
PROCEDURES

OFFICE OF COMPLIANCE**PROCESS FOR HANDLING OSIS NON-CONCURRENCE WITH DECISION TO
DOWNGRADE EIR CLASSIFICATION AT OR AFTER SAM**

Table of Contents

PURPOSE	1
BACKGROUND.....	1
RESPONSIBILITIES	1
PROCEDURES	3
RECORDS MANAGEMENT	4
REFERENCES	5
EFFECTIVE DATE	5
CHANGE CONTROL TABLE	5
ATTACHMENT I – Memo To File Template	6

PURPOSE

To provide direction to CDER's Office of Compliance (OC) Office of Scientific Investigations (OSI) and CDER's Office of Translational Sciences (OTS) Office of Study Integrity and Surveillance (OSIS) on the process for handling OSIS non-concurrence with decisions made at or after Significant Action Meetings (SAMs) to downgrade the classification of Establishment Inspection Reports (EIRs) for Bioequivalence (BE) and Good Laboratory Practice (GLP) inspections.

BACKGROUND

OSIS and OSI will follow this MAPP when OSIS disagrees with a decision made at or after a SAM to downgrade a BE or GLP inspection case with an interim Official Action Indicated (OAI) classification.

RESPONSIBILITIES**OSIS Director**

- Reviews memo to file (MTF) prepared by the OSIS Primary Reviewer, the OSIS Team Leader, or the OSIS Division Director (or designee) who disagrees with downgrade decision. Documents concurrence or non-concurrence with MTF(s).
 - o Notifies individuals who signed MTF(s) in the case of non-concurrence with MTF(s).
-

- o Schedules meeting with OSI Director to discuss downgrade decision in the case of concurrence with MTF(s).
- o Drafts a unique MTF, if desired.

OSI Director

- Meets with the OSIS Director to discuss downgrade decision when the OSIS Director disagrees with downgrade decision made at or after the SAM.
- Consults with OSI staff, as appropriate.
- Notifies OSI Division of Enforcement and Postmarketing Safety Branch (DEPS) Director when OSI Director and OSIS Director agree to change the downgrade decision made at or after the SAM.

OSI Division of Enforcement and Postmarketing Safety Branch (DEPS) Director

- Ensures that cases are processed as OAI according to existing OSI policies and procedures when the OSI Director and OSIS Director agree to change the downgrade decision made at or after the SAM.

OSIS Division Director (or designee)

- Reviews MTF(s) prepared by the OSIS Primary Reviewer, or the OSIS Team Leader. Documents concurrence or non-concurrence with MTF(s).
 - o Notifies individuals who signed MTF(s) in the case of non-concurrence with MTF(s).
 - o Forwards MTF(s) to the OSIS Director for review in the case of concurrence with MTF.
 - o Drafts a unique MTF, if desired.
- If the OSIS Division Director (or designee) is the first person in disagreement with the downgrade decision:
 - o Prepares MTF documenting disagreement and rationale and forwards MTF to OSIS Director for review.
 - o Notifies the OSI Primary Reviewer responsible for the case when the disagreement process is initiated and resolved.
 - o Ensures MTF(s) are collated and archived following resolution of disagreement.

OSIS Team Leader

- Reviews MTF prepared by the OSIS Primary Reviewer who disagrees with downgrade decision. Documents concurrence or non-concurrence with MTF.
 - o Notifies the OSIS Primary Reviewer in the case of non-concurrence with MTF.
 - o Forwards MTF to the OSIS Division Director (or designee) for review in the case of concurrence with MTF.
 - o Drafts a unique MTF, if desired.
- If the OSIS Team Leader is the first person in disagreement with the downgrade decision:
 - o Prepares MTF documenting disagreement and rationale and forwards MTF to OSIS Division Director (or designee) for review.

- o Notifies the OSI Primary Reviewer responsible for the case when the disagreement process is initiated and resolved.
- o Ensures MTF(s) are collated and archived following resolution of disagreement.

OSIS Primary Reviewer

- If the OSIS Primary Reviewer is the first person in disagreement with the downgrade decision:
 - o Prepares MTF documenting disagreement and rationale and then forwards MTF to the OSIS Team Leader for review.
 - o Notifies the OSI Primary Reviewer responsible for the case when the disagreement process is initiated and resolved.
 - o Ensures MTF(s) are collated and archived following resolution of disagreement.

OSI Primary Reviewer

- Receives notice when disagreement process is initiated and ensures that case does not proceed until disagreement is resolved.
-

PROCEDURES**Notification, documentation, and escalation of disagreements with decision to downgrade EIR made at or after SAMs**

- The first person (OSIS Primary Reviewer, OSIS Team Leader, or OSIS Division Director (or designee)) who disagrees with the downgrade decision made at or after a SAM will document the disagreement and the rationale in an MTF if the person wishes to dispute the decision. That person will:
 - o Send the MTF to the next person in the review chain (OSIS Team Leader, OSIS Division Director (or designee), or OSIS Director) for review;
 - o Notify the OSI Primary Reviewer that the disagreement process has been initiated and request that OSI not finalize any downgrade classification or hold any downgrade teleconference with Office of Regulatory Affairs field investigators until the disagreement is resolved.
- Each person in the review chain (OSIS Team Leader, OSIS Division Director (or designee), or OSIS Director) who receives an MTF will document concurrence or non-concurrence with the MTF(s).
 - o If the person receiving the MTF(s) (OSIS Team Leader, OSIS Division Director (or designee), or OSIS Director) non-concurs with the MTF(s), his or her decision is final, and he or she closes the disagreement as described below.
 - o If the OSIS Team Leader or OSIS Division Director (or designee) concurs with the MTF(s), the OSIS Team Leader or OSIS Division Director (or designee) will forward the MTF(s) to the next person in the review chain (OSIS Division Director (or designee) or OSIS Director) for review.

