FY 2001 PERFORMANCE REPORT TO CONGRESS

for the

Prescription Drug User Fee Act of 1992

as reauthorized and amended by the

Food and Drug Administration Modernization Act of 1997

Food and Drug Administration
Department of Health and Human Services

Executive Summary

In 1992, Congress enacted the Prescription Drug User Fee Act (PDUFA). PDUFA provided FDA with additional resources to hire more medical and scientific reviewers to conduct premarket reviews as well as support staff and field investigators to speed up the application review process for human drug and biological products. In 1997, after a successful first five years, Congress reauthorized the program for five additional years. With this reauthorization (PDUFA II) came higher expectations for reviews and additional goals intended to improve FDA's responsiveness to and communication with industry sponsors during the early years of drug development. FDA has been able to respond more rapidly to new drug and biologic applications without compromising review quality. For the consumer, this has meant more products available more quickly.

All of the original applications submitted during FY 2000 have been reviewed and acted upon, and final performance can now be reported. Only a preliminary performance assessment on applications submitted during FY 2001 is possible at this time. FDA exceeded all the review performance goals for original and resubmitted new drug and biological applications and for efficacy and manufacturing supplements submitted in FY 2000. Although it is too early to report final results, the Agency appears to be meeting or exceeding all the review goals for FY 2001 submissions. The Agency also exceeded three of the six "procedural and processing" goals designed to improve its responsiveness to sponsors requests during the early phases of drug development (detailed results of performance on procedural and processing goals are on pages 16 and 17).

Notwithstanding these successes, the Agency has encountered challenges in trying to meet the PDUFA II goals. The fees the Agency has collected have been significantly less than expected due to the reduced number of new drug applications and the increased proportion of applications where fees are waived. Yet the number of goal-driven tasks for which the Agency collects no fees have increased substantially under PDUFA II.

The Agency will continue to work with the industry, the Congress, and all other stakeholders on a reauthorization of the PDUFA program that will continue to bring benefits to American consumers by bringing important new therapies to market quickly without compromising scientific review standards.

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Introduction

In 1992, Congress passed the Prescription Drug User Fee Act (PDUFA). PDUFA authorized FDA to collect fees from companies that produce human drug and biological products. The original PDUFA had a five-year life; it ended in 1997, the same year Congress passed the FDA Modernization Act (FDAMA). FDAMA contained a five-year reauthorization of PDUFA (PDUFA II).

PDUFA requires FDA to submit two annual reports to Congress for each fiscal year during which fees are collected: 1) a performance report due within 60 days of the end of the fiscal year, and 2) a financial report due within 120 days of the end of the fiscal year. This document fulfills the first of these requirements for Fiscal Year 2001.

PDUFA provides FDA with additional revenue to hire more reviewers and support staff and upgrade its information technology to speed up the application review process for pharmaceutical and biological products without compromising review quality.

In consultation with industry and the Congress, FDA agreed to meet a set of review performance goals that become more stringent each year. These goals applied to the review of original new product applications, resubmissions of original applications, and supplements to approved applications. FDA met or exceeded every PDUFA I performance goal and has met or exceeded nearly every PDUFA II performance goal.

Under PDUFA II, the review goals continue to shorten. By 2002, the PDUFA II goals call for FDA to review and act on 90 percent of:

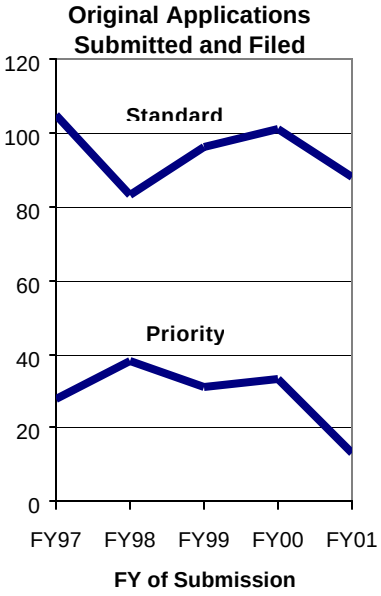
- Priority new drug and biological product applications and efficacy supplements (i.e., for products providing significant therapeutic gains) within 6 months;
- Standard new drug and biological product applications and efficacy supplements within 10 months;
- Manufacturing supplements within 6 months, and those requiring prior approval within 4 months;
- Class 1 resubmissions of original applications within 2 months, and Class 2 resubmissions of original applications within 6 months.

