Office of Pharmaceutical Science

Review of the Same Supplemental Change to More than One NDA or ANDA in More Than One Review Division

CONTENTS

PURPOSE

This MAPP provides a consistent procedure for reviewing chemistry, manufacturing, and controls (CMC) supplements. The goal is to provide consistency when reviewing the same change across more than one NDA (and ANDA if applicable) and in more than one ORM review division.

BACKGROUND

- When firms make identical CMC changes that affect multiple approved applications in more than one ORM review division, the Center needs to have a procedure for reviewing such groups of supplemental applications in an efficient manner to ensure consistency across chemistry review divisions.

REFERENCES

- 21 CFR 314.70

DEFINITIONS

COMIS: The Center-wide Oracle Management Information System (COMIS) is the CDER enterprise-wide database for managing information for pre- and postmarket regulatory activities. COMIS is used to track information about the receipt and review status of investigational new drug applications (INDs), new drug applications (NDAs), and abbreviated new drug applications (ANDAs).

Bundled Supplements: The term is used to describe the group or cluster of supplements to be reviewed using the procedure set forth in this MAPP.

POLICY

- Multiple supplements proposing the same change to approved NDAs (prescription and nonprescription) and ANDAs submitted concurrently will be accepted by the Center.

- The Bundling Coordinator, identified by the Office of Pharmaceutical Science (OPS) as an ONDC contact point, will coordinate the various review processes to provide a consistent and timely review of such supplements.

- The lead review will be performed by ONDC when the bundled supplements include any NDA. Because of the effect of PDUFA goals on ONDC reviews, ONDC reviewers will always be the lead reviewers for bundled supplements. When the bundled supplements are for ANDAs only, the Office of Generic Drugs will coordinate the review within its own office.

- In the event that the change crosses another Center (Center for Biologics Evaluation and Research or Center for Veterinary Medicine), the review process will be determined on a case-by-case basis. The lead review from ONDC will always be made available to any Center noted in the request for a bundled supplement review.
-

RESPONSIBILITIES

- The OPS Bundling Coordinator, an assigned ONDC representative, coordinates and tracks the reviews of the multiple supplements to ensure consistency and communication across chemistry review teams.

- The OGD Bundling Coordinator will forward information on bundled supplements to OGD

personnel, including copies of ONDC chemistry reviews, as they are received.

PROCEDURES

- When the Bundling Coordinator receives communication from an applicant notifying the Agency that they will be submitting supplements for the same change that will affect applications in more than one review team, division or office, the Bundling Coordinator, in conjunction with appropriate ONDC management staff, will evaluate the information that the company has proposed and will determine if the changes are acceptable as a bundled supplement. Once the decision is made to accept the supplements as a bundled set, the lead ONDC chemistry team will be identified for the review. This decision will be based on the team with the largest number of supplements and of that set, the oldest (lowest number) NDA will be designated *the lead* NDA. If there is more that one team with the same number of supplements, the team with the lowest NDA number will be the lead team. If an individual reviewer or team is identified as having specific expertise on the proposed change, they may be asked to accept the role as the lead for that set of supplements.

- The chemistry team leader will assign the reviewer on their team who will be the lead reviewer for the lead NDA in the set of bundled supplements. Once the lead reviewer has been identified, the lead team leader should notify the Bundling Coordinator who the lead reviewer is and what the supplement number is. The coordinator will in turn notify the other teams of this information.

- Applicants will be asked to cross reference all other involved NDAs, DMFs, and/or ANDAs by product name and application number and should provide a list of the clinical divisions responsible for the applications. Bundled supplements should ideally be submitted at the same time. The request for including supplements as a part of the bundle after the original set of bundled supplements has been submitted will be evaluated by the Bundling Coordinator and the management staff of ONDC.

- The Bundling Coordinator will prepare and distribute a memo via e-mail to chemistry team leaders, ONDC management, OGD Bundling Coordinator, chief project managers and appropriate document rooms. The e-mail will contain the name of the firm(s) involved, the date(s) of the supplements, a brief description of the change, the lead chemistry team and lead NDA, a list of all known affected applications, and proposed time lines for the draft and final review cycle. It is expected that the team leaders and chief project managers will forward this e-mail to the appropriate review team to ensure that all team members are aware that a bundled review has been received. It is not intended that the tracking and processing of chemistry, manufacturing, and controls bundled supplements will affect the current review tracking routines set by each ORM review division.

