Duke Virology Quality Assurance

VQA

Executive Summary

Version 1.0

Year 2 VQAAB Annual Review Meeting

October 26 & 27, 2021

Contract # 75N93019C00015

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Dec 1, 2021

(Date)

Bill Meyer,
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DEC 10, 2021

(Date)

NIH National Institute of Allergy and Infectious Diseases

Overall Summary

The Duke Virology Quality Assurance (VQA) Advisory Board (VQAAB) Annual Review (VAR) meeting for Year 2 was held virtually on October 26 & 27, 2021. **Table 1** summarizes all of the attendees external to Duke including the VQAAB members (voting and non-voting), NIH representatives, collaborators (Vitalant Research Institute, VRI; Kilimanjaro Christian Medical Centre, KCMC), and guests that were in attendance for one or both days of the meeting.

Table 1: VQAAB Annual Review Meeting YR 1 Attendees

VQAAB Voting Members		
Bill Meyer (Chair)	Marco Schito	Nicole Tobin (IMPAACT)
Jon Li (ACTG)	Urvi Parikh (MTN)	Jessica Fogel (HPTN)
Belinda Yen-Lieberman (ACTG)		
VQAAB Non-voting Members		
Ron Bosch (SDAC)	Diane Costello (IMPAACT/ACTG)	
HANC		
Tyler Brown		
NIH Representatives		
Keith Crawford (NIAID/DAIDS)	Fatima Jones (NIAID/DAIDS)	Daniella Livnat (NIAID/DAIDS)
Collaborators		
Mike Busch (VRI)	Sonia Bakkour (VRI)	Mars Stone (VRI)
Matt Rubach (KCMC)	Blandina Theophil Mmbaga (KCMC)	
Additional Guests		
Joe Fitzgibbon (former NIAID/DAIDS)	Neil Parkin (WHO consultant)	Allan Levesque

During the meeting, the VQA provided a summary of Year 2 activities and proposed milestones for Year 3. Prior to the meeting, the VQA provided a Meeting Booklet that contained updated and edited versions of the VQA Participation Requirements and Scoring Procedures for the Quantitative HIV-1 RNA, Qualitative HIV Total Nucleic Acid, and HIV-1 Drug Resistance Proficiency Testing (PT) Programs; a memo that will be disseminated to the sites detailing important participation guidelines for sites; a proposed non-technical penalty for data entry errors; and a model letter for closure of the Investigation Reports. Summaries of these documents, were presented to the VQAAB for their approval.

Members of the Duke VQA team presented the actions performed to address the VQAAB Year 1 recommendations, which included a review of a performance survey that was distributed to all of the participating sites. The survey collected information regarding VQA overall performance, quality assurance added value, the VQA web-based system, shipping and quality control materials (QCM), and communications. The Duke Biostatisticians provided a summary of data management and longitudinal trends in data analysis. Additionally, the VQA provided an update on the SARS-CoV-2 work including the development of a pipeline for generating material for a SARS-CoV-2 sequencing program and summary of a second SARS-CoV-2 Neutralization Antibody Concordance Survey (SNACS). Our collaborators from KCMC gave an overview of efforts to acquire non-subtype B HIV-1 strains with drug resistance mutations. Our collaborators from VRI gave a presentation on the HIV Reservoir Assay Validation and Evaluation Network (RAVEN) Program, which was followed by a discussion to determine the need for QCMs for reservoir testing. In the final presentation the Quality Assurance for Duke Vaccine Immunogenicity Program (QADVIP) presented an overview of our ISO 17043 and ISO 17020 accreditations.

