ENCLOSURE

PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES

The performance goals and procedures of the FDA Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER), as agreed to under the reauthorization of the prescription drug user fee program in the "Food and Drug Administration Modernization Act of 1997," are summarized as follows:

I. FIVE-YEAR REVIEW PERFORMANCE GOALS

Fiscal year 1998

1. Review and act on 90 percent of standard original New Drug Application (NDAs) and Product License Applications (PLAs)/Biologic License Applications (BLAs) filed during fiscal year 1998 within 12 months of receipt.

2. Review and act on 90 percent of priority original NDA and PLA/BLA submissions filed during fiscal year 1998 within 6 months of receipt.

3. Review and act on 90 percent of standard efficacy supplements filed during fiscal year 1998 within 12 months of receipt.

4. Review and act on 90 percent of priority efficacy supplements filed during fiscal year 1998 within 6 months of receipt.

5. Review and act on 90 percent of manufacturing supplements filed during fiscal year 1998 within 6 months of receipt.

6. Review and act on 90 percent of all resubmitted original applications filed during fiscal year 1998 within 6 months of receipt, and review and act on 30 percent of Class 1 resubmitted original applications within 2 months of receipt.

Fiscal year 1999

1. Review and act on 90 percent of standard original NDA and PLA/BLA submissions filed during fiscal year 1999 within 12 months of receipt and review and act on 30 percent within 10 months of receipt.

2. Review and act on 90 percent of priority original NDA and PLA/BLA submissions filed during fiscal year 1999 within 6 months of receipt.

3. Review and act on 90 percent of standard efficacy supplements filed during fiscal year 1999 within 12 months of receipt and review and act on 30 percent within 10 months of receipt.

4. Review and act on 90 percent of priority efficacy supplements filed during fiscal year 1999 within 6 months of receipt.

5. Review and act on 90 percent of manufacturing supplements filed during fiscal year 1999 within 6 months of receipt and review and act on 30 percent of manufacturing supplements requiring prior approval within 4 months of receipt.

6. Review and act on 90 percent of Class 1 resubmitted original applications filed during fiscal year 1999 within 4 months of receipt and review and act on 50 percent within 2 months of receipt.

7. Review and act on 90 percent of Class 2 resubmitted original applications filed during fiscal year 1999 within 6 months of receipt.

Fiscal year 2000

1. Review and act on 90 percent of standard original NDA and PLA/BLA submissions filed during fiscal year 2000 within 12 months of receipt and review and act on 50 percent within 10 months of receipt.

2. Review and act on 90 percent of priority original NDA and PLA/BLA submissions filed during fiscal year 2000 within 6 months of receipt.

3. Review and act on 90 percent of standard efficacy supplements filed during fiscal year 2000 within 12 months of receipt and review and act on 50 percent within 10 months of receipt.

4. Review and act on 90 percent of priority efficacy supplements filed during fiscal year 2000 within 6 months of receipt.

5 Review and act on 90 percent of manufacturing supplements filed during fiscal year 2000 within 6 months of receipt and review and act on 50 percent of manufacturing supplements requiring prior approval within 4 months of receipt.

6. Review and act on 90 percent of Class 1 resubmitted original applications filed during fiscal year 2000 within 4 months and review and act on 50 percent within 2 months of receipt.

7. Review and act on 90 percent of Class 2 resubmitted original applications filed during fiscal year 2000 within 6 months of receipt.

Fiscal year 2001

1. Review and act on 90 percent of standard original NDA and PLA/BLA submissions filed during fiscal year 2001 within 12 months and review and act on 70 percent within 10 months of receipt.

2. Review and act on 90 percent of priority original NDA and PLA/BLA submissions filed during fiscal year 2001 within 6 months of receipt.

3. Review and act on 90 percent of standard efficacy supplements filed during fiscal year 2001 within 12 months and review and act on 70 percent within 10 months of receipt.

4. Review and act on 90 percent of priority efficacy supplements filed during fiscal year 2001 within 6 months of receipt.

5. Review and act on 90 percent of manufacturing supplements filed during fiscal year 2001 within 6 months of receipt and review and act on 70 percent of manufacturing supplements requiring prior approval within 4 months of receipt.

6. Review and act on 90 percent of Class 1 resubmitted original applications filed during fiscal year 2001 within 4 months of receipt and review and act on 70 percent within 2 months of receipt.

7. Review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.

Fiscal year 2002

1. Review and act on 90 percent of standard original NDA and PLA/BLA submissions filed during fiscal year 2002 within 10 months of receipt.

