VQA PROGRAM TESTING REQUIREMENTS TO OBTAIN APPROVAL TO PARTICIPATE IN GENOTYPIC HIV DRUG RESISTANCE PROFICIENCY TESTING FOR NIH-FUNDED PROTOCOLS

New Laboratory Pre-Qualification Testing: Participation in any VQA proficiency testing program must be approved by the VQA Contracting Officer Representative (COR, aka Project Officer). In order to be considered for participation in the VQA program, a new laboratory must be doing genotypic HIV drug resistance testing for a NIH-funded program. Once approved, the new laboratory will need to complete an application for participation in the program, which will outline the programs of interest and provide laboratory contact information. A new VQA laboratory number will be assigned to each VQA laboratory to uniquely identify that laboratory within the program.

The VQA genotypic HIV drug resistance proficiency testing program currently evaluates assay performance for reverse transcriptase (RT), protease (PR) and integrase (INT) gene regions. RT and PR genes are evaluated together, and the INT gene region is evaluated separately. Laboratories may opt to participate in one or both programs. Participation rules are the same regardless of the gene region being evaluated.

The VQA program accepts data for genotypic HIV DR (HIV GEN) testing generated using commercially available (ViroSeq, VS and TruGen, TG) and internally developed assays (IH). Sequence files must be submitted to the VQA via web utility programs. All new laboratories must register with the VQA Data Management Group (DMG, FSTRF) at http://www.fstrf.org/ in order to gain access to these web utilities. Information regarding panel labeling requirements and rules for data submission will be provided to the testing laboratory when panels are shipped for testing.

In order to achieve an Approved status for VQA HIV GEN testing, a laboratory must run and pass a total of four (4) five-member panels. Panels may be tested during regular rounds of proficiency testing, which occurs two times per year, or it may be **Fast-Tracked** using historical panels that have been pre-tested in the field. Since consensus sequences are derived using data generated in the field, previous validation of the samples testing is required.

A laboratory must pass two (2) five-member panels in order to prequalify and to become provisionally approved. Panels must be tested as five-member panels. The data must be submitted for scoring before the next panel is tested in order to identify problems early in the process. A score of “C” is required before a laboratory will test the second prequalification panel. A second score of “C” is required to obtain entry into the real-time proficiency testing program. If a score of “PC” is obtained on the second prequalification panel, then a laboratory would need to obtain a score of “C” on the third panel in order to gain entry into the real-time proficiency testing program. A subsequent score of a “PC” or a single score of “P” on the third prequalification panel would require intervention by the VQA laboratory prior to testing any additional panels.

Once the pre-qualification phase is completed, a laboratory will be “provisionally approved” for protocol testing. Full approval may be achieved once a laboratory has successfully

passed two real-time proficiency testing panels. *Note: the VQA will provide a rating for each laboratory based on the results of pre-qualification and ongoing proficiency testing. However, the approval for protocol testing is defined at the network level and thus approval ratings may require additional testing as deemed necessary by the individual networks.*

Pre-certification Testing: Any laboratory may obtain retrospective Genotyping proficiency panels prior to enrollment in the program, or at any time during their participation in the VQA program. Once a panel has been tested and analyzed as a 'practice' panel, it cannot be reclassified for use in laboratory certification. Results from these 'practice' panels will be assessed and results returned to the laboratory, but no certification score will be assigned.

Normal Track Testing: A laboratory participating in the real-time proficiency testing program will receive a panel of 5 coded specimens every six months. The panel members will be analyzed by each participating laboratory and the data will be submitted to the VQA Statistical Analysis Group (SAG) for scoring within the time frame specified by the ***VQA LAB***. Missed panels (due to exceptions) will have to be completed by the next round of testing. A score for each round of testing will be based upon an analysis of the data received from all participating laboratories. Laboratories will be scored within kits, though analyses across kits may eventually also be evaluated.

Cumulative ratings will be assessed as with other VQA proficiency testing programs, except the first two (or three) prequalification panels will be included in the cumulative scoring until four real-time proficiency testing panels have been completed. A laboratory's performance rating (PR) is based on the sum of the scores for the four (4) most recent proficiency panels (Performance Score, PS). Individual proficiency panels are scored a "1" for a Certified (C), "2" for a Provisionally Certified (PC), and "4" for a Probation (P). The Performance Score (PS) results in a Performance Rating (PR) are assigned as listed in the table below.