Overall Recommendations

The overall VQAAB recommendations for the VQA Program include:

- Approval of proficiency test scores will now occur by email after the PT has been analyzed and site-specific reports have been generated. A blinded PT summary will be sent to the VQAAB with a one week deadline to vote on the proposed scores. A meeting will be called if further discussion is warranted.
- Quarterly VQAAB meetings will be held to provide an avenue for receiving critique and advice for future directions to remain innovative and relevant. These meetings will be scheduled, and may be canceled if not required.
- Implement manual tracking of shipments that contain dry ice
    - Request records from courier as to the state of the dry ice when replenished
    - Confirmation of the condition of the package and date received by the site
- Release the proficiency testing memo, circulated prior to the VQAAB Annual Review Meeting, to laboratories via email and upload to the VQA website
- Explore accessing VQA quality control results from Frontier Science that were submitted with clinical testing data.

GCLP-Compliance and ISO/IEC 17043 Accreditation

Kristen Skinner from QADVIP presented an overview of the Good Clinical Lab Practices (GCLP) and ISO/IEC 17043 activities for the second year of the VQA Contract. QADVIP, ledby Marcella Sarzotti-Kelsoe, oversees all GCLP and ISO/IEC 17043 compliance and is ISO/IEC 17020 certified as an inspection body. Duke has received ISO/IEC 17043 accreditations as a PT provider for the Quantitative HIV-1 RNA, Qualitative HIV-1 NAT,and HIV-1 Drug Resistance PT programs.

The VQAAB did not make any additional recommendations.

The Quality Assurance milestones for YR3 of the VQA program are as follows:

- **Milestone 1:** Perform internal audits for all VQA PT programs.
- **Milestone 2:** Maintain ISO/IEC 17043 and 17020 accreditations for all VQA PT Programs

Quantitative HIV-1 RNA

Sal Scianna provided an overview of the Quantitative HIV RNA program for Year 2. Topics that were covered included:

- Production and quality control testing of panels and controls
    - Virus stock for production of controls and PT was obtained from the External Quality Assurance Program Oversight Laboratory (EQAPOL)
    - Panels are tested using the Roche Taqman, Roche cobas 6800, GeneXpert and Abbott m2000.
        - Approximately 15 aliquots per concentration are tested prior to shipment
- Summary of the data analyzed by the Duke VQA Biostatisticians and scoring procedure

The VQAAB recommended continuing to monitor the addition of new assays and the changing assay landscape in order to re-evaluate scoring procedures to avoid penalizing high recovery platforms and to consider dividing analysis based upon platforms.

The milestones for the next year include:

Milestone 1: Ship the VQA RNA2022 panels to be tested as part of the four Quantitative HIV-1 RNA PTs in 2022

Milestone 2: Complete PTs RNA2021_11, RNA2022_02, RNA2022_05, and RNA2022_08

Qualitative HIV-1 NAT

Terese Camp provided an overview of the Qualitative HIV-1 NAT program for Year 2. Topics that were covered included:

- Frequency of PTs
- Composition, production, and shipment of panels
- Summary of the data analyzed by the Duke VQA and scoring procedures

The VQAAB recommended to keep considerations of the new FDA approved HIV qualitative plasma-based assays as a future area of development for the program.

The milestones for the next year include:

Milestone 1: Complete NAT2022_03

Milestone 2: Complete NAT2022_09

Milestone 3: Produce additional cell pellet and DBS controls

HIV-1 Drug Resistance

Sal Scianna and Bhavna Hora provided an overview of the HIV-1 Drug Resistance (GEN DR) program for Year
1. Topics that were covered included:

- Summary of laboratories enrolled in the program
  - VQA / WHO only
- Frequency of PTs
- Composition, production, quality control testing, and shipment of panels
  - Provided a diagram of the Homogeneity and Stability workflow
- Summary of the data analyzed by the Duke VQA and scoring procedures

- Use of phylogenetic clustering to support review and analysis of samples
- Overview of the HIV-1 Drug Resistance Virus Source Material
    - EQAPOL Viral Diversity Repository
    - Pan Resistant sample acquisition
    - Develop molecular clones with random mutations
        - Introduce mutations into subtype A1, B, C, D, and URF_A1D IMCs

The VQAAB recommended to:

