OFFICE OF GENERIC DRUGS

Handling and Processing Requests for Global Reviews

CONTENTS

PURPOSE

- This MAPP outlines the policies and procedures for processing and handling global supplements submitted to the Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research (CDER). This procedure is intended to provide a consistent review of groups of three or more supplements for multiple abbreviated new drug applications (ANDAs) from a single applicant for the same change to each application.

BACKGROUND

- To improve efficiency in the application review process, the Office of Generic Drugs issued a letter on April 8, 1994, to all ANDA sponsors. That letter described procedures to be used by firms wanting to submit multiple supplements to cover an identical change to several different ANDAs. This MAPP formalizes that process.

DEFINITIONS

- **Applicant:** A pharmaceutical firm or other party that submits a drug marketing application to FDA.

- **Establishment Evaluation Request (EER):** A request to identify facilities that may need inspection or favorable current Good Manufacturing Practice (cGMP) status before approval of an application.

- **Global Chemistry and Manufacturing Controls (CMC) Supplement:** A group of supplements for three or more ANDAs that (1) cover an identical change to each application; (2) are submitted by the same ANDA applicant; (3) can be reviewed by one reviewer; and (4) do not include unique data for each supplement.

- **Global Coordinator:** The individual who organizes global submissions, notifies appropriate personnel, and submits an EER to the Office of Compliance, if needed.

- **ONDC Bundled Supplement Coordinator:** The individual who coordinates review of similar ANDA and NDA supplements when applicants make submissions concurrently to one or more Office of New Drug Chemistry (ONDC) divisions and to OGD (**bundled supplements).**[1]

POLICY

- OGD will provide a consistent review of common supplements for multiple applications from a single applicant submitted as a group of supplements for the same changes to each application.

- OGD will check supplemental applications to ensure that they meet the following criteria as *global supplements*:

  1. The supplements must have the same date of submission on Form FDA 356h and must be provided to the OGD document room in a single package. A duplicate copy of each supplement should also be submitted.

  2. Each supplemental application must clearly state the purpose of the proposed change, and indicate that it is a component of a multiple submission intended for a *global* or consolidated review by OGD.

  3. Each supplemental application should be accompanied by an attachment listing the ANDA number and drug product for each supplemental application included in the total submission.

  4. All supplements must provide for the identical change to each application. No variances will be permitted for individual submissions. Changes that include individual stability data to support approval of each application will NOT be considered for a global review.

  5. There must be at least three individual supplements for the same change.

RESPONSIBILITIES AND PROCEDURES

- **The Document Room staff will:**

  1. Receive global supplement submissions and enter the letter "Y" into the appropriate field in COMIS to link the individual supplements to GSS (Global Supplement System).

[1] The Office of New Drug Chemistry (ONDC) typically takes the lead in reviewing bundled supplements. The ONDC contact alerts the OGD coordinator of the expected review completion dates and review status. A copy of the ONDC review is forwarded to the OGD global coordinator who forwards the review to the appropriate OGD chemistry or microbiology team leader and project manager for their concurrence. An action letter is then issued by OGD for the ANDAs affected by the bundled submission.

2. Deliver to the global coordinator the set of duplicate jackets for the ANDAs that may qualify as global CMC supplements.

- **The OGD Global Coordinator will:**

1. Review the cover letter for appropriateness of the submissions (i.e., same dates, Form FDA 356h submitted for each ANDA, identical change, three or more affected ANDAs).

2. Consult the appropriate Chemistry Division Director or Deputy Division Director for any global supplements to determine whether they can be processed as global CMC supplements.

3. If the global supplement submission qualifies for global review, assign it to the chemistry branch with the largest number of the supplements.

4. Create any EERs needed for inspections connected with the global CMC supplements. These are then submitted to the Office of Compliance as soon as global status is granted (using Mass Input feature under Options in EES).

