



THE SECRETARY OF HEALTH AND HUMAN SERVICES  
WASHINGTON, D.C. 20201

March 16, 2007

The Honorable Nancy Pelosi  
Speaker  
United States House of Representatives  
Washington, D.C. 20515

Dear Madam Speaker:

As you are aware, the Prescription Drug User Fee Act of 1992 (PDUFA), as reauthorized by the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, expires at the end of Fiscal Year 2007. Under PDUFA, the additional revenues generated from fees paid by the pharmaceutical and biological prescription drug industries have been used to expedite the process for the review of prescription drugs, in accordance with performance goals that were developed by the Food and Drug Administration (FDA) in consultation with PDUFA stakeholders.

FDA has worked with various stakeholders, including representatives from consumer, patient, and health provider groups, and the pharmaceutical and biological prescription drug industries, to develop a reauthorization proposal for PDUFA that would build upon and enhance the success of the program. In addition, we have complied with the requirements to solicit public comments on our proposals.

We are providing a draft bill entitled "Prescription Drug User Fee Amendments of 2007" and a section-by-section summary for your consideration. The bill reflects changes to the fee mechanisms and other improvements to PDUFA discussed below as well as a new user fee authority for review of direct-to-consumer television advertising. The performance goals referenced in section 5(a) of the bill, entitled "PDUFA Reauthorization Performance Goals and Procedures" and "Performance Goals and Procedures for Advisory Review of Direct-to-Consumer Television Advertising", are also submitted for your consideration. We believe the goals represent a realistic projection of what FDA can accomplish with industry cooperation and both the additional resources identified in the bill and annual FDA appropriations that fully cover the costs of pay and inflation increases for the drug and biologics review process each year. The performance goals will be transmitted to you in final once the PDUFA reauthorization has passed both the Senate and House.

Our proposed recommendations fall into three major categories: proposals to ensure sound financial footing for the human drug review program; proposals to enhance the process for premarket review of human drug applications; and proposals to modernize and transform the postmarket safety system. Although user fees have provided substantial resources to FDA since the beginning of the program, user fees have not kept up with the increasing costs of the program with inflation in pay and benefit costs to the agency, rent and rent-related costs, and workload.

We are proposing changes to the financial provisions of the PDUFA that better reflect these adjustment factors and place FDA on a sound financial footing so we can continue with the program and make enhancements to it. In addition, we are proposing several technical changes to increase the administrative efficiency of the User Fee Program.

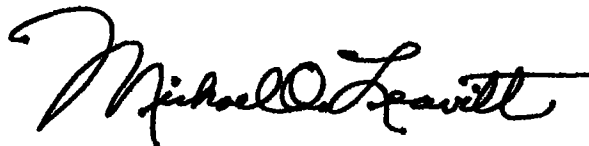
In order to enhance the premarket review process, we are proposing to expand implementation of the Good Review Management Principles (GRMP) to improve notification to applicants about the timeline for review of an application, including the anticipated date for labeling discussions and any FDA requests for postmarketing study commitments (PMCs). We are proposing to expedite drug development by providing guidance to industry to clarify current agency thinking on a variety of topics including clinical trial design. We are also planning to improve information technology activities to help move FDA and the industry to an all-electronic environment. These and other premarket review enhancements should result in faster access to new products without any compromise to FDA's traditional high standards for approval.

We are also proposing to modernize and transform the postmarket drug safety system. New provisions of law and additional funds will be available for FDA to ensure the safety of drugs after they are approved for as long as they remain on the market and will increase FDA's drug safety surveillance capacity. FDA will also be able to adopt new scientific approaches and improve the utility of existing tools for the detection and prevention of adverse events, including obtaining access to the best available databases to better analyze drug safety signals, and enhanced capacity to review proprietary drug names to further prevent medication errors.

In addition, FDA recommends creating a separate new user fee program to collect new fees from companies that seek FDA advisory reviews of their direct to consumer (DTC) television prescription drug advertisements. This will enable FDA to meet the increasing requests from companies for advisory reviews and to address the concerns about the effect of DTC television advertisements on prescribing practices and prescription drug use.

Thank you for the opportunity to present our draft bill to reauthorize this vital program. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accord with the Administration's program.

Sincerely,

A handwritten signature in black ink that reads "Michael O. Leavitt". The signature is written in a cursive style with a large initial "M".

Michael O. Leavitt

Enclosures



THE SECRETARY OF HEALTH AND HUMAN SERVICES  
WASHINGTON, D.C. 20201

March 16, 2007

The Honorable Richard B. Cheney  
President  
United States Senate  
Washington, D.C. 20510

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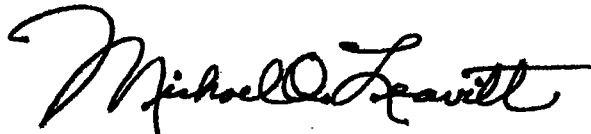
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In addition, FDA recommends creating a separate new user fee program to collect new fees from companies that seek FDA advisory reviews of their direct to consumer (DTC) television prescription drug advertisements. This will enable FDA to meet the increasing requests from companies for advisory reviews and to address the concerns about the effect of DTC television advertisements on prescribing practices and prescription drug use.

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Michael O. Leavitt

Enclosures

## "Prescription Drug User Fee Amendments of 2007"

### Section-by-Section Summary

(Unless otherwise noted, amendments are to the Federal Food, Drug, and Cosmetic Act. For more detailed information regarding these proposed amendments, refer to the HHS *Justification for the Proposed PDUFA IV Statutory Changes*.)

#### **SEC. 2. DEFINITIONS.**

This section would amend section 735 to revise the definitions of certain terms used in the prescription drug user fee provisions, and to add a clarifying definition of the term "person".

#### **SEC. 3. AUTHORITY TO ASSESS AND USE DRUG FEES.**

##### (a) TYPES OF FEES.

This section would amend section 736(a) to clarify (1) that the Secretary will retain 25 percent of the application fees for applications that are withdrawn before filing; and (2) that applications or supplements previously refused for filing or that were withdrawn before filing will be subject to the full user fee under upon being filed over protest or resubmitted, unless otherwise exempted or waived.

##### (b) FEE REVENUE AMOUNTS.

This section would amend section 736(b) to provide that the statutory revenue amount for PDUFA fees in FY 2008 is set at \$392,783,000, subject to adjustment.

Beginning in FY 2009, the adjustments specified in section 736(c) (as proposed to be amended) would be made to the final FY 2008 final revenue amount in years after FY 2008. As in the past, for each fiscal year one-third of the fee revenue will come from application fees, one-third from establishment fees, and one-third from product fees.

##### (c) ADJUSTMENTS TO FEES.

This section would amend section 736(c) to:

- modify the inflation adjustment for the annual statutory revenue target so it includes another factor, relating to costs of personnel compensation and benefits, upon which the calculation of the adjustment amount may be based.
- modify the workload adjuster to use the number of *active* commercial investigational new drug applications (INDs) each year as the surrogate for IND workload in lieu of the number of *new* commercial INDs submitted each year. Active commercial INDs are those that have had at least one submission in the previous 12 month period. This factor

is more representative of FDA's true workload for INDs, which generally remain active and have multiple additional submissions for a number of years after initial submission.

- beginning in fiscal year FY 2010, provide for adjusting the annual fee revenue amount to reflect actual rent and rent-related costs incurred each year. If these actual rent and rent related costs are less than the estimated costs, then FDA will decrease the fee revenue amounts by the projected difference, but not by more than a total of \$11,721,000 each year.

**(d) FEE WAIVER OR REDUCTION**

This section would amend section 736(d) to:

- clarify that only businesses with fewer than 500 employees (including employees of affiliates) and no products already introduced into interstate commerce may qualify for a small business waiver of fees.
- clarify that the person named as the applicant and assessed the user fee is the person who is eligible for a waiver or reduction of fees. Also consistent with the original intent, new section 736(d)(2) is added to make clear that it is only the circumstances and assets of the applicant and its affiliates that are to be considered for waiver purposes

**(e) CREDITING AND AVAILABILITY OF FEES.**

This section would amend section 736(g) to authorize appropriations for prescription drug user fees from fiscal years 2008 through 2012.

**SEC. 4. AUTHORITY TO ASSESS AND USE PRESCRIPTION DRUG ADVERTISING FEES.**

This section would amend Chapter VII, subchapter C, part 2 to establish a new program to assess, collect and user fees for the advisory review of prescription drug direct to consumer (DTC) television advertisements. This program would provide for increased FDA resources to allow for the timely review of DTC television advertisement advisory submissions. First, the program will charge a fee for each advisory review requested. Second, the program will assess a one time fee at the beginning of the program (or at the time a company first elects to participate in the program) to establish stable funding for the program in case the number of advisory submissions fluctuates in future years. These fees would provide sufficient resources for FDA to hire additional staff to review DTC television advisory submissions in a predictable, timely manner.

**SEC. 5. REPORTING REQUIREMENTS.**

This section would require the Secretary to report to Congress for each fiscal year of the PDUFA IV program with respect to (1) the progress of the FDA in achieving the PDUFA IV objectives, as described in the "Goals letter" accompanying the PDUFA IV proposal; and (2) implementation of the PDUFA IV authority and the use by FDA of the user fees collected.

**SEC. 6. SUNSET DATES.**

This section would provide for the amendments made by sections 2, 3, and 4 to sunset on October 1, 2012.

1 **A BILL**

2 To amend the Federal Food, Drug, and Cosmetic Act to reauthorize and amend the prescription drug  
3 user fee provisions, and for other purposes.

4 *Be it enacted by the Senate and House of Representatives of the United States of America*  
5 *in Congress assembled,*

6 **SEC. 1. SHORT TITLE; REFERENCES IN ACT.**

7 (a) SHORT TITLE.— This Act may be cited as the "Prescription Drug User Fee  
8 Amendments of 2007".