In addition, PDUFA II added a new set of goals intended to improve FDA's responsiveness to and communication with industry sponsors during the early years of drug development. These goals specify timeframes for activities such as scheduling meetings and responding to various sponsor requests. Whereas PDUFA's original intent was to speed up the review process, PDUFA II's intent is to speed up the entire drug development process.

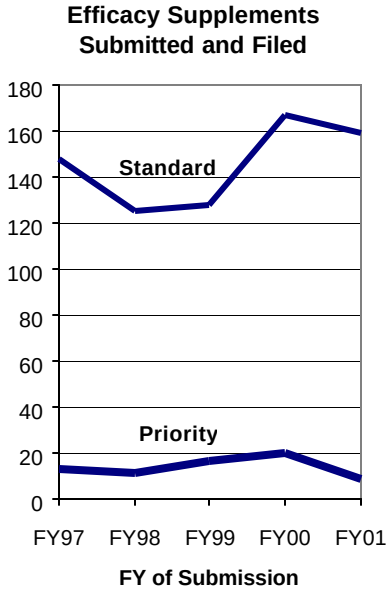
Outcomes

In FY 2001 the Agency exceeded all its review performance goals of PDUFA II[1] despite the goals becoming still more challenging. However, some strains in the program became evident. While some aspects of workload decreased, others, notably those involving pre-submission meetings, increased, and the Agency was unable to achieve all of its procedural and processing performance goals (e.g., goals associated with formal meetings with sponsors).

Fewer Fee-Paying Applications: Original applications and efficacy supplements are the most important component of user-fee revenues. Not only do they generate one-third of the total amount of fees collected, but they also determine the amount to be generated by product and establishment fees, which are set to generate the other two-thirds of the fee revenue. The number of original new product applications submitted and filed each year under PDUFA increased steadily in the early years from 88 in FY 1993 to 133 in FY 1997. From FY 1997 to FY 2000, the growth leveled off, and in FY 2001, application submissions and filings dropped substantially. When applications are submitted, they are reviewed for completeness before they are filed. Even though only three applications were refused for filing, FDA filed 25 percent fewer applications last year than the previous year. The decrease was especially significant for priority applications -- those that represent significant therapeutic gains. The number of priority applications filed last year was down more than 60% from the previous year and was less than half the level of any year since FY 1997.

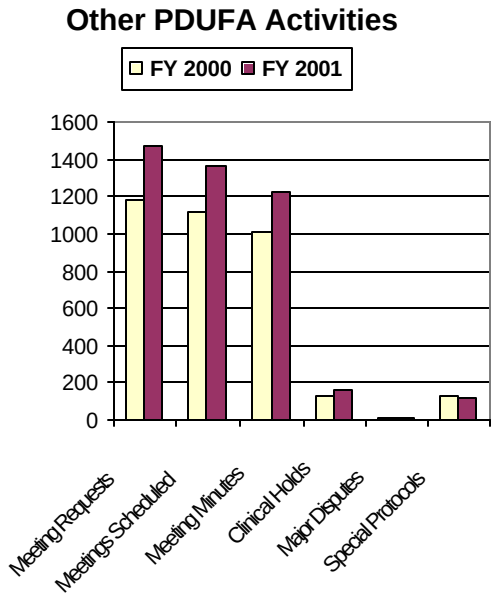


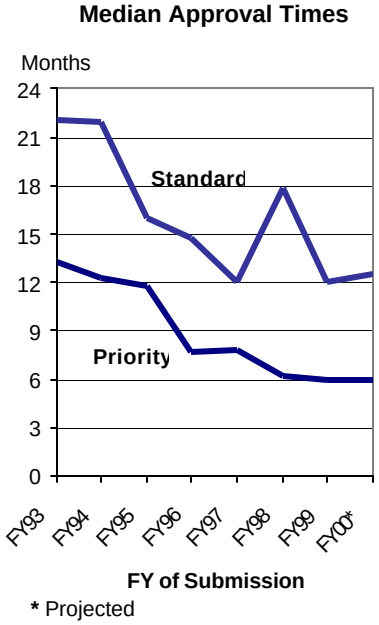
The number of efficacy supplements also decreased last year, from a level of 187 in FY 2000 to 168, a decrease of 10%. Priority efficacy supplements dropped from 20 in FY 2000 to 9 in FY 2001.



Outcomes

Other PDUFA Activities: Although the number of applications the Agency filed dropped last year, pre-submission activity increased. The number of pre-submission meetings requested, scheduled, and transcribed increased from the previous year. Pre-submission meetings play an important role in improving communications between the industry and the Agency and speeding the drug development process, but they consume a significant proportion of the Agency's resources that would otherwise be allocated to the review of applications. The Agency received 1,471 requests for formal meetings from sponsors and scheduled 1,361 meetings. These numbers are increases of 24% and 21% respectively over the previous year.





Approval Times Remain Short: Total approval time is the time from the initial submission of an original application to the issuance of an approval letter for that application. It includes both FDA's review time and the time the sponsor spends answering deficiencies noted by FDA, and can encompass several review "cycles." Not all applications receive approval letters. While PDUFA specifies review-time goals and quicker reviews tend to produce quicker approvals, the quality and completeness of the new drug application and the public health priority of the product also have a significant impact on time to approval.

Median total approval time for priority applications submitted in FY 2000 remained at 6 months, less than half what it was in the early PDUFA years. Median approval time for standard applications increased slightly from an estimated 12.0 months for FY 1999 submissions to 12.5 months for FY 2000[2].

Report on PDUFA Goals

This report updates the Agency's review performance on the FY 2000 application submissions and evaluates its performance in reviewing FY 2001 application submissions and meeting other PDUFA II goals. All of the original applications submitted during FY 2000 have been reviewed and acted upon, and final performance can now be reported (One standard submission was acted on after September 30, 2001, but it is included in the performance statistics). Only a preliminary performance assessment on applications submitted during FY 2001 is possible at this time. For submission categories with a 10- or 12-month review goal, it is too early to measure review performance. For those submission categories with a review goal that is shorter than 10 months, performance on submissions received early in the fiscal year provides an early-indicator of final review performance. Unless otherwise noted, all performance data in this section are as of September 30, 2001.

FDA's Center for Biologics Evaluation and Research (CBER) has changed from counting Product License Applications (PLAs) and Establishment License Applications (ELAs) separately to combining them as Biologic License Applications (BLAs). This report shows CBER's workload and performance on PLAs and BLAs only (i.e., Product Applications). **To simplify notation, it uses BLA as a generic term for both BLAs and PLAs**. Original and resubmitted ELAs have been dropped, both from workload counts and performance measurements. These new counts are reflected in the workload and performance data for the PDUFA I years, so trends into PDUFA II are consistent.

Original New Product Applications

Goal --Review and act upon complete original NDAs and BLAs

The table below summarizes the annually decreasing review-time goals for original New Drug Applications (NDAs) and BLAs under PDUFA II. Over the five-year period, the goal of reviewing 90 percent of priority applications in six months remains constant. For standard applications, the review-time goals drop over the five-year period. For applications filed in FY 1998, the goal was to review 90 percent in 12 months; for FY 2002 applications, the goal is to review 90 percent in 10 months. For standard applications filed in FY 2001, the goal was to review 90 percent in 12 months and 70 percent in 10 months. The statute allows three additional months for review of original NDA and BLA submissions that involve major amendments received within the last three months of their usual review intervals.

Goals		On-Time Performance by Submission Year				
		FY 98	FY 99	FY 00	**FY 01**	FY 02
Priority	6 months	90% on time	90%	90%	**90%**	90%
Standard	12 months 10 months	90%	90% 30%	90% 50%	**90%** **70%**	90%

Workload

The following table shows the number of original NDAs and BLAs filed in each of the last five years. The count of FY 2001 submissions assumes that all submissions received in the last two months of FY 2001 are filed. When FDA files a submission, it is deemed "complete" by PDUFA definition. FDA makes a filing decision within 60 days of an original application's receipt. All calculations of PDUFA review times are made, however, from the original receipt date of the filed application.

Original submissions filed *(Priority/Standard)*:

	FY 97	FY 98	FY 99	FY 00	FY 01[3]
• **NDAs**	117 *(25/92)*	109 *(30/79)*	121 *(30/91)*	121 *(29/92)*	*92 (10/82)*
• **BLAs**	16 *(3/13)*	12 *(8/4)*	6 *(1/5)*	13 *(4/9)*	9 *(3/6)*
• **PDUFA Total**	133 *(28/105)*	121 *(38/83)*	127 *(31/96)*	134 *(33/101)*	*101 (13/88)*
NMEs[4]		*42 (19/23)*	41 *(16/25)*	32 *(17/15)*	*34 (8/26)*

Original New Product Applications

Performance

FY 2000 Submissions

For FY 2000 applications, all but one of the 33 priority submissions were acted upon within the 6-month review goal. FDA met the 12-month goal for standard submissions for 98 of the 101 standard submissions reviewed. Eighty-one percent of all standard applications and 65 percent of the NMEs and BLAs were reviewed and acted upon within 10 months, exceeding the 50 percent review goal in both cases.

FY 00 Submissions			Reviewed and acted upon	Number on time	Percent on time
Priority	6 month goal	All Applications	33	32	97
		NMEs & BLAs	21	20	95
Standard	12 month goal	All Applications	101	98	97
		NMEs & BLAs	24	23	96
	10 month goal	All Applications	101	82	81
		NMEs & BLAs	24	15	62

FY 2001 Submissions

While it is too early to report meaningful review performance statistics for applications submitted in FY 2001, all priority applications that have been reviewed have met the 6 month review goal, and all standard applications that have been reviewed have met the 10 month review goal.

FY 01 Submissions			Reviewed and acted upon	Number on time	Percent on time
Priority	6 month goal	All Applications	8	8	100
		NMEs & BLAs	7	7	100
Standard	12 month goal	All Applications	Too early to report meaningful review performance statistics. Ten standard applications have been reviewed and acted upon, all within 10 months.		
		NMEs & BLAs			
	10 month goal	All Applications			
		NMEs & BLAs			

Resubmitted New Product Applications

Goal -- Review and act upon resubmitted NDAs and BLAs.

A resubmission is a firm's response after an FDA action of "approvable," "not approvable," or "complete response" on an application. The applicable performance goal for a resubmission is determined by the year in which the resubmission itself is received, rather than the year in which the original application was submitted. The definitions of Class 1 and Class 2 resubmissions can be found at the end of Appendix A.