5. Deliver supplements to the team project manager (PM) when appropriate (i.e., changes being effected (CBE) supplements requiring endorsements).

6. When notified by the chemistry team leader and PM that the review clock has reached 130 days before review, reassign the supplements to the team with the next largest number of supplements in the global submission, depending upon workload. The new team leader should formally reassign the global supplements to a reviewer in that team for review.

- **The OGD Chemistry Division Director or Deputy Division Director will:**

1. Determine whether multiple supplements qualify as global CMC supplements for review by one reviewer, then notify the OGD Global Coordinator of this decision. Supplements can be denied global CMC review status if there is any unique data that needs to be evaluated in one or more of the supplements.

2. Return all supplements, whether global review is granted or denied, to the OGD Global Coordinator for appropriate follow-up.

- **The Chemistry Team Leader will:**

1. Assign the global CMC supplements to one of the chemists in the team for review as they come up in the supplement queue.

2. With the PM, maintain awareness of the progress of the inspection status and consults until the first supplement comes up for review in their team.

3. Once a reviewer starts a global review, send an e-mail to that effect to all other reviewers on the assigned team to ensure there is no duplication of review.

4. Monitor the 130-day clock in case reassignment is needed. Inform the global coordinator when the 130-day clock is reached.

- **The OGD Review Support Project Manager will:**

1. In cooperation with the chemistry team leader and the review chemist, monitor the progress of all milestones of all components of the supplements, such as inspection status and consults, as well as the start date of the review.

2. Notify all participants by e-mail once the review has started.

3. If the review clock reaches 130 days before the review begins, notify the team leader and global coordinator.

4. Coordinate the action letter, completed EERs, and consults, including all ANDAs involved, from draft to final letters out.

5. Place entries in the Master Queue, noting the status of the supplements and indicating that the supplements are being handled as global CMC supplements.

EFFECTIVE DATE

This MAPP is effective upon date of publication.

ATTACHMENT

OPERATING THE GLOBAL SUPPLEMENT SYSTEM (GSS)

GRANTING AND DENYING GLOBAL SUPPLEMENTS IN GSS:

- When a set of global supplements meets the required criteria, the supplements are assigned to a team. Before assigning the set to a team, that set has to be either granted or denied global status in the computerized Global Supplement System (GSS). The global assignment appears on the chemistry queues with a designation of GT (tentative global), GD (global denied) or GS plus a number (global granted and team number assigned for review). The GT notation indicates that no decision has been made on the status of the submission and should be brought to the attention of the global coordinator.

  To grant or deny global status to a set of supplements, follow these steps, using the first screen shown after logging into GSS (Screen 1):

  1. Enter the letter date of the submission, using the format DD-MMM-YYYY (i.e., 12-JUN-2003).

  2. Enter the document type into the Doc Type box (e.g., SCS, SCB). Note: Both the letter date and document type MUST be entered.

  3. Click on Display list.

  The sponsor name does not need to be entered.

  The entire list of supplements should appear in the lower left-hand box. Count the number of supplements on the computerized list against the number of supplements the sponsor has listed in the cover letter. If any are missing from the list on your screen, contact the OGD document room by e-mail to have a "Y" placed in COMIS, linking the missing supplements to GSS. You may need to log out of the program and log in again for the update to take effect.

- Once the list displayed on the screen is complete, the entire list may be granted or denied global status. To grant or deny the entire set of supplements, click on >> to move the list to the box on the right-hand side of the screen. Click either Granted or Denied and then click Save. Supplements can be granted or denied individually by highlighting the individual supplement and clicking < or > to move one supplement at a time.

- If the set is being denied, you are finished after clicking on Denied and Save. If the set is to be granted, continue with the following instructions.

ASSIGNING GLOBAL SUPPLEMENTS TO A TEAM IN GSS

1. After granting global status to a set of supplements on Screen 1, click on Go to Global List. Screen 2 should appear.

2. Enter the letter date using the format DD-MMM-YYYY and click on the *eyeglasses icon*. A list of all submissions from all firms made on that date will appear.