9 (b) REFERENCES IN ACT.—Except as otherwise specified, amendments made by this  
10 Act to a section or other provision of law are amendments to such section or other provision of  
11 the Federal Food, Drug, and Cosmetic Act.

12 **SEC. 2. DEFINITIONS.**

13 Section 735 (21 U.S.C. 379g) is amended—

14 (1) in paragraph (1)---

15 (A) in subparagraph (A) by striking "505(b)(1), " and inserting "505(b),

16 or";

17 (B) by striking subparagraph (B); and

18 (C) by re-designating subparagraph (C) as subparagraph (B).

19 (2) in paragraph (3)(C) by striking the period at the end and inserting ", except for  
20 those products on either list that are included in a "discontinued" section of that list.";

21 (3) in paragraph (4) by inserting before the period at the end the following: "(e.g.,  
22 capsules, tablets, lyophilized products before reconstitution)";

23 (4) by amending paragraph (6)(F) to read as follows:

24 "(F) In the case of drugs approved under human drug applications or  
25 supplements, post-marketing safety activities, including: collecting, developing  
26 and reviewing safety information on approved drugs (including adverse event



1 reports); developing and using improved adverse event data collection systems  
2 (including information technology systems); and developing and using improved  
3 analytical tools to assess potential safety problems (including access to external  
4 data bases).";

5 (5) in paragraph (8)—

6 (A) by striking "April of the preceding fiscal year" and inserting "October  
7 of the preceding fiscal year"; and

8 (B) by striking "April 1997" and inserting "October 2006";

9 (6) by re-designating paragraph (9) as paragraph (10); and

10 (7) by inserting immediately after paragraph (8) the following new paragraph:

11 "(9) The term "person" includes an affiliate thereof."

12 **SEC. 3. AUTHORITY TO ASSESS AND USE DRUG FEES.**

13 (a) TYPES OF FEES.— Section 736(a) (21 U.S.C. 379h(a)) is amended—

14 (1) in the matter preceding paragraph (1) by striking "2003" and inserting "2008";

15 (2) in paragraph (1)(D)—

16 (A) in the caption by inserting "OR WITHDRAWN BEFORE FILING"  
17 after "REFUND OF FEE IF APPLICATION REFUSED FOR FILING"; and

18 (B) by inserting before the period at the end the following: "or withdrawn  
19 without a waiver before filing".

20 (3) by re-designating subparagraphs (E) and (F) as subparagraphs (F) and (G),  
21 respectively; and

22 (4) by inserting immediately after subparagraph (D) the following new  
23 subparagraph:

24 "(E) FEES FOR APPLICATIONS PREVIOUSLY REFUSED FOR  
25 FILING OR WITHDRAWN BEFORE FILING.—Applications or supplements  
26 that have been previously refused for filing or that were withdrawn before filing

1 shall be subject to the full fee under subparagraph (A) upon being filed over  
2 protest or resubmitted, unless otherwise exempted or waived."

3 (b) FEE REVENUE AMOUNTS.— Section 736(b) (21 U.S.C. 379h(b)) is amended to  
4 read as follows:

5 "(b) FEE REVENUE AMOUNTS.—Except as provided in subsections (c), (d), (f), and  
6 (g), fees under subsection (a) shall be established to generate the following revenue amounts, in  
7 each fiscal year beginning with fiscal year 2008 and continuing through fiscal year 2012:  
8 \$392,783,000, plus an adjustment for workload, made in accord with the workload adjustment  
9 provisions that were in effect for fiscal year 2007, on \$354,893,000 of this amount, except that  
10 instead of commercial investigational new drug applications submitted to the Secretary, all  
11 commercial investigational new drug applications with a submission during the previous 12  
12 month period shall be used in the determination. One-third of the revenue amount will be  
13 derived from application fees, one-third from establishment fees, and one-third from product  
14 fees."

15 (c) ADJUSTMENTS TO FEES.—

16 (1) INFLATION ADJUSTMENT.— Section 736(c)(1) (21 U.S.C. 379h(c)(1)) is  
17 amended—

18 (A) in the matter preceding subparagraph (A) by striking "The revenues  
19 established in subsection (b)" and inserting "After fiscal year 2008, the revenues  
20 established in subsection (b)";

21 (B) in subparagraph (A) by striking "or" at the end;

22 (C) in subparagraph (B) by striking the period at the end and inserting "  
23 or,";

24 (D) by inserting after subparagraph (B), as so amended, the following new  
25 subparagraph:

26 "(C) the average annual change in the cost, per full-time equivalent  
27 position of the Food and Drug Administration, of all personnel compensation and

1 benefits paid with respect to such positions, for the most recent 5 year period  
2 ending on September 30, 12 months and 1 day prior to the year for which fees are  
3 being established."; and

4 (E) in the matter following subparagraph (C) (as added under this  
5 paragraph), by striking "fiscal year 2003" and inserting "fiscal year 2008".

6 (2) WORKLOAD ADJUSTMENT.—Section 736(c)(2) (21 U.S.C. 379h(c)(2)) is  
7 amended—

8 (A) in the matter preceding subparagraph (A) by striking "2004" and  
9 inserting "2009";

10 (B) in subparagraph (A)—

11 (i) by striking ", commercial investigational new drug applications"  
12 and inserting "(adjusted for changes in review activities)"; and

13 (ii) in the first sentence, as amended under clause (i), by inserting  
14 before the period ", and the change in the number of commercial  
15 investigational new drug applications with a submission during the  
16 previous 12-month period (adjusted for changes in review activities)".

17 (C) in subparagraph (B) by adding at the end the following new sentence:  
18 "Further, any adjustment for review activities made in setting fees and fee revenue  
19 amounts for fiscal year 2009 may not result in the total workload adjustment being  
20 more than 2 percentage points higher than it would be absent the review activity  
21 adjustment."; and

22 (D) by adding after subparagraph (B), as amended under this paragraph,  
23 the following new subparagraph:

24 "(C) FDA will contract with an independent accounting firm to study the  
25 adjustment for changes in review activities applied in setting fees for fiscal year  
26 2009 and to make recommendations, if warranted, on future changes in the  
27 methodology for calculating this adjustment for changes in review activity. After

1 review of the recommendations by the independent accounting firm, the Secretary  
2 shall make appropriate changes to the workload adjustment methodology in  
3 setting fees for fiscal years 2010 through 2012. If this study is not conducted, no  
4 adjustment for review activities will be made after fiscal year 2009."

5 (3) RENT AND RENT-RELATED COST ADJUSTMENT.—Section 736(c) (21  
6 U.S.C. 379h(c)) is amended—

7 (A) by re-designating paragraphs (3), (4), and (5) as paragraphs (4), (5),  
8 and (6), respectively; and

9 (B) by inserting immediately after paragraph (2) the following new  
10 paragraph:

11 "(3) RENT AND RENT RELATED COST ADJUSTMENT.—Beginning in fiscal  
12 year 2010, the Secretary will, before making adjustments under paragraphs (1) and (2),  
13 decrease the fee amounts established in subsection (b), if actual costs paid for rent and  
14 rent related expenses are less than estimates made in fiscal year 2006. The reductions  
15 made under this paragraph, if any, will be no more than the amounts by which costs fell  
16 below estimates made in fiscal year 2006, and will not exceed \$11,721,000 in any fiscal  
17 year."

18 (4) FINAL YEAR ADJUSTMENT.— Section 736(c) (21 U.S.C. 379h(c)) is  
19 amended—

20 (A) in paragraph (4), as re-designated under this subsection—

21 (i) by striking "2007" each place it appears and inserting "2012";

22 and

23 (ii) by striking "2008" and inserting "2013"; and

24 (B) in paragraph (5), as re-designated under this subsection, by striking  
25 "2002" and inserting "2007".

26 (d) FEE WAIVER OR REDUCTION.—Section 736(d) (21 U.S.C. 379h(d)) is  
27 amended—

1 (1) in paragraph (1), in the matter preceding subparagraph (A)—

2 (A) by inserting "to a person who is named as the applicant" after "The  
3 Secretary shall grant"; and

4 (B) by inserting "to that person" after "a waiver from or a reduction of one  
5 or more fees assessed";

6 (2) by re-designating paragraphs (2) and (3) as paragraphs (3) and (4),  
7 respectively;

8 (3) by inserting immediately after paragraph (1) the following new paragraph:

9 "(2) For the purpose of determining whether to grant a waiver or reduction of a fee  
10 under paragraph (1), the Secretary shall consider only the circumstances and assets of the  
11 applicant and any affiliate of the applicant when evaluating a waiver."; and

12 (4) in paragraph (4), as re-designated under this subsection, by inserting before the  
13 period at the end of subparagraph (A) ", and that does not have a drug product that was  
14 approved under a human drug application, and introduced or delivered for introduction  
15 into interstate commerce".

16 (e) CREDITING AND AVAILABILITY OF FEES.—

17 (1) AUTHORIZATION OF APPROPRIATIONS.— Section 736(g)(3) (21 U.S.C.  
18 379h(g)(3)) is amended to read as follows:

19 "(3) AUTHORIZATION OF APPROPRIATIONS.— There are authorized to be  
20 appropriated for fees under this section such sums as are authorized to be assessed and  
21 collected under this section in each fiscal year beginning with fiscal year 2008 and  
22 continuing through fiscal year 2012."

23 (2) OFFSET.— Section 736(g)(4) (21 U.S.C. 379h(g)(4)) is amended to read as  
24 follows:

25 "(4) OFFSET.— If the cumulative amount of fees collected during fiscal years  
26 2008, 2009, and 2010, added to the amount estimated to be collected for fiscal year 2011,  
27 exceeds the amount of fees specified in aggregate in appropriation Acts for such fiscal

1 years, the aggregate amount in excess shall be credited to the appropriation account of the  
2 Food and Drug Administration as provided in paragraph (1), and shall be subtracted from  
3 the amount of fees that would otherwise be authorized to be collected under this section  
4 pursuant to appropriation Acts for fiscal year 2012."

