DIVISION OF MICROBIOLOGY AND INFECTIOUS DISEASES (DMID) NOTES TO FILE GUIDELINES (GUID) AND TEMPLATE

Purpose:

The purpose of this document is to describe the expectations of Notes to File (NTF) provided to DMID to

a. Clarify or add information regarding site specific regulatory file requirements and source document standards;
b. Document and address any issue that is protocol and/or site specific that cannot be resolved without a change from previously approved procedures;
c. Describe the immediate *and* preventative corrective action(s) taken, to resolve the issue;
d. Explain a site-specific process that is not documented in any previously approved procedures.

In general, NTFs are **NEVER** written as an exemption from:

a. Protocol eligibility criteria
b. Protocol amendment
c. Changes to the Manual of Operations (MOP)
d. Protocol deviation reporting
e. Adverse Event reporting
f. Adequate source documentation
g. ICH/GCP compliance, or
h. IRB and any other applicable regulatory and contractual requirements

These guidelines do not apply to reference memos that are used for the location for the storage of documents on site and other administrative items.

Retention and Distribution

1. NTFs should be
    a. Typed (not handwritten) and should include the elements from this template
    b. Kept on file in the site regulatory file
    c. Made available to the clinical site monitors reviewing the site's documents and procedures
    d. Written by the individual responsible for its content, and the author should sign and date the note
        - If the Note File pertains to an item for which the PI is responsible (subject protection, data integrity, etc.), the PI should co-sign and date the note to acknowledge his/her awareness of the issue.

2. Please send a scanned PDF (or electronically signed pdf) of NTF as an email attachment for review, to:

a. DMID Clinical Project Manager/point of contact for the clinical research study,
b. Office of Clinical Research Affairs (OCRA) (email address: OCRAOps@mail.nih.gov), and
c. **If an issue relates to the study product,** the DMID Product Support Team (email address: DMIDProductSupportTeam@mail.nih.gov)
d. **If an issue relates to the study data,** the protocol-specific Data Coordinating Center
e. The site should determine whether the NTF should be submitted to the IRB/EC and submit according the IRB/EC guidelines.

3. The DMID-CROMS clinical site monitor will retrieve a copy of the memo as needed based on the significance of issues addressed in the Note to File.

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Format and Content

The Note to File should be written on institutional letterhead that includes the site's address and include the following elements. Refer to the sample Template, following format guidance.

Element	Element Description
Date the NTF was written:	Date that the NTF was written
To:	DMID Protocol number followed by "Study File". **Note**: for protocol titles or numbers followed by an extended number or letter please provide the full set of characters (i.e., "ACTT 4"), if there is no other reference to the ACTT within the body of the NTF
From:	Name and title/role of the person writing the NTF, all signatories, and their institutional affiliation. If related to an institution with multiple locations/sites, the applicable location/ site should be specified
Subject:	DMID Protocol number [XX-XXXX] and site name. Include a brief note of the overall topic/content, in addition to the protocol and site name (i.e. DMID Protocol 20-0006; <site name>; *eGFR calculation*). This will help to identify Notes to File, when reviewing/reconciling study records. NTFs addressing study product should **NEVER** contain any information that could potentially unblind study team members.
Issue:	This should be used for clarification purposes only. Any noncompliance and protocol deviations should be recorded in the study database according to study specific data entry guidelines. The body of the NTF should *clearly* describe the issue, topic, process and/or problem in a brief paragraph or bulleted outline form. Ensure temporal order to clearly construct events. Please see the **Purpose** section in this guideline regarding content.
Resolution/Outcome:	Describe the resolution of the issue or corrections by the site personnel. If a formal Corrective and Preventive Action (CAPA) plan is required, this should **NOT** be documented in a NTF. • Please use the appropriate DMID form for all CAPAs requested • If the NTF refers to training provided, explain what documents were used to train, who was trained and by whom, and the date they were trained

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Element	Element Description
Effective date of the resolution:	Add an effective date for corrective actions taken
Comments:	(*Optional*) Enter any additional comments or information not noted above including what changes will be made; for example, to site processes, or Quality Management/Quality Assurance plans, to assure future issues will be minimized or eliminated.
Signature block	Signature of person completing the NTF and the PI as necessary, and date. Acceptable signatures include electronic signatures, scanned signatures, digital signature (e.g. signed with a PIV card) and flatten digital signature which must also include the typed name of the person signing and the date signed.
Distribution	NTFs should **not** be submitted via Site Essential Regulatory Document (SERD) portal, or to the Site Monitoring group for review. The completed and signed NTFs **must** be submitted following the distribution noted in **Section 2 of this guideline**.

NOTE TO THE STUDY FILE TEMPLATE ON THE FOLLOWING

NOTE TO FILE TEMPLATE

<Institutional Letterhead>

Date (DD/MMM/YYYY):

To:

From:

Subject:

Issue:

Resolution/Outcome:

Effect date of Resolution (DD/MMM/YYYY):

Comments:

Signature	**Date**