- o If the OSIS Director concurs with the MTF(s), the OSIS Director will arrange to meet with the OSI Director to discuss the downgrade decision. The OSIS Director and OSI Director will jointly determine the final classification.

Closing Resolved Disagreements

- When the OSIS Team Leader, OSIS Division Director (or designee) or OSIS Director non-concurs with the MTF(s), he or she notifies the individuals in OSIS who signed the MTF(s) of the final decision to uphold the downgrade decision made at or after the SAM.
- When the OSI Director and OSIS Director agree to change the downgrade decision made at or after the SAM:
 - o The OSI Director notifies the OSI DEPS Director so the case can be processed as OAI according to existing OSI policies and procedures.
 - o The OSIS Director notifies the individuals in OSIS who signed the MTF(s).
- After receiving notice of the outcome, the person in OSIS (OSIS Primary Reviewer, OSIS Team Leader, or OSIS Division Director (or designee)) who prepared the initial MTF collates all related MTFs into a single .pdf document, bookmarking each MTF. That person archives the document in the appropriate case management system.

RECORDS MANAGEMENT

The processes specified in this MAPP generate records, according to the OC file plan and the procedure described in the *CDER Standard Operating Procedures for Incorporating Records Management into Processes*.

Records Management Table						
Record Generated	Description	Process step that generates the record	Record Owner/ Custodian	Electronic System of Records	Plan for transition to electronic record (if applicable)	Record Control Schedule
FDA-7300 Establishment Inspections and Compliance Action Files	Difference in professional opinion memos with decision to send firm a regulatory letter (includes drafts and finals).	See Procedures Section	The first person by position (Primary Reviewer, Team Leader, or Division Director) who prepared initial Memo to File.	ECMS	N/A	<u>NARA Citation:</u> N/A <u>Disposition:</u> N/A

REFERENCES

- 21 CFR part 10.75 – Internal agency review of decisions.
 - FDA, 2010, Center for Drug Evaluation and Research, MAPP 4151.8 Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions.
 - FDA, 2010, Center for Drug Evaluation and Research, MAPP 4151.1, revision 1, Scientific / Regulatory Dispute Resolution for Individuals Within a Management Chain.
 - FDA, 2010, Center for Drug Evaluation and Research, MAPP 4151.2, revision 1, Resolution of Differing Professional Opinions: Review by Ad Hoc Panel and CDER Director.
-

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
12/20/2020	Initial	Publication of MAPP
01/01/2020	1	Addition of Records Management section; non-substantive, editorial changes

ATTACHMENT I – Memo To File Template

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: *Month, day, year*
TO: ECMS File for Complaint #[*insert*] **or** ANDA #[*insert*]
FROM: [*select one:*]
Name and title
BE Team/GLP Team
Division of New Drug Bioequivalence Evaluation **OR** Division of Generic
Drug Bioequivalence Evaluation
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Non-OAI Classification of Establishment Inspection Report
Inspected Entity: [*insert name and location (city/state; country if outside US)*
of inspected entity]

BACKGROUND:

A Significant Action Meeting (SAM) was held on [*insert date*] to determine the final classification of the Establishment Inspection Report (EIR) for the inspection of [*insert name*]. The Office of Regulatory Affairs had recommended a classification of Official Action Indicated (OAI). [*select one:*] At/After the SAM, OSI determined that an OAI classification could not be supported. Therefore, the final classification will be downgraded to non-OAI, with classification [either Voluntary Action Indicated (VAI) or No Action Indicated (NAI)] to be determined by the branch that will prepare the post-inspectional correspondence.

I do not concur with a downgrade. I believe this EIR should have been classified OAI and have written this memo to document my position.

POSITION ON DOWNGRADE:

Insert summary of disagreement with downgrading, including rationale for why the writer believes that the final classification should have been OAI, reference to relevant inspectional observation(s) and exhibits and supporting argument(s) for the position taken.

[insert electronic signature]

Name and Title

Page 2 – MTF for Complaint #[insert] **or** ANDA #[insert]

CONCURRENCE:

☐ **I concur with the above position.**

Concurrence comments (if applicable):

☐ **I do not concur with the above position.**

Non-concurrence comments (if applicable):

[insert electronic signature]

Name and Title

[Note: As needed, copy and paste here the concurrence blocks and unsigned signature line above to allow for additional level(s) of concurrence/non-concurrence.]

cc:

OSIS Complaint/ANDA File #[insert]

Support Staff/[insert name]

Reviewer/[insert name]

Team Leader/[insert name]

Division Director/[insert name]

Office Director/[insert name]