NEW DRUG CHEMISTRY

Requests for Expedited Review of NDA Chemistry Supplements

CONTENTS

PURPOSE

- To document policy and procedures relating to requests for expedited review of chemistry supplements[1] to new drug applications (NDAs).

BACKGROUND

- For supplements requiring approval by FDA before the applicant may implement the change (prior approval supplements), the regulations at 21 CFR 314.70(b) provide that: "an applicant may **ask** [emphasis added] FDA to expedite its review of a supplement if a delay in making the change described in it would impose an extraordinary hardship on the applicant." The applicant is instructed to mark its supplement and mailing cover: "Supplement - Expedited Review Requested."

- The Office of Generic Drugs (OGD) issued a policy and procedure (Policy and Procedure Guide 18-90, dated March 29, 1990) relating to requests for expedited review of supplements to abbreviated new drug applications (ANDAs). Policy and Procedure Guide 18-90 was subsequently revised by OGD and published in the Center for Drug Evaluation and Research's Manual of Policies and Procedures (Mapp 5240.1, November 1, 1995)

- The Office of New Drug Chemistry (ONDC) has prepared MAPP 5310.3 to document the expedited review policy for NDA chemistry supplements.

POLICY AND PROCEDURE

[1]Chemistry supplements include those relating to microbiology issues (e.g., changes in sterilization procedures). Labeling supplements are not addressed in this MAPP.

- Requests for expedited review will be considered on a case-by-case basis, and will be undertaken if adequate review resources are available. Consideration for expedited review will be given only when the basis for the request is clearly stated by the applicant and sufficient supporting documentation is included. Under the Prescription Drug User Fee Act (PDUFA II) the goal date for review of prior approval NDA chemistry supplements is four months. Expedited review for these supplements will be considered only when there is sufficient documentation to support a need for review in less than four months. Granting of an expedited review does not change the information that should be submitted in the supplement to support the change.

  1. Criteria for Granting Expedited Reviews

     Expedited review may be warranted if the supplement relates to:

     a. Public health need. Events that affect the availability of a drug for which there is no alternative (see also Drug Shortage Management, MAPP 4730.1).

     b. Extraordinary hardship on the applicant.

        (1) Catastrophic events such as explosion, fire, or storm damage.

        (2) Events that could not have been reasonably foreseen, and for which the applicant could not plan. Examples include:

           (i) abrupt discontinuation of supply of active ingredient, packaging material, or container closure.

           (ii) relocation of a facility or change in an existing facility because of a catastrophic event (see item 1.b.(1)). [Otherwise, the applicant should submit its supplement early in the planning stage of a contemplated relocation/change for routine review.]

     c. Agency need.

        (1) Matters regarding the government's drug purchase program, upon request from the appropriate FDA office. ONDC reserves the right to expedite review without a request in this case as well as the one described in item c.(2) below.

        (2) Federal or state legal/regulatory actions, including mandated formulation changes or labeling changes if it is in the Agency's best interest.

This does not include actions taken by FDA Field staff against applicants who put changes into effect that are required to have approved supplements (21 CFR 314.70(b)).

(3) Expiration-date extension or packaging change when the drug product is the subject of a government contract award. (This is usually requested by the Government Wide Quality Assurance Program or by Department of Defense or Department of Veteran's Affairs procurement personnel.)

2. Procedures

a. Initial request

(1) All prior approval supplements requesting expedited review should reference the NDA number and be clearly labeled, "Supplement - Expedited Review Requested." The supplement should not be directed to an individual.

(2) The review chemist will make an initial recommendation. Others will be consulted (e.g., microbiology staff) when necessary.

(3) The initial recommendation will be reviewed by the Chemistry Team Leader, who will concur or not concur with the recommendation.

(4) If the request is granted, the expedited review will be conducted as a high priority review.

(5) If the request for expedited review is denied, the request will be forwarded to the Director of the appropriate Division of New Drug Chemistry (DNDC) for concurrence. After concurrence by the DNDC Director, the Chemistry Team Leader will advise the company by telephone of the decision and the reasons for the denial and then prepare a memorandum of the telephone conversation which will be placed in the NDA archival copy and other appropriate clinical division files.

(6) The Chemistry Team Leader will ensure that the decision is documented (see Attachment A) and filed in the application and other appropriate locations (e.g., division file).

b. Appeal of decision.

(1) The firm may appeal the decision. Supporting documentation (referencing the NDA number) should accompany the request for reconsideration, and be sent to the Director, ONDC. The ONDC Director's decision will be final.

EFFECTIVE DATE

- This Mapp will be effective immediately.

ATTACHMENT A

EXPEDITED REVIEW REQUEST DOCUMENTATION FORM

NDA & Supplement #: _____ Applicant: _____

Date of Submission: _____Drug: _____

MAPP 5310.3 lists the following criteria for granting expedited review status to a prior approval chemistry supplement. At least one of the criteria must be met. Circle those that are applicable.

1. **Public health need.** Events that affect the availability of a drug for which there is no alternative.

2. **Extraordinary hardship on the applicant.**

   A. Catastrophic events such as explosion, fire, or storm damage.

   B. Events that could not have been reasonably foreseen, and for which the applicant could not plan. Examples include:

   - abrupt discontinuation of supply of active ingredient, packaging material, or container closure.
   - relocation of a facility or change in an existing facility because of a catastrophic event (see item 2.A).

3. **Agency need**.

   A. Matters regarding the government's drug purchase program, upon request from the appropriate FDA office.

   B. Federal or state legal/regulatory actions, including mandated formulation changes or labeling changes if it is in the Agency's best interest.

   C. Expiration-date extension or packaging change when the drug product is the subject of a government contract award.

Recommendations (as appropriate):

Review Chemist: □ Grant □ Deny _____
Signature Date

DNDC Team Leader: □ Grant □ Deny _____

DNDC Division Director: □ Grant □ Deny _____

ONDC Director: □ Grant □ Deny _____

Comments: