are available.

The ability to predict IC50 changes using “Virologics” assay may not predict response to drugs in patients. The authors should discuss this in their paper.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Some of the symbols at the top of the screen (e.g. the one for “analyze”) are hard to interpret. I suggest replacing these symbols with words.

The authors should note that Virologics is now called “Monogram Biosciences.”

Discretionary Revisions (which the author can choose to ignore)

I could not use their program effectively until I changed the resolution on my monitor. The authors should consider reducing the size of some of the windows so that they will fit on low-resolution monitors. If this causes too many problems on other monitors they should include a note about the need to change monitor resolutions in the program itself.
When including information on prediction accuracies in the program, the authors should consider categorizing accuracies according to the number of mutations. I suspect that prediction accuracies will be higher for isolates with lots of resistance mutations than for those with only with only a few resistance mutations.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.