Clinical Trials Results Information Submission: Good Cause Extension Request Process and Criteria

I. Good Cause Extension Overview

This document is intended to explain to responsible parties the process of submitting a good cause extension (GCE) request to extend the deadline for submitting clinical trial results information to ClinicalTrials.gov and the information necessary for the National Institutes of Health (NIH) to evaluate and make a determination for GCE requests.

Section 402(j) of the Public Health Service Act (PHS Act) and the Final Rule for Clinical Trials Registration and Results Information Submission ("the Final Rule" or "42 CFR Part 11") establish requirements and deadlines for the submission of clinical trial results information for applicable clinical trials (ACTs). In general, the standard submission deadline for clinical trial results information for ACTs is not later than one year after the study's primary completion date. Section 402(j)(3)(E)(vi) of the PHS Act authorizes the NIH to "provide an extension of the deadline for submission of clinical trial [results] information . . . if the responsible party for the trial submits to the [NIH] a written request that demonstrates good cause for the extension and provides an estimate of the date on which the information will be submitted." The Final Rule at 42 CFR 11.44(e) implemented this provision and clarifies the deadlines and requirements for requesting an extension for good cause. If a responsible party submits a GCE request by the applicable deadline, and if an extension request is granted, the responsible party has until the extended date to submit clinical trial results information.

In addition to Section 402(j) of the PHS Act and the Final Rule, the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information (NOT-OD-16-149) establishes the expectation that all investigators conducting clinical trials funded in whole or in part by the NIH will ensure that these trials are registered at ClinicalTrials.gov and that clinical trial results information for these trials is submitted to ClinicalTrials.gov consistent with timeframes described in Section 402(j) of the PHS Act and the Final Rule. NIH-funded awardees or their designated principal investigators may also submit a GCE request for NIH-funded clinical trials. For additional information on NIH-funded clinical trials, see Section V below.

Section II describes the process for submitting GCE requests. Section III describes general criteria for granting or denying a GCE request. Section IV describes a list of reasons generally considered "good cause" and "not good cause" for granting extension requests. Section V describes additional information specific to the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information (NOT-OD-16-149).

II. Good Cause Extension Request Process

(A) Submission and Deadlines

GCE requests must be submitted[1] through the ClinicalTrials.gov Protocol Registration and Results System (PRS) at any time *prior* to the date of (i.e., the day before) the submission deadline on which clinical trial results information would otherwise be due (i.e., standard results submission deadline or an extended deadline if an extension request was granted or a certification for delay was submitted).[2] NIH *will not* accept requests submitted on or after the submission deadline on which clinical trial results information would otherwise be due. Each GCE request must include (1) a complete description of the reason(s) why clinical trial results information cannot be provided according to the deadline, with sufficient detail to justify good cause for the extension and to allow for the evaluation of the request; and (2) an estimated date on which the clinical trial results information will be submitted. Sufficient detail should be provided, including the steps that will be taken to meet the estimated submission date, a description of mitigating steps to avoid future delay, and any other information needed to address the criteria in Section III of this document.

Consistent with section 402(j)(3)(E)(vi) of the PHS Act, more than one GCE request may be submitted for the same ACT after a previous GCE request was granted. The deadline for submitting subsequent GCE requests is the same as for an initial GCE request. In particular, the request must be made any time *prior* to the date of (i.e., the day before) the submission deadline on which clinical trial results information would otherwise be due. NIH *will not* accept requests submitted on or after the submission deadline on which clinical trial results information would otherwise be due.

(B) GCE Request Review and Decision Notification

The request will be reviewed in accordance with the criteria in Section III of this document.

NIH will provide a response electronically via the PRS ("PRS notification") to the responsible party indicating whether the requested extension demonstrates good cause and has been granted. If the extension request is granted, the responsible party has until the extended date to submit clinical trial results information. If NIH determines that the requested submission date is not commensurate with the explanation provided in the request, NIH may grant the request but identify a submission deadline that is earlier than the requested submission date and the responsible party must either (1) submit clinical trial results information by the

[1] For information on how to submit a GCE request, see "To Request Certification or an Extension" under table 4 of section 8.1.2 of the PRS User's Guide.

[2] 42 CFR 11.44(e)(1)(i), "[t]he responsible party must submit a request for an extension to Clinical Trials.gov prior to the date on which clinical trial results information would otherwise be due in accordance with paragraph (a), (b), (c), (d), (e), or (f) of this section," and the Preamble reiterates this requirement. 81 Fed. Reg. 65076, 65078.

submission deadline identified in the PRS notification; or (2) appeal the NIH-identified earlier deadline.

