08/05/22

VA Office of Research and Development

Response to Elise Gamertsfelder
The London School of Economics and Political Science

Dear Ms. Gamertsfelder:

Thank you for your important work assessing the clinical trial policies and monitoring systems of the largest public and philanthropic medical research funders in the United States, including the Department of Veterans Affairs (VA). The Office of Research and Development (ORD) within the VA's Veterans Healthcare Administration (VHA) is the national office that includes the funding services overseeing VA's intramural research program. ORD appreciates the opportunity to review your assessment of VA's clinical trial transparency policies and provide additional information and comments regarding VHA ORD's policies and approaches to compliance.

The VA is committed to informing Veterans and the public about its research and maximizing the impact of the studies it supports. As a leader in the U.S. clinical trials enterprise, ORD has been making clinical trial information available through ClinicalTrials.gov for more than 15 years. Since 2005, ORD has required all ORD-funded clinical trials to be registered in ClinicalTrials.gov as a condition of the award. Sharing of summary results on ClinicalTrials.gov has been required for all ORD studies active since 2007. Exceeding the federal regulatory requirements, ORD requires results reporting for all trials and not only Applicable Clinical Trials as described in the Food and Drug Administration Amendments Act of 2007, Section 801 (FDAAA801) and the Final Rule for Clinical Trials Registration and Results Information Submission. To date, nearly 2000 ORD trials have been registered with ClinicalTrials.gov.

Although your team completed a search of publicly available policy statements and hyperlinks, there are also ORD clinical trial related practices and policies defined in internal VA documents which ORD implements to facilitate accomplishing what is ORD's standard for clinical trial registration and reporting in clinicaltrials.gov– 100%. These include statements in ORD Requests for Applications (RFA), Intent to Fund letters, and email communications to ORD-funded investigators and individual VA Medical Centers, all of which are not available on public-facing websites for review as part of the assessment scoring. Moreover, for the best practices described as "Protocol onto registry in 12 months" and "PIs' past reporting record," ORD appreciates the opportunity to provide information as ORD's scoring was higher for these categories using documents which were not available for your review, resulting in lower reported scores in your assessment results for VA.

Best Practice: Protocol onto Registry in 12 Months

> **WHO Statement**: "Access to a sufficiently detailed clinical trial protocol is necessary in order to be able to interpret summary results. Therefore we also encourage development of requirements that the protocols are made publicly available no later than the time of the summary results disclosure as part of the clinical trial registry summary results information (including amendments approved by ethics committees/institutional review boards, and either as uploaded electronic document formats such as pdfs or links to the pdf)."

a. ORD Protocol Registration

In the ORD Intent to Award notifications sent to prospective Principal Investigators, it is specified that all related requirements, also known as Just-In-Time (JIT), must be completed within 180 days of the notification. ORD JIT requirements include clinical trial registration. Therefore, clinical trials

registrations are completed within 180 days of notification of the intent to award notification. In addition, registration is required for study funds to be released by ORD.

b. ORD Posting Protocol Document to ClinicalTrials.gov

ORD requires investigators of all trials it funds to report summary results to ClinicalTrials.gov within 12 months of the primary completion date. When submitting results through the ClinicalTrials.gov Protocol Registration and Results System (PRS), the Study Protocol and Statistical Analysis Plan document must be uploaded to PRS; this is a required component. As a result, the ORD requirement for PIs to report summary results to ClinicalTrials.gov with 12 months of the primary completion date also meets the requirement to provide the public with access to a sufficiently detailed clinical trial protocol with 12 months of the primary completion date. See: ClinicalTrials.gov Results Data Element Definitions for Interventional and Observational Studies.

Best Practice: PI's Past Reporting Record

WHO Statement: Reporting of previous trials realizes the value of funding; therefore, the contribution made from reporting previous trials, whatever their results, will be considered in the assessment of a funding proposal. When a PI applies for new funding, they may be asked to provide a list of all previous trials on which they were PI within a specified timeframe and their reporting status, with an explanation where trials have remained unreported.

a. ORD Requests for Application and Scientific Merit Review Process

In internally published RFAs, ORD has specific statements that it will not accept or review an application from an investigator who is not current with clinical trials registration and results reporting requirements for existing and previous awards. During the scientific merit review process, VA staff reviews a PI's reporting record to ensure all requirements including clinical trial requirements have been completed.

Example Statement (from RFA): "The PI must be current with all requirements related to intellectual property (VA invention documents and certifications), submission of annual progress reports (Research Performance Progress Reports (RPPRs)) and Final RPPRs, clinical trials registration, and clinical trials results reporting for existing and previous awards."

b. ORD Withholding of Award Funds

For PIs who fail to meet clinical trial requirements in a timely manner, ORD may withhold funding from existing or future awards.

Example Statement (from Email Communication): "The Office of Research and Development (ORD) requires the PIs of all its registered trials to report summary results in PRS no later than 12 months after the trial Primary Completion Date. This requirement helps fulfill ORD's commitment to informing Veterans and the public about its research and to maximize the impact of the studies it supports. Failure to properly report results to ClinicalTrials.gov may result in current or future project funding to be held or withdrawn by ORD. For some trials, federal law (Final Rule for Clinical Trials Registration and Results Information Submission) requires submitting results in this same time frame."

There are two other practices for which the authors assessed the VA as not fully meeting best practice: (a) results published in journal, and (b) makes monitoring reports public. For these practices, VA ORD plans to evaluate over the course of the next 12 months if and how these referenced practices may be implemented by VA ORD.

Thank you again for the opportunity to respond to the study team's assessment of VA clinical trial policies and monitoring systems. VA welcomes the opportunity to describe our practices as other institutions have used some of our processes to enhance their own respective institutions' clinical trial transparency practices. We appreciate the authors' commitment to strengthening clinical trial quality and transparency. Public access, high-quality data and transparency have been and continue to be a high priority for VA ORD.