2. Review and act on 90 percent of priority original NDA and PLA/BLA submissions filed during fiscal year 2002 within 6 months of receipt.

3. Review and act on 90 percent of standard efficacy supplements filed during fiscal year 2002 within 10 months of receipt.

4. Review and act on 90 percent of priority efficacy supplements filed during fiscal year 2002 within 6 months of receipt.

5. Review and act on 90 percent of manufacturing supplements filed during fiscal year 2002 within 6 months of receipt and review and act on 90 percent of manufacturing supplements requiring prior approval within 4 months of receipt.

6. Review and act on 90 percent of Class 1 resubmitted original applications filed during fiscal year 2002 within 2 months of receipt.

7. Review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.

These review goals are summarized in the following tables:

ORIGINAL NDAs/BLAs/PLAs and EFFICACY SUPPLEMENTS:

SUBMISSION COHORT	STANDARD	PRIORITY
FY 98	90% IN 12 MO	90% IN 6 MO
FY 99	30% IN 10 MO 90% IN 12 MO	90% IN 6 MO
FY 00	50% IN 10 MO 90% IN 12 MO	90% IN 6 MO
FY 01	70% IN 10MO 90% IN 12 MO	90% IN 6 MO
FY 02	90% In 10 MO	90% IN 6 MO

MANUFACTURING SUPPLEMENTS:

SUBMISSION COHORT	MANUFACTURING SUPPLEMENTS THAT DO NOT REQUIRE PRIOR APPROVAL ("CHANGES BEING EFFECTED" OR "30-DAY SUPPLEMENTS"	MANUFACTURING SUPPLEMENTS THAT DO REQUIRE PRIOR APPROVAL
FY 98	90% IN 6 MO	90% IN 6 MO
FY 99	90% IN 6 MO	30% IN 4 MO 90% IN 6 MO
FY 00	90% IN 6 MO	50% IN 4 MO 90% IN 6 MO
FY 01	90% IN 6 MO	70% IN 4 MO 90% IN 6 MO
FY 02	90% IN 6 MO	90% IN 4 MO

RESUBMISSION OF ORIGINAL NDAs/BLAs/PLAs:

SUBMISSION COHORT	CLASS 1	CLASS 2
FY 98	90% IN 6 MO 30% IN 2 MO	90% IN 6 MO
FY 99	90% IN 4 MO 50% IN 2 MO	90% IN 6 MO
FY 00	90% IN 4 MO 70% IN 2 MO	90% IN 6 MO
FY 01	90% IN 2 MO	90% IN 6 MO
FY 02	90% IN 2 MO	90% IN 6 MO

II. NEW MOLECULAR ENTITY (NME) PERFORMANCE GOALS

The performance goals for standard and priority original NMEs in each submission cohort will be the same as for all of the original NDAs (including NMEs) in each submission cohort but shall be reported separately.

For biological products, for purposes of this performance goal, all original BLAs/PLAs will be considered to be NMEs.

III. MEETING MANAGEMENT GOALS

A. Responses to Meeting Requests.

1. Procedure: Within 14 calendar days of the Agency's receipt of a request from industry for a formal meeting (i.e., a scheduled face-to-face, teleconference, or videoconference) CBER and CDER should notify the requester in writing (letter or fax) of the date, time, and place for the meeting, as well as expected Center participants.

2. Performance Goal: FDA will provide this notification within 14 days for 70% of requests (based on request receipt cohort year) starting in FY99; 80% in FY00; and 90% in subsequent fiscal years.

B. Scheduling Meetings

1. Procedure: The meeting date should reflect the next available date on which all applicable Center personnel are available to attend, consistent with the component's other business; however, the meeting should be scheduled consistent with the type of meeting requested. If the requested date for any of these types of meetings is greater than 30, 60, or 75 calendar days (as appropriate) from the date the request is received by the Agency, the meeting date should be within 14 calendar days of the date requested.

   Type A Meetings should occur within 30 calendar days of the Agency receipt of the meeting request.

   Type B Meetings should occur within 60 calendar days of the Agency receipt of the meeting request.

   Type C Meetings should occur within 75 calendar days of the Agency receipt of the meeting request.

2. Performance goal: 70% of meetings are held within the timeframe (based on cohort year of request) starting in FY99; 80% in FY00; and 90% in subsequent fiscal years.