If NIH determines the request does not constitute "good cause," the GCE request will be denied. If the request is denied, the responsible party must either (1) submit clinical trial results information by the later of the date on which clinical trial results information would otherwise be due, or 30 calendar days after the date that the PRS notification was issued by NIH; or (2) submit an appeal as described in subsection (C) below.

(C) Appeals

Responsible parties may appeal denied GCE requests or the NIH-identified earlier deadline specified in a granted extension request. An appeal must provide an explanation of the reason(s) why the initial decision to deny the GCE request or grant the GCE request with a shorter deadline than requested should be overturned or revised, with sufficient detail to allow for the evaluation of the appeal. Responsible parties should provide further elaboration of the grounds for the request or highlight factors that justify an extension. The appeal should only address why the initial decision was incorrect; new bases for an extension request should not be presented for the first time in an appeal and will not be considered. Only one appeal may be submitted for a denied GCE request.

The appeal must be submitted not later than 30 calendar days after the date that the PRS notification was issued by NIH. Appeals should be submitted via the PRS. NIH will provide an electronic notification to the responsible party communicating the determination of whether the appeal is granted or denied.

If the appeal is granted, the responsible party has until the extended date specified in the electronic notification to submit clinical trial results information. If NIH denies the appeal of a denied GCE request, the responsible party must submit clinical trial results information by the later of the date on which clinical trial results information would otherwise be due, or 30 calendar days after the electronic notification denying the appeal was sent by NIH.

As described in section II(B), NIH may grant a GCE request but identify a submission deadline that is earlier than the requested submission date. In other words, the GCE request was granted but the deadline was denied. In such cases, the responsible party may appeal the denied deadline specified in the granted GCE request. If NIH denies an appeal of a denied deadline specified in a granted GCE request, the responsible party must submit clinical trial results information by the later of the date specified in the PRS notification granting the GCE request, or 30 calendar days after the electronic notification denying the appeal was sent by NIH.

III. Good Cause Extension Request Criteria

A GCE request must include (1) a complete description of the reason(s) why clinical trial results information cannot be provided according to the deadline, with sufficient detail to justify good cause for the extension and to allow for the evaluation of the request; and (2) an estimated date on which the clinical trial results information will be submitted. Extension requests will be evaluated on a case-by-case basis using the following general criteria to support a determination of "good cause." These include, but are not limited to:

(A) General Criteria

(1) The impact of the circumstances leading to the GCE request, including steps the responsible party is taking to mitigate the impact of those circumstances.
(2) The extent to which the factors underlying the GCE request are outside of the responsible party's control.
(3) Whether the requested submission date is commensurate with the explanation provided in the request.
(4) Whether information is internally consistent with relevant data element definitions and is consistent with information provided in other sections of the study record.
(5) The number of, and explanations for, previous GCE request(s), and the proposed reporting deadline in previous requests.

(B) General Formatting Criteria and Considerations

(1) The request must be in English.
(2) Acronyms and abbreviations should be spelled out, with the acronym or abbreviation provided in parentheses immediately after, at least the first time they are used in the request.
(3) The responsible party should not include specific personal health information in the request.

IV. Generalized List of Situations That May Be Considered "Good Cause" and "Not Good Cause" for Granting an Extension Request

The situations described below are reasons that would generally be considered to constitute "good cause" and "not good cause," provided the responsible parties demonstrate there was a direct impact on the ability to submit timely clinical trial results information, and other general criteria are met. There are likely to be only a few situations that would constitute "good cause." Even where circumstances exist that are similar to the situations listed below, all extension requests will be evaluated on a case-by-case basis.

(A) Situations That May Be Considered "Good Cause" for Granting an Extension Request

- Need to preserve scientific integrity of study for which data collection is ongoing, including situations in which the submission of results information for the

primary outcome(s) of an ACT would impair or otherwise bias the ongoing collection, analysis, and/or interpretation of data for secondary outcome(s). For example, the protocol or statistical analysis plan prespecified that study data will be blinded for more than one year after the study primary completion date and reporting would introduce bias to the ongoing collection, analysis, and/or interpretation of data for the secondary outcome(s) or adverse events. Such prespecified blinding must have a scientifically valid basis.

- Emergencies that would prevent timely submission of clinical trial results information, including situations in which one or more data collection sites were affected by natural disasters or catastrophic events outside the responsible party or sponsor's control. The responsible party's ability to submit clinical trial results information in a timely manner must be directly affected by the emergency, such as through personnel changes; or changes or damage to facility, study property, or data due to the emergency.

- Study termination near the standard submission deadline: This could occur if the date the decision is made to terminate the study ends up being much later than the date that the final subject in the terminated study was examined or received an intervention for a primary outcome measure (i.e., the actual primary completion date). If the termination date is close to, but not past, the standard submission deadline for clinical trial results information under 42 CFR 11.44(a), there may not be sufficient time to complete data analysis for enrolled subjects and enter clinical trial results information via the PRS.