ASSESSMENT	PS	PR	Action
APPROVED	4-6	A	Eligible for protocol testing
PROVISIONALLY APPROVED	7-9	PA	Eligible for protocol testing at discretion of protocol virologist
NOT APPROVED	10-13	NA	Not eligible for protocol testing
MANDATORY EXPULSION	$\geq$ 14	ME	Not eligible for protocol testing

A new laboratory must obtain an APPROVED performance rating prior to performing any protocol testing. A laboratory will be fully approved for testing after two real-time proficiency testing panels if a score of "C" is obtained on both. If a score of "P or PC" is obtained on the first real-time panel after certification, then the approval rating will be based on the cumulative score obtained by the laboratory once a total of 4 panels (including pre-qualification and real-time proficiency testing) have been tested. Any score of "P" on a panel tested after qualification would require a laboratory to run and pass (with a score of "C") two 5-member panels before full approval may be (re)achieved.

Approval ratings are based on the sum of scores across the four most recent panels. A laboratory will be provisionally approved after successfully completing the pre-qualification process. "B" panel configurations of the real-time proficiency testing panels will be available to permit fast-tracking of the approval rating.

Continued Approval: To retain an 'Approved' status, a laboratory must participate in two rounds of real-time proficiency testing per year as scheduled by the ***VQA LAB***. The ***VQA LAB*** manager or director must approve all requests for exemptions or extensions. A laboratory may be placed 'on hold' for up to 12 months without penalty (see section on withdrawal from the program). Laboratories that are placed on hold for more than 6 months will be expected to run all real-time proficiency testing panels missed (not to exceed 2 panels) upon re-entering the program. A score of "C" must be obtained on both panels in order to resume protocol testing.

Withdrawal/Removal: A laboratory may voluntarily withdraw from the VQA Genotyping proficiency testing program at any time. A laboratory may request to be placed 'on-hold' as a result of operational circumstances (e.g. personnel problems, laboratory issues, etc.) for up to 12 months. A laboratory may not perform protocol testing while 'on hold'. A laboratory that has not participated in the VQA proficiency testing program for more than 12 consecutive months will automatically be removed from the program.

Re-certification: If a laboratory wishes to re-enter the Genotyping proficiency testing program after removal, or has ongoing problems with proficiency panels, the laboratory will need to be requalified as a new laboratory (see section above).

Proficiency Testing:

Once enrolled in the real-time proficiency testing program, laboratories will receive 5 blinded samples every six months. The ***VQA LAB*** will determine a specified time frame for completion of testing the samples. The laboratory must submit a specimen information file (an EXCEL spread sheet developed by the VQA) and the FASTA/sequence text file for each specimen to the VQA SAG for analyses. The project/case file will also be submitted. Panels will be assessed for sequence homology and mutation calls. Scoring criteria for this proficiency testing program may be viewed in the HIV-1 Genotypic Resistance Testing Scoring Criteria document posted on the VQA website.

Protocol Testing Eligibility Based on Proficiency Testing Cumulative Scores: A laboratory's cumulative performance rating will be defined after the first year of the program. "B" panel configurations will be created for each round of testing to permit retesting in the event of problems. Re-approval status may be attained after failure of a panel by obtaining two scores of "C" on two consecutive panels after the first failure. This may be achieved by running a "B" panel configuration for the panel that failed and running the next scheduled panel send-out (two 5-member panels must be completed and passed within 6 months of the first failure). Additionally, other archived panels may be tested if a laboratory wishes to recertify before the next scheduled panel send-out.

Change in Status Letters: Subsequent to review of the VQA score recommendations by the VQA Advisory Board (VQAAB), the ***VQA LAB*** will generate a "Change In Status Letter" if a

laboratory obtains a score on a round of testing that changes their overall performance rating. This letter will document the laboratory's scores over the last four rounds of testing and will indicate when a change in status (performance rating) has resulted. A copy of this letter will be sent to the director of the laboratory and the network leadership for whom the laboratory does testing. Letters will be sent to notify individuals of both negative and positive changes in approval ratings. The **VQA LAB** submits the letters on behalf of the VQAAB, but has no control over the implementation of rules governing the ability of a site to continue protocol testing. All questions surrounding a laboratory's ability to resume or discontinue protocol testing should be directed to the respective network leadership.

Please contact the ***VQA LAB*** manager (vqa@rush.edu) if you have any questions regarding this proficiency testing program.