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Review

Implementation of Good Clinical Laboratory Practice (GCLP) guidelines within the External Quality Assurance Program Oversight Laboratory (EQAPOL)☆

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ABSTRACT

The EQAPOL contract was awarded to Duke University to develop and manage global proficiency testing programs for flow cytometry-, ELISpot-, and Luminex bead-based assays (cytokine analytes), as well as create a genetically diverse panel of HIV-1 viral cultures to be made available to National Institutes of Health (NIH) researchers. As a part of this contract, EQAPOL was required to operate under Good Clinical Laboratory Practices (GCLP) that are traditionally used for laboratories conducting endpoint assays for human clinical trials. EQAPOL adapted these guidelines to the management of proficiency testing programs while simultaneously incorporating aspects of ISO/IEC 17043 which are specifically designed for external proficiency management. Over the first two years of the contract, the EQAPOL Oversight Laboratories received training, developed standard operating procedures and quality management practices, implemented strict quality control procedures for equipment, reagents, and documentation, and received audits from the EQAPOL Central Quality Assurance Unit. GCLP programs, such as EQAPOL, strengthen a laboratory's ability to perform critical assays and provide quality assessments of future potential vaccines.

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1. Introduction

The External Quality Assurance Program Oversight Laboratory (EQAPOL) is a contract awarded by the National Institutes of Health/National Institute of Allergy and Infectious Diseases/Division of AIDS (NIH/NIAID/DAIDS) to support the development of external proficiency testing programs for flow cytometry-, ELISpot-, and Luminex bead-based assays (cytokine analytes). The EQAPOL Program is comprised of a Central Management Team, Central Quality Assurance Unit (CQAU), Statistical Group, Data Management Group, Biorepository, Central Laboratory, A3R5 Neutralizing Antibody Assay Validation Program, and three EQAPOL Oversight Laboratories (EOLs) described in detail in this issue of Journal of Immunological Methods (see Ferrari et al. for ELISpot; Staats et al. for ICS by Flow Cytometry; Sempowski et al. for cytokine-based Luminex). In addition to proficiency testing, EQAPOL is also tasked with creating a diverse panel of high-titer (approximately 10^9 copies/mL), HIV-1 viral culture supernatants grown in PBMC from seed stocks (i.e., from plasma samples and other source material) using a Viral Diversity Core (see Sanchez et al. in this issue) and in validating immunogenicity assays (see Sarzotti-Kelsoe et al. in this issue).

The EQAPOL Laboratory Teams (EQAPOL Viral Diversity Core, Biorepository, Central Laboratory, A3R5 Neutralizing Antibody Assay Validation Program, and each of the EOLs) are required to operate under Good Clinical Laboratory Practices (GCLP), since this is a set of standards designed to facilitate uniform and consistent data generation and reporting. GCLP encompasses both quality assurance (QA) and quality control (QC) principles into its standards. QA proactively and periodically reviews the various components of the research process to assess adherence to standard operating procedures (SOPs) and policies and to determine the accuracy of research records. QC measures are continuous and carried out on all records (QC logs, worksheets, etc.) by the Laboratory Teams. While external laboratories, participating in the EQAPOL proficiency testing programs, are not required to operate under GCLP, many of these laboratories are already GCLP-compliant and perform clinical trial related work. It is for this reason that the program operates in GCLP compliance as it ensures the quality, integrity, and validity of the test data.

GCLP was initially designed by the British Association of Research Quality Assurance (BARQA) in 2003 and later expanded upon by the NIH/NIAID/DAIDS in 2008 to provide a regulatory framework to laboratories performing endpoint assays for HIV-1 human clinical trials (Stiles et al., 2003; Ezzelle et al., 2008). The two sets of GCLP guidelines were harmonized in 2009 in order to provide a single set of recommendations for laboratories to utilize (Sarzotti-Kelsoe et al., 2009). The process of converting laboratories into GCLP-compliant entities includes initial laboratory assessments and GCLP training; establishment of SOPs, Quality Management Systems and Study Plans; quality controlled equipment and reagents; optimization and validation of applicable assays; and laboratory audits and corrective action programs. The EQAPOL CQAU, which has over 10 years of experience in performing audits, document control and study monitoring in GCLP compliance, was tasked with implementing these standards for EQAPOL (Sarzotti-Kelsoe et al., 2009; Ozaki et al., 2012; Todd et al., 2012).

External Quality Assurance (EQA) Programs serve three purposes according to GCLP guidance: 1) provide a way for laboratories to ensure that data generated are timely, accurate, and clinically appropriate; 2) provide sponsors with assurance that data generated are of the highest quality; and 3) ensure that human specimens from clinical trials will be tested accurately and reliably (Ezzelle et al., 2008). Although GCLP is a robust set of guidelines governing the conduct of endpoint assays for clinical trials, there are no specific statements regarding the management of external proficiency testing programs. The International Organization for Standardization (ISO) and International Electrotechnical Commission (IEC) have created a set of guidelines/requirements (ISO/IEC 17043) for external proficiency testing programs to follow, so as to provide extra assurance to participants that the program is operated competently (ISO/IEC, 2010). ISO/IEC 17043 requirements primarily apply to management, planning and design, personnel, quality assurance, and confidentiality (ISO/IEC, 2010). The EQAPOL CQAU implemented GCLP, along with many aspects of ISO/IEC 17043, in an effort to make the program compliant to the most appropriate quality standards.

In addition to the proficiency testing programs, EQAPOL was also charged with establishing and characterizing clade-specific HIV-1 viral culture panels representing world-wide genetic diversity. These HIV-1 viral diversity panels are created from HIV-1 positive plasma specimens received from collaborators or from currently existing viral culture supernatants.

Finally, as an option exercised by the NIAID contract, EQAPOL was also charged with performing formal validation of specific immunogenicity assays to be employed as endpoint assays for HIV vaccine clinical trials. The Neutralizing Antibody Assay for HIV-1 in A3R5 cells was optimized and formally validated (Sarzotti-Kelsoe, et al. in this issue) under the oversight of the EQAPOL CQAU.

This report describes the process by which GCLP compliance was established for the entire EQAPOL Program.

2. Laboratory assessments

Prior to implementing GCLP throughout the EQAPOL Program, the CQAU performed an overall assessment of

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