3. Highlight the desired firm from the list, then click OK.

   Screen 3 then appears, showing a list of all of the global supplements, letter dates, drug names, and reviewers. (Keep in mind that only one of these reviewers will be selected by the Team Leader to perform the review.)

4. Determine which team has the majority of the supplements by reviewer names. If no name is listed in the far right-hand box, use the ANDA number and Master Queue to determine the team associated with the supplement. (You must use the scroll down feature to capture all of the supplements.)

5. Enter the team number of the team with the majority of the supplements into the first box of the Team/Reviewer field (i.e., 7) and click Save.

   The set of supplements has now been assigned to the appropriate team.

6. Print the screen(s) (scroll down to capture all supplements, if necessary). Cut and paste the list to include the entire list of supplements on a sheet of plain paper (2-sided copies are sometimes necessary). Make as many copies as there are supplements. Package the copies with the supplements and send the package to the document room. The document room staff will file a list of the supplements in the jacket of each affected ANDA.

7. If the supplements are **changes being effected** (**CBE) supplements**, handle them as usual after the global assignment is made by delivering the complete package to the appropriate PM so that the CBE form may be endorsed.

8. If EES entries are needed, enter the appropriate information into EES. The Mass Input feature of EES may be used to make the entries and submit them simultaneously.

GENERATING REPORTS

- From Screen 2 of GSS, click Generate Report to show a list of the ANDAs, supplement numbers, letter date, drug names, strengths, and reviewer names.

GENERATING E-MAIL SUPPLEMENT LISTS FOR WORD DOCUMENTS

- E-mailing supplement lists gives the reviewer the option of cutting and pasting lists of supplements to place into their CMC reviews and/or letters.

  To have a report of the global supplements e-mailed to you, follow these steps:

  1. Log into COMIS.
  2. Choose 10, COMIS Main Menu.
  3. Choose 5, ANDA/MIS.
  4. Choose 6, General Reports Menu II.
  5. Choose 10, Global Supplement Report.
  6. Choose 3, E-mail Global Supplements by Family.
  7. Enter any ANDA number from the global set and press enter.

8. The list will be e-mailed to you shortly. If you do not receive the list, enter other ANDA numbers from the submission.

BROWSING BETWEEN SCREENS

- To go back and forth from Screen 1 to Screen 2, click Go to Global Family or Go to Global List.

SEARCHING FOR THE ASSIGNED TEAM

- To find the team to which a set of global supplements has been assigned, choose the following menu options from GSS:

  1. From Screen 1 in GSS, click Go to Global Family.

  2. On Screen 2, enter the letter date of the submission in the box directly adjacent to the box containing the eyeglasses icon. Use the DD-MMM-YYYY format.

  3. Click on the eyeglasses icon.

  4. From the list that appears, highlight the submission of choice and click OK.

  5. The Team/Reviewer box displays the assigned team. As long as the team number is correct, the reviewer name is negligible.

REASSIGNING GLOBAL SUPPLEMENTS TO ANOTHER TEAM

- If the review clock reaches 130 days before the review of a set of global supplements, the set needs to be assigned to the branch with the next largest number of supplements in the global submission. The new team leader should formally reassign the global to a reviewer in that team for review. The global coordinator reassigns the set through GSS.

  To reassign a set of global supplements using GSS, follow the instructions noted below:

  1. Log into GSS.

  2. From Screen 1, click on Go to Global Family. Screen 2 will appear.

  3. In the Document field on Screen 2, enter the letter date of the submission in the box adjacent to the box containing the eyeglasses icon. Use the DD-MMM-YYYY format. Click on the eyeglasses icon.

  4. On Screen 3, change the team number to the new team number and click Save. The assigned team has now been changed and will be reflected on the chemistry review queue.