OFFICE OF GENERIC DRUGS

Productivity Documentation in the Division of Bioequivalence

CONTENTS

PURPOSE

- This MAPP describes the procedures for productivity documentation in the Division of Bioequivalence (DBE) I and DBE II in the Office of Generic Drugs (OGD) and how that productivity is credited to individual reviewers.

BACKGROUND

- A productivity database was created to replace the COMIS system and OGD uses it to keep track of the bioequivalence (BE) divisions' workload. The BE section of an abbreviated new drug application (ANDA) contains data on the demonstration of BE, such as BE studies, studies with clinical endpoints, dissolution data, and waiver requests. The productivity database keeps a record of (1) ANDA number, (2) submission letter date, (3) the reviewer assigned to the submission, (4) the type of studies submitted, in the BE section, and (5) dates when the review was satisfactorily completed by the reviewer. Other work, such as controlled correspondence and protocols, is also tracked in this database. The overall productivity of the division and the reviewers is monitored using the information in the productivity database.

POLICY

- Information entered into the productivity database on the study types in the BE section of an ANDA allows OGD to track the productivity of the DBE reviewers and the DBE divisions. Consistent and fair classification of these study types will ensure objective evaluation of reviewers based on credit earned for their review activities.

- Non-ANDA related work products are also tracked in this database. That information includes a control number, submission letter date, name of assigned reviewer, type of assignment (e.g., control, protocol) and review completion date.

RESPONSIBILITIES

- DBE Reviewer:

  Reviews BE submissions (including correspondence and protocols) as assigned.

  Enters the study types reviewed directly in the productivity database. Exports the records entered in the database into the review.

- Team Leader:

  Verifies study type stated in the last page of the review and the productivity database. Ensures that the study type classifications are consistently applied.

- Tertiary Reviewer (division directors and/or deputies):

  Verifies the entries in the productivity database then signs off on the review. Once the tertiary reviewer completes the review, the productivity data are finalized and archived.

PROCEDURES

Upon completion of the review, the reviewer will identify the study type categories submitted in the application. The reviewer will enter the study types reviewed directly in the productivity database and copy and paste a copy of the records from the productivity database into the review. The team leader will verify the study types entered in the database and the review. The tertiary reviewer will provide their final signature on the review and the productivity database.

A description of the productivity categories follows. The attachment provides a list of the study type categories and subcategories to choose from and the credit each subcategory receives. The following description of the subcategories is provided below to clarify how these subcategories should be applied:

A. BIOEQUIVALENCE STUDIES (BE)

B. DISSOLUTION REVIEWS (**DIS**): A preliminary review of the dissolution data is conducted by a reviewer prior to the review of the BE studies. This is to establish the quality and control method to be used for the stability testing, if needed. The reviewer conducts this preliminary review to provide the stability method to the firm as soon as possible. For certain products that do not require in-vivo BE testing such as those coded as AA[1] drugs in the Orange Book, and supplements for new strengths, the entire review may be completed during this dissolution review. In that case, the review should be credited both as a dissolution review and a dissolution waiver review.

[1] AA: Products in conventional dosage forms not presenting bioequivalence problems.

Dissolution amendments received in response to the initial review of the dissolution portion should go to the reviewer that conducted the dissolution review, if the dissolution amendment is received before assignment to the BE study reviewer. The dissolution reviewer will receive a dissolution amendment credit for it. If the application is assigned to a BE study reviewer before the dissolution amendment is received, the BE reviewer should review the dissolution amendment and will receive the dissolution amendment credit.

NOTE: Dissolution data submitted for the same strength that was the subject of a BE study are not separately coded. The dissolution information is considered to be part of the study.

C. **OTHER** (**OTH**):

1. **STUDY AMENDMENT** - This category is for responses to deficiency comments or additional information the sponsor wishes to provide after the original application is submitted. Whether the amendment contains dissolution data, or addresses a deficiency such as incomplete information on analytical methods or a study, the submission should be coded as a study amendment, unless a new study is submitted for review. If a complete new study is submitted, the appropriate code under BE studies should be selected.

   Re-dosing studies of subjects suspected to have aberrant data when submitted in an amendment are classified as a study amendment.

   Frequently, the DBE telephones sponsors to request information needed to finalize the review. These requests should be made for information the sponsor can respond to within 10 working days and should be coded as STA.