Goals		On-Time Performance by Resubmission Year				
		FY 98	FY 99	FY 00	**FY 01**	FY 02
Class 1	6 months	90% on time				
	4 months		90%	90%		
	2 months	30%	50%	70%	**90%**	90%
Class 2	6 months	90%	90%	90%	**90%**	90%

Workload -- Resubmissions received (*Class 1/Class 2*):

	FY97	FY 98	FY 99	FY 00	FY 01
• **of Original NDAs**	82	50 *(19/31)*	63 *(17/46)*	80 *(25/55)*	61 *(27/34)*
• **of Original BLAs**	8	21 *(5/16)*	14 *(2/12)*	9 *(1/8)*	15 *(6/9)*
• **PDUFA Total**	90	71 *(24/47)*	77 *(19/58)*	89 *(26/63)*	76 *(33/43)*

Resubmitted New Product Applications

Performance

FY 2000 Resubmissions

All 26 Class 1 resubmissions received in FY 2000 were reviewed and acted upon within 4 months, and 25 were acted upon within 2 months. All but one of the 63 Class 2 resubmissions were reviewed and acted upon within 6 months. Review performance on both classes of FY 2000 resubmissions exceeded the PDUFA review goals.

FY 00 Resubmissions		Reviewed and acted upon	Number on time	Percent on time
Class 1	4 months	26	26	100
	2 months		25	96
Class 2	6 months	63	62	98

FY 2001 Resubmissions

As of September 30, 2001, 24 FY 2001 Class 1 resubmissions had been reviewed and acted upon. Twenty-two of these met the 2-month goal. All of the Class 2 resubmissions that have been reviewed and acted upon have met the 6-month goal. With 9 Class 1 and 15 Class 2 resubmissions still pending and not overdue, it is too early to make a final performance determination, but current on-time performance for both classes of resubmissions exceeds the goals.

FY 01 Resubmissions		Reviewed and acted upon	Number on time	Percent on time
Class 1	2 months	24	22	92
Class 2	6 months	28	28	100

Efficacy Supplements

Goal -- Review and act upon complete efficacy supplements to NDAs and BLAs

The table below summarizes the annually decreasing review-time goals for efficacy supplements to NDAs and BLAs under PDUFA II. Review goals for efficacy supplements follow the same progression as the review goals for original NDAs and BLAs. Over the five-year period, the goal of reviewing 90 percent of priority efficacy supplements in six months remains constant. For standard efficacy supplements, the review-time goals drop over the five-year period. For FY 1998 submissions, the goal was to review 90 percent in 12 months; for FY 2002 submissions, the goal is to review 90 percent in 10 months. For standard efficacy supplements received in FY 2001, the goal was to review 90 percent in 12 months and 70 percent in 10 months.

Goals		On-Time Performance by Submission Year				
		FY 98	FY 99	FY 00	**FY 01**	FY 02
Priority	6 months	90% on time	90%	90%	**90%**	90%
Standard	12 months	90%	90%	90%	**90%**	
	10 months		30%	50%	**70%**	90%

Workload -- Efficacy supplements filed *(Priority / Standard)*:

	FY 97	**FY 98**	**FY 99**	**FY 00**	**FY 01**[4]
• **to NDAs**	146 *(10/136)*	126 *(10/116)*	135 *(15/120)*	175 *(18/157)*	*152 (7/145)*
• **to BLAs**	15 *(3/12)*	10 *(1/9)*	10 (2/8)	12 *(2/10)*	16 *(2/14)*
• **PDUFA total**	161 *(13/148)*	136 *(11/125)*	145 *(17/128)*	187 *(20/167)*	*168 (9/159)*

Efficacy Supplements

Performance

FY 2000 Submissions

All 20 of the priority efficacy supplements submitted in FY 2000 were reviewed and acted upon within the 6 month review goal. On-time performance was 100 percent which exceeded the 90 percent goal.

All but one of the standard efficacy supplements were reviewed and acted upon within 12 months and 91 percent were reviewed within 10 months. This performance exceeds the FY 2000 goals of 90 percent and 50 percent respectively.