5 **SEC. 4. AUTHORITY TO ASSESS AND USE PRESCRIPTION DRUG**  
6 **ADVERTISING FEES.**

7 Chapter VII, subchapter C, part 2 (21 U.S.C. 379g et seq.) is amended by adding after  
8 section 736 the following new section:

9 **"SEC. 736A. PROGRAM TO ASSESS AND USE FEES FOR THE ADVISORY REVIEW**  
10 **OF PRESCRIPTION DRUG ADVERTISING.**

11 **"(a) TYPES OF DIRECT-TO-CONSUMER TELEVISION ADVERTISEMENT**  
12 **REVIEW FEES.—** Beginning in fiscal year 2008, the Secretary shall assess and collect fees in  
13 accordance with this section as follows:

14 **"(1) ADVISORY REVIEW FEE.—**

15 **"(A) IN GENERAL.—** Except as provided in subparagraph (B), each  
16 person that on or after October 1, 2007, submits a proposed direct-to-consumer  
17 television advertisement for advisory review by the Secretary prior to its initial  
18 public dissemination shall be subject to a fee established under subsection (c)(3).

19 **"(B) EXCEPTION FOR REQUIRED SUBMISSIONS.—** A  
20 direct-to-consumer television advertisement that is required to be submitted to the  
21 Secretary prior to initial public dissemination will not be assessed a fee unless the  
22 sponsor designates it as a submission for advisory review.

23 **"(C) PAYMENT.—**The fee required by subparagraph (A) shall be due no  
24 later than October 1 of the fiscal year in which the direct-to-consumer television  
25 advertisement will be submitted to the Secretary for advisory review.

26 **"(D) MODIFICATION OF ADVISORY REVIEW FEE.—**

1           "(i) LATE PAYMENT.— If on or before November 1 of the fiscal  
2 year in which the fees are due, a person has not paid all fees that were due  
3 and payable for advisory reviews identified in response to the Federal  
4 Register Notice described in subsection (c)(3)(A), the fees are regarded as  
5 late. Such fees shall be due and payable 20 days before any  
6 direct-to-consumer television advertisement is submitted by such person to  
7 the Secretary for advisory review. Notwithstanding any other provision of  
8 this section, such fees shall be due and payable for each of those advisory  
9 reviews in the amount of 150% of the advisory review fee established for  
10 that fiscal year pursuant to subsection (c)(3).

11           "(ii) LATE NOTICE OF SUBMISSION.—If any person submits  
12 any direct-to-consumer television advertisements for advisory review that  
13 are in excess of the number identified by that person in response to the  
14 Federal Register Notice described in subsection (c)(3)(A), that person  
15 must pay a fee for each of those advisory reviews in the amount of 150%  
16 of the advisory review fee established for that fiscal year pursuant to  
17 subsection (c)(3). Fees under this subparagraph shall be due 20 days  
18 before the direct-to-consumer television advertisement is submitted by  
19 such person to the Secretary for advisory review.

20           "(E) LIMITS.—

21           "(i) A person paying a fee under this paragraph for a fiscal year is  
22 entitled to acceptance for advisory review by the Secretary of one  
23 direct-to-consumer television advertisement and acceptance of one  
24 resubmission for advisory review of the same advertisement. The  
25 advertisement shall be submitted for review in the fiscal year for which the  
26 fee was assessed, except that a person may carry over no more than one  
27 paid advisory review submission to the next fiscal year. Resubmissions

1                   may be submitted without regard to the fiscal year of the initial advisory  
2                   review submission.

3                   "(ii) Except as provided by subsection (f), fees paid under this  
4                   paragraph will not be refunded.

5                   "(iii) The Secretary shall not grant a waiver, exemption, or  
6                   reduction of any fees due or payable under this section.

7                   "(iv) The right to an advisory review is not transferable, except to a  
8                   successor in interest.

9                   “(2) OPERATING RESERVE FEE.—

10                   "(A) IN GENERAL.— Each person that on or after October 1, 2007, is  
11                   assessed an advisory review fee under paragraph (1) shall be subject to an  
12                   operating reserve fee established under subsection (d)(2) only in the first fiscal  
13                   year in which an advisory review fee is assessed.

14                   "(B) PAYMENT.— Except as provided in subparagraph (C), the fee  
15                   required by subparagraph (A) shall be due no later than October 1 of the first  
16                   fiscal year in which the person is required to pay an advisory review fee under  
17                   paragraph (1).

18                   "(C) LATE NOTICE OF SUBMISSION.— If, in the first fiscal year of a  
19                   person's participation in this program, that person submits any direct-to-consumer  
20                   television advertisements for advisory review that are in excess of the number  
21                   identified by that person in response to the Federal Register Notice described in  
22                   subsection (c)(3)(A), that person must pay an operating reserve fee for each of  
23                   those advisory reviews equal to the advisory review fee for each submission  
24                   established under paragraph (1)(D)(ii) of this subsection. Fees required by this  
25                   subparagraph (C) shall be in addition to the fees required under subparagraph (B),  
26                   if any. Fees under this subparagraph (C) shall be due 20 days before any



1 direct-to-consumer television advertisement is submitted by such person to the  
2 Secretary for advisory review.

3 "(b) ADVISORY REVIEW FEE REVENUE AMOUNTS.— Fees under subsection  
4 (a)(1) shall be established to generate revenue amounts of \$6,250,000 each for fiscal years 2008  
5 through 2012, as adjusted pursuant to subsection (c).

6 "(c) ADJUSTMENTS.—

7 "(1) INFLATION ADJUSTMENT.— Beginning with fiscal year 2009, the  
8 revenues established in subsection (b) shall be adjusted by the Secretary by notice,  
9 published in the Federal Register, for a fiscal year to reflect the greater of—

10 "(A) the total percentage change that occurred in the Consumer Price  
11 Index for all urban consumers (all items; U.S. city average), for the 12 month  
12 period ending June 30 preceding the fiscal year for which fees are being  
13 established,

14 "(B) the total percentage change for the previous fiscal year in basic pay  
15 under the General Schedule in accordance with section 5332 of Title 5, as  
16 adjusted by any locality-based comparability payment pursuant to section 5304 of  
17 such title for Federal employees stationed in the District of Columbia, or

18 "(C) the average annual change in the cost, per full-time equivalent  
19 position of the Food and Drug Administration, of all personnel compensation and  
20 benefits paid with respect to such positions, for the most recent 5 year period  
21 ending on September 30, 12 months and 1 day prior to the year for which fees are  
22 being established.

23 "The adjustment made each fiscal year by this subsection will be added on a  
24 compounded basis to the sum of all adjustments made each fiscal year after fiscal  
25 year 2008 under this subsection.

26 "(2) WORKLOAD ADJUSTMENT.— Beginning with fiscal year 2009, after the  
27 fee revenues established in subsection (b) of this section are adjusted for a fiscal year for

1 inflation in accordance with paragraph (1), the fee revenues shall be adjusted further for  
2 such fiscal year to reflect changes in the workload of the Secretary with respect to the  
3 submission of proposed direct-to-consumer television advertisements for advisory review  
4 prior to initial broadcast. With respect to such adjustment:

5 "(A) The adjustment shall be determined by the Secretary based upon the  
6 number of direct-to-consumer television advertisements identified pursuant to  
7 paragraph (3)(A) for the upcoming fiscal year, excluding allowable previously  
8 paid carry over submissions. The adjustment shall be determined by multiplying  
9 the number of such advertisements projected for that fiscal year that exceeds 150  
10 by \$27,600 (adjusted each year beginning with fiscal year 2009 for inflation in  
11 accord with paragraph (1)). The Secretary shall publish in the Federal Register  
12 the fee revenues and fees resulting from the adjustment and the supporting  
13 methodologies.

14 "(B) Under no circumstances shall the adjustment result in fee revenues  
15 for a fiscal year that are less than the fee revenues established for the prior fiscal  
16 year.

17 "(3) ANNUAL FEE SETTING.—

18 "(A) NUMBER OF ADVERTISEMENTS.—The Secretary shall, 120 days  
19 before the start of each fiscal year, publish a notice in the Federal Register  
20 requesting any person to notify the Secretary within 30 days of the number of  
21 direct-to-consumer television advertisements the person intends to submit for  
22 advisory review by the Secretary in the next fiscal year. Notification of the  
23 Secretary of the number of advertisements a person intends to submit for advisory  
24 review prior to initial broadcast shall be a legally binding commitment by that  
25 person to pay the annual advisory review fee for that number of submissions on or  
26 before October 1 of the fiscal year in which the advertisement is intended to be  
27 submitted. A person shall at the same time also notify the Secretary if such

1 person intends to use a paid submission from the previous fiscal year under  
2 subsection (a)(1)(E)(i). If such person does not so notify the Secretary, all  
3 submissions for advisory review shall be subject to advisory review fees.

4 "(B) ANNUAL FEE.— The Secretary shall, 60 days before the start of  
5 each fiscal year, establish, for the next fiscal year, the direct-to-consumer  
6 television advertisement advisory review fee under subsection (a)(1) of this  
7 section, based on the revenue amounts established under subsection (b) of this  
8 section, the adjustments provided under this subsection and the number of  
9 direct-to-consumer television advertisements identified pursuant to subparagraph  
10 (A), excluding allowable previously paid carry over submissions. The annual  
11 advisory review fee shall be established by dividing the fee revenue for a fiscal  
12 year (as adjusted pursuant to this subsection) by the number of direct-to-consumer  
13 television advertisements identified pursuant to subparagraph (A), excluding  
14 allowable previously paid carry over submissions.

15 "(C) FISCAL YEAR 2008 FEE LIMIT.— Notwithstanding subsection (b)  
16 or this subsection, the fee established under subparagraph (B) for fiscal year 2008  
17 may not be more than \$83,000 per submission for advisory review.

18 "(D) ANNUAL FEE LIMIT.— Notwithstanding subsection (b) or this  
19 subsection, the fee established under subparagraph (B) for a fiscal year after fiscal  
20 year 2008 may not be more than 50% more than the fee established for the prior  
21 fiscal year.