- The identified lead reviewer will determine what consults may be needed for the supplement. If a consult from microbiology is needed, a single request from the lead reviewer should be sent to the supervisory microbiologist located in HFD-160 and should include a list of the all applications that will be affected by the change. The Bundling Coordinator should be notified by the lead reviewer that a consult has been initiated and will, in turn, notify the other review teams of the consult request. If an establishment inspection is determined to be necessary, the Bundle Coordinator should be notified by the lead reviewer and will in turn notify the other review teams. Each reviewer assigned to a supplement in the bundle will need to submit an inspection request through the EES system; however, there must be a note in the comments field that the supplement is part of a set of bundled supplements and the lead NDA supplement number should be listed. For tracking purposes, the lead reviewer should notify the Bundling Coordinator if consult requests and/or an establishment inspection is needed.

- The team leaders will ensure that all reviewers are aware of all supplements that are a part of the bundle and keep them up to date on progress of the lead review.

- Upon receipt of the bundled supplements, the Division Document Rooms will enter document and assignment information into COMIS according to the usual procedures for chemistry, manufacturing, and controls supplements. Upon receipt of a consult request form for the lead NDA, the document room personnel should enter the assignment to each of the applications listed as a part of the bundled review in that division.

- The Office of Information Technology's Division of Database Management and Services (DDMS) will use the notification provided by the Bundling Coordinator as a guide in performing consistency checks for COMIS bundled supplement data across and within divisions. DDMS will query COMIS to verify that all supplements in the set have been given the same document type and that all supplements in the group have the same disciplines assigned.

- The Bundling Coordinator will track and record the progress of the review of the bundled supplements and will keep all teams informed of the status of the review.

- The draft lead review (with secondary sign off), including any consult reviews and a draft action letter, should be completed and provided to the Bundling Coordinator 3 months from the submission date for a 4-month supplement and 5 months from the submission date for a 6-month supplement. The Bundling Coordinator will distribute the draft review to the team leaders that have the bundled supplement(s) in their division. It is the responsibility of the team leaders to share this draft review with the chemistry reviewer(s) on their team involved in the review of the bundled submission and then pass concurrence or nonconcurrence along to the Bundling Coordinator. There will be l week for any comments on the draft review. If any team leader or reviewer identifies that any technical information or OPS policy has been interpreted inconsistently, the chemistry team

that identified the discrepancy should inform the Bundling Coordinator (and cc: the other team leaders involved in the bundle review). The Bundling Coordinator should immediately notify all teams reviewing supplements that there is a crosscutting issue needing resolution and that action letters on the supplements may need to be held until they have been notified there is resolution. The Bundling Coordinator will consult ONDC management to determine how best to resolve the issues, which may include having the Bundling Coordinator schedule a meeting with the appropriate staff members to reconcile the issues of concern. If needed, the issue can be presented to the OPS chemistry division directors for resolution.

- At this point, if a meeting is needed to resolve any issues seen in the draft review, the Bundling Coordinator will schedule a meeting. When the draft review has concurrence from the other teams, the Bundling Coordinator will notify the lead reviewer that the review can be finalized and an action letter issued. The review should be endorsed by the reviewer's team leader or other secondary reviewer in keeping with the review component procedures. The lead reviewer or lead team leader should provide directly to the Bundling Coordinator a copy of the final review and action letter as soon as possible for the coordinator to distribute to the other teams and Offices involved in the bundled set of supplements. It is important to meet the time lines listed so that all teams can meet the goal dates for the supplements.

- If the supplement cannot be approved and either a non-approval or approvable letter is issued, the Bundling Coordinator should be notified by the lead reviewer when the response to the action letter is submitted. This will allow tracking and coordination of the supplements until an approval action is issued.

- When applicable, the reviewer assigned to each supplement in the bundled set is responsible for reviewing product specific data (e.g., stability data, product specifications).

- Each team within ONDC will issue its own action letter(s) according to its own procedure with a copy to the Bundling Coordinator.

- Copies of review(s), EER results, consult review(s), and any other related material will be placed in each application in accordance with standard operating procedures of the ORM review divisions.

- A copy of the final review and action letter will be forwarded to the OGD bundle contact person for their information.

- If the action taken on the supplements is a non-approval or approvable and further amendments will be required, the response(s) to the action letters should be handled in the same manner as the original supplements.

EFFECTIVE DATE

This MAPP is effective on the date of publication.