   If the sponsor submits incorrect information, or partial data, the submission should be coded as a study amendment without charge and no credit is given. If the amendment contains new data or information, the submission should be coded as a regular study amendment and credit is given for the evaluation of complete data. If the amendment contains corrections to the application, or information that should have been part of the original submission (such as long term stability data, diskettes, SOPs, chromatograms, potency, expiration dates, lot numbers, typographical errors, etc.), the amendment should be coded "Study Amendment Without Credit," and no credit is given.

2. **WAIVERS** - There is a subcategory available for injectable, ophthalmic, otic, oral, and topical solutions. A formulation in the same concentration that is packaged in different sizes will not be coded separately. Different concentrations of the same product are coded separately.

3. **DISSOLUTION WAIVER** - This code is used for lower strengths that can be approved based on proportionality of the formulation and an acceptable study on the highest strength or the reference listed drug strength. A dissolution waiver should be coded for each strength for which dissolution data are submitted, except the strength for which BE studies have been conducted.

4. **DIVISION OF SCIENTIFIC INVESTIGATIONS INSPECTION REPORT -** The Division of Scientific Investigations (DSI) inspection reports may generate an addendum to the review. If a significant reevaluation of the data is needed based on the recommendation of the DSI or if the issuance of a Form 483 indicates serious violations by the laboratory, a review of the DSI report is generated, and regular credit is given. If the DSI report is acceptable, the DSI report should be filed in the ANDA, and no addendum to the review is necessary.

D. PROTOCOLS (PRO):

There are also protocols sent to the DBE for review to obtain comments on the proposed study design prior to the submission of ANDAs. Pilot studies submitted with a protocol to justify a particular study design are not counted separately. A BE reviewer generates a review and provides comments to the firm by letter.

Occasionally, sponsors submit protocols for products that do not require BE testing (e.g., a waiver request of in-vivo testing). In this case, the additional protocol does not have to be reviewed and credit will not be given.

E. CONTROLLED CORRESPONDENCE (CC):

Bioequivalence information requests sent as correspondence are also assigned to DBE reviewers for evaluation and generation of a review. These reviews are also counted as part of the overall productivity of individual reviewers.

F. ANDA FILING CHECKLIST (P4):

The Regulatory Support Branch sends a checklist to the division for a preliminary review to ensure the BE section is complete and studies submitted meet the current statistical criteria. This checklist is usually sent to the division for first generics and complex drug products. Follow-up amendments which contain the data requested during the checklist review are not credited.

Processing of Work

- When the review is completed, the reviewer will state, on the last page of the review, the study types reviewed in the submission and enter the codes in the productivity database.

- The team leaders verify that the study codes are accurate. Once the review is finalized and has division director's concurrence, the team leaders enter the review in DARRTS. The project manager prepares fax cover sheets and transmits deficiencies to the firm.

- The division directors will verify and finalize the documentation of productivity in the productivity database and will sign off on the review in DARRTS. This closes the submission indicating that the review has been completed. Once the submission is closed, reviewers get credit for their work.

EFFECTIVE DATE

This MAPP is effective upon date of publication.

Attachment

Subcategory Descriptions

Productivity Category	Sub Category	Credit
BE	Fasting Study	1
BE	Fed study	1
BE	Multiple dose study	1
BE	Clinical Endpoint study	1
BE	Pharmacodynamic study	1
BE	Sprinkle study	1
BE	Failed Study	1
BE	Re-dosing study	1
BE	Pilot Study (Blanching)	1
BE	Pivotal Study (Blanching)	1
BE	In-Vitro study (binding)	1
BE	In-Vitro study (nasal or other dosage forms, each study type)	1
BE	Abbreviated Review	1
BE	BCS Permeability Study	1
BE	BCS Solubility Study	1
DIS	Dissolution Review	1
DIS	Dissolution Acknowledgement	0
OTH	Study Amendment	1
OTH	Study Amendment Without Credit	0
OTH	Dissolution Waiver	1
OTH	Waiver Injectable	1
OTH	Waiver Topical	1
OTH	Waiver Oral Solution	1
OTH	Waiver Otic Solution	1
OTH	Waiver Ophthalmic Solution	1
OTH	DSI Inspection report	1
OTH	Citizen's Petition	1
OTH	Addendum	0
OTH	Miscellaneous	0
OTH	BCS Waiver	1
OTH	Dissolution Amendment	1
OTH	In-vitro dose-dumping in Alcohol	1
OTH	Supplement (Audits)	1
		1
PRO	Protocol	

PRO	Protocols Amendment	1
PRO	Bio-IND	1
PRO	Bio-IND Amendment	1
CC	Controlled Correspondence	1
CC	CC Group	1
P4	ANDA Filing Checklist	1