22 "(E) LIMIT.— The total amount of fees obligated for a fiscal year may not  
23 exceed the total costs for such fiscal year for the resources allocated for the  
24 process for the advisory review of prescription drug advertising.

25 "(d) OPERATING RESERVES.—

26 "(1) IN GENERAL. — The Secretary shall establish in the Food and Drug  
27 Administration salaries and expenses appropriation account without fiscal year limitation

1 a Direct-to-Consumer Advisory Review Operating Reserve , of at least \$6,250,000 in  
2 fiscal year 2008, to continue the program in the event the fees collected in any subsequent  
3 fiscal year pursuant to subsection (c)(3) do not generate the fee revenue amount  
4 established for that fiscal year.

5 "(2) FEE SETTING.—The Secretary shall establish the operating reserve fee  
6 under subsection (a)(2)(A) for each person required to pay the fee by multiplying the  
7 number of direct-to-consumer television advertisements identified by that person pursuant  
8 to subsection (c)(3)(A) by the advisory review fee established pursuant to subsection  
9 (c)(3) for that fiscal year. However, in no case shall the operating reserve fee assessed be  
10 less than the operating reserve fee assessed if the person had first participated in the  
11 program in fiscal year 2008.

12 "(3) USE OF OPERATING RESERVE.— The Secretary may use funds from the  
13 reserves only to the extent necessary in any fiscal year to make up the difference between  
14 the fee revenue amount established for that fiscal year under subsections (b) and (c) and  
15 the amount of fees actually collected for that fiscal year pursuant to subsection (a), or to  
16 pay costs of ending the program if it is terminated pursuant to subsection (f) or if it is not  
17 reauthorized beyond fiscal year 2012.

18 "(4) REFUND OF OPERATING RESERVES.— Within 120 days of the end of  
19 fiscal year 2012, or if the program ends early pursuant to subsection (f), the Secretary,  
20 after setting aside sufficient operating reserve amounts to terminate the program, shall  
21 refund all amounts remaining in the operating reserve on a pro rata basis to each person  
22 that paid an operating reserve fee assessment. In no event shall the refund to any person  
23 exceed the total amount of operating reserve fees paid by such person pursuant to  
24 subsection (a)(2).

25 "(e) EFFECT OF FAILURE TO PAY FEES.— Notwithstanding any other law or  
26 regulation of the Secretary, a submission for advisory review of a direct-to-consumer television  
27 advertisement submitted by a person subject to fees under subsection (a) shall be considered

1 incomplete and shall not be accepted for review by the Secretary until all fees owed by such  
2 person under this section have been paid.

3 "(f) EFFECT OF INADEQUATE FUNDING OF PROGRAM.—

4 "(1) If on November 1, 2007, or 120 days after enactment of this provision,  
5 whichever is later, the Secretary has not received at least \$11,250,000 in advisory review  
6 fees and operating reserve fees combined, the Program shall not commence and all  
7 collected fees shall be refunded.

8 "(2) Beginning in fiscal year 2009, if, on November 1 of the fiscal year, the  
9 combination of the operating reserves, annual fee revenues from that fiscal year, and  
10 unobligated fee revenues from prior fiscal years falls below \$9,000,000, adjusted for  
11 inflation (as described in subsection (c)(1)), the Program shall cease to exist, and the  
12 Secretary shall notify all participants, retain any money from the unused advisory review  
13 fees and the operating reserves needed to close down the program, and refund the  
14 remainder of the unused fees and operating reserves. To the extent required to close  
15 down the program, the Secretary shall first use unobligated advisory review fee revenues  
16 from prior fiscal years, then the operating reserves, and finally, unused advisory review  
17 fees from the relevant fiscal year.

18 "(g) CREDITING AND AVAILABILITY OF FEES.—

19 "(1) IN GENERAL.— Fees authorized under subsection (a) of this section shall  
20 be collected and available for obligation only to the extent and in the amount provided in  
21 advance in appropriations Acts. Such fees are authorized to remain available until  
22 expended. Such sums as may be necessary may be transferred from the Food and Drug  
23 Administration salaries and expenses appropriation account without fiscal year limitation  
24 to such appropriation account for salaries and expenses with such fiscal year limitation.  
25 The sums transferred shall be available solely for the process for the advisory review of  
26 prescription drug advertising.

1           "(2) COLLECTIONS AND APPROPRIATION ACTS.— The fees authorized by  
2 this section—

3                   "(A) shall be retained in each fiscal year in an amount not to exceed the  
4 amount specified in appropriation Acts, or otherwise made available for  
5 obligation for such fiscal year, and

6                   "(B) shall be available for obligation only if appropriated budget authority  
7 continues to support at least the total combined number of full time equivalent  
8 employees in the Food and Drug Administration, Center for Drug Evaluation and  
9 Research, Division of Drug Marketing, Advertising, and Communications, and  
10 the Center for Biologics Evaluation and Research, the Advertising and  
11 Promotional Labeling Branch actually supported in fiscal year 2007.

12           "(3) AUTHORIZATION OF APPROPRIATIONS.— There are authorized to be  
13 appropriated for fees under this section no less than \$6,250,000 per year for fiscal years  
14 2008, 2009, 2010, 2011, and 2012, as adjusted to reflect adjustments in the total fee  
15 revenues made under this section, plus amounts collected for the reserve fund under  
16 subsection (d).

17           "(4) OFFSET.— Any amount of fees collected for a fiscal year under this section  
18 that exceeds the amount of fees specified in appropriation Acts for such fiscal year shall  
19 be credited to the appropriation account of the Food and Drug Administration as provided  
20 in paragraph (1), and shall be subtracted from the amount of fees that would otherwise be  
21 collected under this section pursuant to appropriation Acts for a subsequent fiscal  
22 year.

23           "(h) DEFINITIONS.— For purposes of this subchapter:

24                   "(1) The term "advisory review" means reviewing and providing advisory  
25 comments on a proposed advertisement prior to its initial public dissemination.

1           "(2) The term "carry over submission" means a submission for an advisory  
2 review for which a fee was paid in one fiscal year that is submitted for review in the  
3 following fiscal year.

4           "(3) The term "direct-to-consumer television advertisement" means an  
5 advertisement for a prescription drug product as defined in section 735(3) intended to be  
6 displayed on any television channel for less than 2 minutes.

7           "(4) The term "person" includes individual, partnership, corporation, and  
8 association, and any affiliate thereof or successor in interest.

9           "(5) The term "program" means the program to assess, collect, and use fees for the  
10 advisory review of prescription drug advertising established by this section.

11           "(6) The term "process for the advisory review of prescription drug advertising"  
12 means the activities necessary to review and provide advisory comments on proposed  
13 direct-to-consumer television advertisements prior to public dissemination and, to the  
14 extent the Secretary has additional staff resources available under this program that are  
15 not necessary for the advisory review of direct-to-consumer television advertisements, the  
16 activities necessary to review and provide advisory comments on other proposed  
17 advertisements and promotional material prior to public dissemination.

18           "(7) The term "resources allocated for the process for the advisory review of  
19 prescription drug advertising" means the expenses incurred in connection with the  
20 process for the advisory review of prescription drug advertising for—

21           "(A) officers and employees of the Food and Drug Administration,  
22 contractors of the Food and Drug Administration, advisory committees, and costs  
23 related to such officers, employees, and committees, and to contracts with such  
24 contractors;

25           "(B) management of information, and the acquisition, maintenance, and  
26 repair of computer resources;

1                   "(C) leasing, maintenance, renovation, and repair of facilities and  
2 acquisition, maintenance, and repair of fixtures, furniture, scientific equipment,  
3 and other necessary materials and supplies;

4                   "(D) collection of fees under this section and accounting for resources  
5 allocated for the advisory review of prescription drug advertising; and

6                   "(E) closing down the program under subsection (f)(2) if that becomes  
7 necessary.

8                   "(8) The term "resubmission" means a subsequent submission for advisory review  
9 of a direct-to-consumer television advertisement that has been revised in response to the  
10 Secretary's comments on an original submission. A resubmission may not introduce  
11 significant new concepts or creative themes into the television advertisement.

12                   "(9) The term "submission for advisory review" means an original submission of a  
13 direct-to-consumer television advertisement for which the sponsor voluntarily requests  
14 advisory comments before the advertisement is publicly disseminated."

15 **SEC. 5. REPORTING REQUIREMENTS.**

16                   (a) **PERFORMANCE REPORT.**— Beginning with fiscal year 2008, not later than 120  
17 days after the end of each fiscal year during which fees are collected under part 2 of subchapter C  
18 of chapter VII of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379g et seq.), the  
19 Secretary of Health and Human Services shall prepare and submit to the Committee on Energy  
20 and Commerce of the House of Representatives, and the Committee on Health, Education, Labor,  
21 and Pensions of the Senate a report concerning the progress of the Food and Drug Administration  
22 in achieving the goals identified in the letters described in section [502(4) of Public Law 107-  
23 188] during such fiscal year and the future plans of the Food and Drug Administration for  
24 meeting the goals.

25                   (b) **FISCAL REPORT.**— Beginning with fiscal year 2008, not later than 120 days after  
26 the end of each fiscal year during which fees are collected under the part described in subsection  
27 (a), the Secretary of Health and Human Services shall prepare and submit to the Committee on



1 Energy and Commerce of the House of Representatives, and the Committee on Health,  
2 Education, Labor, and Pensions of the Senate, a report on the implementation of the authority for  
3 such fees during such fiscal year and the use, by the Food and Drug Administration, of the fees  
4 collected during such fiscal year for which the report is made.

5 ***SEC. 6. SUNSET DATES.***

6 The amendments made by sections 2, 3, and 4 cease to be effective October 1, 2012.

**ENCLOSURE**  
**SECTION A: PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES**  
**FISCAL YEARS 2008 THROUGH 2012**

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 [cite statute] are summarized below.