- Develop a validation plan that incorporates precision, specificity, interfering specimens (in-house assays) using a sample with pan resistance
- Update Scoring
    - Incorporation of phylogenetic trees results for scoring purposes
    - Apply the PIA (Potential Issue Alert) concept to GEN PT ratings
- Consider the possibility of expanding subtypes represented in GEN DR Panel
- Develop a plan for the addition of real-time samples to participating labs that would be tested with clinical samples. Data will be submitted periodically to VQA for analysis
    - frequent QC samples run in parallel with PT panels
    - Submission real time via VQA Web System

The milestones for the next year include:

Milestone 1: Complete GEN2022_01

Milestone 2: Complete GEN2022_07

Milestone 3: Increase the number of samples with integrase mutations in the repository that can be used for future PTs

VQA Advisory Board October Bi-Monthly Meeting

Terese Camp provided the VQAAB with a summary of the data analyzedfor NAT2021_09, RNA2021_08, and GEN2021_05 in a blinded manner. TheVQAAB reviewed the data and voted to pass the proposed scores with a vote of 6 in favor and none opposing. TheVQAAB also voted to pass the non-technical penalty for data entry errors presented during the meeting with a vote of 6 in favor and none opposing.

SARS-CoV-2

On June 21, 2021, NIAID executed a VQA option to continue SARS-CoV-2 related activities. The funding will support sample acquisition of large volume plasma that will be used to create a second SNACS panel. Miranda Carper provided a brief overview of SNACS I and described proposed panel configuration and collaborations with VRI, the BC Centre for Disease Control and Canadian Blood Service, University of California, San Francisco, and the South African national Blood Service to acquire material from individuals infected with sequence confirmed SARS-CoV-2 variants.

Last year, the VQAAB recommended the VQA develop a SARS-CoV-2 sequencing PT. Bhavna Hora and Manfred Meng discussed activities performed by Duke VQA to model the creation, heat-inactivation, and sequencing of QCMs. The developed pipeline that can be used to create a future SARS-CoV-2 PT if determined to be needed by NIAID.

The VQAAB recommended to benchmark SNACSII material with the WHO standard.

Kilimanjaro Christian Medical Centre (KCMC)

Matthew Rubach from KCMC provided an overview of the collaborative efforts between Duke VQA and KCMC to ensure VQA materials are representative of the global epidemiology of HIV-1.

The VQAAB recommended KCMC capture the history of treatments patients have received and if able, to share this information with VQA.

The milestones for the next year include:

Milestone 1: Finalize Data Transfer Agreement

Milestone 2: National Approval of IRB amendment (obtained late August 2021)

Milestone 3: Ship plasma samples to Duke VQA for sequencing

- Fall 2021: 11 samples had viral load above 10,000 copies/mL
- Spring 2022: Additional samples to be collected and shipped

Milestone 4: DHVI Processes:

- Sequencing of samples
- Select Samples for virus culture

HIV Reservoir Assay Validation and Evaluation Network (RAVEN)

Sonia Bakkour from VRI provided an overview of the RAVEN program's key resources, RAVEN sample collection and repository, assays evaluated at VRI, VQA and VRI collaboration to analyze data from a RAVEN Evaluation panel, and need for a Reservoir PT program.

The VQAAB recommended VRI to reach out to NIAID to get directions for future needs for Reservoir QCM/ PT Program and to focus on QA for novel assays to move field forward including addressing the lack of a gold standard in RAVEN Cohort, creation of cell line standards, and the IPDA assay.

Milestone 1: Sample acquisition in support of SARS-CoV-2 neutralization assay external quality assurance and internal quality controls

Milestone 2: Create HIV cell associated controls to support the ACTG Virology Specialty Labs

Milestone 3: Continue discussion of plans for HIV reservoir assay quality control materials based on current needs of NIAID and the networks

Milestone 4: Collaborate with VQA to analyze data from RAVEN Evaluation Panels and draft manuscripts