FY 00 Submissions		Reviewed and acted upon	Number on time	Percent on time
Priority	6 months	20	20	100
Standard	12 months	167	166	99
	10 months		152	91

FY 2001 Submissions

Four of the nine priority efficacy supplements submitted in FY 2001 have been reviewed and acted upon. All have met the 6-month review goal. Only 19 of the 159 standard efficacy supplements have been reviewed. All of these have met the 10-month review goal.

FY 01 Submissions		Reviewed and acted upon	Number on time	Percent on time
Priority	6 months	4	4	100
Standard	12 months 10 months	Too early to report meaningful review performance statistics. Nineteen standard efficacy supplements have been reviewed and acted upon, all within 10 months.		

Manufacturing Supplements

Goal -- Review and act upon complete manufacturing supplements to NDAs and BLAs

The review performance goals for manufacturing supplements that do not require FDA approval before the changes they specify can be enacted do not change over the five years of PDUFA II. For manufacturing supplements that do require FDA's approval, the goal times decrease from 6 months for FY 1998 submissions to 4 months for FY 2002 submissions.

Goals		On-Time Performance by Submission Year				
		FY 98	FY 99	FY 00	**FY 01**	FY 02
Prior approval not required	6 months	90% on time	90%	90%	**90%**	90%
Prior approval required	6 months	90%	90%	90%	**90%**	
	4 months		30%	50%	**70%**	90%

Workload -- Manufacturing supplements filed *(Prior Approval / No Prior Approval)*:

	FY 97	FY 98	FY 99	FY 00	FY 01[4]
• **to NDAs**	1,262	1,463	1,459 *(900/559)*	1,438 *(684/754)*	1,474 *(585/889)*
• **to BLAs**	338	371	477 *(259/218)*	587 *(239/348)*	595 *(181/414)*
• **PDUFA total**	1,600	1,834	1,936 *(1,159/777)*	2,025 *(923/1,102)*	2,069 *(766/1,303)*

Manufacturing Supplements

Performance:

FY 2000 Submissions

Ninety-eight percent of the manufacturing supplements submitted in FY 2000 that did not require prior FDA approval were reviewed within 6 months. That level of performance exceeded the 90 percent on-time review goal.

Ninety-seven percent of the manufacturing supplements submitted in FY 2000 that required prior FDA approval also were reviewed within 6 months. Seventy-nine percent of these were reviewed within 4 months. That level of performance exceeded FY 2000's goals of 90 percent and 50 percent respectively.

FY 00 Submissions		Reviewed and acted upon	Number on time	Percent on time
Prior approval not required	6 months	1102	1077	98
Prior approval required	6 months	923	897	97
	4 months		725	79

FY 2001 Submissions

As of September 30, 2001, almost 64 percent of the manufacturing supplements that do not require prior approval, and 72 percent of those that do require prior approval had been reviewed. Ninety-nine percent of both categories of manufacturing supplements had been reviewed within 6 months, and 89 percent of those requiring prior approval had been reviewed within 4 months. Although it is too early to make a final determination with only 67 percent of the submissions reviewed, performance in all categories is well above the FY 2001 review goals.

FY 01 Submissions		Reviewed and acted upon	Number on time	Percent on time
Prior approval not required	6 months	831	824	99
Prior approval required	6 months	551	547	99
	4 months		490	89

Procedural and Processing Goals

This section reports on a number of PDUFA II goals that had no precedent under PDUFA I. These goals relate to the IND phase of drug development and some aspects of the infrastructure of drug review. A detailed description of the goals, the annual performance targets, and definitions of terms can be found in Appendix A. This section reports on actions on items that occurred in FY 2001.

Meeting Management:

- **Meeting Requests:** Notify requestor of formal meeting in writing within 14 days of request.
- **Scheduling Meetings:** Schedule meetings within goal date (within 30 days of receipt of request for Type A meetings, 60 days for Type B meetings, and 75 days for Type C meetings). If the requested date for any of these types of meetings is greater than 30, 60, or 75 days, as appropriate, from the date the request is received by the Agency, the meeting date should be within 14 days of the requested date.
- **Meeting Minutes:** Agency prepared minutes, clearly outlining agreements, disagreements, issues for further discussion and action times will be available to sponsor within 30 calendar days of meeting.