C. Meeting Minutes

1. Procedure: The Agency will prepare minutes which will be available to the sponsor 30 calendar days after the meeting. The minutes will clearly outline the important agreements, disagreements, issues for further discussion, and action items from the meeting in bulleted form and need not be in great detail.

2. Performance goal: 70% of minutes are issued within 30 calendar days of date of meeting (based on cohort year of meeting) starting in FY99; 80% in FY00; and 90% in subsequent fiscal years.

D. Conditions

For a meeting to qualify for these performance goals:

1. A written request (letter or fax) should be submitted to the review division; and

2. The letter should provide:

   a. A brief statement of the purpose of the meeting;
   b. A listing of the specific objectives/outcomes the requester expects from the meeting;
   c. A proposed agenda, including estimated times needed for each agenda item;
   d. A listing of planned external attendees;
   e. A listing of requested participants/disciplines representative(s) from the Center;
   f. The approximate time that supporting documentation (i.e., the "backgrounder") for the meeting will be sent to the Center (i.e., "x" weeks prior to the meeting, but should be received by the Center at least 2 weeks in advance of the scheduled meeting for Type A or C meetings and at least 1 month in advance of the scheduled meeting for Type B meetings); and

3. The Agency concurs that the meeting will serve a useful purpose (i.e., it is not premature or clearly unnecessary). However, requests for a "Type B" meeting will be honored except in the most unusual circumstances.

IV. CLINICAL HOLDS

A. Procedure: The Center should respond to a sponsor's complete response to a clinical hold within 30 days of the Agency's receipt of the submission of such sponsor response.

B. Performance goal: 75% of such responses are provided within 30 calendar days of the Agency's receipt of the sponsor's response starting in FY98 (cohort of date of receipt) and 90% in subsequent fiscal years.

V. MAJOR DISPUTE RESOLUTION

A. Procedure: For procedural or scientific matters involving the review of human drug applications and supplements (as defined in PDUFA) that cannot be resolved at the divisional level (including a request for reconsideration by the Division after reviewing any materials that are planned to be forwarded with an appeal to the next level), the response to appeals of decisions will occur within 30 calendar days of the Center's receipt of the written appeal.

B. Performance goal: 70% of such answers are provided within 30 calendar days of the Center's receipt of the written appeal starting in FY99; 80% in FY00; and 90% in subsequent fiscal years.

C. Conditions

1. Sponsors should first try to resolve the procedural or scientific issue at the Division level. If it cannot be resolved at that level, it should be appealed to the Office Director level (with a copy to the Division Director) and then, if necessary, to the Deputy Center Director or Center Director (with a copy to the Office Director).

2. Responses should be either verbal (followed by a written confirmation within 14 calendar days of the verbal notification) or written and should ordinarily be to either deny or grant the appeal.

3. If the decision is to deny the appeal, the response should include reasons for the denial and any actions the sponsor might take in order to persuade the Agency to reverse its decision.

4. In some cases, further data or further input from others might be needed to reach a decision on the appeal. In these cases, the "response" should be the plan for obtaining that information (e.g., requesting further information from the sponsor, scheduling a meeting with the sponsor, scheduling the issue for discussion at the next scheduled available advisory committee).

5. In these cases, once the required information is received by the Agency (including any advice from an advisory committee), the person to whom the appeal was made, again has 30 calendar days from the receipt of the required information in which to either deny or grant the appeal.

6. Again, if the decision is to deny the appeal, the response should include the reasons for the denial and any actions the sponsor might take in order to persuade the Agency to reverse its decision.

7. N.B. If the Agency decides to present the issue to an advisory committee and there are not 30 days before the next scheduled advisory committee, the issue will be presented at the following scheduled committee meeting in order to allow conformance with advisory committee administrative procedures.

VI. SPECIAL PROTOCOL QUESTION ASSESSMENT AND AGREEMENT

A. Procedure: Upon specific request by a sponsor (including specific questions that the sponsor desires to be answered), the agency will evaluate certain protocols and issues to assess whether the design is adequate to meet scientific and regulatory requirements identified by the sponsor.

1. The sponsor should submit a limited number of specific questions about the protocol design and scientific and regulatory requirements for which the sponsor seeks agreement (e.g., is the dose range in the carcinogenicity study adequate, considering the intended clinical dosage; are the clinical endpoints adequate to support a specific efficacy claim).

2. Within 45 days of Agency receipt of the protocol and specific questions, the Agency will provide a written response to the sponsor that includes a succinct assessment of the protocol and answers to the questions posed by the sponsor. If the agency does not agree that the protocol design, execution plans, and data analyses are adequate to achieve the goals of the sponsor, the reasons for the disagreement will be explained in the response.

