Scoring System (version 3) for the TREAT Asia Participants in HIV-1 GENOTYPIC DRUG RESISTANCE HIVG425 EXTERNAL QUALITY ASSESSMENT

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PREFACE

TREAT Asia (Therapeutics Research, Education, and AIDS Training in Asia) is a network of clinics, hospitals, and research institutions working to ensure the safe and effective delivery of HIV/AIDS treatments throughout Asia and the Pacific. Facilitated by amfAR, TREAT Asia seeks to strengthen HIV/AIDS care, treatment, and management skills among health care professionals through education and training programs developed by experts in the region (www.amfar.org/cgi-bin/iowa/asia/about/index).

Part of the role of the TREAT Asia Network is the evaluation of HIV drug resistance in the Asian region. The aims are to facilitate surveillance for antiretroviral (ARV)-resistant HIV-1 virus across subtypes and to monitor the development of resistance in individuals receiving ARV therapy. To ensure the quality of the laboratory test outcome, NRL has been charged with delivering an on-going External Quality Assessment Scheme (EQAS) code name: HIVG425 to laboratories in the TREAT Asia Network (known as TAQAS laboratories) that perform HIV genotypic resistance testing (genotyping) for the surveillance of ARV-resistant virus and patient management.

Participation in EQAS helps to assure the quality of testing. By comparing a participant's results of testing a panel of samples with either reference results or with a consensus of participants' results, the testing process is assessed. The value of EQAS lies in continuous participation in the scheme and depends on the results being generated in the usual way that clinical specimens are processed. Privacy and confidentiality are maintained by giving all participants an identifier known only to them, NRL and TREAT Asia. Mistakes or aberrant results alert the participant to review their test procedures. In addition, potential problems can be averted by reviewing aberrant results and the causes proposed for these. Thus EQAS can be conducted and viewed as an educational process.

Laboratories worldwide participate in HIVG425 and test two panels of five samples per annum. Participants' results are analysed and a detailed report of the participants' results is prepared and posted on the NRL Website. As part of the analysis each TAQAS participant's performance on a HIVG425 panel is scored according to the criteria detailed in this document.

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CRITERIA for SCORING TAQAS RESULTS

1. Participation

Consecutive participation is required. Penalties apply for late or failed submission of results.

2. Submission of edited nucleotide sequences (sequences)

Participants are scored on submission of sequences suitable for analysis. Participants are required to submit sequences from no less than 4 of 5 samples per panel. "No Score" is applied for any laboratory submitting sequence from fewer than 4 samples but results will be analysed.

3. Sequence clustering by phylogenetic analysis

Clustering of sequences reported by participants is assessed to determine accuracy of sequencing and lack of contamination. Results derived from a sequence that is identified as outlying are not scored on the remaining criteria. Participants are required to submit no less than 80% of sequences that cluster with sequences from the same sample. "No Score" is applied for participants submitting > 20% of outlying sequences.

4. Sequence Alignment

Participants' sequences must align with the Target Genotype (TG). (TG: the edited nucleotide sequences returned by participants are aligned to make a consensus sequence for each sample, known as the TG).

5. Sequence Agreement

Level of agreement between the participants' sequences across all regions sequenced and the TGs is expressed as a percentage.

6. Detection of drug resistance mutations (DRMs)

Participants' detection of DRMs across all samples is expressed as a percentage of DRMs in the TGs.

7. Detection of major DRMs

Participants' detection of DRMs as per the list given in Table 2 (overleaf).

8. Agreement in interpretation of ARV resistance

Agreement of a participant's interpretation with that of the majority of participants when a single interpretation system is used. This assessment is graded but NOT scored. Agreement <75% is graded as "Low". Agreement between 76% and 95% is graded as "Moderate". Agreement >95% is graded as "High".

9. Nucleotide mixtures (NMs)

Participants' detection of nucleotide mixtures (NMs) across all samples, expressed as a percentage of NMs in the TGs. This is included to highlight the importance of detection of NMs but NOT scored.

Table 1. TAQAS Scoring System version 3

The lower the score, the better the result. A score up to 33 is acceptable.

	Scoring Criterion	Points lost	Best possible Score	Worst possible Score	Acceptable Score
1	**Participation** [a.]	Failure to submit results: 10 points. Late submission of results: 1 point per week or part thereof.	0	10	2
2	**Submission of nucleotide sequences** [b.]	PR or RT sequence per sample not submitted: 1 point. Less than 4 of 5 sample sequences submitted **NO SCORE**.	0	**NO SCORE**	2
3	**Sequence clustering** [b.]	Poor sequence clustering per PR or RT sequence 5 points. Less than 80% of sequences cluster **NO SCORE**.	0	**NO SCORE**	10
4	**Sequence Alignment**	Lack of alignment with consensus per PR or RT sequence per sample: 1 point.	0	10	2
5	**Sequence Agreement** [b.]	% agreement with TG: 2 points ≥98% but <99%; 5 points ≥95% but <98%; 10 points ≥90% but < 95%; 15 points < 90%.	0	15	10
6	**Drug resistance mutations (DRMs)**	% agreement with TG: 2 points < 95% but >90%; 5 points < 90% but >85%; 10 points <85% but >80%; 15 points < 80%.	0	15	2
7	**Detection of major DRMs**	DRM(s) identified as different from majority: 5 points per major DRM.	0	?	5
	Total		**0**	**>50**	**33**

a. Points are not accrued if TAQAS provider is informed of delays that occurred as an outcome of circumstances beyond the participant's control or testing difficulties were encountered.

b. "Hurdle requirement" participant must return ≥ 80% of sequence data suitable for analysis to be scored on their performance.

Table 2. Protease Inhibitor (PI), Nucleoside Reverse Transcriptase Inhibitor (NRTI), and Non-nucleoside RTI (NNRTI) Drug Resistance Mutations considered in the TAQAS Scoring System version 3.

PI Mutations	NRTI Mutations	NNRTI Mutations
L23I	M41L	L100I
L24I	A62V	K101EP
D30N	K65RN	K103NS
V32I	D67N	V106AM
M46IL	69 ins	V108I
I47VA	K70R	Y181CIV
G48VM	L74VI	Y188LHC
I50LV	V75ITM	G190ASE
F53L	F77L	P225H
I54VTALM	Y115F	F227LC
G73ST	F116Y	M230L
L76V	Q151M	P236L
V82AFSTL	M184VI	K238T
I84VAC	L210W	
N88DS	T215FY	
L90M	K219QE	