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1.0 PURPOSE

1.1 The DAIDS Protocol Change Process Job Aid is a companion to the DAIDS Protocol Change Process Policy and provides more detailed information to guide DAIDS staff and external stakeholders.

2.0 SCOPE

2.1 This job aid is to assist protocol teams/protocol principal investigators, DAIDS staff and other stakeholders determine the appropriate method to make changes or clarifications to a DAIDS approved protocol.

2.2 The methods described in this job aid apply to all clinical trials (IND and Non-IND) for which DAIDS serves as the regulatory sponsor and/or funder. Because these methods are DAIDS specific, they may not apply to clinical trials in which DAIDS is not the regulatory sponsor.

3.0 DEFINITIONS

For additional definitions, see DAIDS glossary

3.1 Refer to the DAIDS Protocol Change Process Policy.

4.0 RESPONSIBILITIES

4.1 **Protocol Team/Protocol Principal Investigator:** The Protocol Team/Protocol Principal Investigator is responsible for protocol development including drafting and revising the protocol document and sample informed consent throughout the course of a clinical trial.

4.2 **DAIDS Medical Officer (MO):** The DAIDS MO works with the Protocol Team/Protocol Principal Investigator to assess if proposed modifications require a Full Version Protocol Amendment, LOA, or CM

4.3 **DAIDS Regulatory Affairs Branch (RAB) Sponsor's Authorized Representative (SAR):** The DAIDS RAB SAR is responsible for reviewing the proposed modification and for making the final decision regarding the appropriate method to change or clarify the protocol.

5.0 PROCEDURE

The three DAIDS approved methods for making changes or clarifications to a protocol are Full Version Protocol Amendment, Letter of Amendment (LOA) and Clarification Memo (CM). These methods are mutually exclusive and apply to both IND and Non-IND protocols.

5.1 Full Version Protocol Amendment:

5.1.1 Is required when changes to a protocol are substantive in number and/or nature.

5.1.2 Results in a new protocol version number (e.g., Version 2.0, 3.0, etc.).

5.1.3 Changes are incorporated directly into the protocol document.

5.1.4 Must incorporate all LOAs and CMs implemented since the last DAIDS approved version of the protocol.

5.1.5 The following examples require a Full Version Protocol Amendment:

5.1.5.1 An increase or decrease of more than 10% of the total number of participants to be enrolled.

5.1.5.2 A change to the protocol design that includes but is not limited to:

5.1.5.2.1 Inclusion of a new study arm

5.1.5.2.2 Inclusion of a new sub-study

5.1.5.2.3 Inclusion of a new informed consent form or significant changes to the existing form

5.1.5.2.4 A change in the schedule of study product dosing which results in a higher dosage being given in the study or frequency in which study product is given.

5.1.5.2.5 The introduction of a new study product or study product formulation.

5.1.5.3 If the FDA requires significant changes during the 30-day review period to avoid a clinical hold, a Full Version Protocol Amendment is required before initiating a study.

5.2 Letter of Amendment (LOA):

5.2.1 Can be used when there are specific changes to the protocol that result in the addition of new information or the deletion of incorrect or unnecessary information.

5.2.2 May result in minor changes to the Sample Informed Consent (SIC).

5.2.3 If the collective changes are extensive and cannot be implemented easily and immediately, the DAIDS RAB SAR may require a Full Version Protocol Amendment.

5.2.4 If multiple LOAs have been implemented for a single version of the protocol and additional changes are requested by the Protocol Team/Protocol Principal Investigator, the DAIDS RAB SAR may require the Protocol Team/Protocol Principal Investigator to develop a Full Version Protocol Amendment to maintain Good Clinical Practice (GCP).

5.2.5 The following examples are instances when a LOA would be the appropriate method to make changes to a protocol:

5.2.5.1 Changes to the volume of blood or number of samples that will be collected at a specific study visit.

5.2.5.2 Changes to procedures or lab tests that will be conducted at a specific study visit. Any new lab test or procedure should not increase the risk to the participants. The addition of a blood draw would be acceptable while the addition of a lumbar puncture would require a Full Version Protocol Amendment.

5.2.5.3 A change to the inclusion/exclusion criteria that results in slightly broadening parameters to help increase enrollment (e.g., reducing the CD4 count from 350/mm3 to 300/mm3 or increasing the upper age limit from 13 to17 years of age).

5.2.5.4 Allowing an addition/deletion in background therapy.

5.2.5.5 Dropping a protocol arm based on the recommendation of the Data Safety Monitoring Board (DSMB)

5.3 Clarification Memo (CM):

5.3.1 Provides additional detail or further explanation to information that is already included in the protocol.

5.3.2 Does not affect participant safety or the risk assessment of the protocol.

5.3.3 Does not change the SIC.

5.3.4 The following examples are instances in which a CM would be the appropriate method for implementing a clarification to a protocol:

5.3.4.1 Updates or corrections to phone numbers and/or addresses for protocol team members/laboratories already listed in the protocol.

5.3.4.2 To correct inconsistent information in the protocol (e.g., the schedule of events specifies a lab test or blood volume to be collected at a specific study visit and conflicting information is included in the corresponding section of the protocol document.).

	Full Version Protocol Amendment	Letter of Amendment	Clarification Memo
IRB/EC Approval Required	YES	YES	NO*
Submitted to FDA (IND studies)	YES	YES	NO
Protocol Registration Required	YES	YES	NO

Copy Sent to Drug Company Collaborator	YES	YES	NO
RAB Makes Final Determination	YES	YES	NO
Change in Protocol Version Number	YES	NO	NO

5.3.4.3 To specify a specific type of collection tube to be used for drawing a lab specimen.

5.4 Summary of Operational Requirements for Protocol Changes and Clarifications:

*DAIDS does not require IRB/EC/RE approval of CMs. Each site must follow the requirements of their IRB/EC/RE as required prior to implementation.

6.0 REFERENCES

6.1 21 CFR 312.30, Code of Federal Regulations Title 21

6.2 ICH Guideline for Good Clinical Practice E6(R2) 4.5 Compliance with Protocol

7.0 APPENDICES

Not applicable

8.0 REVISION SUMMARY

8.1 APP-A15-OPC-008.00 is the original version of this Appendix. The information in this job aid had been in effect since March 2000 (updated in May 2012, Version 2.0 and updated in May 2018, Version 3.0) in the form of a guidance document

8.2 DAIDS-OPC-A15-GUD-00008 rev 01 is the first revision of this guidance document in MasterControl. The document format and numbering were updated to reflect current requirements.