3. Protocols that qualify for this program include: carcinogenicity protocols, stability protocols, and Phase 3 protocols for clinical trials that will form the primary basis of an efficacy claim. (For such Phase 3 protocols to qualify for this comprehensive protocol assessment, the sponsor must have had an end of Phase 2/pre-Phase 3 meeting with the review division so that the division is aware of the developmental context in which the protocol is being reviewed and the questions being answered.)

4. N.B. For products that will be using Subpart E or Subpart H development schemes, the Phase 3 protocols mentioned in this paragraph should be construed to mean those protocols for trials that will form the primary basis of an efficacy claim no matter what phase of drug development in which they happen to be conducted.

5. If a protocol is reviewed under the process outlined above and agreement with the Agency is reached on design, execution, and analyses and if the results of the trial conducted under the protocol substantiate the hypothesis of the protocol, the Agency agrees that the data from the protocol can be used as part of the primary basis for approval of the product. The fundamental agreement here is that having agreed to the design, execution, and analyses proposed in protocols reviewed under this process, the Agency will not later alter its perspective on the issues of design, execution, or analyses unless public health concerns unrecognized at the time of protocol assessment under this process are evident.

B. Performance goal: 60% of special protocols assessments and agreement requests completed and returned to sponsor within timeframes (based on cohort year of request) starting in FY99; 70% in FY00; 80% in FY 01; and 90% in FY02.

VII. ELECTRONIC APPLICATIONS AND SUBMISSIONS

The Agency shall develop and update its information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of INDs and human drug applications, as defined in PDUFA, and related submissions.

VIII. ADDITIONAL PROCEDURES

A. Simplification of Action Letters

To simplify regulatory procedures, the CBER and the CDER intend to amend their regulations and processes to provide for the issuance of either an "approval" (AP) or a "complete response" (CR) action letter at the completion of a review cycle for a marketing application.

B. Timing of Sponsor Notification of Deficiencies in Applications

To help expedite the development of drug and biologic products, CBER and CDER intend to submit deficiencies to sponsors in the form of an "information request" (IR) letter when each discipline has finished its initial review of its section of the pending application.

IX. DEFINITIONS AND EXPLANATION OF TERMS

A. The term "review and act on" is understood to mean the issuance of a complete action letter after the complete review of a filed complete application. The action letter, if it is not an approval, will set forth in detail the specific deficiencies and, where appropriate, the actions necessary to place the application in condition for approval.

B. A major amendment to an original application submitted within three months of the goal date extends the goal date by three months.

C. A resubmitted original application is a complete response to an action letter addressing all identified deficiencies.

D. Class 1 resubmitted applications are applications resubmitted after a complete response letter (or a not approvable or approvable letter) that include the following items only (or combinations of these items):

1. Final printed labeling

2. Draft labeling

3. Safety updates submitted in the same format, including tabulations, as the original safety submission with new data and changes highlighted (except when large amounts of new information including important new adverse experiences not previously reported with the product are presented in the resubmission)

4. Stability updates to support provisional or final dating periods

5. Commitments to perform Phase 4 studies, including proposals for such studies

6. Assay validation data

7. Final release testing on the last 1-2 lots used to support approval

8. A minor reanalysis of data previously submitted to the application (determined by the agency as fitting the Class 1 category)

9. Other minor clarifying information (determined by the Agency as fitting the Class 1 category)

10. Other specific items may be added later as the Agency gains experience with the scheme and will be communicated via guidance documents to industry.

E. Class 2 resubmissions are resubmissions that include any other items, including any item that would require presentation to an advisory committee.

F. A Type A Meeting is a meeting which is necessary for an otherwise stalled drug development program to proceed (a "critical path" meeting).

G. A Type B Meeting is a 1) pre-IND, 2) end of Phase 1 (for Subpart E or Subpart H or similar products) or end of Phase 2/pre-Phase 3, or 3) a pre-NDA/PLA/BLA meeting. Each requestor should usually only request 1 each of these Type B meetings for each potential application (NDA/PLA/BLA) (or combination of closely related products, i.e., same active ingredient but different dosage forms being developed concurrently).

H. A Type C Meeting is any other type of meeting.

I. The performance goals and procedures also apply to original applications and supplements for human drugs initially marketed on an over-the-counter (OTC) basis through an NDA or switched from prescription to OTC status through an NDA or supplement.