- Reporting delays due to unexpected personal emergency circumstances: This may include emergency situations faced by the responsible party or key personnel, such as death or extended personal illness.

(B) Situations That Would Be Considered "Not Good Cause" for Granting an Extension Request

- Certification of delay should have been submitted rather than a good cause extension request: A good cause extension request should not be submitted under circumstances where a certification of delay under 42 CFR 11.44(b) or (c) would be available.

- Awaiting journal publication: A study must report clinical trial results information even if the data have not yet been published.[3]

[3] Note: the International Committee of Medical Journal Editors (ICMJE) has stated that results information submission to ClinicalTrials.gov in compliance with FDAAA 801 will not be considered "prior publication" and will not preclude future publication.

- Pending FDA or other regulatory/health agency review: A study must report clinical trial results information even if the data are under FDA or other regulatory/health agency review, consistent with any certification of delay submission, as applicable.

- Ongoing data analysis without sufficient explanation: All studies are expected to be able to complete data analysis within one year of the primary completion date unless there are unexpected circumstances that prevent the timely completion of the analysis. Analysis that is not yet complete, without further explanation, is not adequate justification for "good cause."

- Events that might reasonably have been avoided or anticipated through standard contingency planning (e.g., transition planning for key staff members who leave an organization or change of vendor) will generally not be considered to constitute "good cause."

Hypothetical Examples of Extension Requests

The following hypothetical examples with fictional data are provided to illustrate the type of information and level of detail needed in good cause extension requests to allow NIH to evaluate whether the requests demonstrate good cause. Please ***note*** that these examples may or may not constitute good cause and are only provided for illustrative purposes.

Emergencies or Other National Public Health Emergency

The responsible party for an ACT with a standard submission deadline of December 1, 2020, had work redirected during a national public health emergency and work on the data analysis for the ACT was delayed. Beginning in March 2020, the principal investigator for the ACT, an infectious disease physician, had work priorities shift heavily from research to clinical care during the COVID-19 pandemic. In addition, access to the study site was strictly limited after March 2020, delaying completion of the data analysis. Therefore, the responsible party submitted a good cause extension request on November 1, 2020, describing this situation and requesting a 6-month extension until June 1, 2021, to submit summary results information for the ACT.

Natural Disaster or Other Catastrophes

The responsible party for an ACT with a standard submission deadline of September 1, 2022, lost all ongoing analyses and results data for the ACT when Hurricane Anna hit its facilities on August 26, 2022. Further, access to the necessary technology to recreate the analyses was significantly affected. However, the data were backed up on servers in another location and the responsible party anticipated being able to replace the needed technology by late September 2022 and to recreate the analyses from the backed-up data by late November 2022. Therefore, the responsible party submitted a good cause extension request on August 31, 2022, describing this situation and requesting a 3-month extension until December 1, 2022, to submit summary results information for the ACT.

Need to Preserve Scientific Integrity of Study: Study Blinding

All study personnel will remain blinded to individual treatment assignment from the time of randomization until the final database lock on [August 1, 2023]. Therefore, it will not be possible to submit unblinded summary results information until October 1, 2023, and the responsible party submitted a good cause extension request.

Study Termination Near the Standard Submission Deadline

The study was terminated on December 31, 2023, by the data monitoring committee due to low enrollment over the past year. The Primary Completion Date was backdated to February 25, 2023 (Actual). Due to this unanticipated change to the Primary Completion Date, summary results information is due in 2 months. The responsible party needs 6 months total to prepare summary results information. Accordingly, they submit a request for an extension for 6 months until August 25, 2024, to allow time to clean and analyze data and submit to ClinicalTrials.gov.

Personal Illness

Due to an unexpected personal illness of the study statistician between April 2023–July 2023, progress on data analysis has been delayed for 3 months and it has not been possible to replace the statistician in that time. Results are due on September 15, 2023. The responsible party submitted a good cause extension request for a 3-month extension until December15, 2023, to allow for time to finish the data analyses.

NOTE: The responsible party should not include personal medical information in the extension request justification. An explanation of the impact of the illness on the study and an estimated date on which clinical trial results information will be submitted is sufficient.

V. Special Considerations for NIH Awardees

For NIH-funded and supported clinical trials, awardees should be aware that any good cause extension request could impact other aspect of the contract or grant award. Therefore, the submission of a "Request for an Extension for Good Cause" does not constitute a prior approval request submission (e.g., No Cost Extension and Carryover) or a request for contract modification (e.g., contract extension or change to deliverable due date).