			Total	Met Goal	Missed Goal[5]	Pending Within Goal[6]	% On Time[7]
On-time Goal							**90%**
Meeting Requests		CBER	387	376	9	2	
		CDER	1084	942	123	19	
		Combined	1471	1318	132	21	**91%**
Scheduling Meetings	Type A	CBER	22	18	2	2	
		CDER	36	25	11	0	
	Type B	CBER	229	191	11	27	
		CDER	386	258	116	12	
	Type C	CBER	89	75	2	12	
		CDER	599	564	28	7	
	All	CBER	340	284	15	41	
		CDER	1021	847	155	19	
		Combined	1361	1131	170	60	**87%**
Meeting Minutes		CBER	243	216	6	21	
		CDER	979	440	229	310	
		Combined	1222	656	235	331	**74%**

Procedural and Processing Goals

Clinical Holds: Respond to sponsor's complete response to a clinical hold within 30 days of receipt

	Total	Met Goal	Missed Goal[5]	Pending Within Goal[6]	% On Time[7]
On-time Goal					**90%**
CBER	125	115	10	0	
CDER	34	25	8	1	
Combined	159	140	18	1	**89%**

Major Dispute Resolution: Respond to sponsor's appeal of decision within 30 days of receipt

	Total	Met Goal	Missed Goal[5]	Pending Within Goal[6]	% On Time[7]
On-time Goal					**90%**
CBER	2*	2*	0	0	
CDER	9	9	0	0	
Combined	11	11	0	0	**100%**

* *Both are for the same dispute: one for the original submission, the other for the response to an information request.*

Special Protocol Question Assessment and Agreement: Respond to sponsor's request for evaluation of protocol design within 45 days of receipt

	Total	Met Goal	Missed Goal[5]	Pending Within Goal[6]	% On Time[7]
On-time Goal					**80%**
CBER	1	1	0	0	
CDER	120	88	18	14	
Combined	121	89	18	14	**83%**

Notes:

[1] This report uses the terms PDUFA I and PDUFA II to distinguish between the original Prescription Drug User Fee Act of 1992 and the Act as reauthorized and amended by the Food and Drug Administration Modernization Act of 1997 (FDAMA) respectively. Where no distinction is needed or where the reference is obvious, the term PDUFA is used.

[2] Although the last approvals for FY 2000 submissions (as well as for earlier years) have not yet occurred, the median statistic can be estimated from approvals to date and estimates of the percent of submissions that will ultimately be approved.

[3] The count of FY 2001 submissions assumes that all submissions received in the last two months of FY 2001 are filed. When FDA files a submission, it is deemed "complete" by PDUFA definition. FDA makes a filing decision within 60 days of an original application's receipt. All calculations of PDUFA review times are made, however, from the original receipt date of the filed application.

[4] The term NME in this report refers exclusively to NMEs that are NDAs. For FDAMA purposes, BLAs are considered to be equivalent to NMEs; however, workload and performance statistics for BLAs are reported separately. The counts of NMEs in the workload table are of 'discrete,' filed NMEs. CDER often receives multiple submissions for the same new molecular entity, for different dosage forms for example. All are initially designated as NMEs, but, when the first of the multiples is approved, the others are redesignated as non-NMEs. In FY 2001, CDER designated 38 filings as NMEs initially (8 priority, 30 standard). Only 34 of these are 'discrete' (8 priority, 26 standard).

[5] Includes those with late actions and those still pending whose goal date has passed and which have not had actions.

[6] Includes actions that are pending within goal, as well as those whose goal date has passed, but whose action status is deemed incomplete because the database had not been updated to reflect the action in time for this report.

[7] Actions pending were excluded from the calculation.