**Unless otherwise stated, goals apply to cohorts of each fiscal year (FY).**

**I. REVIEW PERFORMANCE GOALS**

**A. NDA/BLA Submissions and Resubmissions**

1. Review and act on 90 percent of standard original NDA and BLA submissions within 10 months of receipt.
2. Review and act on 90 percent of priority original NDA and BLA submissions within 6 months of receipt.
3. Review and act on 90 percent of Class 1 resubmitted original applications within 2 months of receipt.
4. Review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.

**B. Original Efficacy Supplements**

1. Review and act on 90 percent of standard efficacy supplements within 10 months of receipt.
2. Review and act on 90 percent of priority efficacy supplement within 6 months of receipt.

**C. Resubmitted Efficacy Supplements**

1. Review and act on 90 percent of Class 1 resubmitted efficacy supplements within 2 months of receipt.
2. Review and act on 90 percent of Class 2 resubmitted efficacy supplements within 6 months of receipt.

**D. Original Manufacturing Supplements**

1. Review and act on 90 percent of manufacturing supplements within 6 months of receipt and review and act on 90 percent of manufacturing supplements requiring prior approval within 4 months of receipt.

**E. These review goals are summarized in the following tables:**

**ORIGINAL and RESUBMITTED NDAs/BLAs and Efficacy Supplements:**

<b>SUBMISSION COHORT</b>	<b>STANDARD</b>	<b>PRIORITY</b>
Original Applications	90% IN 10 MO	90% IN 6 MO
Class 1 Resubmissions	90% IN 2 MO	90% IN 2 MO
Class 2 Resubmissions	90% IN 6 MO	90% IN 6 MO
Original Efficacy Supplements	90% IN 10 MO	90% IN 6 MO
Class 1 Resubmitted Efficacy Supplements	90% IN 2 MO	90% IN 2 MO
Class 2	90% IN 6 MO	90% IN 6 MO

**MANUFACTURING SUPPLEMENTS**

FY 2008-2012	90% IN 6 MO	90% IN 4 MO
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**II. NEW MOLECULAR ENTITY (NME) PERFORMANCE GOALS**

- A. 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.
- B. For biological products, for purposes of this performance goal, all original BLAs 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 Type A meeting, or within 21 calendar days of the Agency's receipt of a request from industry for a formal Type B or Type C 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 90% of Type A meeting requests and within 21 days for 90% of Type B and Type C meeting requests.

**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.

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

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

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

**2. Performance goal:** 90% of meetings are held within the timeframe.

### **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:** 90% of minutes are issued within 30 calendar days of date of meeting.

### **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 meetings and at least 1 month in advance of the scheduled meeting for Type B and Type C 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.

Sponsors are encouraged to consult available FDA guidance to obtain further information on recommended meeting procedures.

#### 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:** 90% of such responses are provided within 30 calendar days of the Agency's receipt of the sponsor's response.

#### 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 signatory authority level (including a request for reconsideration by the signatory authority 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:** 90% of such answers are provided within 30 calendar days of the Center's receipt of the written appeal.

C. **Conditions:**

1. Sponsors should first try to resolve the procedural or scientific issue at the signatory authority level. If it cannot be resolved at that level, it should be appealed to the next higher organizational level (with a copy to the signatory authority) and then, if necessary, to the next higher organizational level.
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 grant or deny 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:** 90% of special protocols assessments and agreement requests completed and returned to sponsor within timeframes.

**C. Reporting:** The Agency will track and report the number of original special protocol assessments and resubmissions per original special protocol assessment.

## **VII. ADDITIONAL PROCEDURES**

### **A. Simplification of Action Letters**

To simplify regulatory procedures, CBER and 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 a “discipline review” (DR) letter when each discipline has finished its initial review of its section of the pending application.

## **VIII. ENHANCEMENT AND MODERNIZATION OF THE FDA DRUG SAFETY SYSTEM**

FDA will use user fees to enhance and modernize the current U.S. drug safety system. FDA will adopt new scientific approaches, improve the utility of existing tools for the detection, evaluation, prevention, and mitigation of adverse events, and continue to enhance and improve communication and coordination between post-market and pre-market review staff. Enhancements to the post-market drug safety system will improve the public health by increasing patient protection while continuing to enable access to needed medical products. User fees will provide support for 1) preparing and implementing a 5-year plan to modernize drug safety, including improving communication and coordination between the post-market and pre-market review staff, 2) conducting and/or supporting activities designed to modernize the process of pharmacovigilance, 3) developing with sponsors, reviewing, and monitoring implementation of risk management plans, and 4) related activities.

### **A. Development of 5-year plan, and Communications and Technical Interactions**

1. The FDA will develop and periodically update a 5-year plan describing activities that will lead to enhancing and modernizing FDA's drug safety activities/system. The activities described in the 5-year plan will include:
  - a) Assessment of current and new methodologies to maximize the public health benefit associated with collecting adverse event information at various points during the product lifecycle;
  - b) With input from academia, industry, and others from the general public, identifying epidemiology best practices and developing guidance(s) describing these practices;
  - c) Expanding CBER/CDER's database acquisition and use for the purposes of targeted post-marketing surveillance and epidemiology;
  - d) Developing and validating risk management and risk communication tools, including assessing the effectiveness of risk management plan agreements and developing, implementing, and evaluating mechanisms for public communications about the benefits and risks of drugs and biological products;

e) Improving post-market IT systems (e.g., AERS 2, safety tracking system, and opportunities for linked data management).

f) Enhancing and improving communication and coordination between the Office of Surveillance and Epidemiology and the Office of New Drugs in CDER and the Office of Biostatistics and Epidemiology and the pre-market product review Offices in CBER, including activities to assess the impact and value of routinely including post-market review staff on pre-market review teams

2. The plan will be drafted, published on the FDA website, and updated as follows:

a) FDA will publish a draft of the plan by March 31, 2008. At that time, FDA will solicit and consider comments from the public on the draft plan. The public comment period will be at least 45 calendar days. FDA will complete revisions to the plan and publish the final version no later than December 31, 2008.

b) By the end of FY 09, FDA will conduct an annual assessment of progress against the plan to be published on the FDA website. The report will describe progress on issues outlined in the five year plan. In addition, the report will include FDA efforts to facilitate the interactions between OND/OSE related to the process of evaluating and responding to post-marketing drug safety/adverse event reports.

c) FDA will publish updates to the plan as FDA deems necessary. FDA will publish on the FDA website draft revisions to the plan, solicit comments from the public on those draft revisions, and consider the public comments before completing and publishing updates to the plan.

## **B. Conduct and support activities designed to modernize the process of pharmacovigilance**

1. Maximize the Public Health Benefit of Adverse Event (AE) Collection Throughout the Product Life Cycle: By the end of FY 08, FDA will publish a Request for Proposals (RFP) to solicit proposals from outside research organizations to conduct research on determining the best way to maximize the public health benefit associated with collecting and reporting serious and non-serious adverse events occurring throughout a product's life cycle. Central to addressing this question are determining the number and type of safety concerns discovered by AE collection, the age of products at the time safety concerns are detected by AE collection, and the types of actions that are subsequently taken to protect patient safety. Contractor(s) should study adverse event collection both within and outside the U.S. Contract(s) will be awarded during FY 09 and the completion of study(ies) targeted for FY 11.

2. Epidemiology Best Practices and Guidance Document Development: During FY 08, the FDA, with input from academia, industry, and others from the general public, will hold a public workshop to identify epidemiology best practices. The workshop will examine current epidemiology practices both within and outside the U.S. By the end of FY 10, CDER and CBER jointly will develop and issue a draft guidance document that addresses epidemiology best practices and



provides guidance on carrying out scientifically sound observational studies using quality data resources. A final guidance will be issued in FY 11.

3. **Expanding Database Resources:** A critical part of the transformation of the drug safety program is maximizing the usefulness of tools used for adverse event signal detection and risk assessment. To achieve this end, data other than passive spontaneous reports, including population-based epidemiological data and other types of observational data resources will be used and evaluated. Access to these types of data will expand the FDA's capability to carry out targeted post-marketing surveillance, look at class effects of drugs, and potentially carry out signal detection using data resources other than reports from AERs system. PDUFA funds will be used to obtain access to additional databases, to train existing staff, and to hire additional epidemiologists and programmers to be able to use these new resources.

4. **Development and Validation of Risk Management and Risk Communication Tools:** During FY 08, FDA will develop a plan to 1) identify, with input from academia, industry, and others from the general public, risk management tools and programs for the purpose of evaluation and 2) conduct assessments of the effectiveness of identified Risk Minimization Action Plans (RiskMAPS) and current risk management and risk communication tools. A public workshop will be held during FY 09 to obtain input from industry and other stakeholders regarding the prioritization of the plans and tools to be evaluated. Starting in FY 09, FDA will conduct annual systematic public discussion and review of the effectiveness of one to two risk management program(s) and one major risk management tool. Reports of these discussions will be posted on the FDA website.

### **C. Review of risk management plans**

FDA may use user fees for the review of risk management plans and related activities (e.g., meeting with sponsors, collaborations between review divisions and the appropriate safety group in CDER or CBER, and reviews of periodic reports on the implementation of any risk management plan).

### **D. Other Activities**

FDA will establish the following standards-based information systems to support how FDA obtains and analyzes post-market drug safety data and manages emerging drug safety information:

1. Enhanced adverse event reporting system and surveillance tools;
2. IT infrastructure to support access and analyses of externally-linked databases; and
3. Workflow tracking system.

## **IX. REVIEW OF PROPRIETARY NAMES TO REDUCE MEDICATION ERRORS**

To enhance patient safety, FDA will utilize user fees to implement various measures to reduce medication errors related to look-alike and sound-alike proprietary names and such factors as unclear label abbreviations, acronyms, dose designations, and error prone label and packaging design.

