POLICY AND PROCEDURES

OFFICE OF PHARMACEUTICAL QUALITY

Review of Grouped Product Quality Supplements

Table of Contents

PURPOSE

This MAPP outlines the policies and procedures for grouping supplements submitted concurrently that provide for the same chemistry, manufacturing, and controls (CMC) changes to multiple approved new drug applications (NDAs), abbreviated new drug applications (ANDAs), and biological license applications (BLAs) and are submitted by the same applicant. The goal is to improve efficiency and provide consistency when reviewing these grouped supplements.

BACKGROUND

- When applicants make identical CMC post-approval changes that affect multiple approved applications, the Center needs procedures for reviewing these groups of supplements. Implementing these procedures helps the Office of Pharmaceutical Quality (OPQ) manage the review of these changes in an efficient manner and ensures consistency.

- This MAPP has been revised to replace the term "bundled supplements" with "grouped supplements."

- The previous version of this MAPP (5015.6) applied only to supplements to NDAs (sNDAs). A related MAPP applied only to supplements to ANDAs (sANDAs) [the Office of Generic Drugs (OGD) (MAPP 5240.9 *Processing Requests for the Review of Grouped Supplements*)].

- The current version of this MAPP combines and supersedes the aforementioned documents.

POLICY

- The term "grouped supplements" is used to describe two or more supplements reviewed and processed using the procedures set forth in this MAPP.

- Supplements cannot be grouped if submitted by a different applicant or if the supplements provide for different CMC changes. The supporting data necessary for the review of the CMC changes should be the same for each of the grouped supplements. Any supplement that provides for the same CMC changes but necessitates the review of data that is unique to that supplement (e.g., product-specific data) should not be grouped.

- Supplements are grouped at the discretion of the Center for the purpose of ensuring review efficiency and consistency. Supplements will be grouped when the following criteria are met:

    1. The cover letter for the supplements clearly states the purpose of the proposed CMC changes and indicates that the supplement is one of multiple submissions for the same change
    2. Each supplement includes a list of the application numbers (NDA, BLA, and ANDA, as appropriate) and identifies the drug products that will be covered by the CMC changes
    3. The supplements have the same submission date on Form FDA 356h

- On a case-by-case basis, the Center may also group supplements that do not meet some or any of the criteria described above, if grouping the supplements is advantageous to the review process. If all of the criteria above are met, the Center may recognize an opportunity to group supplements.

- If an applicant submits a group of supplements for the same CMC change and then, at a later date, submits additional supplements for the same change and requests the Center to include the second set of supplements in the group, the Regulatory Business Project Manager (RBPM) and Branch Chief (BC) of the relevant review division will decide whether this is appropriate on a case-by-case basis. Consideration will be given to whether the goal date for the original group of supplements could still be met if the second set of supplements is added to the review.

- Typically for grouped supplements, the lead application is the supplement with the earliest goal date. In cases where multiple applications have the same earliest Prescription Drug User Fee Act (PDUFA) or Generic Drug User Fee Act (GDUFA) goal date, the supplement within the earliest goal date group, with the

lowest application number will be designated as the lead.

- Grouped supplements will be assigned for review (i.e., identify the RBPM and the primary reviewer) based on the supplement designated as the lead. The review division assigned to the lead application will be responsible for the review of all of the supplements in a group.
    - As an exception, Office of New Drug Products (ONDP) will review the group only in cases where all submissions in the group, not just the lead submission, would be assigned to ONDP.
- Typically, a single drug product review will be completed per discipline for the group by the lead reviewer.
    - As an exception, if the group also includes BLAs, then the Office of Biotechnology Products (OBP), the Office of Lifecycle Drug Products (OLDP), and ONDP will provide a review for their respective products. In this case, the lead office and review process will be determined on a case-by-case basis.

RESPONSIBILITIES

- The Office of Programs and Regulatory Operations (OPRO) RBPM triages and prepares the action letters or other necessary correspondence for grouped supplements. The RBPM also ensures that all relevant metadata (i.e., action status, effective date, filing category, assigned review division) for each of the supplements in the group are updated.
- The initially assigned BC (or designee) from the relevant review division resolves any issues regarding the grouping of supplements or designation of the lead application.
- The lead reviewer or review team completes a review for the entire group of supplements as a single review per discipline.

PROCEDURES

1. The OPRO RBPMs triage the incoming supplements and confirm that the initial grouping in Panorama is accurate, and subsequently, identify the proposed lead application and assigned review division (as provided in the policy section above).

2. The BC (or designee) for the assigned review division within OPQ (e.g., OLDP, ONDP) re-confirms the grouping and decides whether an application does not belong within the initial group and informs the RBPM that there is an application that needs to be removed from the group.

3. Upon re-confirmation that the supplements can be grouped, the review team is identified and assigned to the group by the BC or designee. Reviewer assignments are made by the supervisors of the team members. In some cases, this determination may be driven by resource issues or a need for specific review expertise.

4. If the initial grouping cannot be re-confirmed, the supplements will be ungrouped and each application may be reviewed separately or grouped in a separate manner.

5. After the review is complete (as per currently established procedures), the OPRO/RBPM prepares one action letter for the BC (or designee) which includes all the sNDAs and sANDAs. For a group that includes sBLAs, the decision whether to include the sBLA in the action letter will be determined on a case-by-case basis.

6. If the grouped supplements include sANDAs, the RBPM forwards a copy of the final review and action letter to the OLDP Division of Post-Marketing Activities II for informational purposes. The RBPM is also responsible for updating the relevant metadata for all supplements in the group and for closing out all projects for the group.

7. If the action taken on the supplements is a complete response, subsequent submissions to address the complete response issues will be appropriately grouped in the same manner as the original supplement submissions.

REFERENCES

- 21 CFR 314.70
- Form FDA 356h

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
01/19/2000	Initial	N/A
04/19/16	Rev.1	Combines NDA/ANDA procedures for grouping supplements requesting CMC changes.
12/9/2022	N/A	Recertified: no changes

ATTACHMENT – Grouped Product Quality Supplements Flowchart