## **A. Review Performance Goals – Drug/Biological Product Proprietary Names**

### **1. Proprietary names submitted during IND phase (as early as end-of-phase 2)**

- a) Review 50% of proprietary name submissions filed during FY 09 within 180 days of receipt. Notify sponsor of tentative acceptance or non-acceptance.
- b) Review 70% of proprietary name submissions filed during FY 10 within 180 days of receipt. Notify sponsor of tentative acceptance or non-acceptance.
- c) Review 90% of proprietary name submissions filed during FYs 11 and 12 within 180 days of receipt. Notify sponsor of tentative acceptance or non-acceptance.
- d) If proprietary name is found to be unacceptable, sponsor can request reconsideration by submitting a written rebuttal with supporting data or request a meeting within 60 days to discuss the initial decision (meeting package required).
- e) If proprietary name is found to be unacceptable, the above review performance goals also would apply to the written request for reconsideration with supporting data or the submission of a new proprietary name.
- f) Complete submission is required to begin the review clock.

### **2. Proprietary names submitted with NDA/BLA**

- a) Review 50% of NDA/BLA proprietary name submissions filed during FY 09 within 90 days of receipt. Notify sponsor of tentative acceptance/non-acceptance.
- b) Review 70% of NDA/BLA proprietary name submissions filed during FY 10 within 90 days of receipt. Notify sponsor of tentative acceptance/non-acceptance.
- c) Review 90% of NDA/BLA proprietary name submissions filed during FYs 11 and 12 within 90 days of receipt. Notify sponsor of tentative acceptance/non-acceptance.
- d) A supplemental review will be done meeting the above review performance goals if the proprietary name has been submitted previously (IND phase after end of phase 2) and has received tentative acceptance.
- e) If proprietary name is found to be unacceptable, sponsor can request reconsideration by submitting a written rebuttal with supporting data or request a meeting within 60 days to discuss the initial decision (meeting package required).
- f) If proprietary name is found to be unacceptable, the above review performance goals apply to the written request for reconsideration with supporting data or the submission of a new proprietary name.

g) Complete submission is required to begin the review clock.

### 3. Guidance Document Development

a) By the end of FY 08, FDA will publish a final guidance on the contents of a complete submission package for a proposed proprietary drug/biological product name.

b) By the end of FY 09, FDA will prepare a MaPP (Manual of Policies and Procedures) to ensure that FDA internal processes (e.g., Division of Medication Errors and Technical Support, Division of Drug Marketing, Advertising, and Communications, Office of New Drugs, CDER and Advertising and Promotional Labeling Branch, CBER) are consistent with meeting the proprietary name review goals.

c) By the end of FY 10, after public consultation with academia, industry, and others from the general public, FDA will publish a draft guidance on best practices for naming, labeling and packaging drugs and biologics to reduce medication errors. Final guidance will be published by the end of FY 11.

d) By the end of FY 12, after public consultation with industry, academia and others from the general public, FDA will publish a draft guidance on proprietary name evaluation best practices. Publication of final guidance on proprietary name evaluation best practices will follow as soon as feasible.

### B. Pilot Program

During PDUFA IV, FDA will develop and implement a pilot program to enable pharmaceutical firms participating in the pilot to evaluate proposed proprietary names and submit the data generated from those evaluations to the FDA for review.

1. FDA will hold a public technical meeting to discuss the elements necessary to create a concept paper describing the logistics of the pilot program, the contents of a proprietary name review submission, and the criteria to be used by FDA to review submissions under the pilot program. Subsequently, by the end of FY 08, FDA will publish the concept paper.

2. By the end of FY 09, FDA will begin enrollment into the pilot program.

3. By the end of FY 11, or subsequent to accruing two years of experience with pilot submissions, FDA will evaluate the pilot program.

### C. Other Activities

1. FDA and industry are interested in exploring the possibility of “reserving” proprietary names for companies once the names have been tentatively accepted by the Agency. By the end of FY 08, FDA will initiate a public process to discuss issues around “reserving” proprietary names.

2. FDA will provide the full source code and supporting technical documentation for the Phonetic and Orthographic Computer Analysis (POCA) tool and make it

available on disk for use by industry and others from the general public by end of FY 08.

**X. FIRST CYCLE REVIEW PERFORMANCE PROPOSAL**

**A. Notification of Issues Identified during the Filing Review**

1. Performance Goal: For original NDA/BLA applications and efficacy supplements, FDA will report substantive review issues identified during the initial filing review to the applicant by letter, telephone conference, facsimile, secure e-mail, or other expedient means.
2. The timeline for such communication will be within 14 calendar days after the 60 day filing date.
3. If no substantive review issues were identified during the filing review, FDA will so notify the applicant.
4. FDA's filing review represents a preliminary review of the application and is not indicative of deficiencies that may be identified later in the review cycle.
5. FDA will notify the applicant of substantive review issues prior to the goal date for 90% of applications.

**B. Notification of Planned Review Timelines**

1. Performance Goal: For original NDA/BLA applications and efficacy supplements, FDA will inform the applicant of the planned timeline for review of the application. The information conveyed will include a target date for communication of feedback from the review division to the applicant regarding proposed labeling and postmarketing study commitments (PMCs) the Agency will be requesting.
2. The planned review timeline will be included with the notification of issues identified during the filing review, within 14 calendar days after the 60 day filing date.
3. The planned review timelines will be consistent with the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products (GRMPs), taking into consideration the specific circumstances surrounding the individual application.
4. The planned review timeline will be based on the application as submitted.
5. FDA will inform the applicant of the planned review timeline for 90% of original BLA and NME NDA applications beginning in FY 09; 90% of efficacy supplements for new or expanded indications beginning in FY 10; 90% of all original NDAs/BLAs beginning in FY 11; and 90% of all efficacy supplements beginning in FY 12 (see table below).

	FY08	FY09	FY10	FY11	FY12
Original BLAs and NME NDAs	---	90%	90%	90%	90%
Efficacy supplements for	---	---	90%	90%	90%

new/expanded indications					
All original NDAs	---	---	---	90%	90%
All efficacy supplements	---	---	---	---	90%

6. Should the applicant submit any unsolicited major amendment(s) to the application (e.g., a major new clinical safety/efficacy study report, major re-analyses of previously submitted study(ies)) and if the division chooses to review such amendment(s) during that review cycle, the planned review timeline will no longer be applicable (even if the unsolicited major amendment leads to an extension of the overall PDUFA review clock). No new planned review timeline need be provided in such cases; however, the overall PDUFA action goal date, including any extension, will still apply. The division will notify the applicant promptly of its decision regarding review of the unsolicited major amendment(s) and whether the planned review timeline is still applicable.

7. In the event FDA determines that significant deficiencies in the application preclude discussion of labeling or PMCs by the target date identified in the planned review timeline (e.g., failure to demonstrate efficacy, significant safety concern(s), need for a new study(ies) or extensive re-analyses of existing data before approval), FDA will communicate this determination to the applicant in accordance with GRMP and no later than the target date. In such cases the planned review timeline will be considered to have been met. Communication of FDA's determination may occur by letter, telephone conference, facsimile, secure e-mail, or other expedient means. Communication of the deficiencies identified will generally occur through issuance of a discipline review letter(s) in advance of the planned target date for initiation of postmarketing study commitments and labeling discussions.

8. Should the applicant submit a major amendment(s) (e.g., a major new clinical safety/efficacy study report, major re-analyses of previously submitted study(ies)) to provide information or data requested by FDA during the review (e.g., a solicited major amendment) and if the division chooses to review such amendment(s) during that review cycle, the planned review timeline initially communicated will generally no longer be applicable. If the solicited major amendment does not result in an extension of the overall PDUFA review clock, and depending upon the circumstances, the review division may choose to retain the previously communicated planned review timeline (e.g., the solicited major amendment is submitted early in the review cycle, review of the amendment is not expected to significantly alter the division's planned review timeline). If the solicited major amendment is submitted during the last 90 days of the review cycle and results in an extension of the PDUFA action date (review clock), the review division will establish a new review timeline for communication of feedback on proposed labeling and PMCs. The division will notify the applicant promptly of its decision regarding review of the major amendment(s) and whether the planned review timeline is still applicable. If the solicited major amendment results in an extension of the overall PDUFA review clock, the division will communicate a new planned review timeline to the applicant at the time of the clock extension.

### **C. Report on Review Timeline Performance**

1. FDA will report its performance in meeting the goals for inclusion of a planned review timeline with the notification of issues identified during the filing review in the annual PDUFA performance report.
2. FDA will report its performance in meeting the planned review timeline for communication of labeling comments and PMC requests in the annual PDUFA performance report. The report will include the percentage of applications for which the planned target dates for communication of labeling comments and PMC requests were met. The report will also note how often the planned review timeline was met based on communication of labeling comments and PMC requests by the target date and how often such communication did not occur due to FDA's determination that significant deficiencies in the application precluded communication of labeling comments and PMC requests at the time initially projected. Communication of labeling comments and PMC requests, or communication of FDA's determination that significant deficiencies preclude initiation of such discussions, within 7 calendar days of the target date stated in the planned review timeline will be considered to have met the target date. FDA will also report the number of times that the review timelines were inapplicable due to the Agency's decision to review an unsolicited major amendment or a solicited major amendment that did not result in an extension of the review clock (unless the review division chose to retain the previously communicated planned review timeline.)
3. FDA will engage an independent outside consultant to conduct an analysis of the Agency's success in adhering to the planned review timelines. The contractor will assess the factors, based on input from both the FDA and the applicants, that contributed to the ability of the Agency to adhere to the planned review timelines and those factors attributable to either the FDA or the applicant that contributed to failure to adhere to the planned review timeline. A final report will be provided to FDA at least 6 months before the end of FY 11. FDA will make available a releasable version of the final report within 2 months of receipt from the independent outside consultant.

### **D. Standard Operating Procedures and Training**

FDA will develop harmonized (CBER/CDER) standard operating procedures (SOPs) regarding the notification of planned review timelines. These SOPs will be finalized and implemented by the end of FY 08. Training will be provided to all CBER and CDER review staff on the harmonized (CBER/CDER) standard operating procedures. Training will continue for all new review staff and refresher training will be provided to all review staff as necessary through FY 12.

## **XI. EXPEDITING DRUG DEVELOPMENT**

- A. Guidance Development:** FDA will develop and publish for comment draft guidances on the following topics by the end of the indicated Fiscal Year of PDUFA-IV. FDA will complete the final guidances within one year of the close of the public comment period.
1. Clinical Hepatotoxicity – FY 2008
  2. Non-inferiority Trials – FY 2008
  3. Adaptive Trial Designs – FY 2008

4. End of Phase 2(a) Meetings – FY 2008
5. Multiple Endpoints in Clinical Trials – FY 2009
6. Enriched Trial Designs – FY 2010
7. Imaging Standards for Use as an End Point in Clinical Trials – FY 2011

**B. Ongoing Scientific Collaboration:** FDA will participate in workshops with representatives from the scientific community (including industry, academia and other interested stakeholders) to further the science toward development of guidance documents in the following areas:

1. Predictive Toxicology
2. Biomarker Qualification
3. Missing Data

**C.** FDA will participate in workshops and other public meetings to explore new approaches to a structured model for benefit/risk assessment. The results of these interactions will be used to assess whether pilot(s) of such new approaches can be conducted during PDUFA-IV. These efforts may lead to the development of guidance documents.

## **XII. POSTMARKETING STUDY COMMITMENTS**

FDA will develop harmonized (CBER/CDER) standard operating procedures that articulate the Agency's policy and procedures (e.g., timing, content, rationale and vetting process) for requesting that applicants agree in writing to voluntary postmarketing study commitments. The SOPs will be finalized prior to the end of FY 08. In developing these SOPs, the Agency will take into consideration the findings of the contractor study of current Agency procedures to be completed during FY 07. FDA will make available a releasable version of the final report within 2 months of receipt from the contractor. Training will be provided to all CBER and CDER review staff on the harmonized (CBER/CDER) standard operating procedures. Training will continue for all new review staff and refresher training will be provided to all review staff as necessary through FY 12.

## **XIII. IMPROVING FDA PERFORMANCE MANAGEMENT**

**A. The studies conducted under this initiative are intended to foster:**

1. Development of programs to improve access to internal and external expertise
2. Reviewer development programs, particularly as they relate to drug review processes
3. Advancing science and use of information management tools
4. Improving both inter- and intra-Center consistency, efficiency, and effectiveness
5. Improved reporting of management objectives
6. Increased accountability for use of user fee revenues
7. Focused investments on improvements in the process of drug review

8. Improved communication between the FDA and industry

**B. Studies will include:**

1. Assessment of the impact of the electronic submission and review environment on the efficiency and effectiveness of the overall process for the review of human drugs.
2. Assessment of the progress toward full implementation of Good Review Management Principles, focusing on both FDA reviewer practices and industry sponsor practices affecting successful implementation.
3. Assessment by an independent accounting firm of the review activity adjustment methodology (as described in section 736(c)(2) that is applied in FY 09 with recommendations for changes, if warranted

**XIV. INFORMATION TECHNOLOGY GOALS**

**A. Objectives**

1. FDA is committed to achieve the long-term goal of an *automated standards-based* information technology (IT) environment for the exchange, review, and management of information supporting the process for the review of human drug applications throughout the *product life cycle*. Towards this goal, FDA will work toward the accomplishment of the following objectives by the end of FY 12:
  - a) Develop and periodically update an IT plan, as defined in Sections B) and C) below, covering a rolling five-year planning horizon.
  - b) Develop, implement, and maintain new information systems consistently across all organizational divisions participating in the process for the review of human drug applications, and in compliance with the IT plan, the FDA's program-wide governance process, the FDA's target enterprise architecture, and with HHS enterprise architecture standards. The consistency of development, implementation, and maintenance of new information systems will be determined by the FDA based on considerations of program efficiency and effectiveness. *Emphasis will be placed on the consistency of interactions with regulated parties and other external stakeholders.*
  - c) Update technical specifications and IT-related guidance documents as necessary to reflect consistent program-wide implementation of new information systems supporting electronic information exchange between FDA and regulated parties and other external stakeholders.
  - d) Extend the capability of the secure electronic single point of entry to include two-way transmission of regulatory correspondence.
  - e) Establish an automated standards-based regulatory submission and review environment for INDs, NDAs, and BLAs, and their supplements, that enables the following functions over the life cycle of the product:
    - (1) Electronic IND, NDA, and BLA submissions received by FDA can be archived to enable retrieval through standardized automated links;



(2) Electronic IND, NDA, and BLA submissions can include cross-references to previously submitted electronic materials through standardized automated links; and

(3) Archived electronic IND, NDA, and BLA submissions can be retrieved through standardized automated links.

f) Establish a system for electronic exchange and management of human drug labeling information in a modular manner (e.g., at the label section level) that is based on FDA standards and that enables revision tracking.

g) Establish standards-based information systems to support how FDA obtains and analyzes post-market drug safety data and manages emerging drug safety information, as described in Section VIII addressing the enhancement and modernization of the FDA drug safety system.

## **B. Communications and Technical Interactions**

1. FDA will develop and periodically update a five-year IT plan for improving the automation of business processes and acquiring and maintaining information systems to achieve the objectives defined above in PDUFA IT Goal A. The plan will include measurable or observable milestones toward achievement of those objectives.

2. The IT plan will be reviewed and approved through the appropriate FDA governance process to ensure it conforms to the Agency's overall long-term automation strategy.

3. The IT plan will be drafted, published on the FDA web site, and updated as follows:

a) FDA will publish a draft of the IT plan by December 31, 2007. At that time, FDA will solicit and consider comments from the public on the draft IT plan. The public comment period will be at least 45 calendar days. FDA will complete revisions to the IT plan and publish the final version no later than May 30, 2008.

b) FDA will conduct an annual assessment of progress against the IT plan and publish on the FDA web site a summary of the assessment within 2 months after the close of each fiscal year.

c) FDA will publish updates to the IT plan as FDA deems necessary to achieve the objectives defined in PDUFA IT Goal A. FDA will publish on the FDA web site draft revisions to the IT plan; solicit comments from the public on those draft revisions; and consider the public comments before completing and publishing updates to the IT plan.

4. The FDA and industry stakeholders will meet on a quarterly basis to discuss ongoing implementation of the IT plan, status of IT metrics as available, and potential impacts that future activities may have on stakeholders. These meetings will also be used to discuss potential FDA revisions to the IT plan based on operational experience.

### **C. Standards and IT Plan**

The IT plan referenced in PDUFA IT Goal B will provide a vision for FDA standards and technical infrastructure supporting the process for the review of human drug applications and will address the following:

1. A description of the scope and approach for an evaluation and design of the target enterprise architecture necessary to achieve the objectives defined in PDUFA IT Goal A.
2. The business processes targeted for automation to achieve business-driven objectives.
3. Which electronic data standards, including the associated Standards Development Organization, are being considered for adoption or development. (Note: The FDA's process for adopting or developing standards includes the consideration of existing open consensus standards prior to the development of new standards. FDA participates in international Standards Development Organizations and supports global harmonization of data standards through open structured processes.)
4. Implementation of information systems that are based on the electronic data standards.
5. Training for system users, stakeholder adoption, and communications for transitioning to new or reengineered information systems supporting the process for the review of human drug applications.
6. A description of FDA's processes for
  - a) evaluating business processes for electronic information exchange between FDA and regulated parties or external stakeholders;
  - b) evaluating, adopting or developing electronic data standards for information exchange between FDA and regulated parties or external stakeholders; and
  - c) developing, piloting, and deploying information systems that use those standards in supporting the process for the review of human drug applications.

### **D. Metrics and Measures**

FDA will measure progress toward achievement of the objectives defined in PDUFA IT Goal A. Measures will include:

1. The number and percentage of IND, NDA, and BLA submissions received in valid electronic format in compliance with FDA standards, categorized by types of submissions. Increasing the number and percentage of IND, NDA, and BLA submissions received in valid electronic format is a goal that is supported by the FDA and industry stakeholders. Achievement of this goal requires the cooperation of regulated industry. To support the assessment of this goal, the following information will be tracked and reported at least annually:

- a) Total number of submissions categorized by type of submission;
  - b) Total number of submissions in valid electronic format in compliance with FDA standards
  - c) Total number of submissions received through the secure electronic single point of entry versus other methods; and
  - d) Total number of submissions received substantially on paper.
2. Total number of standards-based electronic submissions that fail to comply with FDA electronic submission standards, along with a distribution of these submission failures across categories of failure or problem type.
  3. Annual spending on maintenance of legacy IT systems and IT systems that are common across the organizational divisions participating in the process for the review of human drug applications.
  4. Other measures and milestones to be identified in the IT plan addressed under Sections B and C above.

## **XV. 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, efficacy supplement, or resubmission of any of these applications, submitted within three months of a goal date, may extend the goal date by three months. A major amendment to a manufacturing supplement submitted within two months of the goal date extends the goal date by two months. Only one extension can be given per review cycle.

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
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 items 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) or to address an important safety issue.

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/BLA meeting. Each requestor should usually only request 1 each of these Type B meetings for each potential application (NDA/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.

J. IT Definitions (see section XI)

1. "Automation of business processes" refers to the development and deployment of information systems that support program activities (i.e., business processes) conducted under the process for the review of human drug applications. The purpose of business process automation is to support decision making by FDA program managers and reviewers. The scope of business process automation is determined by program managers toward the objective of more efficient and effective program operations.

2. "Program" refers to the organizational resources, procedures, and activities assigned to conduct "the process for the review of human drug applications," as defined in the Prescription Drug User Fee Act.

3. "Standards-based" means compliant with published specifications that address terminology or information exchange between the FDA and regulated parties or external stakeholders, as adopted by the FDA or other agencies of the federal government, and often based on the publications of national or international Standards Development Organizations.

4. "FDA Standards" means technical specifications that have been adopted and published by the FDA through the appropriate governance process. FDA standards may apply to terminology, information exchange, engineering or technology specifications, or other technical matters related to information systems. FDA standards often are based on the publications of other federal agencies, or the publications of national or international Standards Development Organizations.

5. "Product life cycle" means the sequential stages of human drug development, regulatory review and approval, post-market surveillance and risk management, and where applicable, withdrawal of an approved drug from the market. In the context of the process for the review of human drug applications, the product life cycle begins with the earliest regulatory submissions in the Investigational New Drug (IND) phase, continues through the New Drug Application (NDA) or Biological Licensing Application (BLA) review phase, and includes post-market surveillance and risk management activities as covered under the process for the review of human drug applications.

6. "The FDA's program-wide IT governance process" includes centralized oversight of all data and technology standards adoption, technology acquisition, and funding allocation.

7. "The FDA's target enterprise architecture" includes data and technology standards for the electronic exchange and management of information supporting the process for the review of human drug applications.

**SECTION B: PERFORMANCE GOALS AND PROCEDURES FOR ADVISORY REVIEW OF  
DIRECT-TO-CONSUMER TELEVISION ADVERTISING  
FISCAL YEARS 2008 THROUGH 2012**

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 direct-to-consumer television advertising user fee program in Section 736A of the Federal Food, Drug, and Cosmetic Act are summarized below.

**I. FINDINGS**

A. FDA's advisory review of proposed prescription drug television advertisements helps to ensure that these advertisements communicate information to consumers that is accurate, balanced, and adequately substantiated, thereby improving the quality of these advertisements.

B. It is important to industry and FDA to provide predictability in the timeframe for reviewing and providing written comments on direct-to-consumer television advertisements submitted to FDA for advisory review before initial dissemination.

C. FDA needs additional resources to ensure that it has adequate staff to provide advisory reviews of direct-to-consumer television advertisements in a timely manner.

D. A program that requires payment of user fees by those who choose to voluntarily submit direct-to-consumer television advertisements for advisory review by FDA is established to provide needed resources to FDA and improve the timeliness of FDA advisory reviews while maintaining the quality of the reviews.

E. Each submission for advisory review will be assessed a fee, but the sponsor may resubmit that advertisement one time after receiving comments without further fee assessment.

F. Under this program, it is important to ensure that FDA has the resources needed to hire and retain adequate staff to meet review performance goals.

G. Because reviews from this program are dependant on submissions which are unpredictable, the statute establishes a reserve fund to maintain a staff that can meet the review performance goals in case user fees for any year of the program are not adequate. In addition, user fees for all submissions during a fiscal year are to be paid at the start of each fiscal year or late fees will be assessed.

**II. REVIEW PERFORMANCE GOALS**

**A. Goals for First 150 Advisory Review Submissions**

**Fiscal Year 2008**

1. Review and provide advisory comments for 75 original submissions within 45 days (50% of 150).

2. Review and provide advisory comments for 37 resubmissions of original submissions within 30 days (50% of 75 resubmissions).

**Fiscal Year 2009**

1. Review and provide advisory comments for 90 original submissions (60% of 150) within 45 days.
2. Review and provide advisory comments for 45 resubmissions (60% of 75) within 30 days.

**Fiscal Year 2010:**

1. Review and provide advisory comments for 105 original submissions (70 % of 150) within 45 days.
2. Review and provide advisory comments for 52 resubmissions (70% of 75) within 30 days.

**Fiscal Year 2011**

1. Review and provide advisory comments for 120 original submissions (80% of 150) within 45 days.
2. Review and provide advisory comments for 60 resubmissions (80% of 75) within 30 days.

**Fiscal Year 2012**

1. Review and provide advisory comments for 135 original submissions (90% of 150) within 45 days.
2. Review and provide advisory comments for 68 resubmissions (90% of 75) within 30 days.

**NOTE:** For any goal year, if the number of submissions or resubmissions received is not greater than the number for which the Agency has committed to provide advisory comments on within the goal timeframe, then the goal will be to provide comments on 90% of the number received within the goal timeframe. For example, if FDA receives only 30 resubmissions in fiscal year 2008, then the goal would be to review 27 resubmissions within 30 days.

**B. Goals after 150 Submissions**

If in any fiscal year after FY 2008, participants in the program indicate (in response to the Federal Register notice) the intent to submit more direct-to-consumer broadcast advertisement submissions for advisory review than were subject to the goals in the prior year, the following performance goals will apply (see Appendix B-1 for specific examples):

1. In the first year of the increase, FDA will review and provide advisory comments for:
  - a) 50% of the additional paid original submissions over the cohort of original submissions from the previous fiscal year, up to a maximum of 50 additional submissions, within 45 days.
  - b) 50% of the additional resubmissions over the cohort of resubmissions from the previous fiscal year, up to a maximum of 24 additional resubmissions, within 30 days.

2. In each subsequent year, the performance goals will increase in the same manner as in section A. for each additional cohort of up to 50 additional submissions over the cohort of the prior year (i.e., in the second year after the increase, the goal will be to review 60% of the additional cohort from the prior year (up to 50 submissions) and 50% of any further additions (up to an additional 50 submissions).

3. For purposes of this adjustment, it is assumed that the number of submissions subject to review metrics cannot decrease from one year to the next even if actual submissions decrease.

4. For purposes of this adjustment, it is assumed that 150 submissions are subject to performance goals in fiscal year 2008.

5. The goals described in this subsection will be calculated based solely on the number of submissions identified in response to the Federal Register notice for that fiscal year.

### **III. DEFINITIONS AND EXPLANATION OF TERMS**

1. The term "amendment" shall mean additional documents submitted to FDA to complete an original submission or resubmission. For example, references that have been cited in the original submission but were omitted from the original submission package could be submitted as an amendment.

2. The term "original submission" shall mean a proposed television advertisement submission for which a sponsor paid for an advisory review. The proposed television advertisement may not be more than two minutes long.

3 The term "resubmission" shall mean a subsequent submission of a revised version of the advertisement contained in an original submission. Any revisions made to the proposed television advertisement must be based on FDA comments on the original submission. The resubmission may not introduce significant new concepts or creative themes into the television advertisement, or FDA will designate it as an original submission. Revisions that require a consult to another division will be considered to introduce "significant new concepts or creative themes."



**Appendix B-1**

**Example 1: Original Submissions**

If participants indicate the intent to submit 150 submissions in fiscal year 2008; 200 submissions in fiscal year 2009; 224 submissions in fiscal year 2010; 200 submissions in fiscal year 2011; and 250 submissions in fiscal year 2012, the review metrics will be as follows:

	<b>FY 08: 150 submissions</b>	<b>FY 09: 200 submissions</b>	<b>FY 10: 224 submissions</b>	<b>FY 11: 200 submissions</b>	<b>FY 12: 250 submissions</b>
Cohort 1 (150 submissions)	75 (50% of 150)	90 (60% of 150)	105 (70% of 150)	120 (80% of 150)	135 (90% of 150)
Cohort 2 (50 submissions)		25 (50% of 50)	30 (60% of 50)	35 (70% of 50)	40 (80% of 50)
Cohort 3 (24 submissions)			12 (50% of 24)	0 (60% of 0)	17 (70% of 24)
Cohort 4 (0 submissions)				0 (50% of 0)	0 (70% of 0)
Cohort 5 (26 submissions)					13 (50% of 26)
<b>Total Target for 45 Day Review Metric</b>	<b>75</b>	<b>115</b>	<b>147</b>	<b>155</b>	<b>205</b>

**Example 2: Original Submissions**

If participants indicate the intent to submit 150 submissions in fiscal year 2008; 200 submissions in fiscal year 2009; 250 submissions in fiscal year 2010; 300 submissions in fiscal year 2011; and 350 submissions in fiscal year 2012, the review metrics will be as follows:

	<b>FY 08: 150 submissions</b>	<b>FY 09: 200 submissions</b>	<b>FY 10: 250 submissions</b>	<b>FY 11: 300 submissions</b>	<b>FY 12: 350 submissions</b>
Cohort 1 (150 submissions)	75 (50% of 150)	90 (60% of 150)	105 (70% of 150)	120 (80% of 150)	135 (90% of 150)
Cohort 2 (50 submissions)		25 (50% of 50)	30 (60% of 50)	35 (70% of 50)	40 (80% of 50)
Cohort 3 (50 submissions)			25 (50% of 50)	30 (60% of 50)	35 (70% of 50)
Cohort 4 (50 submissions)				25 (50% of 50)	30 (60% of 50)
Cohort 5 (50 submissions)					25 (50% of 50)
<b>Total Target for 45 Day Review Metric</b>	<b>75</b>	<b>115</b>	<b>160</b>	<b>210</b>	<b>265</b>

### Example 3: Resubmissions

If participants submit 75 resubmissions in fiscal year 2008; 99 resubmissions in fiscal year 2009; 123 resubmissions in fiscal year 2010; 147 resubmissions in fiscal year 2011; and 171 resubmissions in fiscal year 2012, the review metrics will be as follows:

	<b>FY 08: 75 resubmissions</b>	<b>FY 09: 99 resubmissions</b>	<b>FY 10: 123 resubmissions</b>	<b>FY 11: 147 resubmissions</b>	<b>FY 12: 171 resubmissions</b>
Cohort 1 (75 submissions)	37 (50% of 75)	45 (60% of 75)	52 (70% of 75)	60 (80% of 75)	68 (90% of 75)
Cohort 2 (24 submissions)		12 (50% of 24)	14 (60% of 24)	17 (70% of 24)	19 (80% of 24)
Cohort 3 (24 submissions)			12 (50% of 24)	14 (60% of 24)	17 (70% of 24)
Cohort 4 (24 submissions)				12 (50% of 24)	14 (60% of 24)
Cohort 5 (24 submissions)					12 (50% of 24)
<b>Total Target for 30 Day Review Metric</b>	<b>37</b>	<b>57</b>	<b>78</b>	<b>103</b>	<b>130</b>